

## Message from the President

In this issue of the College Newsletter, I am saddened to bring the news to all Members and Fellows that one of our Honorary Fellows, Professor WU Bing Quan passed away peacefully on 21 June 2020. Professor WU was a pioneer in the development of Pathology in China. He was one of the first group of scientists to be sent to the United States for training where he met Professor Joseph CK LEE, Former Dean and current Honorary Clinical Professor of The Chinese University of Hong Kong. They became good friends during their time together in the United States and hence Professor WU became associated with our College. Professor LEE has kindly written an obituary for Professor WU and our College also sends its condolences to Professor WU's family.

The 15th Trainee Presentation Session, the 28th Annual General Meeting and Conferment Ceremony, the 28th T.B. TEOH Foundation Lecture and Dinner were successfully held on 23rd November 2019 when the social unrest was quietening down. All attending Members, Fellows and their families enjoyed a wonderful evening. Professor KWONG Yok Lam, our 28th T.B. TEOH Foundation Lecturer, delivered a lecture entitled "An amazing journey from micro to macro and back" with a human touch of his interest in reading science fiction. The winner of the 15th Trainee Presentation Session was Dr. CHENG Hua Tse Timothy who presented his work on 'Comprehensive characterization and resolution of eltrombopag interference on bilirubin measurement'.

The Academies of Medicine for Singapore and Malaysia organised the 53rd Singapore Malaysia Congress of Medicine in Singapore in January 2020. I attended the Congress as well as the Joint Academy Council Meeting on behalf of the College. In the Congress Symposium, a fascinating talk on how big data and social media affects the hierarchical relationship and massive manipulation was presented by Mr. George YEO, the Former Cabinet Minister of Singapore.

The Topical Update in this issue was on "Liver Injury associated with Immune Checkpoint Inhibitors – An Update on Clinicopathological Features", by Dr. LO Cheuk Lam Regina of The University of Hong Kong.

In response to the recent COVID-19 pandemic, Professor LAI Koon Chi Christopher of The Chinese University of Hong Kong, and Professor Siddharth SRIDHAR of The University of Hong Kong, jointly published an article on "Coronavirus Diversity and Infection through Host Receptor" in Ming Pao on 7th April 2020. On 29th April 2020, our College also released a press statement to the general public on the "Use of Over-the-Counter COVID-19 Test Kits", explaining the risks associated with false positives and false negatives of the point-of-care test kits based on IgG and IgM antibodies. Apart from numerous reports in various newspapers, our College also noted about 40,000 'shares' on social media.

Different parts of College Examinations have been or will be conducted from July to September 2020. It is challenging to conduct examinations in a pandemic situation, but with the approval from the Academy Council, Colleges are allowed to conduct examinations using telecommunication technology where appropriate and possible. I would like to thank our External Examiners, Chief Examiners, Deputy Chief Examiner and Local Examiners in advance for their tremendous effort in making it possible for the College Examinations to be conducted as scheduled.

Finally, allow me to wish you all 'good health' going forward !

Dr CHAN Ho Ming  
President  
July 2020



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## President's Activities:

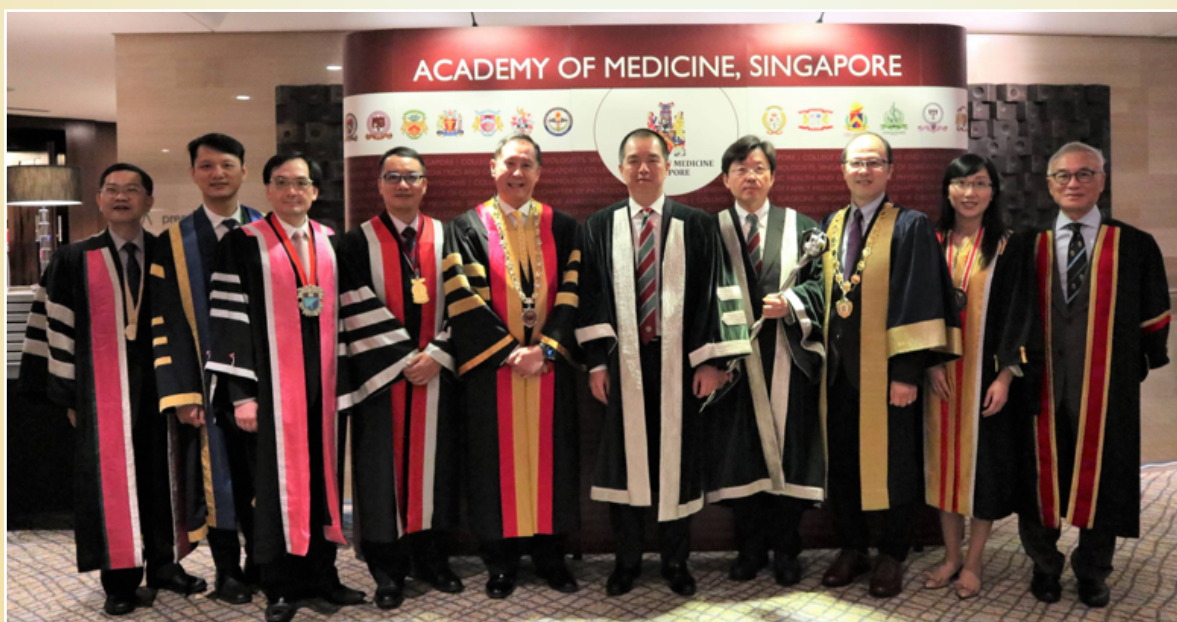
### The 53rd Singapore Malaysia Congress

The 53rd Singapore-Malaysia Congress was held on 18th January 2020 in Singapore. It was a rescheduled meeting after the initial plans for the meeting to be held in Hong Kong in December, were deferred due to the social situation in Hong Kong at the time.

The meeting was co-organised by the Academy of Medicine, Singapore (AMS) and the Academy of Medicine of Malaysia (AMM). The Congress was held in conjunction with the AMS's Induction Comitia, where Hong Kong Academy of Medicine Vice President (Education and Examinations), Professor Gilberto Leung appraised the great achievements of the new Fellows admitted by the AMS.

The 24th Gordon Arthur Ransome Oration was delivered by Former Cabinet Minister of Singapore, Mr George Yeo. In his speech entitled 'Human Solidarity in a Fragmenting World', Mr Yeo focused on four 'Forces' that result in moral challenges in the world today; namely the social media revolution and how it has impacted on hierarchical relationships; fragmentation and reconfiguration of human society which is occurring at all levels from the family to companies to political structures; growing wealth and income inequality which exacerbates existing class and ethnic divisions in society; and mass manipulation by new masters of the universe, meaning the way that big data and the social media are being used to influence and manipulate the way we think.

The Academies from all three countries (Singapore, Malaysia and Hong Kong) also took the opportunity to update each other on their latest developments at the Joint Council Meeting.





# The 15<sup>th</sup> Trainee Presentation Session

The 15th Trainee Presentation Session was successfully held in the afternoon on 23rd November 2019. Four fellows from different Pathology Disciplines were invited to be judges: Dr. CHAN Fuk Woo Jasper (Clinical Microbiology & Infection, Queen Mary Hospital), Dr. KWOK Sung Shing Jeffrey (Chemical Pathology, Prince of Wales Hospital), Dr. SIN Chun Fung Albert (Hematology, Queen Mary Hospital), and Dr. WU Cherry (Anatomical Pathology, United Christian Hospital). On behalf of the Education Committee, I would like to express grateful appreciation to our invited judges for spending their Saturday afternoon participating in the Trainee Presentation Session to provide critical judgements and invaluable comments to our trainees.

The Trainee Presentation Session aims to provide a platform for our trainees to undertake research study and sharpen presentation skills. A total of 16 trainees took part in this session. I would like to congratulate all participants for their nice preparation and impressive presentation. Due to time constraints, only 10 participants were nominated to do an oral presentation, while the 6 remaining participants were invited to do poster presentations. The best presentation was awarded to Dr. CHENG Hua Tse Timothy (Chemical Pathology, Prince of Wales Hospital). The topic of his presentation was: "Comprehensive characterization and resolution of eltrombopag interference: A hepatotoxic drug that interferes with bilirubin measurement". The abstract of his study was:



▲ Judges of the 15th Trainee Presentation Session. From left to right: Dr. CHAN Fuk Woo Jasper, Dr. KWOK Sung Shing Jeffrey, Dr. CHAN Wing Hung Anthony (Vice Chairman of the Education Committee and Organiser of the Trainee Presentation Session), Dr SIN Chun Fung Albert, Dr WU Cherry.

## Background

Eltrombopag is a thrombopoietin receptor agonist that is increasingly being prescribed in recent years to treat chronic thrombocytopenic conditions (~260 patients in Hong Kong, 2018). Hepatotoxicity occurs in ~15% of patients, and the regular biochemical monitoring of liver function is an important part of the follow-up process. Eltrombopag can cause pH-dependent discoloration of serum and affect the assessment of hyperbilirubinemia because of its i) absorbance at ~450 nm (bilirubin) ii) absorbance at ~550 nm (diazo-bilirubin) and iii) it can cause yellowish discoloration of the eyes at normal circulating bilirubin levels. Depending on which hospital a patient is followed-up, the serum bilirubin concentration for a single serum sample can vary by more than 8-fold, up to 64  $\mu\text{mol/L}$ , with the true concentration unknown.

## Methods

We collected 66 samples from patients on a range of eltrombopag dosages 25-150 mg daily. Bilirubin was measured using nine assays including the Reference method (Dumas) and High Performance Liquid Chromatography (HPLC). Plasma/serum eltrombopag concentrations were determined using Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS).

## Results

49 of 52 samples from patients on  $\geq 50$  mg daily eltrombopag therapy showed significantly discrepant inter-analyzer total bilirubin results. There was a positive correlation between total bilirubin difference and plasma eltrombopag concentration ( $r=0.679$ ). Spike-in experiments demonstrated that Beckman AU and Dumas Reference methods were susceptible to positive interference, and that metabolites likely contribute. HPLC quantified bilirubin after separating eltrombopag, and results demonstrate that different analyzers are affected to varying degrees by eltrombopag and its metabolites.

## Conclusions

We are the first to demonstrate which bilirubin assays can accurately quantitate bilirubin concentration in patients on eltrombopag therapy, and also provided evidence for the first time that metabolites likely contribute to the interference. Accurate measurement of total bilirubin may improve our understanding of the prevalence of hyperbilirubinemia, and prevent misdiagnosis of hepatotoxicity in patients on eltrombopag therapy.



▲ Chairman of the Education Committee, Dr LAI Koon Chi Christopher, presenting the prize for the Best Presentation to Dr CHENG Hua Tse Timothy.





# Annual General Meeting 2019

The 28th Annual General Meeting (AGM) was convened on 23rd November 2019, after the 15th Trainee Presentation session. In the AGM, Dr. CHAN Ho Ming, Michael was re-elected as President. Dr. CHAN Chak Lam Alexander and Dr. POON Wai Ming were re-elected as Vice-Presidents. Dr. MAK Siu Ming was elected as Registrar and Dr. LEUNG Ying Kit was elected as Deputy Registrar. Dr. CHAN Kui Fat and Dr. WONG Lap Gate, Michael were elected as Council Members. Dr. CHEONG Renee Constance Yue-Kew and Dr. LAI Koon Chi Christopher were re-elected as Council Members.



▲ **Council Members of The Hong Kong College of Pathologists 2019-2020:**

*Front row (from left to right): Dr. LUNG David Christopher, Honorary Treasurer; Dr. POON Wai Ming, Vice-President; Dr. CHAN Ho Ming, Michael, President; Dr. CHAN Chak Lam, Alexander, Vice-President; Dr. MAK Siu Ming, Registrar; Dr. LEUNG Ying Kit, Deputy Registrar.*

*Back row (from left to right): Council Members, Dr. LAM Woon Yee, Polly, Dr. LAI Koon Chi, Christopher; Dr. CHAN Kui Fat, Dr. WONG Lap Gate, Michael, Dr. LEUNG Yuk Yan, Rock, Dr. CHEONG Renee Constance Yue-Kew, Dr. LI Hiu Lui.*

*Absent with apology: Dr. CHEN Pak Lam, Sammy, Council Member*



### Conferment Ceremony

The conferment ceremony admitted 9 Fellows and 11 Members to the College. Our honourable guests included Professor Sophia CHAN, Secretary for Food and Health, Food and Health Bureau, Hong Kong Special Administrative Region (HKSAR); Professor LAU Chak Sing, President, Hong Kong Academy of Medicine; Dr. the Honorable Pierre CHAN, Legislative Councillor, HKSAR; and Dr. Doris TSE, Cluster Chief Executive, Kowloon West Cluster, Hospital Authority.



▲ Professor LAU Chak Sing, President, The Hong Kong Academy of Medicine, addressing newly admitted Fellows and Members, and the audience.



▲ Group photo of Stage Party and newly admitted Members and Fellows of The Hong Kong College of Pathologists.



# CONGRATULATIONS

## to our newly admitted Fellows!



▲ Dr. CHAN Wing Chai, Raymond



▲ Dr. CHENG Shui Ying



▲ Dr. KWONG Hoi Yi, Joyce



▲ Dr. LIU Kwan Leung



▲ Dr. NG Wai Yan



▲ Dr. LEE Wai Kwan



▲ Dr. WONG Hung Fan



▲ Dr. WONG Ching Ching, Alice



▲ Dr. WAN Judith Vonnice





▲ *Anatomical Pathologists celebrating with their newly admitted Fellows.*

▼ *Haematologists with their graduates.*



◀ *President Dr CHAN Ho Ming, with Professor Sophia Chan, Dr Doris TSE and Vice President, Dr CHAN Chak Lam Alexander.*



# The T.B. Teoh Foundation Lecture

The 28th T.B. Teoh Foundation Lecture was delivered by Prof. KWONG Yok Lam, Chui Fook-chuen Professor in Molecular Medicine, Chair of Haematology and Haematological Oncology, Department of Medicine, The University of Hong Kong. The topic of his lecture was “An amazing journey from micro to macro and back”.

In his lecture, Prof. KWONG recollected how he practised haematopathology (“micro”) in his early career and how he discovered oral arsenic trioxide in the treatment of acute promyelocytic leukaemia (APL) when he returned to the field of clinical haematology (“macro”). Throughout his career as a clinical haematologist, Prof. KWONG has devoted substantially to the treatment of various haematological malignancies (e.g. APL, extranodal NK/T cell lymphoma, Hodgkin lymphoma) and increasingly engages in molecular treatments that target pathways of tumourigenesis. It is this molecular landscape that he eventually found himself back into “micro”. Prof. KWONG also shared his interest of reading science fictions and referred to various quotations from Kazuo Ishiguro and Isaac Asimov throughout his lecture, lending a humanistic touch to his scientific discoveries and research endeavours.



▲ Professor Kwong with fellow Haematologists.

**We would like to thank our College Fellow, Dr. TSE Pui Wai Victoria, for being the Mistress of Ceremonies, and our College Secretary Ms Adrienne YUNG for her support in organising and ensuring the smooth-running of events that evening.**



◀ College Vice-President and Chairman of The Training and Examinations Committee, Dr CHAN Chak Lam Alexander, with Mistress of Ceremonies, Dr TSE Pui Wai Victoria.















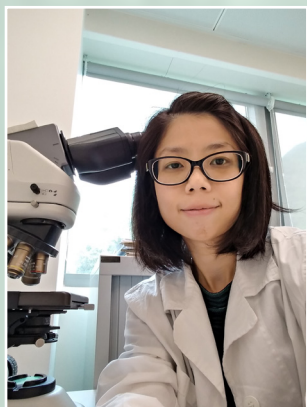


# TOPICAL UPDATE

Volume 15, Issue 1 January 2020

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**Editorial note:** Immune checkpoint inhibitors revolutionize the field of immuno-oncology. They have demonstrated great potential in a wide range of adult cancers by reaching long-lasting objective responses and prolonging survival. Through completed and on-going clinical trials, their indications continue to expand among different cancer types. However, one of their limitations is immune-related adverse events, which are most frequently reported in skin, gastrointestinal tract, and endocrine organs. Immune-related adverse events in liver are less common hepatotoxicity but still reported up to 4 to 10% of patients receiving immune checkpoint inhibitors. This Topical Update provides a concise review on the clinicopathological features of liver injury associated with immune checkpoint inhibitors. We welcome any feedback or suggestions. Please direct them to Dr. Anthony Chan (e-mail: [awh\\_chan@alumni.cuhk.net](mailto:awh_chan@alumni.cuhk.net)) of Education Committee, the Hong Kong College of Pathologists. Opinions expressed are those of the authors or named individuals, and are not necessarily those of the Hong Kong College of Pathologists.



## Liver injury associated with immune checkpoint inhibitors – An update on clinicopathological features

**Dr. Regina Lo**

*Department of Pathology & State Key Laboratory of Liver Research  
The University of Hong Kong*

### Current applications of immune checkpoint inhibitors

Immune checkpoint inhibitors [ICPI] have been introduced as a form of targeted therapy for human cancers. They exert anti-tumor effects by potentiating T cell functions via removing the inhibitory signals. Programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) are receptors located on T cells. Ligand-receptor interactions lead to inhibition of T cell activation, therefore suppressing T cell activity against tumor cells<sup>(1)</sup>. Currently, anti-PD1/PD-L1 ligand (PD-L1) and anti-CTLA-4 are the two major forms of ICPI by exploiting an antagonistic approach using specific antibodies that target PD-1 and CTLA-4, respectively. Thus far, several ICPIs were

approved by the US Food and Drug Administration for treating cancers<sup>(2)</sup>. Nivolumab and pembrolizumab are FDA approved frontline anti-PD1 agents, while ipilimumab is an anti-CTLA-4 agent. These drugs are given either alone or in combination. Currently there are a number of on-going phase III/IV clinical trials with ICPI for various types of cancers<sup>(3)</sup>.

### Clinical features of hepatotoxicity associated with ICPI

Despite the encouraging clinical efficacy, adverse reactions related to ICPI administration have been observed, among which dermatological, gastrointestinal, endocrine manifestations were most frequently reported. These reactions are believed to result from the immune response elicited toward various organs. A meta-analysis of 17 studies revealed an increased risk of all-grade hepatotoxicity with ICPI compared with controls (pooled OR 4.10; PD-1 subgroup 1.94; CTLA-4 5.01)<sup>(4)</sup>. Among all immune-related adverse reactions, hepatotoxicity was observed in a relatively small proportion of cases (up to 4-10%) in most reports<sup>(2, 5-9)</sup>. Susceptibility of adverse reactions in the liver appears to be dependent on the primary cancer, regimen/dose of ICPI, and host factors. It was reported that patients receiving ICPI for HCC were at a higher risk of hepatotoxicity in terms of transaminases levels compared with lung cancer and melanoma<sup>(10)</sup>. Moreover, combination therapy or a higher dose of ICPI was associated with increased risk of hepatic injury<sup>(6, 9, 11, 12)</sup>.



Patients may present with fever and jaundice but can also be asymptomatic <sup>(13, 14)</sup>. The median time from the first dose to immune-related hepatotoxicity was 14.1 weeks (9.4–19.7) for anti-PD-1, 9.9 weeks (6.1–14.7) for anti-CTLA4, and 2.9 weeks for combined therapy <sup>(15)</sup>. The biochemical derangement is usually of a hepatitic or mixed hepatitic/cholestatic pattern. Radiological findings most of the time do not offer additional diagnostic information. In general, hepatotoxicity associated with ICPI is classified according to Common Terminology Criteria for Adverse Events by the National Cancer Institute (CTCAE). This system comprises grades 1–5 (with grade 5 being fatal) based on the serum levels of AST, ALT, ALP, GGT and total bilirubin. Having said that, elevated bilirubin is a less frequent phenomenon than most forms of drug-induced liver injury.

### Histological features of liver injury associated with ICPI

The commonest histological features of ICPI-associated hepatotoxicity are lobular hepatitis, portal lymphoid infiltrates and variable degrees of hepatocytic necrosis <sup>(16–19)</sup>. A predominant biliary pattern has been reported but is much less frequently encountered <sup>(20, 21)</sup>. Cholestasis is not commonly seen, with bland cholestasis reported in 1 of 10 cases treated with pembrolizumab <sup>(22)</sup>. Two cases of ICPI-induced hepatitis histologically presenting with fibrin-ring granulomas have also been reported <sup>(23)</sup>. Steatosis is rare. Some histological features may be more readily observed with the use of a specific type of inhibitor. For instance, microgranulomas and central vein endotheliitis were seen in patients who received anti-CTLA4 therapy. With anti-PD1 therapy, more prominent portal tract inflammation was encountered. In contrast to autoimmune hepatitis, plasma cells are usually low in number <sup>(24)</sup>, which is line with the observation that serum IgG level is mostly normal and autoimmune serological markers are negative. Likewise, in a report comparing 7 cases of ICPI-associated hepatitis versus 10 cases of AIH and 10 cases of drug-induced liver injury (DILI) <sup>(24)</sup>, hepatocytic rosettes

and emperipolesis were less commonly observed than AIH. When compared with DILI, bile plugs and eosinophils were less readily seen in ICPI-associated hepatitis. On immunohistochemical delineation of the lymphoid cell population in ICPI-associated hepatitis, several reports have consistently demonstrated a predominance of CD8+ lymphocytes <sup>(17, 18, 22)</sup>. This could be distinguishing feature with AIH, in which CD20+ or CD4+ lymphoid cells are frequently encountered.

### Diagnostic considerations and implications

The diagnosis of ICPI-liver injury can seldom be made by histology alone as there are no pathognomonic features. Before attributing the cause to ICPI, potential etiologies for liver function derangement should be considered. In particular, exclusion of hepatic involvement by tumor and viral hepatitis is needed. According to a recent report, among 491 patients treated with pembrolizumab for melanoma, lung cancer or urothelial cancer, 70 developed liver injury. Among which, a probably drug-related cause was only made in 20 cases after adjudication <sup>(25)</sup>. Liver histology can help to exclude some differential diagnoses and assess the severity of liver tissue injury, which could be useful to guide management plan. The treatment options for adverse reactions would depend on the severity, and include withdrawal/discontinuation of ICPI, corticosteroids (oral or IV) +/- additional immunosuppressant e.g. mycophenolate mofetil <sup>(26)</sup>. The drugs are usually permanently discontinued in cases presenting with Grade 3 or Grade 4 adverse reactions. There are no standard guidelines with reference to reintroducing ICPI after recovery from Grade 1–2 adverse reactions. As far as histology is concerned, it remains an open question whether histological parameters could offer added values in the grading of ICPI-associated hepatotoxicity. Besides, further studies are awaited to better understand the histological features associated different types of ICPI, and to depict the development and progression of fibrosis in this subset of drug-induced liver injury.

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## OBITUARY: PROFESSOR WU BING QUAN (1930-2020)



It saddened me to learn of the passing of Professor Wu Bing Quan on 21 June 2020.

The first time I met Professor Wu was in 1980 in Washington, DC. We were both visiting fellows at the National Institutes of Health (NIH)—he from China and I from the University of Rochester, NY. We did not know each other. At around June of 1980, I was told by a NIH staff that there was a visiting

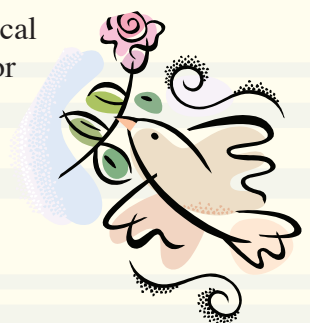
Chinese pathologist who would like to meet US pathologists. And it happened that the annual meeting of Canadian and US pathologists (as part of the IAP—the International Academy of Pathologists) was coming up in a few weeks. I took Wu to the IAP meeting in Los Angeles. We flew from Washington, DC to Los Angeles. We shared a room and went to the meetings together daily.

At the meeting he impressed me by his friendliness; he was eager to meet people and made many friends. Although the IAP programs were slanted towards pathology education and practice unfamiliar to him since he was an experimental pathologist, Professor Wu was nevertheless keen to make friends, to observe and learn. He was particularly interested in information on all new instruments and new tools and reagents. He collected much to bring home intending for future purchases.

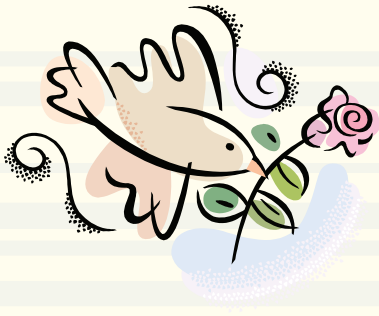
After the meeting he visited Loma Linda University Medical school in Los Angeles. I came to Hong Kong in 1981 to join The Chinese University of Hong Kong.

Professor Wu was among the first group of promising scientists in China who were sent overseas for advanced training after normalization of relation between China and the US. In the early 1980s Wu was already known among Chinese pathologists as one of the ‘Two Wus of Pathology’ in China, one in the north and one in the south. He was the northern Wu—being in Beijing, and the other, a Professor Wu at Xiang Ya Medical School, of Yale-in-China fame, at Changsha in Hunan province in the south. Both were leading scientists and highly respected pathologists in China.

In 1983 I visited Professor Wu’s department at Beijing Medical University (BMU). (The State Council had approved 10 institutions for priority development. Among them, Beijing Medical College was the only medical institution. In 2000, BMU was incorporated into Peking University and formally renamed Peking University Health Science Center.) In 1983 the facilities and equipment in the department were







rather primitive. However, there were group of young minds eager to learn (since they missed a 10-year duration of the Cultural Revolution with no teaching or research.) Wu reached out to America and he worked closely with Don King and Cecilia Fenoglio of Columbia University on cell biology and academic pathology. Wu had arranged exchange programs for his staff--a quick way to leapfrog the slow process of local training. At that time, experienced staff were few.

By now after three or four generations of development and growth, many capable pathologists are scattered all over the country. In his recent publications I note topics such as quantification of telomerase activities, telomerase in lung cancer, immunodeficient animals in experimental medicine, *Helicobacter pylori* infection and risk of gastric cancer in China.

Wu was a soft spoken and sincere person. He commanded respect from those around him, particularly the young ones who looked upon him for guidance and connections. He was hard working and I had seen him working late into the night on many occasions in his office in Beijing.

Professor Bing Quan Wu had been the right person to modernize pathology in China as the country rapidly modernizes.

Contributed by : Professor Joseph C K LEE



▲ Professor WU Bing Quan (3rd from left, and Professor Joseph C K LEE (2nd from left). Photograph of a group of Pathologists from various parts of China following a national meeting, taken c.1986.



## PRESS STATEMENT

### Use of Over-the-counter COVID-19 Test Kits

The College has noticed that a variety of over-the-counter Coronavirus Disease 2019 (COVID-19) self-test kits are being promoted in the market. We are concerned that the public could be misled by the results of these kits.

These over-the-counter test kits usually utilize pinprick blood samples to detect IgG or IgM antibodies against the SARS-CoV-2 virus. Antibodies are produced over days to weeks after infection; the level and timing of response vary among individuals. The performance of these kits, including sensitivity and specificity (i.e. respectively whether the test can accurately exclude COVID-19 infection and whether a positive result is reliable to indicate actual infection), also varies among assays. Thus the public must be aware of the risk of false negative and false positive results.

A false negative result may cause a false sense of security, which could potentially increase transmission of the virus to others and result in delay in seeking medical consultation and management. On the other hand, a false positive result will lead to undue anxiety and unnecessary investigations, and even public health measures such as isolation of the person and his or her close contacts.

The College reiterates that the current test of choice for the diagnosis of active COVID-19 infection remains polymerase chain reaction (PCR)-based tests detecting viral nucleic acids. The detection of antibodies is neither a suitable nor a reliable alternative. The College urges the public to seek advice from medical professionals if COVID-19 infection is suspected.

End / Wednesday / 29 April 2020

Issued at HKT 17:00

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### 就市面上出售的新型冠狀病毒快速測試之聲明

近日坊間出現各式各樣的新型冠狀病毒快速測試，並透過不同媒體銷售。惟快速測試結果存疑，有誤導公眾之嫌，本學院非常關注。

市面上售賣之試劑盒，一般採用針刺血液樣本來檢測SARS-CoV-2病毒的IgM或IgG抗體。抗體於感染後數天至數週方能達至可偵測的水平，抗體之濃度及產生之時間亦因人而異。市場上不同牌子之測試劑，其敏感性 (sensitivity) 和特異性 (specificity) 不盡相同，因此市民應注意有假陰性和假陽性結果之風險。

假陰性結果會令市民錯誤以為自己未有受感染，從而潛在增加將病毒傳播給他人的風險，及導致延誤最佳診治的時間。另一方面，假陽性結果則會引致不必要的焦慮，多重覆檢，甚至需要採取公共衛生措施，如本人及密切接觸者的隔離檢疫。

本學院重申，目前診斷新型冠狀病毒以聚合酶鏈反應 (PCR) 測試病毒核酸為首選。現時市場上出售之快速抗體測試並不適合及不可靠。本學院呼籲公眾如懷疑自己受感染，須及早向醫生求醫。

2020年4月 29日 (星期三) 5 時正

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《科學專輯》每月首個周二刊出，以有趣角度解構日常生活背後各種科學知識，由飲食、醫療、設計到運動等，每月來一次全面科學大解構。

# 冠狀病毒大解構 竊宿主受體入侵

2003年SARS、2012年MERS（中東呼吸綜合症），今天的COVID-19，在過去十多年，冠狀病毒一次又一次帶來嚴重、致命的傳染病。其中新型冠狀病毒肺炎（COVID-19）自去年尾在中國湖北省爆發以來，至今已蔓延超過200個國家及地區，世界衛生組織在3月11日宣布「全球大流行」（pandemic）。

為何冠狀病毒能對人類健康造成威脅？往後會否繼續有新的冠狀病毒出現？

文：李祖怡

香港大學微生物學系臨床助理教授薛達指出，目前已知有7種與人類有關的冠狀病毒，其中4種較常見，會引起輕微上呼吸道感染，包括HCoV-229E、HCoV-NL63、HCoV-OC43、HCoV-HKU1，可引起流鼻涕、喉嚨痛等徵狀；另外3種原為動物冠狀病毒，累積基因突變後入侵人體引起嚴重感染，並可「人傳人」，包括SARS、MERS、COVID-19。

## 「溫和派」與人類和平共處數百載

冠狀病毒與人類「和平」共處一段很長的時間，科學家推算，較溫和的HCoV-NL63和HCoV-229E，分別約在500至800年前和200年前出現。為何新品種的冠狀病毒如此兇猛？香港中文大學醫學院微生物學系臨床助理教授、香港病理學專科學院委員賴貫之估計，現時常見的人類冠狀病毒，可能在幾百年前曾經大流行，引致嚴重疾病，只是當時未有診斷，而病毒亦慢慢變成現在與人類共存。

## 侵入人體4部曲

### 1. S-蛋白王冠竊出禍

一粒小小的冠狀病毒，究竟如何攻擊人體？答案在S-蛋白。賴貫之指出，在電子顯微鏡下，S-蛋白呈王冠模樣，「冠狀病毒」因而得名。S-蛋白會「竊住」宿主細胞受體，從而入侵人體。

### 2. 對應受體不同

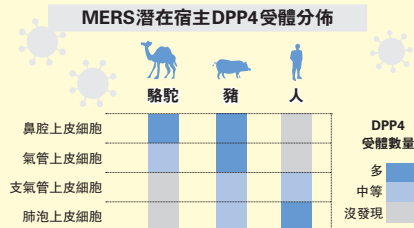
每種冠狀病毒對應的受體都不盡相同，例如SARS及COVID-19，宿主受體為ACE2（血管緊張素轉化酶2/angiotensin-converting enzyme 2），MERS的受體是DPP4（二肽基肽酶4/dipeptidyl peptidase 4）。

### 3. 藉相應受體入侵

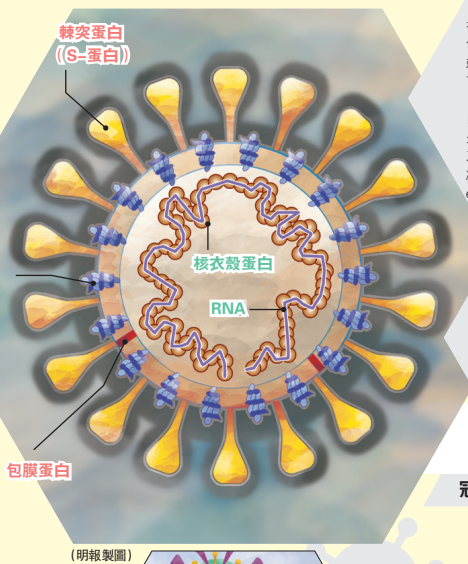
賴貫之將S-蛋白和受體比喻成八達通和八達通機，「有八達通都要有八達通機，才可上車！想搭的士用八達通，但原來沒有八達通機，司機會請你下車」。病毒要透過相應受體，才能進入人類或動物細胞。

### 4. 受體分佈影響病徵

以MERS為例，人類、蝙蝠、駱駝、豬和兔子都是MERS的潛在宿主，因為病毒的S-蛋白能識別及侵入宿主體內的DPP4；其中駱駝的DPP4主要分佈於鼻腺上皮細胞，人類的DPP4則集中在肺細胞（pneumocyte），因此人類感染MERS後，大多引起肺炎，少有上呼吸道感染。至於新型冠狀病毒，ACE2受體亦多見於下呼吸道。



（明報製圖）



（明報製圖）

## 外層：

有一層包膜（envelope），包膜表面有3種結構蛋白：棘突蛋白（spike protein，下稱S-蛋白）、包膜蛋白（envelope protein）、膜蛋白（membrane protein）。少數冠狀病毒如HCoV-OC43及HCoV-HKU1，還含有血凝素酯酶（Hemagglutinin esterase）。

## 內層：

含有RNA及核衣殼蛋白（nucleocapsid protein）。冠狀病毒屬於正單鏈RNA病毒（positive-sense single-stranded RNA virus），比起DNA病毒更容易變異。

## 新型冠狀病毒

▲電子顯微鏡下，新型冠狀病毒外層有一層包膜（envelope），由磷脂（phospholipids）和蛋白質組成。（賴貫之提供）

## 冠狀病毒有幾細？

✱——冠狀病毒  
直徑80至160納米

流感病毒——  
直徑88至200納米

紅血球  
直徑10000納米

大腸桿菌  
300納米（闊）×1000納米（長）

## SARS、MERS、COVID-19比較

| 傳染病    | 嚴重急性呼吸綜合症 (SARS)           | 中東呼吸綜合症 (MERS)                  | 新型冠狀病毒肺炎 (COVID-19) |
|--------|----------------------------|---------------------------------|---------------------|
| 微狀     | 發燒、發冷、顫抖、肌肉痛、疲倦、乾咳、頭痛、呼吸困難 | 發燒、咳嗽、呼吸急促、腸胃道微狀；20%感染者無微狀或輕微微狀 | 發燒、發冷、咳嗽、呼吸急促、消化道微狀 |
| 潛伏期    | 可長達10天                     | 2至14天                           | 3至7天，可長達14天         |
| 病例     | 8098                       | 2519                            | 1,136,862*          |
| 死亡人數   | 774人 (9.6%)                | 886人 (35%)                      | 63,025人 (未知)*       |
| 宿主     | 果子狸                        | 駱駝                              | ? 未知                |
| 人傳人傳播力 | 有效率                        | 有限度而斷續                          | 很有效                 |

\*世界衛生組織截至今年4月6日數據

資料提供：香港中文大學醫學院微生物學系臨床助理教授賴貫之、世界衛生組織

## 知多啲

## 愈多人感染 新冠消失機率愈小

由SARS、MERS，到今天的COVID-19，接連帶來致命威脅。同樣是來自動物傳人的冠狀病毒，為何SARS會消失，而COVID-19卻大規模傳播？

### 病徵輕微反致廣傳

「如果你是一隻病毒，想在人類之中繼續生存的話，你應該要怎樣做呢？在傳聞之前，你已經殺掉宿主的話，這樣已經失敗了！」賴貫之認為，SARS「失敗」，在於其病徵比較嚴重，而且在有微病徵的時候才具傳染力；新型冠狀病毒的「成功」，反而是因為沒那麼

致命，加上在病徵輕微甚至沒有病徵的情況下，感染者可將病毒傳染給別人而不自知。薛達補充，SARS之所以能夠「消失」，原因是成功堵截病毒源頭，而且病徵較明顯，可及早發現和隔離患者。另外，天氣回暖亦是SARS銷聲匿迹的其中一個因素。理論上，冠狀病毒在溫度高的環境下，傳染力減弱。有人認為夏天來臨時，新冠疫情可望結束。然而，「當愈來愈多人感染，病毒完全消失的機率愈小」。對於是次疫情在夏天完結並不樂觀，加上當北半球夏天開始時，位於南半球的澳洲、南美洲地區則是冬天，疫情可能

在當地爆發。

### 動物家園招惹果

即使捱過COVID-19一疫，賴貫之和薛達均認為，未來還會繼續出現新的冠狀病毒。人口密集、全球暖化、森林開伐，令人與動物之間隔離縮短，新病毒出現的機率因而增加。蝙蝠原本居住的地方被人類砍伐，因而遷往其他地方，並感染新的宿主。氣候變化令到生態改變，新的宿主和新的病毒就會相遇，又有可能出現大爆發。

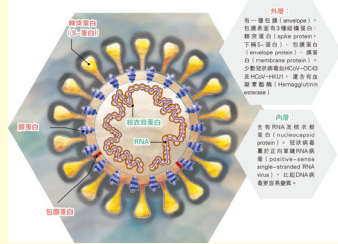


### 砍伐森林

專家認為，砍伐森林令人與動物之間隔離縮短，新病毒出現的機率因而增加。（資料圖片）



## 冠狀病毒大解構 竊宿主受體入侵



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為何冠狀病毒接連對人類健康造成威脅？往後會否繼續有新的冠狀病毒出現？

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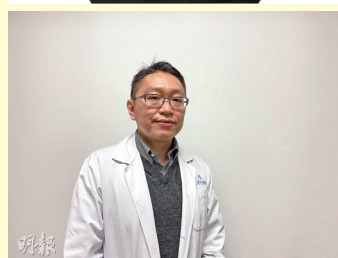
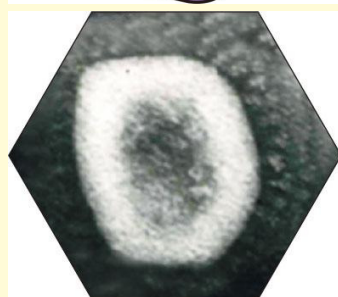
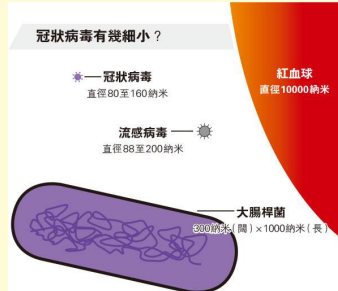
### ■專家意見

◆賴貫之（香港中文大學醫學院微生物學系臨牀助理教授、香港病理學專科學院委員）

◆薛達（Siddharth Sridhar）（香港大學微生物學系臨牀助理教授）

| SARS · MERS · COVID-19比較 |                      |                       |                      |
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\*世界衛生組織截至今年4月4日數據。資料來源：香港中文大學醫學院微生物學系臨牌助理教授賴貫之、香港大學微生物學系臨牌助理教授薛達。



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## ERRATUM

*On pages 8 and 9 of the last issue of Pathologue (Volume 28 issue 2, January 2020), the caption of the two photographs showing the 'Examiners for Anatomical Pathology (Membership and Fellowship Vivas) 2019', should include Professor John NICHOLLS and not Dr Robert COLLINS as previously published. We sincerely apologise to Professor NICHOLLS and Dr COLLINS for the error.*