

# HONG KONG PHARMACEUTICAL *JOURNAL*

VOL 26 NO 2 Apr - Jun 2019 ISSN 1727-2874



## News & Short Communications

Pushing the Pharmacy Profession to a New Era –  
Interview with Jason Tong

An Overview and Update on the Management of  
Severe Asthma

Evaluation of GenoFlow Bacterial Meningitis Array  
Testing Kits with Reference to Conventional Method  
for the Diagnosis of Bacterial Meningitis Pathogens

The Beijing Forbidden City International Pharmacist  
Forum 2019 Student Experience Reflection

PPAHK Introduce USP 800 New Standards and  
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*The Pharmaceutical Society of Hong Kong  
The Practising Pharmacists Association of Hong Kong  
The Society of Hospital Pharmacists of Hong Kong*

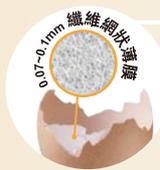
# 領鈣入骨 舒痛護膝<sup>[1-3]</sup>

## 關節活到 120歲

### 持續服用有助修復受損軟骨<sup>[4]</sup>

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## 健骨活絡寶 - 膝康寧



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### 八大功能 科研實證

#### 強健骨骼

維他命K2(MK-7)&D3 協同  
幫助吸收鈣質，提高骨骼密度<sup>[5]</sup>。

#### 領鈣入骨

維他命K2(MK-7) 降低  
血管鈣化風險，緩解骨質  
疏松困擾。

#### 強化韌帶

銅 促進膠原增生，強化韌帶。

#### 抗氧化保護

維他命C及維他命E 可去除  
引致細胞老化的自由基。

#### 舒緩疼痛

天然蛋膜素 經臨床證實，  
7-10天 有效舒緩關節痛症<sup>[1-3]</sup>。

#### 修復軟骨

非變性 II 型膠原蛋白  
有助修復關節軟骨<sup>[4]</sup>。  
葡萄糖胺及硫酸軟骨素  
提供軟骨再生所需原料。

#### 潤滑關節

透明質酸 增加關節潤滑，  
減少軟骨磨損。

#### 撲滅炎症

南非鈣麻根提取物及乳香  
提取物 可舒緩炎症反應。

## 關節活到120歲 建議每日組合使用 1+3

### 健骨活絡寶

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- 方便隨身 快速舒痛
- 特別適合 年長人士



3粒 膝康寧

針對膝蓋部位

- 片劑配方 易於吞服
- 及早保養 集中修復
- 特別適合 年輕人士

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## INSTRUCTIONS FOR AUTHORS

The Hong Kong Pharmaceutical Journal is a journal of the pharmacists, for the pharmacists and by the pharmacists. Submissions are welcome for the following sections:

- Pharmacy Education & Practice
- Primary Care
- Medication Safety
- Society Activities
- Drugs & Therapeutics
- Pharmaceutical Techniques & Technology
- Herbal Medicines & Nutraceuticals
- New Products

Comments on any aspects of the profession are also welcome as Letter to the Editor.

There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The Editorial Committee may make editorial changes to the articles but major amendments will be communicated with the authors prior to publishing.

It is preferable to have original articles submitted as an electronic file, in Microsoft Word, typed in Arial 9pt. Files can be sent to the following address:

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**address: Room 1303, Rightful Centre,  
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Hong Kong.**

For detail instructions for authors, please refer to the first issue of each volume of HKPJ.

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## District Health Centre- more opportunity for community pharmacists



In her 2017 Policy Address, the Chief Executive directed that, to further illustrate the effectiveness of medical-social collaboration, the Food and Health Bureau (FHB) should set up a District Health Centre (DHC) with a brand new operation mode in Kwai Tsing District within two years. In this relation, FHB has established the Steering Committee on Primary Healthcare Development in

November 2017, to formulate the development strategy and devise a blueprint for primary healthcare services. FHB has also established the Working Group on DHC Pilot Project in Kwai Tsing District, to provide advice on the planning, implementation and evaluation of the DHC pilot project. Primary Care Office would provide professional advice to FHB in their planning and implementation of the DHC pilot project in Kwai Tsing.<sup>(1)</sup>

As reported in News & Short Communication on **page 45**, on March 4, 2019, the Food and Health Bureau (FHB) announced that the operation service contract for the Kwai Tsing District Health Centre (DHC) has been awarded through open tender to the Kwai Tsing Safe Community and Healthy City Association. On the advice of the Steering Committee, the Kwai Tsing DHC will accord priority to handling the following chronic diseases and health risk factors-

- (a) Hypertension;
- (b) Diabetes mellitus;
- (c) Overweight / obesity;
- (d) Fall risk; and
- (e) Lifestyle risk factors, such as smoking, alcohol consumption, physical inactivity, unhealthy diet, etc.

The DHC Operator would be expected to develop and manage a DHC Network of Service Providers. This network may include doctors, nurses, pharmacists, allied health professionals (such as physiotherapists, occupational therapists, dietitians), and Chinese Medicine Practitioners.<sup>(2)</sup> The pharmacist in the DHC can provide disease screening, conducting medication review, drug education and counselling patients on proper way of taking drugs and also set up a network with local community pharmacies where patients can be referred for follow up. Pharmacists in the local community pharmacies can provide treatment for minor ailments, dispense prescription and conduct Medication Therapy Management to help individual patients. I look forward to the development of a new and innovative mode of primary care services.

Starting with this issue, we have changed the section of "OTC & Health" to "Primary Care", I like to welcome Jacky Chung and Janet Wong alongside with Celeste Ewig as section editors. In the article on **page 50**, LEUNG, Philip Win-Kin & CHONG, Donald Wing-Kit wrote on "An Overview and Update on the Management of Severe Asthma". The advancement on the understanding of severe asthma has led to the concepts of phenotyping and endotyping of the disease, which has become invaluable to formulating individualized treatment based on the severe asthma

endotype. The evolution of immunological therapies (e.g. anti-IgE and anti-IL5 monoclonal antibodies) extends the treatment portfolio for better severe asthma control. It is of paramount importance to the management of severe asthma for patients to have appropriate inhaler technique. Before using individualized biological agents, pharmacists should optimize the inhaler therapy of the patient. Not only the choice and dose of the inhaler are important, but the way of using the inhaler is also pivotal and affects the therapeutic outcome of the patient.

On **page 47**, is an interview of Mr. Jason Tong. Jason Tong is a young pharmacist from Australia, returned to Hong Kong in 2015 and is currently working as a pharmacist in a clinic. Inspired by the healthcare system in Australia, he has a strong passion in enhancing the health and medications literacy of the public. Together with other young pharmacists, Jason has, co-founded a non-governmental pharmacy society called Pharmacists Connect two years ago, hoping to connect the future and existing pharmacy leaders from all sectors to shape and secure the future of the profession and promote the roles of pharmacists in Hong Kong.

On **page 58**, MA, Dongli, SZABÓ, Edina, LEE, Rebecca Hui Kwan et al wrote the article on "Evaluation of GenoFlow Bacterial Meningitis Array Testing Kits with Reference to Conventional Method for the Diagnosis of Bacterial Meningitis Pathogens". The results showed that the array test kit had a 96.5% concordant rate with the reference methods. They further analyzed the discrepant results using PCR and Sanger sequencing and confirmed that the array test kit indeed showed 100% sensitivity and 100% specificity for all the pathogens detected by various reference methods. The GenoFlow Bacterial meningitis array test kit represented a sensitive, accurate and rapid laboratory method to help with diagnosis suspected bacterial meningitis cases. The use of this multiplex detection array test could provide prompt and appropriate antibiotic treatment in managing meningitis patients.

On **page 65**, we read about the description and reflection by the first year Pharmacy Students of the Chinese University of Hong Kong of the visit to the Forbidden City Conference and the Peking University Third Hospital in Beijing. As the saying goes, "Traveling is a more valuable learning experience than going to school". The students said that the study visits are their most memorable experiences in year one pharmacy school.

I hope you will spend time to read the content of this issue and I look forward to the submission of articles from you. Have a nice summer!

*Cheng Mary Catherine*  
Managing Editor  
24 June 2019

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Prepared by Howard Chan; Chiu Tsz Ching

## Contract awarded for Kwai Tsing District Health Centre

Date: March 4, 2019

On March 4, 2019, the Food and Health Bureau (FHB) announced that the operation service contract for the Kwai Tsing District Health Centre (DHC) has been awarded through open tender to the Kwai Tsing Safe Community and Healthy City Association (the operator). Under the contract, the operator is required to commence three-year operation of a Core Centre no later than October 1 this year. It will also set up five satellite centres in different parts of Kwai Tsing within one year after commencement of the Core Centre. The total contract amount is \$284.06 million.

Located at Kowloon Commerce Centre in Kwai Chung with about 1 500 square metres of net operating floor area, the Core Centre will provide various healthcare services including health promotion and educational activities, health assessment and chronic disease management. It will open 10 hours a day and six days a week.

The operator is required to develop a network of medical and healthcare practitioners including doctors, nurses, pharmacists, allied

health professionals such as physiotherapists, occupational therapists, dietitians and Chinese medicine practitioners, with a view to providing multiple access and service points for a good range of co-ordinated care and support services within the district, offering a convenient alternative to frequenting hospitals.

The Kwai Tsing DHC is a pilot scheme with a brand new operation mode and funding support from the Government. It aims to illustrate the effectiveness of public-private partnership and medical-social collaboration in providing primary healthcare services which cater for the needs and characteristics of the district, as well as to enhance public awareness of a healthy lifestyle, disease prevention and self-management of health. Taking into account the experience of the pilot DHC in Kwai Tsing District, the Government will gradually set up DHCs in all 18 districts.

Source: [www.fhb.gov.hk/en/press\\_and\\_publications/press/2019.html](http://www.fhb.gov.hk/en/press_and_publications/press/2019.html)

## FDA Approves First Two-drug Complete Regimen for HIV-infected Patients Who Have Never Received Antiretroviral Treatment

Date: April 8, 2019

The Food and Drug Administration (FDA) approved Dovato (dolutegravir and lamivudine), a two-drug, fixed dose once-daily formulation, as a complete regimen for the treatment of HIV-1 infection in adults without antiretroviral treatment (ART) history and with no known or suspected substitutions with resistance to individual components of Dovato.

The current standard of care for HIV-infected treatment-naïve patients is a three-drug regimen. This approval permits treatment-naïve patients to have the option of taking a two-drug regimen in a single tablet while eliminating additional toxicity and potential drug interactions from a third drug, which the FDA believes is beneficial to patients who may have issues taking multiple medications over prolonged period.

The efficacy and safety of Dovato were demonstrated in two identical, randomized, double-blind, controlled clinical trials in 1,433 HIV-infected treatment-naïve adults. Results showed that drug regimen containing dolutegravir and lamivudine had a similar effect of reducing HIV viral load compared to another drug regimen which included

dolutegravir, emtricitabine, and tenofovir. Treatment was considered successful if the patient maintained low levels (<50 copies/mL) of HIV RNA in blood for at least 48 weeks.

The Dovato labeling includes a Boxed Warning, cautioning that patients infected with both HIV and hepatitis B should add additional treatment for their hepatitis B or consider a different drug regimen. Patients with both HIV and hepatitis B taking lamivudine, an ingredient in Dovato, have developed resistance-associated hepatitis B variants and may develop severe liver problems, including liver failure, when they stop taking relevant drugs. Such population should be closely monitored by their healthcare provider upon discontinuing Dovato.

The most common adverse reactions with Dovato were headache, diarrhea, nausea, insomnia and fatigue. As there is a known risk of neural tube defects with dolutegravir, patients are advised to avoid using Dovato at the time of conception through the first trimester of pregnancy.

Source: [www.fda.gov](http://www.fda.gov)

## FDA Approves New Treatment for Osteoporosis in Postmenopausal Women at High Risk of Fracture

Date: April 9, 2019

FDA approved Evenity (romosozumab-aqqg) to treat osteoporosis in postmenopausal women at high risk of fracture. Risk factors include a history of osteoporotic fracture and those who have failed or are intolerant to other osteoporosis therapies.

Evenity is a monoclonal antibody that increases bone formation through blocking the effects of sclerostin. Each dose consists of two injections, one immediately following the other, given once a month by a healthcare professional. The bone-forming effect of Evenity wanes after 12 doses; if further treatment is needed, one should select a regimen that reduces bone breakdown.

The safety and efficacy of Evenity were demonstrated in two clinical trials involving a total of over 11,000 women with postmenopausal osteoporosis. In the first trial, one-year treatment with Evenity lowered the risk of new vertebral fracture by 73% compared to placebo. This benefit was maintained over the second year when Evenity was followed by one year of denosumab compared to placebo followed

by denosumab. In the second trial, one-year treatment with Evenity followed by one year of alendronate reduced the risk of a new vertebral fracture by 50% compared to two years of alendronate alone. Such regimen also reduced the risk of nonvertebral fractures.

Evenity increased the risk of cardiovascular death, myocardial infarction and stroke in the alendronate trial, but not in the placebo one. Therefore, a Boxed Warning is added on its labelling, stating that it may increase the risk of such events and should not be used in patients who have had myocardial infarction or stroke within the previous year. Healthcare professionals should also consider whether the benefits of Evenity outweigh its risks in those with other cardiovascular risk factors and should discontinue Evenity whenever a patient experiences cardiovascular events during treatment.

Common side effects of Evenity included joint pain and headache; injection site reactions were also observed.

Source: [www.fda.gov](http://www.fda.gov)

## Acclidinium Bromide Shows No Increased Risk of Major Cardiovascular Events in High-risk Patients with COPD

Date: May 7, 2019

Long-term use of acclidinium bromide for chronic obstructive pulmonary disease (COPD) management in patients with high cardiovascular risk did not result in greater likelihood of major cardiovascular events (MACE), a clinical trial reported.

From October 2013 to September 2017, ASCENT-COPD, a randomized, placebo-controlled, double-blind parallel design trial, was carried out to investigate the cardiovascular safety of acclidinium. Participants, who had stable moderate-to-severe COPD, a history of cardiovascular events or at least two atherothrombotic risk factors, and previous use of inhaled corticosteroids (ICS) and/or long-acting beta agonists (LABA), were enrolled and randomized in 1:1 ratio to receive either acclidinium or placebo. Primary efficacy and safety outcomes were exacerbation rate and MACE (cardiovascular death, nonfatal myocardial infarction or nonfatal stroke) respectively.

In terms of efficacy, acclidinium bromide significantly reduced exacerbation rate in subjects over the first year (0.44 vs 0.57; rate

ratio, 0.78; 2-sided 95% CI, 0.68 to 0.89;  $p < 0.001$ ). From the safety standpoint, overall MACE occurrence in acclidinium group was non-inferior to that in placebo group (3.9% vs 4.2%; HR, 0.89; 1-sided 97.5% CI, 0 to 1.23), with notable differences observed in nonfatal myocardial infarction and stroke.

Results suggested that acclidinium is effective in COPD maintenance over placebo without significantly elevating cardiovascular risk in high-risk patients. Nevertheless, further studies are required to investigate its safety in new-onset treatment.

Acclidinium bromide is a long-acting muscarinic receptor antagonist that is available in Hong Kong as both single (HK-64504) and combination (HK-64503) dry powder inhalers. Common side effects include headache, nasopharyngitis and cough.

Source: [www.jamanetwork.com](http://www.jamanetwork.com)

## Restrictions in Use of Xeljanz (tofacitinib) While EMA Reviews Risk of Pulmonary Embolism

Date: May 17, 2019

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended that doctors must not prescribe 10 mg twice daily dose of Xeljanz (tofacitinib) in patients who are at high risk of pulmonary embolism, including patients with heart failure, cancer, inherited blood clotting disorders or relevant history, as well as those taking combined hormonal contraceptives, receiving hormone replacement surgery or undergoing major surgery. PRAC also recommends doctors to consider other factors that may increase the risk of pulmonary embolism including age, obesity, smoking or immobilization.

PRAC recommendation follows results from an ongoing open-label clinical trial (study A3921133) evaluating the safety of tofacitinib 5mg twice daily and 10mg twice daily compared with a tumour necrosis factor (TNF) inhibitor in patients with rheumatoid arthritis, aged 50 or above and have at least one additional cardiovascular risk factor. Preliminary results showed that there were 19 cases of pulmonary embolism out of 3,884 patients in the tofacitinib 10mg twice daily arm

of the study compared with 3 cases out of 3,982 in the TNF inhibitor arm. Additionally, there were 45 deaths from all causes out of 3,884 patient-years in the 10mg twice daily arm, whereas the number was 25 cases out of 3,982 patients in the TNF inhibitor arm.

As 10mg is the only recommended initial dose in ulcerative colitis, patients with this condition who are at high risk of blood clots must not be started on Xeljanz. For patients with rheumatoid arthritis and psoriatic arthritis, prescribers should continue to adhere to the authorized dose of 5mg twice daily. Patients at high risk currently taking 10mg twice daily dose for any condition must be switched to alternative treatments. Patients receiving tofacitinib, irrespective of indication, should be monitored for signs and symptoms of pulmonary embolism, and are advised to seek medical attention immediately if they experience such events.

Source: [www.ema.europa.eu](http://www.ema.europa.eu)

## The Novel START trial – Controlled Trial of Budesonide-Formoterol as Needed for Mild Asthma

Date: May 19, 2019

In double-blind, placebo-controlled trials, as-needed budesonide-formoterol use resulted in lower risk of severe asthma exacerbation than as-needed use of a short-acting  $\beta_2$ -agonist (SABA); the risk was similar to that of budesonide maintenance therapy plus as-needed SABA. However, whether the findings translate to clinical practice outside the setting of a rigidly controlled trial is unclear. The Novel START trial was conducted to investigate budesonide-formoterol reliever therapy used on as-needed basis among adults with mild asthma who had been treated with as-needed SABA only.

Novel START was a 52-week, randomized, open-label, parallel-group, multicentre controlled trial. Patients were randomly assigned to one of three treatment groups: albuterol group (albuterol 100 $\mu$ g, two inhalations from a pressurized metered dose inhaler as needed), budesonide maintenance group (budesonide 200 $\mu$ g, one inhalation through Turbuhaler twice daily plus as-needed albuterol) or budesonide-formoterol group (budesonide 200 $\mu$ g and formoterol 6 $\mu$ g, one inhalation through Turbuhaler as needed). Electronic monitoring of inhalers was used to measure medication use. The primary outcome was annualized rate of asthma exacerbations.

Analysis included 668 of 675 patients who underwent randomization. Annualized exacerbation rate in budesonide-formoterol group was lower than that in albuterol group (absolute rate, 0.195 vs 0.400; relative rate, 0.49; 95% CI, 0.33 to 0.72;  $p < 0.001$ ) and did not differ significantly from the rate in budesonide maintenance group (absolute rate, 0.195 vs 0.175; relative rate, 1.12; 95% CI, 0.70 to 1.49;  $p = 0.65$ ). Number of severe exacerbations was lower in budesonide-formoterol group than in both albuterol (9 vs 23; relative risk, 0.40; 95% CI, 0.18 to 0.86) and budesonide maintenance groups (9 vs. 21; relative risk, 0.44; 95% CI, 0.20 to 0.96). The mean ( $\pm$ SD) dose of inhaled budesonide in budesonide-formoterol group and budesonide maintenance groups were 107 $\pm$ 109 $\mu$ g/day and 222 $\pm$ 113 $\mu$ g/day respectively. Incidence and type of adverse events reported were consistent with those in previous trials and reports in clinical use.

In an open-label trial involving adults with mild asthma, budesonide-formoterol used as needed was superior to albuterol used as needed for the prevention of asthma exacerbations.

Source: [www.nejm.org](http://www.nejm.org)

## Pushing the Pharmacy Profession to a New Era – Interview with Jason Tong

**CHUNG, Winnie WY<sup>a</sup>; CHONG, Donald WK<sup>b\*</sup>**

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<sup>b</sup> GSK (Consumer Healthcare) HK Limited, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong SAR, China (\*Corresponding author)

### INTRODUCTION

**Jason Tong**, a young pharmacist from Australia, returned to Hong Kong in 2015 and is currently working as a pharmacist in a clinic. Inspired by the healthcare system in Australia, he has a strong passion in enhancing the health and medications literacy of the public. He, then, co-founded a non-governmental pharmacy society called Pharmacists Connect two years ago, hoping to connect the future and existing pharmacy leaders from all sectors to shape and secure the future of the profession and promote the roles of pharmacists in Hong Kong.



Pharmacists Connect expressed pharmacist roles via different channels.

### BACKGROUND

Jason was born in Australia and received his primary school education in Hong Kong. After that, he went back to Australia for his secondary school and university study of Pharmacy in The University of Queensland. With the one-year pre-registration training in a community pharmacy, shadowing a community pharmacist, and the written and oral registration examinations, he became a registered pharmacist in Australia.

#### *From Australia to Hong Kong*

**PJ: You came back to Hong Kong in 2015. What makes you decided to come back?**

Jason: I decided to return to Hong Kong as I hoped to spend more time with my family. Another reason for my return is that I saw the healthcare system in Hospital Authority appeared not functioning properly, as reflected by the long waiting time of pharmacy and specialty service and insufficient time to give medication advises to patient. While the healthcare system in Australia has its own merit, I hope to make an effort to be part of the change in the healthcare system in Hong Kong, with my pre-registration experience in community pharmacy in Australia.

**PJ: Coming back from Australia, how did you start your career as a pharmacist in a clinic?**

Jason: As you know, pharmacists holding a qualification of pharmacy degree outside Hong Kong are required to undergo a conversion examination. While preparing for the examination, I worked as a dispenser in a clinic. After passing the conversion examination, I was promoted to be a pharmacist position and later become the pharmacy manager in the clinic.

#### *Life as a Pharmacist in Clinic*

**PJ: Why did you choose to work in a clinic?**

Jason: Through job interviews and talking with seniors, I understood more on the roles of pharmacists in Hong Kong, which are quite different from Australia. The role of pharmacists in Hong Kong is mostly highlighted in hospitals, with a lighter emphasis in community pharmacy, while there is a more established pharmacy service and primary care model in community pharmacies in Australia.

When I attended the job interview for a pharmacist position in clinic, I found that the job nature of pharmacists in clinic is very similar to the community pharmacies in Australia. We have counselling and regular follow-up with patients through which we can establish relationship with them. I found it very enjoyable.

Being a pharmacist in a clinic is a relatively new role in Hong Kong, when compared to the three traditional sectors that pharmacists usually work, namely hospitals, community pharmacies and pharmaceutical companies. Pharmacists in a clinic will oversee the whole operation of a pharmacy, from the procurement of drugs to detailed drug counselling with patients. I value the close relationship and drug counselling time with patients.



*Pharmacists Connect participated in health-related activities and provide medication counselling service.*

**PJ: What do you do in the clinic?**

Jason: My work mainly focuses on drug counselling with patients and I have the help from dispensers to dispense medications. In the clinic, nurses and doctors may not be very clear about the dosage and administration of drugs. In this case, I will also provide drug information services to them. Also, as doctors may not be familiar with the legislation of dangerous drug, disposing expired medications and children vaccination program, pharmacists are more than capable to provide such information to the doctors and other colleagues.

**PJ: Is there any difference between working in clinics in Hong Kong and Australia?**

Jason: To be honest, I have not worked as a pharmacist in a clinic before as there is no pharmacist in clinics in Australia. Under the Separation of Prescribing and Dispensing (SPD) in Australia, very often there is a pharmacy near medical centre, where the pharmacy is owned and operated by a registered pharmacist, which means the pharmacist is financially independent from the medical centre. This prevents the conflicts of interest between doctors and pharmacists. Pharmacists have the autonomy in not dispensing or rejecting a prescription when it is not in the best interest of the patient due to an allergy or contraindication

On the contrary, in the situation of Hong Kong, as pharmacists are employed under the doctor or the medical centre, there may be conflict of interest when pointing out the mistakes on prescriptions. We will be at a relatively embarrassing position. Nevertheless, I think it is all about our communication skills and whether the pharmacist can establish a close relationship and

gain trust from doctors. If yes, pharmacists can still make recommendations and advices to doctors on the prescription to safeguard the patients' medication safety.

In terms of the liability of pharmacists upon dispensing, it is quite different in Australia and Hong Kong as well. In Australia, both parties share half of the responsibility on a mistake on prescription. If the pharmacist cannot spot the mistake and issues a prescription, he is liable to the mistake made, whereas in Hong Kong, pharmacists working in a clinic seemingly do not have a legal liability in medication errors on prescription. In other words, there is no penalty if a pharmacist working in clinic forgot or failed to identify errors on prescription. I will not say the current situation is optimal. I believe all pharmacists endeavour to safeguard patient safety in terms of prescription, though it is not a legal requirement to do so. Yet, rendering pharmacists a legal liability on checking prescription not only provides a double-checking on prescription for the sake of patient safety, but also increase the recognition and status of pharmacist in Hong Kong.

**PJ: It seems that the work of pharmacists in clinics is very meaningful but challenging. Do you have any advices to students who would like to enter this sector?**

Jason: The pharmacist working in a clinic has to be familiar with everything in a clinic, from procurement to dispensing and counselling. Yet, pharmacy school does not teach you everything and there are no guidelines for you to follow in the clinic. We have to explore the process and procedures by ourselves. I remembered when I just registered in Hong Kong, I was not familiar with the pharmacy laws and legislations in Hong Kong. Therefore, I approached and asked Department of Health. Finally, I received a much better understanding of the local requirements. In short, pharmacist in clinic should be able to solve the issues independently and are willing to learn.



*Jason Tong, a registered pharmacist working in a clinic.*

*A Revolution in Pharmacy Profession Development in Hong Kong*

**PJ: Apart from a pharmacist in clinic, I know that you are also the President of Pharmacists Connect. Could you tell me more about Pharmacists Connect?**

Jason: Sure. Pharmacists Connect is not just an effort from myself. It was founded by five pharmacists from different sectors, including pharmacists from non-governmental organizations, community pharmacy, hospital, and a consultancy two years ago. We hope to unify the profession and enhance the image of pharmacist in our community. More importantly, we would like to improve the knowledge and awareness of patients on their medications and health conditions. Ideally speaking, we really hope that with our effort, patients can ultimately recognize their need for pharmacy service to understand more the medications they are taking in the future.



As the president of Pharmacists Connect, Jason meets different stakeholders to express his view on the pharmacy profession.

**PJ: Compared to the three traditional pharmacists' association, namely The Society of Hospital Pharmacists of Hong Kong (SHPHK), The Pharmaceutical Society of Hong Kong (PSHK) and The Practising Pharmacists Association of Hong Kong (PPA), Pharmacists Connect is an association composed of young pharmacists. How did you make noise on the issues related to pharmacy?**

Jason: We believe advocacy is always the golden step to promote the role of pharmacists and even the SPD in Hong Kong. Therefore, we send letters and proposals to government officials and they hold meetings with us. This gives a chance to express our thoughts on the policy.

We also hold different gatherings to unify the profession. Both young and experienced pharmacists are welcome, whatever sectors you are working in. You are correct that we are different from the three traditional pharmacists' association as we do not want to divide pharmacists into groups according to the sectors they are working in. Instead, we hope to "connect" passionate pharmacists from all sectors and come up with solutions to promote the pharmacist's role in the community and fight for SPD in the future.

Other than that, we also make use of the internet and social media to promote our profession. One of the unique features of Pharmacists Connect is that we do not accept donations from pharmaceutical industry. In other words, we have no strings attached and we have

the freedom to hold any campaigns and services. Like this year, we raised an online campaign that the general public can ask drug-related questions online and we would answer them with our professional knowledge to promote the role of pharmacists. We sometimes cooperate with organizations and attend outreach services, drug talks and pharmacy exhibitions, through which we hope that more people can know who we are in the future. From the previous two years since the establishment of Pharmacists Connect, I think we have made some progress and we will keep going on with our work.

**PJ: The ultimate goal of promoting pharmacists' role is for the SPD in Hong Kong. What do you think about the hurdle in implementing SPD in Hong Kong?**

Jason: The largest problem is that patients do not know who we are. Wearing a white coat in clinic, it is common for patients to call me doctor or nurse. The limited understanding of pharmacists' role from patients can also be reflected on their conservative mindset that doctors are the only ones they can seek for help when they are sick. They do not recognize that pharmacists in community pharmacy can give medical advice on minor ailments like thrush or migraine. This poses a huge financial burden to the public healthcare system.

Despite the long road to SPD in Hong Kong, I think we can make it shorter by the collective efforts from all the pharmacists in Hong Kong. We may start with people around us by telling them the roles of pharmacists and encouraging them to use the service from pharmacists in community. We work hand in hand and it will definitely make us one step closer to our destination. If each of us can tell at least 10 people of what pharmacist is capable of doing, then with Hong Kong having around 2600 pharmacist registered, we already increase the number of people finding a pharmacist dramatically.

## CONCLUSION

The story from Jason has shown his tremendous efforts on promoting the role of pharmacists in the community, via his drug counselling in clinic and cofounding Pharmacists Connect. With time and collective efforts of pharmacists, we can make a difference in our profession and provide patients with a premium pharmacy service, which is a win-win situation that we would like to see in the near future.

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# An Overview and Update on the Management of Severe Asthma

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### ABSTRACT

Severe asthma represents one-tenth of the asthmatics cases and poses extensive negative impacts to the quality of life in this group of patients. This enduring disease not only brings hardship to the sufferers, but also delivers a huge financial burden to the healthcare system. Effective treatment of severe asthma requires its affirmative diagnosis in asthmatics, while regular assessments on the control of severe asthma are essential to guide the selection of treatment regimens. The advancement on the understanding of severe asthma has led to the concepts of phenotyping and endotyping of the disease, which has become invaluable to formulating individualized treatment based on the severe asthma endotype. Current immunologic agents, namely omalizumab, mepolizumab, reslizumab, and benralizumab are introduced in this article. Additional roles of pharmacists are also proposed to improve the therapeutic outcomes in severe asthma patients. As the treatment options of severe asthma are expanding, pharmacists are in the most advisable position to engage patients to a better management of this disease.

**Keywords:** Severe asthma; phenotypes and endotypes of severe asthma, omalizumab, mepolizumab, reslizumab, benralizumab

### DEFINITION OF SEVERE ASTHMA

Asthma is a heterogeneous syndrome that is characterized by a predisposition to chronic airway inflammation.<sup>(1)</sup> It is often associated with airway hyper-responsiveness and bronchoconstriction (narrowed airway) due to airway thickening and increased mucus secretion.<sup>(2)</sup> These pathological features lead to the recurrent episodes of classical respiratory symptoms including wheezing, coughing, chest tightness, and breathlessness. The associated symptoms vary over time and in intensity, and the severity of asthma does not necessarily progress from mild to severe disease.<sup>(3)</sup>

Special emphasis should be put on the fact that around 5% to 10% of the asthma patient populations are classified as having severe asthma.<sup>(4)</sup> According to a survey conducted by the Hong Kong Asthma Society (HKAS) in 2011, there are more than 330,000 patients suffering from asthma locally.<sup>(5)</sup> This statistical finding extends to the projection that there are more than 16,500 to 33,000 severe asthma patients in Hong Kong. The American Thoracic Society (ATS) and the European Respiratory Society (ERS) taskforce defines severe asthma in patients aged 6 years and older as a form of asthma that requires treatment with either one of the following:<sup>(4)</sup>

- (a) High-dose inhaled corticosteroids (ICS) plus a second controller medication (e.g. long-acting  $\beta_2$ -agonists (LABA), or leukotriene-receptor antagonists, or theophylline) for the previous year, or treatments following the recommendations from Global Initiative for Asthma (GINA) Guideline 2018 Step 4-5, or;
- (b) Systemic corticosteroids for more than half of the time of the previous year to prevent asthma from becoming “uncontrolled” or which remains “uncontrolled” despite this therapy. “Uncontrolled” asthma is defined by ANY ONE of the following:
  - (i) Poor symptom control with Asthma Control Questionnaire (ACQ) consistently  $\geq 1.5$ , ACT (Asthma Control Test)  $< 20$ , or “not well controlled” defined by the National Asthma Education and Prevention Program (NAEPP)/GINA guidelines;<sup>(1)</sup>
  - (ii) Frequent severe exacerbations, including the need of two or more bursts of systemic corticosteroids in the previous year;
  - (iii) Serious exacerbations that require at least one hospitalization, intensive care stay; or mechanical ventilation in the previous year;
  - (iv) Airflow limitation, with Forced Expiratory Volume (FEV<sub>1</sub>)  $< 80\%$  after withholding bronchodilators for an appropriate period.

Severe asthma heavily increases the burden on the health quality of the patients, as well as the resource consumptions of the healthcare system.<sup>(6)</sup> Comparing patients with severe asthma against patients with generally milder asthma, the former group of patients is more likely to suffer from various comorbidities.<sup>(7)</sup> These include rhinosinusitis, obstructive sleep apnoea (OSA), hyperventilation syndrome, vocal cord dysfunction, and gastroesophageal reflux disease (GERD). Patients with severe asthma are also exposed to an increased mortality risk, which is largely due to the greater asthma severity, poorer health status and poorer perceived asthmatic control.<sup>(6)</sup> Another study also found that patients with severe asthma showed a 5-fold higher rate of disease exacerbations (i.e. resulting in emergency visits, hospitalization, or administration of oral corticosteroids), compared to the mild or moderate asthma patients.<sup>(8)</sup> Patients with severe asthma were also twice more likely to experience loss of productivity and impairments in their everyday life versus patients with mild or moderate patients.<sup>(9)</sup> In terms of economic burden, patients with severe asthma consume 1.7-fold to 5-fold greater costs than those with milder asthma.<sup>(10)</sup> This might be due to the results of the higher medication usage, higher costs related to hospitalization or emergency department visit, and other indirect costs. Therefore, severe asthma noticeably leads to a wide spectrum of negative short-term and long-term outcomes.

## **PATHOPHYSIOLOGY OF SEVERE ASTHMA**

The pathogenesis of asthma always encompasses inflammation, injury, and remodelling of the airway.<sup>(11)</sup> Chronic inflammation of the airways induces airway hyper-responsiveness (AHR), which is correlated with a varying extent of airflow obstruction. Although the major cellular components of airway inflammation have been elucidated, the explicit mechanisms involved in chronic inflammation of the airway are still not fully discerned.<sup>(12)</sup> Here, the pivotal cellular components of three major asthma phenotypes are introduced:

- A. *Allergic (atopic) eosinophilic asthma*  
T-helper (Th2) lymphocytes and mast cells activate the eosinophilic airway inflammation in an allergen-specific and IgE-dependent manner.<sup>(13)</sup>
- B. *Non-allergic (atopic) eosinophilic asthma*  
Innate lymphocytes such as natural killer T-cells and innate lymphoid cells type-2 might contribute to airway eosinophilia through the production of interleukin-5 (IL-5).<sup>(13)</sup>
- C. *Neutrophilic asthma*  
Despite the fact that this inflammatory pathway is not well understood, it is known that the IL-17 pathway and IL-8 are involved in activating neutrophils in the airway.<sup>(13)</sup>

Since severe asthma is characterized by an insensitivity to corticosteroids (i.e. with continuous lack

of control even though the patient is already having corticosteroid therapy), alternative targeted therapies may become advantageous to regulate the inflammation in these patients. Examples of the targeting cytokines include IL-4 and IL-13 that are Th2-associated cytokines and induce the production of IgE from B-cells.<sup>(14)</sup> IL-13 also triggers the proliferation and hyper-contractility in airway smooth muscle cells and promotes Goblet cells hyperplasia and mucus hyper-secretion.<sup>(15)</sup> Another paramount cytokine that is involved in the pathogenesis of severe asthma is IL-5, which plays an elemental role in the proliferation and maturation of eosinophils in the bone marrow, as well as their recruitment and activation at the sites of allergic inflammation.<sup>(16)</sup> The binding of IL-5 to the IL-5 receptors results in the differentiation and maturation of eosinophils in the bone marrow, and also enhanced their cellular migration, increased release of granular proteins and respiratory burst. Elevated numbers and activation of eosinophils are also found to be associated with exacerbations of severe asthma.<sup>(17)</sup> Nevertheless, the choice of immunologic targeted therapy, apart from the conventional non-immunologic asthma therapies, should be selected based on the targeting cytokines that corresponds to a particular severe asthma phenotype.<sup>(13)</sup>

## **DIAGNOSIS AND ASSESSMENT OF SEVERE ASTHMA**

### **Differentiating Severe Asthma, Difficult-to-treat Asthma, and Other Comorbidities**

Diagnosing severe asthma and distinguishing severe asthma from difficult-to-treat asthma has always been vital because the treatments of these two forms of asthma are not similar. For instance, severe asthma patients might be suitable candidates for biologic and immunological therapies, while difficult-to-treat asthma patients are not.<sup>(4)</sup> The GINA 2018 guideline defines difficult-to-treat asthma as a form of asthma that is interfered from achieving good asthma control due to some persistent factors including comorbidities, poor medication adherence, and exposure to allergens.<sup>(1)</sup> Severe asthma is often confused with difficult-to-treat asthma as they share many co-existing symptoms such as dyspnoea, coughing, wheezing, chest tightness, nocturnal awakenings, etc. However, difficult-to-treat asthma can be hard to control regardless of the use of high-intensity asthma medications. This is due to the patient's poor medication adherence and inhaler techniques, psychological issues, ongoing exposure to environmental allergens, and other untreated comorbidities.<sup>(18)</sup> Furthermore, many non-asthmatic conditions are often misdiagnosed as uncontrolled severe asthma due to their similar presentations of symptoms (e.g. vocal cord dysfunction, chronic obstructive pulmonary disease (COPD), etc.). Since misdiagnosis happens in 12% to 30% of non-asthmatic patients, clinicians should therefore exclude other conditions by reviewing the patient's medical history, before diagnosing the patient with severe asthma and prescribing the pertinent treatments<sup>(4)</sup>. On the other

hand, if a patient has been diagnosed with severe asthma and remains uncontrolled in spite of appropriate investigations and treatments, referral to specialist care should be considered <sup>(1)</sup>.

### Stepwise Approach to Confirm the Diagnosis of Severe Asthma

The current ATS/ERS guideline suggests a stepwise approach for confirming the diagnosis of severe asthma <sup>(4)</sup>:

1. Identify or exclude difficult-to-treat asthma. Concurrently manage comorbidities that may affect asthma control including chronic rhinosinusitis, GERD, obesity, depression, anxiety, OSA, etc. Evaluate regularly the inhaler technique and adherence.
2. Differentiate severe asthma from milder forms of asthma. Check if high-dose ICS with a second controllers medication are needed to prevent asthma from becoming uncontrolled, or asthma remains uncontrolled despite receiving high-dose therapy.
3. Assess regularly whether asthma is controlled or uncontrolled while on high-dose therapy (“uncontrolled asthma” is defined according to the 4 criteria listed in the guideline).<sup>(4)</sup>

Unlike milder forms of asthma that are managed by primary care services, patients with severe asthma are often referred to secondary or specialist care.

### Assessment of Severe Asthma Control

The Asthma Control Questionnaire (ACQ) and the Asthma Control Test (ACT) are recommended in the ATS/ERS Guideline to assess the severe asthma control. The ACQ contains seven questions, six of which probing the patient to recall the symptoms that he/she experienced during the past week.<sup>(19)</sup> These symptoms include nocturnal awakening, symptoms upon waking, wheezing,

shortness of breath, restrictions in daily activities, and the use of rescue medications. The remaining question is a measurement of the prebronchodilator-use FEV<sub>1</sub> percent of the predicted value.<sup>(20)</sup> ACT is a comparable questionnaire but does not involve the measurement of FEV<sub>1</sub>.<sup>(21)</sup>

Periodic lung function assessment is also indispensable as patients may not realize their symptoms until airflow has become markedly hampered.<sup>(22)</sup> Patients may possibly adapt to the tolerable airflow obstruction unconsciously. Spirometry is the most solid measurement for airflow restriction, but it is not commonly adopted in the primary care setting. Suboptimal values of FEV<sub>1</sub>, forced vital capacity, and FEV<sub>1</sub>/forced vital capacity ratio can be used to quantify the extent of airflow restriction.

The frequency of exacerbations, including the use of oral corticosteroids, emergency department visits, hospitalizations, and the triggers of asthma exacerbations should also be recorded to provide additional information for the assessment of severe asthma control.<sup>(23)</sup>

### FROM PHENOTYPING TO ENDOTYPING OF SEVERE ASTHMA

It is becoming more apparent that severe asthma is not a single and isolated disease, as seen from its wide variety of symptoms presentations, physiological characteristics and outcomes.<sup>(4)</sup> Therefore, the concept of phenotyping has emerged to incorporate biological features (e.g. molecular, cellular, and morphological) into patient’s characteristics to improve the therapeutic outcome of severe asthma. A phenotype is defined as a set of characteristics resulting from the interaction between genetics and the environment.<sup>(4)</sup> A number of asthma phenotypes are proposed to be associated with environmental exposures, symptoms or clinical features, and biomarkers (**Table 1**). The biomarker phenotyping is relatively more promising because it relates to the

	<b>Clinical Features / Presentations</b>	<b>Pathophysiology</b>	<b>Biomarkers</b>	<b>Proposed Agents for Treatment</b>
<b>Early-onset Allergic</b>	<ul style="list-style-type: none"> <li>• Symptoms are associated with allergen exposure</li> <li>• Related to hereditary atopy</li> </ul>	<ul style="list-style-type: none"> <li>• Allergen-specific IgE</li> <li>• Th2 pathway</li> </ul>	<ul style="list-style-type: none"> <li>• Eosinophils count from blood or sputum</li> <li>• FeNO, periostin, positive skin prick test or serum specific IgE level</li> </ul>	<ul style="list-style-type: none"> <li>• More responsive to steroids</li> <li>• Th2-targeted biologics (e.g. anti-IgE, anti-IL-13, anti-IL-5)</li> </ul>
<b>Late-onset Eosinophilic</b>	<ul style="list-style-type: none"> <li>• More severe</li> <li>• Less related to atopy but more sinus disease</li> </ul>	<ul style="list-style-type: none"> <li>• Th2 and leukotriene pathways</li> </ul>	<ul style="list-style-type: none"> <li>• Eosinophils count from blood or sputum</li> </ul>	<ul style="list-style-type: none"> <li>• Anti-IL-5 biologics, leukotriene modifiers</li> </ul>
<b>Neutrophilic</b>	<ul style="list-style-type: none"> <li>• Reduced lung function</li> <li>• Production of purulent mucus</li> </ul>	<ul style="list-style-type: none"> <li>• Neutrophilic inflammation</li> <li>• Non-Th2 pathway</li> </ul>	<ul style="list-style-type: none"> <li>• Polymorphonuclear neutrophils in sputum</li> </ul>	<ul style="list-style-type: none"> <li>• Less responsive to ICS</li> <li>• Possibly responsive to macrolides</li> </ul>
<b>Fixed Airflow Limitation</b>	<ul style="list-style-type: none"> <li>• Partially reversible or irreversible airway obstruction</li> </ul>	<ul style="list-style-type: none"> <li>• Considerable airway remodelling</li> </ul>	<ul style="list-style-type: none"> <li>• None (persistent airflow limitation)</li> </ul>	<ul style="list-style-type: none"> <li>• Should adopt more aggressive treatments</li> </ul>
<b>Obesity-related</b>	<ul style="list-style-type: none"> <li>• More common in obese females</li> <li>• Difficult to control</li> </ul>	<ul style="list-style-type: none"> <li>• Non-Th2 pathways</li> <li>• Systemic inflammatory cytokines</li> <li>• Oxidative stress</li> </ul>	<ul style="list-style-type: none"> <li>• Non-Th2 biomarkers</li> </ul>	<ul style="list-style-type: none"> <li>• Weight reduction</li> </ul>

The classification of the severe asthma phenotypes was adapted from the referenced review articles.<sup>(31-33)</sup>

underlying mechanisms so that therapies can be better targeted.<sup>(24)</sup>

More specifically, when an association can be made between the clinical characteristics of an asthma subtype and the molecular pathways involved, the term endotype can be used to describe the distinctive asthma subtypes with a defined aetiology and consistent pathophysiological mechanisms. A specific endotype has a consistent natural history, genetics, and clinical characteristics from an underlying specific pathobiology that are associated with identifiable biomarkers and a predictable response to a specific therapy.<sup>(25)</sup> Type-2 asthma is one of the well-studied asthma endotypes.<sup>(26)</sup> This endotype is correlated with elevated plasma levels of inflammatory mediators that are associated with type-2 immunity, including eosinophils, basophils, Th2 cells, group 2 innate lymphoid cells, as well as type-2 cytokines such as IL-4, IL-5, and IL-13 in the epithelium of the airway. The identification of the severe asthma endotype in patients is valuable to guide the selection of novel biologics agents in both clinical practice and clinical trials, which in turn recommends delicately a felicitous treatment to patients accordingly.

## **INDIVIDUALIZED TREATMENT OF SEVERE ASTHMA BASED ON ENDOTYPES**

The most commonly adopted biomarkers include the serum IgE level and eosinophil counts in blood or sputum samples. These serve as an initial step to determine if the patient is classified as type-2 endotype of severe asthma in order to devise the proper treatment.<sup>(26)</sup> Elevated IgE plasma level can aggravate the inflammatory response of allergic asthma through the production of mediators, including histamine, prostaglandin, and leukotrienes that lead to bronchoconstriction consequently. Still, haematological values of IgE solely is not absolutely diagnostic.<sup>(23)</sup> However, the measurement of IgE plasma level can primarily serves as a guidance for the dosing of the anti-IgE monoclonal antibody, omalizumab, and the screening for allergic bronchopulmonary aspergillosis.<sup>(26)</sup> On the other hand, elevated eosinophil counts usually lead to more drastic forms of severe asthma, along with more recurrent exacerbations through the IL-5 and IgE-mediated pathways.<sup>(27)</sup> Eosinophils are responsible for the production of a diversified range of inflammatory mediators that ultimately cause tissue damage and airway remodelling.<sup>(28)</sup> Fractional exhaled nitric oxide (FENO) is also an indicative biomarker of airway inflammation in asthma,<sup>(1)</sup> which was shown to be related to eosinophilia. Although measurements of FENO is becoming more accessible, FENO can still be uplifted under non-asthmatic conditions, including allergic rhinitis, atopy, and eczema. Therefore, the ATS/ERS guideline still does not suggest using FENO to guide the choice of therapy in adults or children with severe asthma.<sup>(4)</sup>

### **Anti-IgE Monoclonal Antibody – Omalizumab (Xolair)**

Omalizumab is a chimeric (human-murine) but humanized

anti-IgE monoclonal antibody. It is the first monoclonal antibody used in the treatment of asthma that inhibits the production of pro-inflammatory mediators from mast cells and basophils. In the United States, omalizumab is approved as an adjunct agent over ICS and LABA in patients older than 12 years old with moderate-to-severe persistent allergic asthma that could not be well controlled with ICS.<sup>(23)</sup> This indication is further approved in children aged 6 years or above in Europe<sup>(29)</sup> and the United Kingdom.<sup>(30)</sup>

Omalizumab demonstrated efficacy in reducing exacerbations and hospitalizations in patients with moderate-to-severe asthma, and increasing the probability of ICS withdrawal from these patients.<sup>(34)</sup> It also showed its efficacy in adolescents (12 – 17 years old) with moderate-to-severe allergic asthma, where omalizumab was associated with a reduced number usage of rescuing oral corticosteroids, improved FEV<sub>1</sub>, and a decreased number in missed school days.<sup>(35)</sup> Children aged 6 to 12 years old were also included in several clinical trials, but conclusions are yet to be made from the results.<sup>(34)</sup> Patients with elevated levels of biomarkers (e.g. FENO or eosinophil level in peripheral blood) were particularly shown to have reduced rates of asthma exacerbations with the use of omalizumab.<sup>(36)</sup> Improved quality-of-life was also demonstrated in patients with allergic asthma through the assessment of the Juniper Asthma Quality of Life Questionnaire (AQLQ).<sup>(37)</sup> Nonetheless, a cost-effectiveness analysis was conducted in 2007 and suggested that omalizumab may not be a cost-effective option for patients with severe asthma.<sup>(38)</sup> However, considering that the significant drop in medication cost after 2007 and its demonstrated efficacy, omalizumab is still a viable option for patients with severe asthma nowadays.

Dosing of omalizumab requires the measurements of both body weight and plasma IgE level before initiation of treatment.<sup>(39)</sup> The most common associated side effect is injection site reactions. However, a boxed warning was also issued for omalizumab because there were adverse events of life-threatening anaphylaxis being reported. Therefore, patients with their first three injections of omalizumab should be closely monitored for at least 2 hours post-injection by healthcare providers for any signs of anaphylaxis. Thereafter, omalizumab could be self-administered in an out-patient setting either every two or four weeks.

### **IL-5 Monoclonal Antibody – Mepolizumab (Nucala) and Reslizumab (Cinqair)**

Mepolizumab and reslizumab are recombinant, DNA-derived, and humanized monoclonal antibodies directed against IL-5.<sup>(40)</sup> They intervene the IL-5 signalling pathway and hence inhibit the growth, differentiation, activation, recruitment, and survival of eosinophils.<sup>(41)</sup> As a result, the eosinophil-mediated inflammation in severe asthma is diminished. Mepolizumab is approved as an adjunctive maintenance therapy in severe eosinophilic asthma in patients of 12 years of age or above, while

reslizumab is approved in patients aging 18 years old or above.<sup>(42)</sup>

Both mepolizumab and reslizumab demonstrated efficacy by decreasing the rates of asthma exacerbation,<sup>(43)</sup> enhancing the quality of life, and improving the lung function that was noted by an increased FEV<sub>1</sub> compared to the baseline value.<sup>(44, 45)</sup> In addition, mepolizumab was also shown to lessen the use of oral corticosteroid.<sup>(43, 44, 46)</sup> It should be noted that both mepolizumab and reslizumab are not indicated for the relief of acute conditions, including acute bronchospasm and status asthmaticus, as well as other eosinophilic conditions.<sup>(40, 42)</sup>

Mepolizumab is administered subcutaneously every 4 weeks by a clinician.<sup>(40)</sup> Reslizumab is infused slowly (20 – 50 minutes) intravenously to prevent anaphylaxis.<sup>(42)</sup> It is also administered every 4 weeks at a clinical setting, where healthcare providers are available in case of anaphylaxis occurs.

### IL-5 Receptor Monoclonal Antibody – Benralizumab (Fasenra)

Benralizumab is a humanized and afucosylated monoclonal antibody that targets the alpha-subunit of the IL-5 receptor.<sup>(47)</sup> It activates an enhanced antibody-dependent cell-mediated cytotoxicity that rapidly and thoroughly exhausts the eosinophils and basophils reservoirs. Similar to mepolizumab, benralizumab is approved as an adjunctive therapy in severe eosinophilic asthma in patients of 12 years or above. Benralizumab demonstrates its efficacy in reducing the exacerbation rates in moderate to severe asthma. It also improves lung function by increased FEV<sub>1</sub> and spare the use of oral corticosteroids.<sup>(48-50)</sup>

Benralizumab is administered subcutaneously every four weeks for the first three doses, with the subsequent doses every eight weeks.<sup>(51)</sup> Similar to reslizumab,

the patient should receive the benralizumab dose in a setting where it is capable to manage any anaphylactic reactions.

A summary of the approved immunologic agents indicated for severe asthma are listed in **Table 2**.

### PROPOSED ROLES OF PHARMACISTS IN THE MANAGEMENT OF SEVERE ASTHMA

Patients having appropriate inhaler technique is of paramount importance to the management of severe asthma. Before using individualized biological agents, pharmacists should optimize the inhaler therapy of the patient. Not only the choice and dose of the inhaler are important, but the way of using the inhaler is also pivotal and affects the therapeutic outcome of the patient. Pharmacists may request the patients to demonstrate how they use their inhalers (i.e. the teach-back method) during each visit. Pharmacists may then observe the administration process and evaluate the procedure using an “inhaler checklist”. This assessment should be conducted during each visit to safeguard the capability of the patient’s inhaler technique. A study showed that patients who received face-to-face counselling on the usage of inhalers from a pharmacist, no matter as brief as two minutes, have demonstrated better inhaler technique than those who read the product insert or watching online demonstration videos.<sup>(52)</sup>

Moreover, pharmacists should be responsible for resolving the poor inhaler adherence of patients. Pharmacists can initiate consultations with these patients and discuss the factors that contribute to the poor adherence. For instance, the patients may be inquired sincerely on their beliefs concerning the medications or the disease (e.g. if the poor adherence is due to disbelief of the efficacy of the medications), any issues on affording the medications, as well as the routine refilling frequency of their medications.

Compound (Brand Name)	Manufacturer (Approval Year)	Molecular Entity and Target	Formulation and Dosage of Administration	Specific Asthma Indication
<b>Omalizumab (Xolair)</b>	Genentech / Novartis (2003)	Humanized monoclonal antibody targeted against IgE	<ul style="list-style-type: none"> <li>Subcutaneous injection of 75 – 375mg every 2 to 4 weeks.</li> <li>Limit the dose to 150mg per injection site. Divide the doses to more than 1 injection site if the total dose is greater than 150mg.</li> </ul>	<ul style="list-style-type: none"> <li>Moderate to severe asthma in patients aged 6 years or above</li> <li>Symptoms are inadequately controlled by ICS</li> </ul>
<b>Mepolizumab (Nucala)</b>	GlaxoSmithKline (2015)	Humanized monoclonal antibody targeted against IL-5	Subcutaneous injection of 100mg every 4 weeks.	Adjunctive maintenance therapy in severe asthma with eosinophilic phenotype in patients aged 12 years or above
<b>Reslizumab (Cinqair)</b>	Teva Pharmaceuticals (2016)	Humanized monoclonal antibody targeted against IL-5	Intravenous infusion of 3mg/kg over 20 – 50 minutes every 4 weeks.	Adjunctive maintenance therapy in severe asthma with eosinophilic phenotype in patients aged 18 years or above
<b>Benralizumab (Fasenra)</b>	AstraZeneca (2017)	Humanized monoclonal antibody targeted against IL-5Rα	Subcutaneous injection of 30mg every 4 weeks for the first 3 doses, then 30mg every 8 weeks for the subsequent doses.	Adjunctive maintenance therapy in severe asthma with eosinophilic phenotype in patients aged 12 years or above

The summary of the approved immunologic agents (biologics) are adapted from a review article on the management of severe asthma.<sup>(54)</sup>

Managing modifiable risk factors and preventing triggers of asthma are also beneficial for the remission of the disease. Smoking cessation is indispensable for severe asthma patients because there are numerous noxious chemicals present in the tobacco smoke. Occupational exposures to allergens or triggers are also a significant issue and therefore, pharmacists may collaborate with patients to devise action plans to stay away from those persistent triggers. In addition, several classes of medications, such as beta-blockers and non-steroidal inflammatory drugs (NSAIDs), may also exacerbate the symptoms of asthma. Pharmacists are in the best position to conduct medication reconciliation in these patients to review their medications on hand. When necessary, pharmacists should recommend dose adjustments or alternative medications to substitute the culprits of symptoms exacerbation. Furthermore, some comorbidities may also aggravate the symptoms of severe asthma, including allergic rhinitis, obesity, gastro-esophageal reflux disease (GERD), obstructive sleep apnoea (OSA), depression, and anxiety. Pharmacists should recognize the relevant comorbidities and advise appropriate treatments accordingly.

Pharmacists-led severe asthma clinic should also be advocated as pharmacists are influential in health promotion and disease prevention.<sup>(53)</sup> Pharmacists should be established in primary care settings and conduct regular interviews or consultations with asthma patients. Assessments on the asthma control of the patients are warranted as patients themselves may not fully comprehend how to measure asthma control. Pharmacists should ask direct questions and guide the patients to recall the previous asthmatic events so as to assess the severity and frequency of asthma exacerbations. Apart from the subjective reminiscence from the patient, pharmacists should also look for objective information of asthma control. Pharmacists may document the details of each exacerbation episode, including the use of oral corticosteroids, the frequency of attending the emergency department or hospitalization, as well as the severity and frequency of the symptoms during exacerbations. Thereafter, pharmaceutical care should be delivered that encompasses medications compliance check, patient counselling on medications and their potential side effects, self-monitoring adverse events, ways to prevent or diminish their occurrence, and the corresponding action plans to manage these adverse events. Nonetheless, collaboration between various healthcare professionals is essential to augment the desired therapeutic outcome.

## CONCLUSIONS

Although the population with severe asthma in Hong Kong only represents a small portion among asthma patients, the impact of severe asthma is tremendous. Severe asthma not only deteriorates the quality of life of the patients, but also poses a heavy financial burden to the society. Therefore, primary prevention of severe asthma is urgently important, and there are so

many channels that pharmacists can contribute to, as proposed in this article. Regular assessments, including patient questionnaires about inhaler techniques and symptoms control, and evaluating lung functions such as spirometry, could already restrain the progression of asthma. The conventional stepwise therapy treatment algorithms for asthma may not be effective for severe asthma patients. Therefore, a better understanding on differentiating asthma phenotypes and endotypes, and the evolution of immunological therapies (e.g. anti-IgE and anti-IL5 monoclonal antibodies) extend the treatment portfolio for better severe asthma control

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# Questions for Pharmacy Central Continuing Education Committee Program

( Please be informed that this article and answer sheet will be available on PCCC website concurrently. Members may go to PCCC website (www.pccchk.com) to fill in their answers there.)

1. Which of the following is NOT a criterion of the definition of severe asthma according to the American Thoracic Society (ATS) and the European Respiratory Society (ERS)?

- Taken systemic corticosteroids for more than half of the time in the previous year to control asthma
- Used low-dose inhaled corticosteroids (ICS) plus a second controller medication (e.g. long-acting  $\beta_2$ -agonists (LABA), leukotriene-receptor antagonists, or theophylline) in the previous year for managing asthma
- An exacerbation that lead to hospitalization, intensive care stay, or mechanical ventilation in the previous year
- Airflow limitation, with Forced Expiratory Volume (FEV<sub>1</sub>) < 80% after withholding bronchodilators for an appropriate period.

2. Which of the following is TRUE when comparing severe asthma with milder forms of asthma?

- Patients with severe asthma are more likely to endure various comorbidities, including rhinosinusitis, obstructive sleep apnoea (OSA), hyperventilation syndrome, vocal cord dysfunction, and gastroesophageal reflux disease (GERD).
- Patients with severe asthma are in poorer health status and has unsatisfactory asthma control, therefore the patients are exposed to a higher mortality risk.
- Patients with severe asthma are also more likely to experience loss of productivity and impairments in their daily life.
- All of the above

3. Which of the following components of the immune system play a major role in the development of allergic (atopic) eosinophilic asthma?

- T-helper (Th2) lymphocytes
  - Mast cells
  - Neutrophils
- i & ii
  - i & iii
  - ii & iii
  - i & ii & iii

4. Which of the following is NOT crucial in the assessment of severe asthma control?

- The Asthma Control Questionnaire (ACQ) and the Asthma Control Test (ACT)
- Periodic lung function assessment
- Records of the details of exacerbation episodes, including the triggers of the exacerbation, the need of hospitalization, the use of oral corticosteroids, etc.
- The total number of medications required for managing severe asthma

5. Which of the following correctly describes the Type-2 asthma endotype?

- It has a consistent medical history, genetics, and clinical features that are associated with identifiable biomarkers.

- Diagnosing a patient with Type-2 asthma endotype definitely guides the choice of treatment regimen.
- It is associated with elevated levels of neutrophils and memory B cells.

- iii
- ii
- i & ii
- i & ii & iii

6. Which of the following statements regarding omalizumab are correct?

- It is the first monoclonal antibody used for the management of asthma.
- Patients should be closely monitored when receiving their first three doses of omalizumab due to the risk of anaphylaxis.
- It demonstrated its clinical efficacy in children aged 6 to 12 years old.

- iii
- ii
- i & ii
- i & ii & iii

7. What did mepolizumab and reslizumab demonstrated in clinical trials on asthmatics?

- They reduced the frequency of bronchodilators administration.
- They decreased the rates of exacerbation, increased quality of life, and improved the lung function.
- They were shown to be effective even under acute bronchospasm and status asthmaticus.
- Rates of hospitalization were lower in patients receiving mepolizumab than those taking placebo.

8. Please arrange the approval year of the biologics in chronological order.

- Omalizumab → Reslizumab → Mepolizumab → Benralizumab
- Omalizumab → Benralizumab → Reslizumab → Mepolizumab
- Omalizumab → Reslizumab → Benralizumab → Mepolizumab
- Omalizumab → Mepolizumab → Reslizumab → Benralizumab

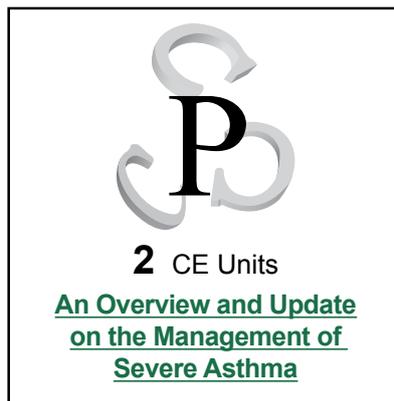
9. Pharmacists are in the best position to

- Counsel inhaler techniques and check patients' compliance
- Review the medications that may exacerbate asthma
- Promote smoking cessation

- iii
- ii
- i & ii
- i & ii & iii

10. The proposed pharmacists-led severe asthma clinic should be responsible for

- Assessing the asthma control on the patients
- Providing pharmaceutical care
- Collaborating with other healthcare professionals to enhance the treatment outcome
- All of the above



Answers will be released in the next issue of HKPJ.

CE Questions Answer for 261(D&T)

Dronedaron: A Review in Atrial Fibrillation

1. A 2. B 3. C 4. D 5. A 6. B 7. D 8. B 9. B 10. C

## Evaluation of GenoFlow Bacterial Meningitis Array Testing Kits with Reference to Conventional Method for the Diagnosis of Bacterial Meningitis Pathogens

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### ABSTRACT

Bacterial meningitis continuously threatens public health with its high morbidity and mortality rates. Due to complex etiological and aggressive nature of bacterial meningitis, a rapid and sensitive diagnostic method is needed before deciding a proper treatment, e.g., the use of antibiotics. In this study, we collected 604 clinical samples from Hungary and Shenzhen, China and compared the performance of DiagCor's GenoFlow Bacterial meningitis array test kit against the gold standard, i.e., bacterial culture and latex agglutination. The results showed that the array test kit had a 96.5% concordant rate with the reference methods. We further analyzed the discrepant results using PCR and Sanger sequencing and confirmed that the array test kit indeed showed 100% sensitivity and 100% specificity for all the pathogens detected by various reference methods. In conclusion, the GenoFlow Bacterial meningitis array test kit represented a sensitive, accurate and rapid laboratory method to help of diagnosis suspected bacterial meningitis cases. The use of this multiplex detection array test could provide prompt and appropriate antibiotic treatment in managing meningitis patients.

**Keywords:** Bacterial Meningitis, Cerebrospinal Fluid, Molecular Diagnostics, Multiplex PCR, Flow Through Hybridization

### Abbreviations

BLAST, Basic Local Alignment Search Tool; CSF, cerebrospinal fluid; EFM, *Enterococcus faecium*; EFS, *Enterococcus faecalis*; EC, *Escherichia coli* K1; WBC, white blood cell; PCR, polymerase chain reaction; HA, *Haemophilus influenza*; NM, *Neisseria meningitidis*; SP, *Streptococcus pneumonia*; SAG, *Streptococcus agalactiae*; SPY, *Streptococcus pyogenes*; PA,

*Pseudomonas aeruginosa*; LM, *Listeria monocytogenes*; MP, *Mycoplasma pneumoniae*; SE, *Staphylococcus epidermidis* and Limit of detection (LOD);

### INTRODUCTION

Bacterial meningitis causes significant morbidity and mortality, and it continually threatens public health globally. The mortality rate of bacterial meningitis can be as high as 30%, especially in newborns and older patients,<sup>(1)</sup> and it is associated with various bacterial pathogens. For example, *Haemophilus influenzae* is one of the major causes of bacterial meningitis, and this pathogen has led to 45% of all bacterial meningitis cases in the US before the launch of the conjugated vaccine.<sup>(2)</sup> *Streptococcus pneumoniae* is another important bacterium that causes meningitis, and it accounted for 60% of the total meningitis cases in US and Turkey.<sup>(1, 3)</sup> It was also the most observed meningitis pathogen in Italy, Israel and Brazil.<sup>(4-6)</sup> *Neisseria meningitidis* infection rate could be up to 1% of the population, and severe infection rate was found globally including Brazil, Nepal, China, and several sub-Saharan African nations.<sup>(7-11)</sup> Due to its high infection rate, an 'African Meningitis belt' was mapped out.<sup>(12)</sup> *N. meningitidis* associated meningitis cases were also common in some developed countries such as the United States.<sup>(13)</sup> *Streptococcus agalactiae* (GBS), on the other hand, is an important pathogen which caused 59% of neonatal meningitis cases in France,<sup>(14)</sup> and it was the most common cause of neonatal meningitis in England.<sup>(15)</sup>

Owing to the complexity and high mortality rate of bacterial meningitis infection, a rapid diagnostic method is crucial to provide proper treatment. Currently, the most common bacterial meningitis diagnosis is based on white blood cell (WBC) counting of CSF (cerebrospinal fluid), turbidity observation, Gram staining, latex agglutination,

and bacterial culture.<sup>(16)</sup> These conventional diagnostic methods are relatively slow with low sensitivity, which may not be able to cope with the aggressive and complex nature of bacterial meningitis infection. On the other hand, the nucleic acid amplification test represents a quick and versatile diagnostic tool against bacterial meningitis (PCR) over the bacterial culture method as a diagnostic tool has been demonstrated previously.<sup>(16)</sup>

GenoFlow Bacterial meningitis array test kit is a PCR based diagnostic test kit, which was developed specifically to detect the most common pathogens found in bacterial meningitis infection by DiagCor (**Table 1**). Amplified bacterial DNA in the CSF sample is hybridized with specific probes on the nitrocellulose membrane by flow-through hybridization technique. This technology enables the simultaneous detection of multiple targets in the sample and shortens the hybridization time to 30 minutes dramatically.<sup>(17)</sup> The potential uses of this test kit include rapid laboratory diagnosis of suspected bacterial meningitis cases, revealing various infection cases, and providing clues for proper antibiotic treatment.

Target pathogens	Abbreviations
<i>Haemophilus influenzae</i>	HI
<i>Neisseria meningitidis</i>	NM
<i>Streptococcus pneumoniae</i>	SP
<i>Streptococcus agalactiae</i>	SAG
<i>Streptococcus pyogenes</i>	SPY
<i>Pseudomonas aeruginosa</i>	PA
<i>Listeria monocytogenes</i>	LM
<i>Mycoplasma pneumoniae</i>	MP
<i>Enterococcus faecium</i>	EFM
<i>Enterococcus faecalis</i>	EFS
<i>Staphylococcus epidermidis</i>	SE
<i>Escherichia coli</i> K1	EC

This study aimed to evaluate the performance of the DiagCor's GenoFlow Bacterial meningitis array test kit in comparison with different traditional diagnostic methods such as bacterial culture and latex agglutination tests.

## MATERIALS AND METHODS

### Clinical Specimens

Six hundred and four (604) CSF samples in total were collected from patients with suspected bacterial meningitis. Among them, 98 samples were collected from St. Laszlo Hospital in Hungary and 506 samples from Shenzhen Children's Hospital in China. The samples reached the laboratory in the respective hospital within four hours after lumbar puncture and underwent conventional microbiologic testing, including

Gram staining, WBC counting, and bacterial culture. All visibly cloudy samples were tested by latex agglutination. Aliquot of two hundred microliters (200 µL) of CSF samples were stored at -80°C for a comparison study using DiagCor's GenoFlow Bacterial meningitis array test kit. Consent was obtained from all patients or their parents for those younger than the age of 18 years old.

### Synthetic Plasmid Generation and Bacterial Genomic DNA

Synthetic plasmids containing sequences specific to the targets were constructed using pUC57 vector. The plasmids were manufactured from GenScript (Piscataway, USA). Bacterial genomic DNA was purchased from ATCC (Manassas, USA). *Haemophilus influenzae* (ATCC® Number: 51907D); *Neisseria meningitidis* (ATCC® Number: 53415D-5); *Streptococcus pneumoniae* (ATCC® Number: BAA-255D-5); *Streptococcus agalactiae* (ATCC® Number: BAA-611D-5); *Streptococcus pyogenes* (ATCC® Number: BAA-1315D-5); *Pseudomonas aeruginosa* (ATCC® Number: 47085D-5); *Listeria monocytogenes* (ATCC® Number: BAA-679D-5); *Mycoplasma pneumoniae* (ATCC® Number: 29342D); *Enterococcus faecium* (ATCC® Number: 51559D-5); *Enterococcus faecalis* (ATCC® Number: 700802D-5); *Staphylococcus epidermidis* (ATCC® Number: 35984D-5).

### Bacterial Culture and Latex Agglutination

In Hungary, the samples from St. Laszlo Hospital were cultured on Columbia blood agar and chocolate agar and parallel in brain heart infusion broth (Bio-Merieux, Marcyll' Etoile, France). Incubation time was 72 hours. Identification was with MALDI-TOF (Bio-Merieux, Marcyll' Etoile, France). Susceptibility is according to EUCAST recommendations. The samples collected from Shenzhen Children's Hospital in China were cultured on blood agar plates and chocolate blood plate for 72 hours at 35°C in a 5-10% CO<sub>2</sub> atmosphere. The observed colonies were identified using the Vitek2 Compact system (Bio-Merieux, Marcyll' Etoile, France) according to the manufacturer's instruction. For latex agglutination test performed in Hungary, the samples were evaluated by using Wellcogen Bacterial Antigen Rapid Latex Agglutination Test (ThermoFisher Scientific, MA, USA) according to the manufacturer's instruction.

### DNA Extraction, Amplification and Detection Using DiagCor's GenoFlow Bacterial Meningitis Array Testing Kit

DNA was isolated from 200 µL CSF samples using the QIAamp DNA Blood Mini Kit (No. 51104; Qiagen, Hilden, Germany) according to the manufacturer's instruction. The extracted DNA was further analyzed with the GenoFlow Bacterial meningitis array test kit to detect the presence of pathogens in the clinical samples according

to the manufacturer's manual. Briefly, a 25 µL reaction containing 5 µL plasmid DNA, 14.1 µL PCR reaction mix, 2.5 µL primer mix, 1 µL GC enhancer, 2 µL internal amplification control and 0.4 µL DNA Taq polymerase was set up for each sample. The PCR mixtures were amplified under the following thermal cycling profile: initial denaturation at 95°C for 5 mins; 45 cycles at 95°C for 30s, annealing at 58°C for 30s, extension at 72°C for 30s; and a final extension step at 72°C for 10 min. Following PCR amplification, the amplicons were subjected to flow-through hybridization as instructed. Bacterial genomic DNA (10<sup>6</sup> copies) and human DNA (20 ng, equivalent to 5.79×10<sup>3</sup> copies) were used to determine the cross-reactivity of the detection signals. The obtained results were used to compare with those from culture and latex agglutination results.

### Sanger Sequencing

Samples with discrepant results were further analyzed by standard Sanger sequencing using a pair of 16S rRNA primers or UMD-Universal (No. U-010-048, Molyzm, Bremen, Germany) according to our in-house method or the manufacturer's instruction, respectively. Amplicons were purified using PureLink QuickGel Extraction and PCR purification combo kit (No. K220001, Thermo Fisher Scientific, Waltham, MA, USA) and were sequenced using the BigDye Terminator Cycle Sequencing Kit (PE Applied Biosystems, Foster City, CA, USA) and an ABI PRISM 3130 DNA analyzer (PE Applied Biosystems). Sequences were analyzed using the Basic Local Alignment Search Tool (BLAST) provided by the National Centre for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/BLAST>).

## RESULTS

### Analytical Sensitivity and Specificity of DiagCor's GenoFlow Bacterial Meningitis Array Testing Kit

The upper and lower LOD for all 12 target pathogens (Table 1) of the GenoFlow Bacterial meningitis array test kit was determined. Serially diluted synthetic plasmids were used to determine the analytical sensitivity and specificity. The detection range of the GenoFlow Bacterial meningitis array test kit was from 100 to 10<sup>6</sup>copies, except PA that can only achieve 500 copies at the lowest LOD. Genomic DNA of human and other reference bacteria were used to test the specificity of the array test, and not cross-reactivity signal was observed (data not shown).

### Comparison of GenoFlow Bacterial Meningitis Array Testing kit Verse Conventional Culture and CSF Latex Agglutination Results

A total of 604 samples were collected from patients with suspected bacterial meningitis, 44 positive and

560 negative samples were identified using reference methods, including traditional culture and latex agglutination as shown in Table 2. Of the 44 positive samples, 31 samples were determined as positive by both reference method and GenoFlow Bacterial meningitis array test kit. Twelve of the leftover 13 samples were identified as negative results since the assay panel did not include the causative pathogens. Reference methods detected the remaining positive sample as *Staphylococcus aureus*, while GenoFlow Bacterial meningitis array test identified them as *Streptococcus pyogenes*. The Sanger sequencing confirmed the results of GenoFlow kit. The sequencing result was concordant with the array test with 98-100% matched as SPY in the BLAST search (data not shown). Of the 560 negative samples, 19 discordant results were detected in the presence of bacterial DNA by the GenoFlow Bacterial meningitis array test. These discrepant samples were further analyzed by Sanger sequencing, and the identities of all these bacteria were concordant with the GenoFlow Bacterial meningitis array test results.

Pathogens	No. of positive by reference methods	No. of positive by GenoFlow Bacterial meningitis array test kit	** No. of Discrepant result
<i>Haemophilus influenzae</i>	0	2	2
<i>Neisseria meningitidis</i>	8	9	1
<i>Streptococcus pneumoniae</i>	16	17	1
<i>Streptococcus agalactiae</i>	1	4	3
<i>Streptococcus pyogenes</i>	0	1	1
<i>Pseudomonas aeruginosa</i>	0	3	3
<i>Listeria monocytogenes</i>	0	2	2
<i>Staphylococcus epidermidis</i>	6	11	5
<i>Escherichia coli K1</i>	0	2	2
*Other pathogens	13	0	n/a
Total no. of positives	44	51	n/a
Total no. of negatives	560	553	n/a
Total no. of samples	604	604	20

\* Other pathogens were out-panel pathogens in GenoFlow Bacterial meningitis array test kit which includes 1 *Streptococcus equinus*, 1 *Staphylococcus hominis*, 4 *Staphylococcus aureus*, 2 *Coagulase-negative Staphylococcus*, 1 *Staphylococcus haemolyticus*, 1 *Bacteroides thetaiotaomicron*, 1 *Cryptococcus neoformans*, 1 *Ochrobactrum anthropic*, and 1 *Acinetobacter lwoffii*.

\*\* All the discrepant samples were subjected to Sanger sequencing, and results were concordant with GenoFlow Bacterial meningitis array test kit.

### Clinical Sensitivity and Specificity of DiagCor's GenoFlow Bacterial Meningitis Array Testing Kit

Clinical sensitivity and specificity of GenoFlow Bacterial meningitis array test kit were calculated according to the results obtained from reference methods as shown in Table 3. The overall sensitivity and specificity were 100%. The sensitivity and specificity of individual targets were also determined and listed in Table 4. However, the sensitivity and specificity of targets for MP, EFM, and EFS could not be evaluated due to the lack of clinical samples.

**Table 3. Clinical Performance of GenoFlow Bacterial Meningitis Array Testing Kit**

GenoFlow Bacterial meningitis Array test kit	N = 604	Reference methods (Bacterial culture and latex agglutination) and Sanger sequencing		
		Positive	Negative	
Positive		51	0	Positive Predictive Value = 100%
Negative		0	553	Negative Predictive Value = 100%
		Sensitivity = 100%	Specificity = 100%	
		False Negative Rate = 0%	False Positive Rate = 0%	

Clinical performance of GenoFlow Bacterial meningitis array test kit was evaluated by reference methods, including bacterial culture, latex agglutination as the gold standard. The discrepant result was further analyzed using Sanger sequencing.

**Table 4. Sensitivity and Specificity of Individual Target in GenoFlow Bacterial Meningitis Array Testing Kit**

Targets	Sensitivity (%)	Specificity (%)
<i>Haemophilus influenzae</i>	100	100
<i>Neisseria meningitidis</i>	100	100
<i>Streptococcus pneumoniae</i>	100	100
<i>Streptococcus agalactiae</i>	100	100
<i>Streptococcus pyogenes</i>	100	100
<i>Pseudomonas aeruginosa</i>	100	100
<i>Listeria monocytogenes</i>	100	100
<i>Staphylococcus epidermidis</i>	100	100
<i>Escherichia coli K1</i>	100	100

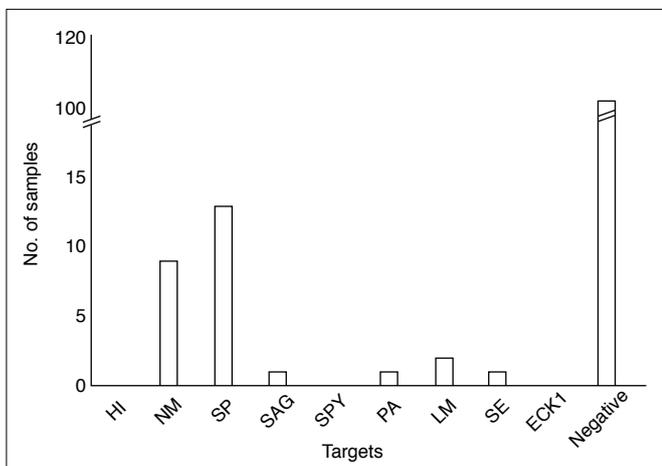
Sensitivity and specificity were calculated from both reference and Sanger sequencing results. The sensitivity and specificity of MP, EFM, and EFS cannot be determined in this study.

### Incidence Rate of Pathogens Detected by DiagCor's GenoFlow Bacterial Meningitis Array Testing Kit in Hungary and Shenzhen

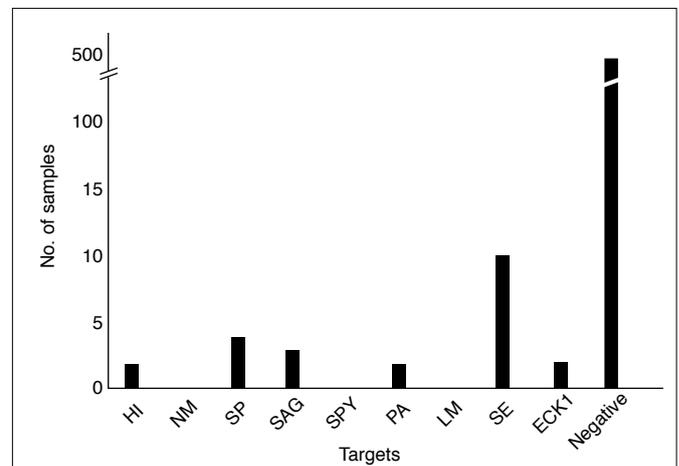
We expect the prevalence of bacterial meningitis varied in different countries and age groups. In this study, the most common pathogens found in the United St. Isvan and Laszlo Hospital in Hungary were SP and NM, which are found frequently in bacterial meningitis cases worldwide (**Figure 1A**). The age of these patients in the hospital in Hungary varied from newborn to 93 years old. While in the Shenzhen region of China, SE was found to be the most prevalent bacterial causing pathogen, followed by SP and SAG (**Figure 1B**).

### DISCUSSION

Patients with bacterial meningitis require proper and prompt treatment to avoid adverse clinical outcomes, such as brain damage, hearing loss, or learning disabilities.<sup>(18)</sup> Therefore, it is essential to identify the causative agent(s) to initiate appropriate antibiotic treatment. Routine laboratory practice employs conventional cytological examinations, e.g., Gram staining, cell counting, and latex agglutination tests for immunological identification, to diagnose bacterial meningitis in suspected cases. Although these methods are relatively rapid and low-cost, they often lack specificity, and their sensitivities might diminish with preceding empirical antibiotic therapy.<sup>(19)</sup> CSF culture is considered as the gold standard to identify causative pathogens in bacterial meningitis. However, the long reporting time of CSF culture prevents specific antibiotic treatment in early disease stage. Molecular diagnostic assays were recently applied in clinical decision making and surveillance.<sup>(20, 21)</sup> Several detection kits are currently available commercially based on multiplex PCR principle, while the GenoFlow Bacterial meningitis array test employs flow-through hybridization technology and offers the capability to detect 12 most prevalence bacteria causing meningitis simultaneously. Furthermore, we found that the LOD revealed the detection range to as low as 100 copies of plasmid DNA and 500 copies for PA, which is comparable to other attainable multiplex array test series developed to identify common viral and bacterial



**Figure 1A.** Distribution of sample identity detected in GenoFlow bacterial meningitis array test kit collected in St. Laszlo Hospital, Hungary



**Figure 1B.** Distribution of sample identity detected in GenoFlow bacterial meningitis array test kit collected in Shenzhen Children's Hospital, China

pathogens. For instance, the GenoFlow HPV Array Test Kit and the Genoflow DR-MTB Array Test Kit, are meanwhile being used and evaluated in different clinical laboratories.<sup>(22-24)</sup>

In this study, it showed that the GenoFlow Bacterial meningitis array test offered high detection sensitivity and specificity for nine pathogens observed in the clinical samples suspected with bacterial meningitis (**Table 3**). Excluding pathogens that were out of the detection panel, the overall concordant rate was 3.5% in comparison to the reference methods. Furthermore, 19 out of 20 discrepant samples were identified as negative in reference methods but positive in the GenoFlow Bacterial meningitis array test. All the 19 discordant samples were further confirmed as positive with sequencing data. The discrepancies observed might be due to the low amount of pathogens presented in CSF. GenoFlow Bacterial meningitis array test was sensitive enough to detect a trace amount of pathogens presented in the samples. It is critical to provide a prompt and precise antibiotic treatment to minimize treatment failure rate and reduce clinical complications. The workflow of the array test can be completed within three hours, whereas the golden standard culture method takes up to few days for pathogen identification. This test kit provides a significant advantage for pathogen detection as it is highly sensitive, accurate and fast. Although this assay offers the capability to identify 12 specific pathogens, it is still restricted to a discrete number of targets based on the most common meningitis-causing pathogens. In this study, the array test kit was unable to identify any pathogen in 14 positive clinical samples, which were later confirmed as the pathogens not included in the array. It showed the limitation of this array test kit to detect rare bacteria strain out of the panel. We recognize that molecular assay could be used as an adjunct to culture method, which will remain essential for antibiotic susceptibility testing.

The epidemiology of bacterial meningitis has changed substantially since the administration of conjugate vaccines.<sup>(1, 25, 26)</sup> The statistical data from this study suggested that, in children, SP and NM remained as the leading cause of bacterial meningitis in Hungary while SE was the most common pathogens in Shenzhen region in China. Previous studies demonstrated that SP, NM, and HI are the most prevalence etiological agents of bacterial meningitis.<sup>(27)</sup> Vaccination strategy targeting the most common community-acquired pathogen was introduced in developed countries, which were associated with the prominent reduction of bacterial meningitis cases for disease control.<sup>(28)</sup> On the other hand, bacterial meningitis is mostly found for the child, elderly and immunocompromised patients.<sup>(27)</sup> The epidemiology of bacterial meningitis has to be studied

thoroughly in different regions as well as various age groups to develop a proper vaccination strategy which can effectively control the most common community-acquired pathogens that cause bacterial meningitis.

Viral meningitis accounts for most cases of acute meningitis. Bacterial and viral meningitis cannot be reliably differentiated clinically, and all suspected cases should be referred to a hospital.<sup>(29)</sup> In most cases, no treatment is necessary for viral meningitis. Certain medications can be useful, depending on the virus that caused the infection. Therefore, there are considerable benefits in making the differentiation between bacterial and viral meningitis swiftly, in terms of both reducing antibiotic usage and hospital admission. A more comprehensive molecular panel is needed to provide immediate and precise therapy to the patients.

In conclusion, our results demonstrated that the GenoFlow Bacterial meningitis array test kit had high sensitivity and specificity for the 12 most common bacteria which cause bacterial meningitis. It can be used to provide rapid identification of pathogens in patients with suspected bacterial meningitis to initiate suitable antibiotic treatments promptly and offer better patient management.

## ACKNOWLEDGMENT

The authors would like to thank Dr. Enders Ng for suggestions and critical reading of the manuscript.

## Declaration

The author declares that the research methods and results obtained in this study are pertinent and do not deliberately favor any brand mentioned in the manuscript.

### Author's background

**MA Dongli** and **LIU, Xiaorong** are currently working in the Department of Clinical Laboratory, Shenzhen Engineering Laboratory for High-throughput Gene Sequencing of Pathogens, Shenzhen Children's Hospital, Shenzhen, Guangdong, China. **Mr. SZABÓ, Edina** is currently working in the United St. Isvan and Laszlo Hospita, Budapest, Hungary. **Miss WONG, Wing Yan** and **Miss LAW, Ngau Ling** worked as Research Scientist in the R&D Department of the DiagCor Bioscience Incorporation Limited. **Dr. LEUNG Andrew** obtained his PhD in Foundation Medicine from The Chinese University of Hong Kong and worked as an R&D manager at the DiagCor Bioscience Incorporation Limited. **Mr. CHU, Yan Sing** is working as a Research Scientist in the R&D Department of the DiagCor Life Science Limited. **Dr. LEE Rebecca** obtained her PhD from the National Institute for Basic Biology, Japan. She works as an R&D manager at the DiagCor Life Science Limited. **Dr. YANG Mei** obtained her PhD in Biomedical Sciences from the City University of Hong Kong. She is working as a scientist on the molecular diagnostics of infectious and genetic diseases in the R&D Department of the DiagCor Life Science Limited.

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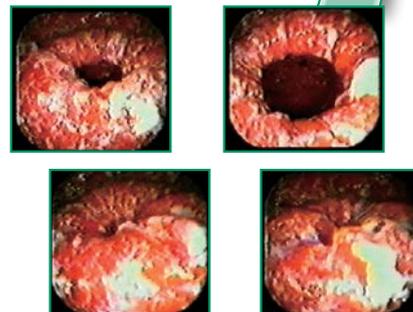
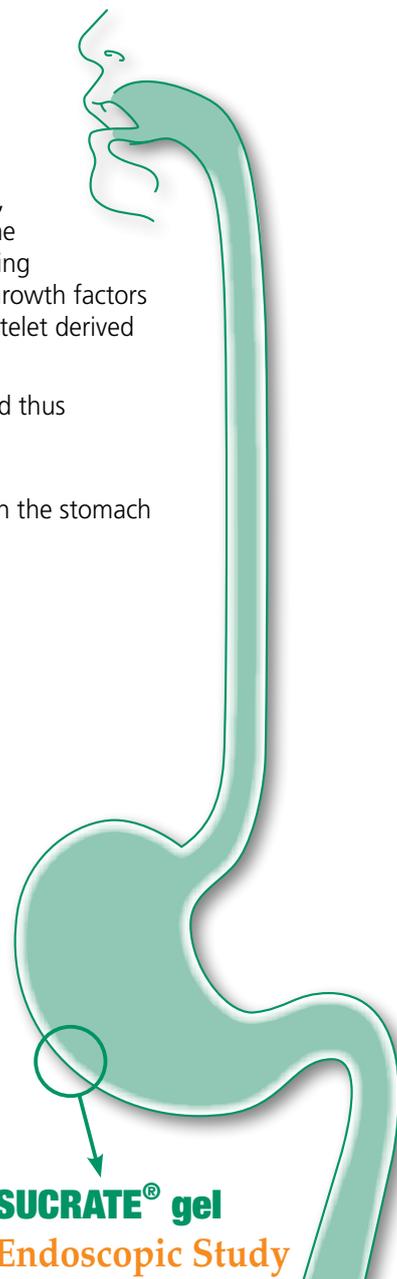
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Cosentino F. et al., Società Italiana di Endoscopia Digestiva, VII Simp. Naz, Napoli, 1992

# The Beijing Forbidden City International Pharmacist Forum 2019 Student Experience Reflection

**LAI, Yat Wing Betty\***; **LAM, Hei Yiu Jessie**; **LEUNG, Yin Mei Crystal**; **SO, Ho Yin Steven**; **TUNG, Yan Tung Anisa**

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As future pharmacists, it is important for us students to stay up-to-date and keep up with the global trend in pharmacy. We are so grateful to be granted an opportunity by the Pharmaceutical Society of Hong Kong (PSHK) to travel alongside experienced and passionate pharmacists to participate in the Beijing Forbidden City International Pharmacist Forum 2019 in early May. The PSHK delegation was led by Mrs. Mary Cheng, together with Mr. Peter Suen, Benjamin Kwong, Mr. Wong Chi Ming, Mr. Hubert Suen and Ms. Susanna Choi (Photo 1).



**Photo 1.** Pharmacists & students from the Pharmaceutical Society of Hong Kong & Macau

## HOSPITAL VISIT

### PEKING UNIVERSITY THIRD HOSPITAL

We visited the Pharmacy Department of Peking University Third Hospital (Photo 2, 3), a Class A tertiary comprehensive hospital in China. In 2016 and 2017, the department topped the list in the aspect of clinical pharmacy in the hospital ranking conducted by Hospital Management Institute, Fudan University. Clinical pharmacists in the hospital participate in ward round actively to provide medication-related recommendation for physicians. In addition, the hospital has established physician-pharmacist joint clinics and pharmacists actively participate in multiple disciplinary teams.

The department has adopted various kinds of technology to facilitate the handling of enormous amount

of prescriptions per day. For inpatient pharmacy, Unit Dose Automatic Tablet Dispensing System is installed (Photo 4). The machine is able to distribute medications of a specific patient to a labelled plastic bag automatically. All the required information, for instance, the ward, bed number, patient name and ID, dosage and route of administration etc. are printed on the label. Pharmacists will double check the unit dose to ensure that everything is perfectly correct. This measure effectively minimizes dispensing errors and contamination of medications.



**Photo 2.** Visit to Pharmacy Department of Peking University Third Hospital



**Photo 3.** Peking University Third Hospital



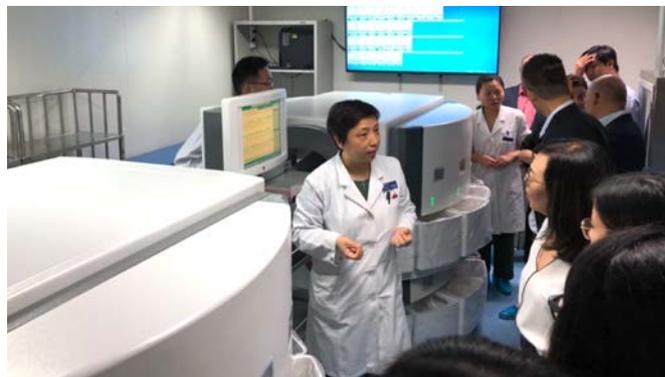
**Photo 4.** Inpatient Pharmacy & Unit-dose dispensing machine

For outpatient pharmacy, the department makes use of Yuyama Box Package Dispense Robot System to aid the dispensing process. After the code on the prescription is scanned, the system automatically locates the medications and gathers them into a basket installed with an RFID chip (**Photo 5**). The chip records the patient's prescription information and is used for final verification before the medications are sent out. The basket will then be transferred back to the shelf, which is equipped with RFID reader, and wait for counselling step by pharmacist. Upon the scanning of patient's ID, the compartment of the shelf placed with the corresponding basket will light up to remind the pharmacist to locate the basket containing patient's medications. The system greatly improves the efficiency and accuracy of dispensing. The storage condition of medication is also controlled to the optimal conditions by the machine as well. Furthermore, the workload of pharmacists can be relieved, especially those who work in hospitals that process massive amount of prescription per day. Nevertheless, there still exists some technical problems. The refill of medications has to be done manually by technicians, which may induce errors. Also, the types of medication capable to be stored in and distributed by the machine are limited. Some medications still require manual dispensing.



**Photo 5.** Basket to gather medications in outpatient pharmacy

The hospital has also established the Pharmacy Intravenous Admixture Services (PIVAS) in 2004 to ensure the safety of IV injecting products, TPN, antibiotic and cytotoxic drugs. PIVAS provided by the pharmacy department covers more than 50 wards, 1400 beds in the hospital. In-patient ward sorting machine (**Photo 6**) is used to ensure that the products are delivered to the corresponding wards correctly.



**Photo 6.** In-patient medication ward sorting machine

All in all, the pharmacy department of Peking University Third Hospital demonstrated their professionalism and capability of making good use of modern technology to provide the optimal outcome for patients. The hospital has cooperated with UKCOP as well as different universities to provide advanced pharmacy practice experience for pharmacy student or postgraduates.

## **PARTICIPATION BY HONG KONG PHARMACIST IN THE FORUM**

On 3 May 2019, there was a seminar on Pharmaceutical Care Practice in Hong Kong, Macao, Taiwan and Mainland China. Mr. Peter Suen from Hong Kong and Ling Jiang from China co-chaired the seminar. As representatives from Hong Kong, Mr. Wong Chi Ming, council member of PSHK, participated in the seminar by giving a talk titled Pharmaceutical Society of Hong Kong preparing Community Pharmacists to Advance in Emerging Primary District Healthcare. With solid data and statistics, Mr. Wong first pointed out the fact that Hong Kong people are having the highest life expectancy in the world, which implies that a large portion of the society may experience more diseases. The result of this phenomenon is the increase in burden to the public healthcare system of Hong Kong. Thus, it becomes important for pharmacists to take part in the work of promoting primary healthcare in the community.

In order to devote themselves into the primary healthcare sector, there are a few roles that pharmacists should undertake. One of the most significant roles played by a pharmacist in the community is to provide Medication Therapy Management (MTM) service. Under the MTM mode of practice, pharmacists deliver drug related information, educate and conduct counselling to

patients. As the effect of drugs on the body is greatly affected by patients' drug compliance, pharmacists also have the responsibility of uncovering the reason behind the low compliance in specific patients. Besides these roles, pharmacists can make efforts in detecting chronic diseases in an early stage by offering services such as fast screening test for NCD like blood glucose and cholesterol test. They can even further enlarge their scope of service to providing vaccination to patients, which has become an increasing trend in different countries in recent years.

Different from the conventional perception that pharmacists only dispense medications, in our modern society the cruciality of pharmacists processing qualities as healthcare professionals is emphasized. On top of learning basic pharmaceutical and medical knowledge, pharmacists should constantly renew their understanding towards the field by lifelong learning. Also, it is of utmost importance that they equip themselves with a variety of skills other than dispensing ability. These include good communication skills that will certainly be useful when pharmacists work in a cross professional environment. Besides, as mentioned above, as there is an increasing tendency of pharmacists providing alternative services, they should also acquire first aid and IV injection skills. In this way, pharmacists can dedicate themselves in improving the primary health condition in the community level.

As another member of the PSHK delegation, Mrs. Mary Cheng participated as moderator of the opening ceremony keynote speech with presentation by pharmacists from China, Japan, United Kingdom and USA. The topic of the section was Ability and Responsibility, Service and Charge – Pharmacists Are in Actions Again. Throughout the forum, Hong Kong pharmacists did not only get to know the current healthcare situations from different countries, but also introduced the Hong Kong way of practice onto this international platform. On 4 May 2019, Mr. Benjamin Kwong participated as moderator for the morning session, Topic Pharmaceutical Economics and Real World Studies.

## **COMPARISON OF PHARMACY SYSTEMS BETWEEN HONG KONG AND OTHER REGIONS**

We believe every country and region has their unique pharmacy system that caters for the distinctive needs of their citizens. Some may include the participation of insurance firms in the healthcare system, while in other systems, the pharmacy department might target more on out-patient service, depending on the differences in cultural backgrounds and acceptance of patients.

Throughout the forum and our visit to Peking University Third Hospital, we discovered several differences between pharmacy systems as follows:

In Hong Kong, the pharmacy system in the hospital setting usually includes the participation of a few pharmacists and more dispensers. Dispensers' daily working routine mainly involves manual picking, packaging and labelling of prescribed medications. Then, pharmacists review the prescription and provide a simple counselling to patients over the outpatient pharmacy counter, during which instructions on drug usage are given. Seldom do pharmacists take place in the outpatient clinic to provide diagnostic services or suggest health advice to patients with mild symptoms like common cold and cough. Even though in recent years, more pharmacists play a role in the clinical setting to reconcile medications from different specialities and clinics, or take part in various specializations such as in the oncology department or paediatric department to give drug advises, the majority of Hong Kong pharmacists would work in the hospital pharmacy, or in a community setting.

Like Hong Kong, pharmacists around the world also regard dispensing as one of their duties. However, the situation is changing in China in recent years, as there is an increasing level of participation by pharmacists in the outpatient department in the hospitals. For instance, in the sub-forum presented by Dr Lin Hua from the Guangdong Provincial Hospital of Traditional Chinese Medicine, Lin mentioned that the hospital he is working in has been currently and actively developing outpatient pharmacy counselling services for their patients, in a step by step manner. At first, the service was provided with the collaboration between pharmacists and practitioners; it then extended to comprehensive services, including the provision of information on drug usage and drug safety. Afterwards, a specialized pharmacy outpatient services was developed. Finally, pharmacists can work with other healthcare professions to treat patients in a concerted effort. It is observed that the pharmacy profession is constantly improving itself, no matter in which part of the world.

After our hospital visit, we found that the major difference between the pharmacy systems in Hong Kong and Beijing is that the pharmacies in Beijing are fully operated and monitored by pharmacists, without the presence of dispensers. To cope with the heavy workload of the pharmacy department, especially in "first-tier city" in China like Beijing, the hospitals make use of multiple types of machinery in the drug dispensing process. For example, RFID baskets that run on conveyor belts are used to initiate an automatic dispensing process. There are chips installed at the bottom of the baskets, which alert pharmacists when the prescriptions are delivered to a wrong place, so as to prevent errors in the busy setting. To further facilitate patients in taking medications, the hospital has implemented the Unit Dose Automatic Tablet Dispensing System to pre-pack drugs with the appropriate dose into small packets according to the time patients consume the drugs, which may make it easier for patients, especially those who are having polypharmacy. This practice

may be adopted in Hong Kong for the favour of elderly patients who live in an elderly home, as a means of drug management.

As pharmacists-in-training, we truly believe that every pharmacy system has its own advantages and strengths, which deserve learning. However, it is also important to consider the reality conditions in our home city when we try to adopt the mode of practice of other places. Only by learning and integrating can we improve our own pharmacy services.

## REFLECTION

While we are truly grateful to be given this precious opportunity to join in the trip, we have also learnt a lot and reflected on the experience in Beijing.

In the Forbidden City International Pharmacist Forum, pharmacists from all over the globe exchanged their experience, knowledge and opinions. They shared how pharmacists work in their countries and their views on specific medical issue. Also, they listened and communicated with each other. Seeing this, we students realized that being a pharmacist is not only about the 4-year training in the university. It is instead a life-long learning process that requires one to keep on learning new knowledge and be aware of the current development of the sector.

The forum involved a fruitful amount of presentations given by pharmacist speakers not only from China, but also from other countries and regions such as America, Japan and the UK. These presentations included

sharing on respective country's experience on topics like medication in children and nutrition therapy. We attended presentations that we were interested in and wanted to know more about. It was surely a good opportunity for us to practice self-motivated learning and we did gain comprehensive knowledge on various aspects.

The visit to the Pharmacy Department of Peking University Third Hospital was also very impressive. Peking University Third Hospital is a large-scale hospital and the number of prescriptions each pharmacist handle per day is far more than that in Hong Kong. We were amazed by their high efficiency and accuracy. During the visit, we could see that they utilized the help of machines in dispensing medicines. This greatly reduced pharmacists' workload and prevented error which ensured the safety of patient. This may be what Hong Kong can learn from mainland China.

## CONCLUSION

As the old saying goes, "he that travels far knows much". This trip had not only widened our horizons in the pharmacy profession but had also reinforced our passion to be a pharmacist. No matter the trip was long or short, these 3 days are certainly one of our most memorable experiences in year one pharmacy school.

### Author's background

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# PPAHK Introduce USP 800 New Standards and Practices to Hong Kong

by Iris Chang , President, The Practising Pharmacists Association of Hong Kong

**PPAHK** President Iris Chang conducted a Study Mission to USA to attend the USP 800 Train the Trainer Education Event and Site Visit in hospitals and primary healthcare centers in the USA.

The PPAHK aims to always stay one step ahead in advancing pharmacy practice and makes focused efforts to learn of the cutting edge practices around the world with the purpose of introducing valuable best practices to Hong Kong in a timely manner.

In June 2019, the PPAHK President Iris Chang travelled to the USA to join the Train the Trainer Education Event for the implementation of the USP General Chapter 800 in the USA and went to conduct a site visit to the Backus Hospital where the transition to upgrade to USP 800 standards had been recently completed.

The USP (United States Pharmacopeia) is a non profit, science driven organization that has an established process for convening independent experts in the development and maintenance of healthcare quality standards.

The USP General Chapter 800 provides standards for safe handling of hazardous drugs to minimize the risk of exposure to healthcare personnel, patients, and the environment.<sup>(1)</sup> While the USP 797 focus on sterile compounding activities only, the USP 800 takes a 360 degree approach for processing hazardous drugs and expands controls for the protection of healthcare personnel and environments against the risks of exposures to hazardous drug compounds.<sup>(2)</sup>

According to the National Institute for Occupational Safety and Health, about 8 million US healthcare workers are potentially exposed to hazardous drugs. Exposures to hazardous drugs (HDs) can cause both acute and chronic health effects.

Those that may potentially become exposed to HDs may include pharmacists, pharmacy support staff, nurses, physicians, patient's family members, laboratory staff, environmental services and other healthcare facilities staff.

The implementation of the USP 800 will aim to reduce the risk of harm to both the environment and workers when compounding or packaging HDs including anti neoplastic drugs, hormonal therapies, radio pharmaceuticals, bacteria, and viruses.<sup>(3)</sup>

The PPAHK believes the concept of the USP 800 is important to the development of higher standards of

Medication safety in Hong Kong to protect pharmacists, pharmacy support staff, doctors, nurses, patient's family and others that may potentially be harmed by being exposed to hazardous drugs.

The PPAHK will take the lead to drive new commitment amongst pharmacists and stakeholders together with the government to promote higher levels of occupational safety and health for all pharmacists and all those involved in handling hazardous drugs.

We look forward to your support.

#### References

1. USP 800 Hazardous Drugs ~ Handling in Healthcare Settings July 1, 2018
2. USP 800 Compounding Overview ~ A Guide to USP 800 Requirements
3. USP 800 and hazardous Medications. Trung H. Nguyen, PharmD and Alesha Davis, CPhT

## PPAHK Forms Strategic Alliance to Gain Service Provider Status for Pharmacists in the Hong Kong Government's Elderly Healthcare Voucher Scheme

On 11 June 2019, a press conference was held to announce the establishment of the Strategic Alliance for Improving the Elderly Healthcare Voucher Scheme (the EHVS Alliance) with The Practising Pharmacists Association of Hong Kong, the Hong Kong Academy of Pharmacy, the Hong Kong General Chamber of Pharmacy, Patient groups, and other local and global supporting organizations. **(Photos A,B)**. As the PPAHK had been advocating and had been in continuous dialogue with the government over the past years to include the professional advisory services of the Pharmacist, such as the Medication Check Up Service, to the Government's Elderly Healthcare Voucher Scheme (EHVS) so that the Scheme can offer more choices to patients seeking for their desired primary healthcare services, it is timely that a Strategic Alliance be formed together with the key stakeholder groups to strengthen and magnify our voice to the government to take immediate actions accordingly.



Photo A



Photo B

The EHVS Alliance will formulate strategies and action plans to ensure our proposals to the government are being seriously considered and taken forward.

While the Medication Check Up Services continue to be provided in community pharmacies in Hong Kong with patients paying "out of pocket" and we will commence the 6<sup>th</sup> intake of the Official Certification Training for Delivery the Medication Check Up and Medication Therapy Management (MTM) Services In the community with the partnership support of the American Society of Consultant Pharmacists who were the original Innovators of the MTM practice model.

Because The PPAHK believes it is our professional duty to make our valuable Pharmacists advisory services more readily available to all of the elderly in need to use the Elderly Healthcare Voucher for obtaining important primary healthcare services such as a Medication Check Up, the PPAHK have started a Petition to gather 100,000 signatures from local Hong Kong and international supporters. We would like to raise to the attention of the Hong Kong Government the urgent need to improve the service scope of the Elderly Healthcare Voucher Scheme by way of adding highly trained and qualified pharmacists as service providers recognized by the Elderly Healthcare Voucher Scheme to support the quality use of Medicines In the elderly population.

Many signatures of supporters and partners in Hong Kong and in the USA have already been placed on a big banner to be used for giving the petition letter to the government. We look forward to your support to sign the PPAHK Petition Letter And Banner for this important cause for the benefit of all of the elderly in Hong Kong.

## SHPHK – Opportunity is everywhere!

The 32<sup>nd</sup> Annual General Meeting (AGM) of the Society of Hospital Pharmacists of Hong Kong (SHPHK) was successfully held on 22<sup>nd</sup> March 2019 at Cordis Hotel, Mongkok. Prior to the meeting, we were honored to have Dr. Lam King Yun Joanne, Specialist in Endocrinology, Diabetes and Metabolism, Queen Mary Hospital to share her expertise in type 2 diabetes mellitus with us.

In the AGM, Mr. William Chui, President of SHPHK reported that over 30 educational activities were organized by the Society and the Drug Education Resources Centre (DERC) in 2018. Mr. Chui also shared with the Members the career opportunities available to pharmacists, pharmacy interns and students, as well as the future development of hospital pharmacy in Hong Kong in the meeting.



The 32<sup>nd</sup> SHPHK annual general meeting cum educational seminar was held on 22<sup>nd</sup> March 2019. From left: Dr. Lam King Yun Joanne, Specialist in Endocrinology, Diabetes and Metabolism, Queen Mary Hospital and Mr. William Chui, President, SHPHK.

### Official Visit to Shenzhen Bay

SHPHK welcomes different collaboration opportunities from different parties, hoping to explore different platforms for its Members to connect with pharmacists of different region.

On 15<sup>th</sup> April 2019, four delegates of the SHPHK Committee had an official meeting with the representatives of various parties of Shanghai, including the Shanghai Pharmaceutical Association; Zhongshan Hospital, Shanghai Medical College of Fudan University, Shanghai; Changhai Hospital, Second Military Medical University, Shanghai; Shanghai Municipal Health Commission and; the China Resources Pharmaceutical (Shanghai) Co., Ltd.

The meeting took place at the China Resources Headquarters in Shenzhen Bay. It was a very productive meeting. The idea of organising a clinical pharmacy

forum for pharmacists of Shanghai, Hong Kong, Macao and Taiwan was discussed. Watch this space!



In the meeting at the China Resources Headquarters in Shenzhen Bay, delegates from Hong Kong and Shanghai were exploring the possibility of organising a Shanghai-Hong Kong Clinical Pharmacy Forum in the near future.

### Seminar on Influenza Outbreak and Sharing Session on Kindergarten Vaccination Programme

On 26<sup>th</sup> April 2019, SHPHK organized a seminar on influenza outbreak and a sharing session on kindergarten vaccination programme for kindergarten principals in Hong Kong. During the seminar, Mr. William Chui reported the results of the survey on the knowledge of parents towards flu vaccination. Two doctors and a nurse who are specialised in public health were invited to give a detailed presentation on the control of influenza outbreak and on the community outreach vaccination programme in Hong Kong. The principal of Kowloon True Light School (Kindergarten Section) was also invited to share her experience in prevention of kindergarten influenza outbreak in the sharing session.

The Society will organise more educational activities for the public to raise their awareness on the prevention of different diseases.



A seminar on influenza outbreak and a sharing session on kindergarten vaccination programme were held on 26<sup>th</sup> April 2019. From left: Mr. William Chui, President, SHPHK; Dr. Ip Kai Ming, Clinical Associate Professor and Division Head, School of Public Health, LKS Faculty of Medicine, The University of Hong Kong and; Ms. So Hau Chi, Registered Nurse and the Coordinator of the research on 'The Relationship of Flu Infection Between School Children and Family Members'.

## Workshops for Pharmacy Students and Interns

The Society values the personal development of Pharmacy Students and Interns in Hong Kong. The General Committee Members of SHPHK are always willing to share their invaluable experience with the young pharmacists selflessly. In May and June 2019, two workshops were organised to help our pharmacists-to-be and young pharmacists to better prepare themselves for their oral exams and job interviews.

The Society would like to thank Ms. Chiang and Mr. Michael Ling, advisors of SHPHK as well as the instructors of the two workshops for their time to deliver two inspiring and interesting workshops to the participants.

## The ABC Seminars Are Back!

This year, the Society is organising a lecture series on HIV/AIDS, hepatitis B and hepatitis C in June, August and October, respectively. This lecture series is the second part of the ABC course held in 2017.

The first lecture on HIV/AIDS was already held on 13<sup>th</sup> June 2019 at the Cityview Hotel. If you would like to learn more about the latest antiviral therapies for hepatitis B and C, do not miss the chance to sign up for

the two remaining lectures of the series. More details will be announced by the Society's News Reporter in due course.



*Antiviral ABC Seminar (Part II) – HIV/AIDS was successfully held on 13<sup>th</sup> June 2019. From left: Ms. Selma Lai, Pharmacist, Princess Margaret Hospital; Dr. Jacky Chan, Associate Consultant, Department of Medicine and Geriatrics, Princess Margaret Hospital and; Mr. William Chui, President, SHPHK.*

You are most welcome to follow the Society's Facebook page (@SHPHK) to know more about the Society's development and activities. You may also visit the Drug Education Resources Centre (DERC) Website: [www.derc.org.hk](http://www.derc.org.hk) to keep abreast of the latest news and development of drugs in Hong Kong. Join us now as new member or renew your membership at the Society's website: [www.shphk.org.hk](http://www.shphk.org.hk).

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