NEWSLETTER OF THE HONG KONG COLLEGE OF PATHOLOGISTS

The Hong Kong College of Pathologists, Incorporated in Hong Kong with Limited Liability

Message from the President

We are honoured to stand on the shoulders of giants so that we can continue to enhance the development of pathology based on the achievements of our senior Fellows and colleagues. In this newsletter, tributes are paid to two distinguished pathologists who have contributed tremendously to the development of pathology in Hong Kong. Professor Sir Roddy MACSWEEN and Professor Li Chong CHAN left us in the winter of 2015. This is a personal loss to me, as I have been fortunate enough to have worked with and learnt from them for decades. To express our appreciation and grieve, Professor Faith HO and Professor John NICHOLLS, with the help of Fellows, colleagues and friends, have contributed two articles to pay tributes to these two giants in the field of pathology.

Indeed, pathology is facing significant challenges, from manpower shortage to technological advancement and raised expectations from community. Our College will continue to safeguard the standard of our profession and quality of service to our patients. To achieve this, our College will enhance representation in various local task forces and committees so that our views can be heard. A Task Force on Training for Genetics and Genomics, led by TEC Chairman Dr Michael CHAN, with membership including Chief Examiners and Specialty Board Chairmen, is finalizing the preparation for establishing the post-specialty Fellowship in Genetic and Genomic Pathology.

Introduction of pathology to the general public continues to be enhanced through the International Pathology Day. Last year, we have focused on high school students and a two days' workshop was conducted with great success. I must thank Dr Michael WONG and the team of young pathologists who made such success possible.

We continue our collaboration with the Hong Kong Academy of Medicine and our sister Colleges. Internationally, I participated in the International Liaison of Pathology Presidents (ILPP) meeting in Melbourne so that knowledge and views can be shared with international pathology professionals.

In 2016, the quinquennial (five-yearly) inspection of laboratories for training of the various specialties will be conducted. This is an enormous exercise that demands joint effort of the large number of inspectors involved. I would like to thank in advance the great contribution from all the Educational Supervisors, inspectors and particularly the Convenors for this inspection exercise.

Professor CHEUNG Nga Yin, Annie May 2016







Dr LAI Sai Chak (Chief Editor) Dr CHAN Chak Lam, Alexander Dr LO Cheuk Lam, Regina Dr LO Yee Chi, Janice Dr TANG Wai Lun Dr WU Cherry

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President's activities



Conferment Ceremony of The Hong Kong College of Emergency Medicine.

Fund raising dinner for The Hong Kong Museum of Medical Sciences.







▲ ▼ Group Photos at the ILPP 2016 in Melbourne.



International Pathology Day at Hong Kong 2015 Group Photo.





International Pathology Day at Hong Kong 2015 with student participants.

The 24th Annual General Meeting

The 24th Annual General Meeting (AGM) was held after the 11th Trainee Presentation Session on 28 November 2015. Eight Councillors were elected in AGM 2015. All of them were in previous Council 2014/2015, of which three were elected to a new post in AGM 2015 as follows. Dr TANG Wai Lun was elected as Registrar, succeeding Dr CHAN Chak Lam, Alexander, who was elected as Council Member. Dr MAK Siu Ming was elected as Deputy Registrar to fill the vacancy left behind by Dr TANG Wai Lun.



Annual General Meeting. From left to right: Dr Michael Chan, Dr Michael Wong, Prof. Annie Cheung, Dr Alexander Chan, Dr Bobby Shum.

Council 2015/16, The Hong Kong College of Pathologists.





Prof. Annie Cheung presenting certificate to newly admitted Member of the College.

In the Conferment Ceremony, II Fellows and 9 Members were admitted to the College. The honourable guests included Prof. William WEI (Honorary Treasurer of the Hong Kong Academy of Medicine), Dr KO Wing Man (Secretary for Food & Health of the Food & Health Bureau of the Hong Kong Special Administrative Region Government) and Dr Derrick AU (Director (Quality & Safety) of the Hospital Authority). College President Prof. Annie CHEUNG shared with the audience her work during her tenure as the President of the College.



- Prof. William Wei delivers a speech at the Conferment Ceremony.
- A photo of the Stage Party at the Conferment Ceremony and new Fellows.



The 24th T.B. Teoh Foundation Lecture was delivered by Dr CHAN Yuk Tat, Eric, Consultant Pathologist (Immunology), Department of Pathology and Clinical Biochemistry, Queen Mary Hospital. In the lecture titled "The Allergy Epidemic", Dr Chan enlightened the audience on the various aspects of allergy. Guests and members of the College enjoyed the subsequent Chinese banquet dinner.

We would like to thank Dr Regina LO for being the Mistress of Ceremonies in the AGM. We thank Ms NG Tsz Kwan, Ms LIU Cheuk Lam and Ms CHONG Lai Shan for taking photos during the Trainee Presentation Session, AGM, Conferment Ceremony, T.B.Teoh Foundation Lecture and the dinner. We would also like to express our gratitude towards our College Secretary, Ms Adrienne YUNG, as well as Ms Maizie CHAN and Ms Heidi CHU, for their continuous support in organizing the AGM.

Looking forward to seeing you all in the coming AGM.



- Dr Eric Chan receives a souvenir from the President.
 - Nice reunion time at the Chinese banquet dinner.

Upcoming event The 25th AGM will be held on 26 November 2016.

Mark your diaries!

The 11th Trainee Presentation Session

The LIth Trainee Presentation Session was successfully held in the afternoon on 28 November 2015. Four fellows in different disciplines from different institutions were invited to be judges: Prof. Rossa CHIU (Chemical Pathology, Prince of Wales Hospital), Dr William CHOI (Haematology, United Christian Hospital), Dr Mamie HUI (Clinical Microbiology & Infection, Prince of Wales Hospital) and Dr Philip IP (Anatomical Pathology, Queen Mary Hospital).



Dr Siddharth Sridhar receives the prize from Dr Anthony Chan of the Education Committee.

The Trainee Presentation Session provides a good opportunity for our trainees to undertake research study and sharpen presentation skills. The number of participants continuously broke our previous records. A total of 17 trainees across different subspecialties participated in the Trainee Presentation Session this year. Due to the overwhelming response of participation in recent years, the poster presentation has been introduced since 2014. Both oral and poster presentations are recognized education activities that fulfil the training requirement of our College. All participants of oral and poster presentations received a certificate of participation but the best presentation was selected from the oral presentations only. In order to provide a chance of practising presentation (4 minutes without question & answer sessions) was first introduced this year, in addition to preparing a poster. Among the 17 participating trainees, 10 made oral presentations, and 7 prepared posters. Herein, I would like to congratulate all participants for their nice works and excellent presentation, and on behalf of the Education Committee, express grateful appreciation to the invited judges and helpers assisting the Trainee Presentation Session.

Dr Anthony Chan Vice-Chairman, Education Committee



Judges and participants of the 11th Trainee Presentation Session.

The best presentation of the Trainee Presentation Session this year was awarded to Dr Siddharth SRIDHAR (Clinical Microbiology & Infection, Queen Mary Hospital). The abstract of the study was:

Discovery of a novel psittacine adenovirus during an outbreak of psittacosis: human zoonotic infection associated with virusbacterium coinfection in birds

Chlamydophila psittaci is a common pathogen among psittacine birds in tropical and subtropical regions that can be transmitted to humans as a zoonosis. While investigating a human psittacosis outbreak that was associated with avian chlamydiosis in Hong Kong, a novel adenovirus was identified in epidemiologically linked Mealy Parrots, which was not present in healthy birds unrelated to the outbreak or in other animals. The novel adenovirus (tentatively named Psittacine adenovirus HKU1) was most closely related to Duck adenovirus A in the Atadenovirus genus. The C. psittaci bacterial load in the lungs of epidemiologically linked parrots correlated positively with adenovirus viral load in the birds' lungs. Immunostaining for fibre protein expression was positive in lung and liver tissue cells of affected parrots, confirming active viral replication as opposed to a carrier or latent state. No other viruses were found. This is the first documentation of an adenovirus-C. psittaci co-infection in an avian species that was associated with a human outbreak of psittacosis. Viral-bacterial co-infection in animals leading to animal-to-human transmission of zoonotic agents has not received sufficient attention and should be emphasized in the investigation of disease outbreaks in human and animals.

International Pathology Day Workshop 2015

International Pathology Day Workshop 2015 was held at University Pathology Building of Queen Mary Hospital from 21 – 22 November 2015. This workshop was open to the public and attracted nearly 200 students to join. The students enjoyed performing pathology tests under the guidance of pathologists and medical student volunteers. Professor Sophia CHAN JP, Under Secretary for Food and Health, was the officiating guest. Dr Michael WONG, our PGAC Chairman, Dr Calvin CHONG, Dr Candy NG, Ms Carmen POON, Dr Billy PANG, Dr Elison KAM, Dr Kristine LUK, Dr Regina LO and Dr Rosalina IP helped in the preparation of the workshop.



Students having fun while learning pathology at the same time.

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THE HONG KONG COLLEGE OF PATHOLOGISTS:



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The Hong Kong College of Pathologists, Incorporated in Hong Kong with Limited Liability **Editorial note:** With increasing international travel, awareness and knowledge on the microbiology aspects of the returning traveller is essential, in order for timely diagnosis of infectious diseases acquired abroad and for administration of effective clinical management and public health control measures. In this issue of the Topical Update, Dr Samson Wong presents a synopsis of the conditions associated with the returned traveller, which will be of practical application to any medical professional. We welcome any feedback or suggestion. Please direct them to Dr Janice Lo (e-mail: janicelo@dh.gov.hk), 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.

The Sick Returned Traveller

Dr Samson SY WONG Assistant Professor, Department of Microbiology, The University of Hong Kong Queen Mary Hospital, Hong Kong



Introduction

The number of international travellers has been increasing over the past 20 years. In 1995, there were 530 million international arrivals; this figure increased to 1,138 million in 2014^[1]. This rising trend has only been punctuated in 2003 and 2009, coinciding with two infectious disease epidemics, SARS and pandemic influenza, respectively. With the unprecedented volume, speed, and reach of international travel comes an increasing number of patients who developed travel-related health issues. About 15-64% international travellers may develop health problems during their travel [2-5]. The risk depends on the duration of travel, destination, behaviour of the travellers, and the use of prophylactic measures. In most studies, gastrointestinal (usually in the form of travellers' diarrhoea) and respiratory illnesses are the commonest complaints, followed by skin problems, fever, and other conditions such as altitude sickness, envenoming, accidents and injuries. In this article, we shall focus on the concerns and precautions in the laboratory diagnosis of some important infections in the returned travellers.

With the unprecedented volume, speed, and reach of international travel comes an increasing number of patients who developed travel-related health issues.

Spectrum of infections and approach to the sick returned traveller

The spectrum of travel-related infections is diverse. A large body of information is available from individual centres and from GeoSentinel which consists of 63 travel clinics in 29 countries on 6 continents (http://wwwnc.cdc.gov/travel/ page/geosentinel. Accessed on 2 December 2015). However, similar data are lacking in Hong Kong, and one should note that the prevalence of different infections in the literature may not be applicable locally because of differences in the adoption of prophylactic measures and habits of travel. Data from the more recent GeoSentinel surveillance are consistent with earlier studies in that the commonest illnesses in returned travellers affected the gastrointestinal tract, respiratory system, skin, or presented as fever or systemic illnesses (Table 1)^[6-9]. Fever is a common manifestation in such patients, which may occur as an undifferentiated febrile illness or be associated with specific symptoms such as rash, arthritis/arthralgia, or other localizing symptoms. The presence of localizing signs and symptoms helps to narrow the differential diagnoses. Most studies in the literature described malaria as one of the commonest causes of fever, followed by dengue in the more recent series (Table 2). Although malaria is certainly a diagnosis not to be missed, it is not the commonest aetiology of fever in returned travellers in Hong Kong. For example, in 2014, 23 cases of malaria and 112 cases of dengue were notified to the Department of Health ^[10]. Given that both diseases are

primarily imported from endemic countries, dengue would be commoner as a cause of fever in the travellers in Hong Kong.

The clinical approach should always begin with a thorough history including a detailed itinerary (with stopovers), potential exposure history, and prophylactic measures. Despite the long list of differential diagnoses to each clinical syndrome, the most likely causes can often be suggested by the geographical areas visited, the likely incubation period of the disease, and the relevant exposure history. Some important infections associated with specific exposures are listed in Table 3. Subsequent choice of organ imaging and laboratory investigations is guided by the most likely diagnosis. It is important that after the initial assessment, one must not miss conditions that are clinically severe and potentially treatable, as well as those that have a high risk of hospital or community transmission. Severe infections must be investigated and treated urgently, such as sepsis, severe malaria, haemorrhagic fevers, and central nervous system infections. Examples of diseases that require prompt infection control precautions include viral haemorrhagic fevers, Middle East respiratory syndrome (MERS), avian influenza and infections caused by other novel influenza viruses.

The clinical approach should always begin with a thorough history including a detailed itinerary (with stopovers), potential exposure history, and prophylactic measures.

Important clinical syndromes and laboratory investigations

Malaria

Malaria must always be considered as a potential cause of fever occurring in anyone who develops fever seven days after travelling to an endemic area ^[11]. Missing a case of malaria, especially falciparum malaria, can lead to serious and often fatal outcomes which in turn, may lead to medicolegal litigations. There are no pathognomonic clinical signs and symptoms of malaria. Patients are sometimes erroneously diagnosed to have influenza or gastroenteritis initially because of the non-specific clinical symptoms ^[12–15]. The textbook description of periodic fever is only present in 8–23% of malaria patients ^[12, 13]. Appropriate laboratory testing must be performed in any patient with a compatible travel history.

The diagnosis of malaria is conventionally made by examination of the thin and thick blood films. The four species of human Plasmodium, P. vivax, P. ovale, P. malariae, and P. falciparum are distinguished morphologically. In the past decade, the simian malaria P. knowlesi has emerged as an important cause of human malaria in some Southeast Asian foci, especially in Malaysian Borneo. P. knowlesi infection of travellers has been well reported. The difficulty with P. knowlesi is that its morphology closely resembles other human plasmodia, especially P. malariae. Definitive speciation can generally be made using molecular techniques ^[16]. Quantification of the level of parasitaemia is essential for falciparum malaria both upon initial diagnosis and serial examination of the blood smear because the level of parasitaemia carries prognostic

Country	USA [6]	USA [7]	Canada [8]	Global centres [9]
Years	1997-2011	2000-2012	2009-2011	2007–2011
Number of travellers studied	10,032	9,624	4,365	42,173
Systems involved				
Gastrointestinal tract	45%	58.4%	43.7%	34.0%
Respiratory system	8%	10.8%	5.4%	10.9%
Skin	12%	16.6%	14.7%	19.5%
Fever or systemic illness	14%	18.2%	10.8%	23.3%
Neurological system				1.7%
Genito-urinary tract and				2.9%
gynaecological system,				
sexually-transmitted infections				

Table 1: Illnesses in returned international travellers from GeoSentinel surveillance.

Country	USA [6]	USA [7]	Canada [8]	Global centres [9]
Years	1997-2011	2000-2012	2009-2011	2007-2011
Number of patients presenting with fever or systemic illness	1802	1748	675	9817
Diagnoses				
Malaria	19.4%	27.4%	11.9%	28.7%
Dengue	11.1%	12%	7.1%	15.0%
Chikungunya			0.9%	1.7%
Enteric fever		6.1%	4.1%	4.8%
Respiratory tract infections			6.7%	
Active tuberculosis			7%	
Urinary tract infection			1.5%	
Rickettsioses		4.7%	0.7%	3.0%
Leptospirosis				0.8%
Brucellosis			0.9%	0.3%
Hepatitis A and E				1.7%
Acute HIV infection			0.9%	
Viral syndrome	17.1%	18.5%		
Unspecified febrile illness	8.2%			
Epstein-Barr virus	4.4%	8.7%		
infection and infectious				
mononucleosis-like syndrome				

Table 2: Causes of fever in returned international travellers from GeoSentinel surveillance.

significance and failure to reduce the level of parasitaemia after antimalarial treatment could signify drug resistance.

Any positive blood smear results must be conveyed to the attending clinician immediately. This is especially critical for P. falciparum which is a medical emergency in the nonimmune travellers. It is important to remember that one single negative blood smear cannot exclude malaria. It is generally recommended that in patients with a negative blood smear but with a high clinical suspicion for malaria, at least three blood smears must be repeated over 48 hours to exclude the diagnosis^[17–19]. Alternatives to microscopic diagnosis of malaria include antigen detection and nucleic acid amplification tests (NAAT) from peripheral blood. Immunochromatographic antigen detection kits are widely accepted as a form of rapid diagnostic test [20]. These are particularly useful as a form of point-of-care testing and in situations where experienced microscopists are not available. The major drawbacks include the limited sensitivity in patients with low level parasitaemia and their inability to differentiate all four species of human plasmodia. Speciation is clinically essential because P. vivax and P. ovale infections require radical cure with primaquine. NAAT is currently the most sensitive method for detection of bloodborne parasites and mixed infections, and also allows definitive speciation in problematic cases, including P. knowlesi infection ^[21]. Availability is, however, currently limited to a few centres and the turnaround time is often too long for routine diagnostic purposes.

Arboviruses

The arthropod-borne viruses are fast becoming some of the most important causes of emerging and re-emerging infectious disease outbreaks in tropical and subtropical countries. This is contributed by the global climate and environmental changes, as well as the geographic spread of the vectors, especially mosquitoes. There is a long list of arboviruses, many of which belong to the families of Togaviridae (mosquito-borne; e.g. Chikungunya, Ross River; Eastern, Western, and Venezuelan equine encephalitis viruses), Flaviviridae (e.g. mosquito-borne dengue, yellow fever, Japanese encephalitis, Zika, Murray

Exposure	Potential infective complications
Sex, blood, body fluids, surgical operations, intravenous drug use	Hepatitis B and C, HIV infection, syphilis
Tattoos, body piercing, other body modification procedures	Hepatitis B and C, HIV infection, syphilis, non-tuberculous mycobacterial infections
Hospitalization	Antibiotic-resistant bacteria (colonization or infection)
Ingestion of raw or	Various foodborne infections including bacterial and viral
undercooked food	gastroenteritis, protozoal and helminth infections, brucellosis, listeriosis, toxoplasmosis, hepatitis A and E
Soil	Histoplasmosis, coccidioidomycoses, other endemic
	mycoses, cutaneous larva migrans, strongyloidiasis
Freshwater	Schistosomiasis (Katayama fever), leptospirosis
Arthropod bites	Various arthropod-borne infections, such as dengue, chikungunya, Zika virus infection, rickettsioses, relapsing fevers, malaria, babesiosis, leishmaniasis, trypanosomiasis, dirofilariasis
Dog, bat and other animal bites	Rabies, bat rabies, herpes B virus infection, bite wound infections
Animals and animal products	Hantaviruses, Lassa fever, Crimean-Congo haemorrhagic fevers, avian influenza, MERS, plague, rat-bite fevers, leptospirosis, Q fever, brucellosis, tularaemia, anthrax, psittacosis.

Note that the exact risk of specific infections depends not only on the exposure history, but the geographical location of exposures.

Table 3: Exposure history that should raise suspicion to specific infections.

Valley encephalitis viruses; tick-borne encephalitis virus), and Bunyaviridae (e.g. mosquito-borne Rift Valley fever virus; tickborne Crimean-Congo haemorrhagic fever virus; sandflyborne Toscana and sandfly fever viruses)^[22].

The global incidence and geographical extent of dengue have been growing over the past five decades with regular outbreaks in different parts of the world ^[23]. The most recent outbreak is the ongoing epidemic (at the time of writing) in Taiwan, with 39,350 indigenous cases in 2015 (as of I December 2015) ^[24]. This is also the commonest notifiable arbovirus infection in Hong Kong with occasional local transmissions. Dengue is a relatively common cause of fever in returned travellers, causing 2–16.5% of the cases ^[25]. The disease is traditionally classified into uncomplicated dengue fever, dengue haemorrhagic fever, and dengue shock syndrome. The last two entities are usually associated with

secondary infections due to serotypes of the virus that are different from the one causing the first episode of infection. Since 2009, the World Health Organization re-classified the disease into dengue fever and severe dengue, the latter being characterized by severe plasma leakage, bleeding, and organ impairment^[23].

Chikungunya is another arbovirus infection that has gained much attention in the past decade since an outbreak started in Kenya in 2004, with subsequent spread to the Indian Ocean islands till 2006, and infected over one third of the population in La Réunion^[26]. Outbreaks of this togavirus have been repeatedly reported in recent years, affecting countries in Asia, Africa, the Pacific islands, Central and South Americas. Likewise, infections due to Zika virus received little attention until it caused large outbreaks in the Yap State of Federated States of Micronesia in 2007 and the French Polynesia in 2013 ^[27]. Zika virus is endemic in various countries in Africa, Asia, Oceania, the Pacific islands, and since 2014, in Latin and South America (especially Brazil, but also Chile, Colombia, Suriname, Jamaica, and Dominican Republic)^[27, 28].

Given the large number of arboviruses, the choice of diagnostic tests should be guided by the geographical area(s) of travel and clinical syndrome. Arbovirus infections commonly manifest as systemic febrile illnesses with or without rash, arthralgia or arthritis, encephalitis or meningoencephalitis, or viral haemorrhagic fever (Table 4)^[22,29]. Many of the viruses are geographically restricted. Requests for investigations against specific viruses should be guided by the travel history and clinical manifestations. Viral culture can be performed for some viruses, but this is generally not the test of choice in most circumstances. Viral serology, preferably with paired sera for antibody testing, is one of the options of investigation, though the availability of serological tests for rarer infections is limited. Antibody testing is readily available for arboviruses such as dengue, Japanese encephalitis, and chikungunya. It should be remembered that antibody testing may be negative in the very early stage of disease, and a second serum should always be obtained. The paired antibody profile in dengue patients can also help to differentiate primary from secondary infections. Another drawback in viral antibody testing is the potential cross reactivity between different viruses, which is common among flaviviruses for example. In terms of dengue diagnostics, detection of the viral NSI antigen in serum is superior to IgM antibody detection in the first two to three days after disease onset, a window period where IgM is often negative ^[30] A combined NSI antigenaemia and IgM antibody testing is currently a common approach to initial diagnosis of dengue. The use of NSI lateral flow assay kits may even allow pointof-care testing for dengue, and if the roles of urine and saliva NSI are substantiated by further studies, this will facilitate the diagnosis of dengue in resource-limited settings^[31, 32]. NAAT is another option for early diagnosis of dengue which also permits detection of co-infection by different serotypes (and with other arboviruses) and genotyping of the infecting viral strains^[33-35]. Antibody detection (IgM and IgG) and NAAT can also be used for the diagnosis of chikungunya and Japanese encephalitis. Consultation with clinical virologists should be made in order to choose the most appropriate tests, especially when unusual viral agents are suspected.

Enteric syndromes

Important enteric infections encountered in returned travellers include travellers' diarrhoea, enteric fever, and amoebiasis. Travellers' diarrhoea is the commonest travelrelated infection, affecting 10–40% of individuals travelling from developed to developing countries ^[36]. It is most often a bacterial infection caused by various diarrhoeagenic Escherichia coli (especially enterotoxigenic strains) and other enteorpathogens such as Campylobacter, Salmonella, and Shigella. Other pathogens include viruses (especially Norovirus, classically associated with passenger ships) and parasites (such as Cryptosporidium, Giardia, Cyclospora) as well as mixed infections. Most cases of travellers' diarrhoea are self-limiting. Specific microbiological investigations may not be necessary in milder cases, but should be considered in those with more severe manifestations (such as fever, dysentery, bloody diarrhoea, cholera-like symptoms), persistent symptoms, or in immunocompromised individuals [36]. Specific requests for viral agents (antigen detection or NAAT for Rotavirus, NAAT for Norovirus) or special concentration and staining for protozoa (e.g. modified acid-fast staining for Cryptosporidium, Cyclospora, and Cystoisospora) are necessary if routine bacterial cultures are unremarkable.

Enteric fever in Hong Kong can be indigenous or imported. This is most commonly due to typhoid and paratyphoid fevers, caused by Salmonella enterica Typhi and Paratyphi (A, B, C) respectively. Laboratory diagnosis of typhoid and paratyphoid fevers remains problematic. A positive culture from blood or other specimens (stool, urine, bone marrow) provides the definitive diagnosis, though this is not always possible due to the kinetics of bacterial shedding and circulation at different sites or prior antibiotic usage, and that bone marrow culture (the most sensitive type of specimen) is not routinely performed in this setting. Serological testing has been an important adjunct to diagnosis. Unfortunately, the widely available Widal's test is neither sensitive nor specific for this purpose, especially when only a single serum is tested. Newer serological assays such TUBEX TFTM (IDL Biotech, Sweden) and TyphidotTM (Reszon Diagnostics, Malaysia) have improvements over the Widal's test, but their performance in the field has not been encouraging [37, 38]. Perhaps more promising in the future is the detection of Salmonella Typhi and Paratyphi in peripheral blood by NAAT^[39]. This approach has the additional benefit of detecting other circulating pathogens as a panel (e.g. using multiplex PCR) for systemic febrile illnesses in travellers, such as Plasmodium, Babesia, Rickettsia, Orientia, and other pathogenic bacteria and viruses^[40].

Entamoeba histolytica infection most often manifests as amoebic colitis; extraintestinal amoebiasis is less frequently seen and the usual presentation is amoebic liver abscess. Intestinal infection is mainly diagnosed by faecal microscopy. As in the case of other enteric parasites, multiple stool samples (usually at least three) should be examined. E. histolytica is morphologically identical to at least three other species of Entamoeba, viz. E. dispar, E. moshkovskii, and E. bangladeshi. Definitive identification is best achieved by molecular methods. Antigen detection assays are viable alternatives for

Common clinical syndromes	Common causative agents
Systemic febrile illness ± rash	Dengue virus, West Nile virus, Yellow fever virus, Zika virus, chikungunya virus
Arthralgia, arthritis ± rash	Chikungunya virus, Ross River virus, Barmah Forest virus, dengue virus, West Nile virus, O'nyong'nyong virus
Encephalitis or	Japanese encephalitis virus, Murray Valley encephalitis virus, St. Louis
meningoencephalitis	encephalitis virus, West Nile virus, tick-borne encephalitis virus, California encephalitis virus, La Crosse virus, Rift Valley fever virus, Toscana virus, Eastern equine encephalitis virus, Venezuelan equine encephalitis virus, Western equine encephalitis virus
Viral haemorrhagic fevers	Crimean-Congo haemorrhagic fever, Rift Valley fever virus, yellow fever virus, dengue virus, Kyasanur Forest disease virus, Omsk haemorrhagic fever, severe fever with thrombocytopenia syndrome virus

Note that the clinical syndromes and severity of disease caused by any single arbovirus can vary substantially. For example, many infections can either be subclinical or manifest as undifferentiated fever or produce a fulminant disease, such as viral haemorrhagic fever or meningoencephalitis. The likelihood of various potential pathogens depends on the exact geographical areas involved.

Table 4: Some common arboviruses and their typical clinical syndromes.

the detection E. histolytica in stool ^[41]. Some of these kits can concurrently detect other enteric protozoa such as Giardia intestinalis and Cryptosporidium. Not all of the antigen detection assays, however, are able to differentiate E. histolytica and E. dispar. Microscopy is less useful in amoebic liver abscesses; amoebae are seen in only 20% or less of liver aspirates ^[42]. Stool samples of patients with amoebic liver abscesses have positive microscopy for E. histolytica in only 8–44% of the cases ^[42]. Antibody testing is helpful in the diagnosis of amoebic liver abscess; a positive serology is present in over 95% of the patients ^[41–43]. The major drawback of serology is that it cannot differentiate active from past infections with E. histolytica, and hence it is less useful for populations in endemic areas.

Other issues

Space does not permit further discussion on other travel-related infections. Two more recent issues may require attention from clinical and laboratory colleagues. Firstly, the transmission of epidemic-prone infectious diseases through travel, and in particular, air travel, has caused much concern in the past few years. Examples include avian influenza and other novel influenza viruses, MERS-CoV (and the SARS-CoV in 2003), Ebola virus and other agents of viral haemorrhagic fevers. Although these are relatively uncommon causes of infection in returned travellers (with the exception of pandemic influenza in 2009), transnational spread of these infections remains a constant threat to non-endemic countries and contingency plans for surveillance, screening, clinical management, infection control, and laboratory diagnostics must be formulated in anticipation^[44].

Secondly, the importation of antibiotic-resistant bacteria from travellers has emerged as another menace [45-47]. The main microbes of concern include extendedspectrum beta-lactamase and carbapenemase-producing multidrug-resistant Acinetobacter Enterobacteriaceae, baumannii and Pseudomonas aeruginosa, methicillin-resistant Staphylococcus aureus, and vancomycin-resistant enterococci. These may be causing active infections or merely colonizing the travellers. Areas with the highest risks are the Indian subcontinent, Southeast Asia, and Africa [48-51]. Encounters with hospitals or medical facilities abroad could be due to medical problems that appeared during travel or being part of an increasingly popular medical tourism. Admission screening for multidrug-resistant organisms should be considered for patients with recent hospitalization in overseas facilities.

And not just for the microbiologists

Although the majority of tests for infective complications among the returned travellers are performed by the clinical microbiology laboratory, other specialties of clinical pathology may sometimes be involved in the investigation. The commonest scenario is the examination of peripheral blood films by haematology colleagues for malaria parasites. In addition to Plasmodium species, other pathogens that may be seen in the blood films include Babesia spp., Trypanosoma spp. (the African T. brucei gambiense and T. brucei rhodesiense, as well as the American T. cruzi), microfilariae, and the spirochaete bacterium Borrelia spp. The identification of Babesia spp. is sometimes mistaken for Plasmodium spp. because of the presence of intra-erythrocytic ring forms [52]. The travel history, especially when the destination is not a malaria-endemic region, should alert the microscopist to the possibility of babesiosis. Other morphological features that are suggestive of Babesia include the absence of stipplings and malarial pigments, presence of multiple pleomorphic rings within a single erythrocyte, and arrangement of the parasites in a Maltese cross appearance. Borrelia burgdorferi, the cause of Lyme disease, is possibly the best-known Borrelia species. However, B. burgdorferi is not normally seen in the peripheral blood smear. When spirochaetes are observed, the possibility of tick-borne or louse-borne relapsing fever should be considered. Tick-borne borrelioses are zoonoses caused by over 30 species of Borrelia and they have a global occurrence. Louse-borne relapsing fever, on the other hand, is restricted to countries in the Horn of Africa (Ethiopia, Eritrea, Somalia, and Sudan) nowadays. It is caused by Borrelia recurrentis which causes infection in humans only. The significance of louse-borne relapsing fever as a potential reemerging infection is highlighted by the recent cases reported amongst asylum seekers who travelled to Europe from East

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Africa^[53-56]. Definitive identification of Borrelia species requires molecular testing of the blood sample by sequencing of the I 6S rRNA gene and other targets.

In addition to blood smear examination, the anatomical pathologist may encounter unexpected or unusual infections. Some of these infections may present as subacute or chronic lesions and may be seen in immigrants from foreign countries rather than recent travellers. Examples include colonic or liver biopsies with E. histolytica or Schistosoma; soft tissue or visceral lesions due to larval stages of nematodes (such as dirofilariasis or onchocerciasis) or cestodes (such as sparganosis, cysticercosis); skin biopsy in patients with cutaneous or mucocutaneous leishmaniasis; bone marrow, liver, spleen, or lymph node biopsies in patients with visceral leishmaniasis. Most of these are relatively rare in Hong Kong, but they may spice up our otherwise mundane everyday routines.

Although the majority of tests for infective complications among the returned travellers are performed by the clinical microbiology laboratory, other specialties of clinical pathology may sometimes be involved in the investigation.

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TRIBUTE TO PROFESSOR LI CHONG CHAN

Professor John Malcolm NICHOLLS

Swige Con

Professor Li Chong ("LC") CHAN was the MB Lee Professor in the Humanities and Medicine, Chair Professor in Department of Pathology in the Li Ka Shing (LKS) Faculty of Medicine, and a Director of the Centre for the Humanities and Medicine (CHM) at The University of Hong Kong (HKU).

LC had a distinguished academic career in high school in Malaya before going to Trinity College, Cambridge and King's College Hospital, where he graduated in 1978 with an MB BChir, and then obtained the MRCP (UK) in 1981. From 1981 to 1987 he was at the Imperial Cancer Research Fund and the Leukaemia Research Fund (LRF) Centre, where he worked with Professor Mel GREAVES, FRS, on his PhD study on immunophenotyping of leukaemias; and later at the Royal Marsden Hospital with Professor Daniel CATOVSKY. It was during his time at the LRF when he published a large number of manuscripts on the mechanisms of leukaemia development, including a seminal Nature paper on the mechanisms of acute leukaemia involving the Philadelphia chromosome and a novel *ab*/protein. Further work at HKU showed how some leukaemias with a normal karyotype actually had a fusion of the mixed leukaemia lineage (*MLL*)

gene with partner genes including *EEN*, leading to the development of acute and chronic leukaemias in humans and mice, thus widening the knowledge of the aetiology of acute and chronic leukaemias.

During LC's time in London, he met and studied with colleagues who are now in key haematology positions around the world, including Professors Shuki MITZUTANI, Leanne WIEDEMANN and Zhu CHEN, the former Minister of Health in China. After training as a clinical haematologist in the United Kingdom, LC came to the Department of Pathology of HKU in 1989, where he rose from Senior Lecturer to Reader, and then Professor. When he moved to Hong Kong he continued his research interest in the molecular biology of leukaemia, and his PhD students have also followed in this area, especially in the field of MLL-EEN translocations, where LC developed a mouse model of human leukaemia by introducing MLL-EEN into embryonic



- Official opening of the LRF Centre (1984): LC (left) with Professor Greaves (centre) and HRH the Duke of Kent (right).
- LC (second from right) as a professional skier with Professor Greaves (second from left) and Professor Mitzutani (right).





LC (right) at dinner at Professor Mitzutani(centre)'s house after Professor Mitzutani's retirement international conference and party (2014).



stem cells by homologous recombination, the first in Asia and the second using this approach for *MLL* fusion genes worldwide.

LC had a special interest in curriculum development, problem-based learning in medicine, general education, and mindfulness practice. He was a Co-Director of the Medical Ethics and Humanities Unit, and the Chairman of the Medical Humanities Planning Group, responsible for the development and the teaching and learning of medical humanities, which is now part of the core undergraduate medical curriculum. In 1996 he was a core member of the planning group involved in the overhaul and reformatting of the undergraduate MBBS education programme, and visited The University of Liverpool Medical School and Harvard Medical School to understand how curriculum change should take place, and later attended the Harvard Macy Institute for Leaders in Education. His teaching philosophy was driven by the recognition that "The student of today is the teacher of tomorrow". Implicit in this statement was the responsibility of teachers to nurture students to develop not only self-directed learning and critical thinking skills but also a spirit of inquisitiveness and the courage to challenge scientific and medical dogma. LC believed that through the teaching and learning of medical humanities, students should generate new inquiries and reflections which would enable them to understand illness and health in the wider context of the lives of people. They should become aware of the complexities and ambiguities of issues involved in medical care and practice; and should explore the nature of suffering and healing so as to enable patients to live a life of meaning despite their illness.

His passion for medical humanities was a realization that biomedical research and cutting edge medical technology have dominated the medical curricula in many schools over the past few decades. This has resulted in illness being managed through biomedical perspectives, with little understanding of how an individual or community's experience of illness was influenced by social and cultural factors. To redress the imbalance and help develop humanistic care, LC was at the forefront of helping the LKS Faculty of Medicine to pioneer a core medical humanities curriculum from 2012 which would span the entire 6 years of the undergraduate curriculum, starting with first year students. He instituted the concept that narrative medicine would develop humanistic care through



LC and his family (left) with Professor Wiedemann (third from right), Professor Mai Har SHAM (second from right) and Professor Robb KRUMLAUF (first from right) in LC's home.

a better understanding of self and others and our interconnectedness. He promoted mindfulness training - a special feature of the MBBS programme - to maximize the potential of delivery of such care by enabling health care professionals to work in situations which are difficult and challenging, hence opening up opportunities to turn towards and work with instead of away from dissonance. His regular "dinging" of the small cymbals before meetings, to "bring us to the current moment" was a regular feature in the past few years. He started teaching a course "Mindfulness, Stress Reduction and Psychotherapy" in the Master of Buddhist Studies programme in HKU in 2015, and practiced mindful living

which enabled the experience of joy and peace in our busy and demanding world.



Through this medical humanities programme, students learned to understand and experience who they were beneath the white coat, the nature of suffering and healing, the role of empathy and compassion, and the importance for health care professionals to take care of themselves and to build resilience. This programme included development and running of interdisciplinary courses, seminars and symposia, which enhanced teaching, scholarship and research in the humanities and medicine. LC co-ordinated the first symposium in April 2015 "Linking Leadership in Ethics, Art and Professionalism" organized between the Medical Ethics and Humanities Unit, LKS Faculty of Medicine and CHM, in which medical and art educators, bioethicists and museum curators were invited to share their work and discuss how interdisciplinary teaching and learning could enhance medical training and ethical reasoning. One of the more memorable meetings that he helped organize in 2010 was with the Insitut Pasteur in Hong Kong on the "Nature of Altruism".

In recognition of his expertise and leadership in education, LC received an Outstanding Teaching Award (OTA) from HKU in 2009 and OTA (Team) in 2013.



Like many of his close colleagues, LC was a keen lover of music and food, and a keen advocate of his home Malaysian cuisine. He was renowned for his hospitality to previous research colleagues when they visited Hong Kong, taking them shopping in old and new markets, eating in dai pai dongs and chatting about music, food and philosophy. LC is survived by his wife, Penny, and their son Min Wei and daughter Wen Yen.

LC published in Nature in the first decade of his distinguished career. (Available at http://www.nature.com/nature/journal/v325/ n6105/abs/325635a0.html)



LC (third from left) and his research team.

LC (left) and his former PhD student Professor Eric SO (right) celebrating their paper in Nature Cell Biology in Professor So's home in London (2007).



PROFESSOR SIR RODERICK NORMAN MCIVER MACSWEEN (1935 – 2015): OBITUARY AND APPRECIATION

Professor Faith Ho



Fig. | Professor Sir Roderick N M MacSween Professor Sir Roddy MacSween was well known to pathologists in Hong Kong, not only through his writings, but also as a teacher, mentor and friend to many of us. It was therefore with much sadness and regret that we learnt of his passing on 11 December 2015. He had been fighting a chronic illness bravely for some time, and for the last 5 months of his life was well cared for in a nursing home where he peacefully passed his last hours in the presence of his devoted wife, Marjory and his family. It was comforting to know from Marjory that he had been his usual cheerful self and, mentally, fully in control of what was happening around him almost right till the end. A private funeral was held on 21 December at his church in Glasgow, and a Memorial Service at the University Chapel, University of Glasgow was held on 19 February 2016. Both were extremely well attended.

Roddy MacSween was born in February 1935 in Kinloch on the Isle of Lewis, which is at the northwest corner of the group of Islands known as the Hebrides, or Western Isles, near the West coast of Scotland. The island has an area of 683 square miles which compares favourably with Hong Kong with a total land area of 426 square miles. Gaelic was his mother tongue, as Roddy never allowed anyone who came into his orbit to fail to know. In fact, during the time I spent in the Department of Pathology at the Western Infirmary, Glasgow, he was regularly contributing to the Gaelic channel of the local radio station and I did try once to tune into the programme out of curiosity, even though I failed to understand a word. After primary schooling, he studied at the Inverness Royal Academy and at Glasgow University, graduating with BSc (Hons) in 1956 and MB ChB in 1959. His wife Marjory (nee Brown) was a fellow student in the Glasgow medical school and they were married in 1961. They have two children, Ruth who became a dermatologist and Gordon, an engineer and business consultant.

After a period spent in clinical medicine, specializing in infectious disease and virology, Roddy determined to enter Pathology as a career and never looked back. In 1963, he joined the Department of Pathology at the Western Infirmary under Professor Dan Cappell and became a lecturer in 1965. Obtaining his MRCPath in 1967, he was awarded a postgraduate fellowship which allowed him to cross the Atlantic to study at the University of Colorado Medical Centre in Denver. It was in Denver that he developed his interest in hepatology, studying the disease hemochromatosis and iron metabolism. Returning to the Western Infirmary in 1970, he continued his research interest in liver pathology and was awarded a Wellcome Senior Research



Fellowship, gaining an MD with honours in 1973 with a thesis on Clinico-Pathological and Immunological Studies in Liver Disease. Professor John Anderson had by 1970 succeeded Professor Cappell in the Chair and Roddy in turn

succeeded Professor Anderson in 1984. He held the Chair of Pathology at the Western Infirmary and was Head of Department until his retirement in 1999. Amongst other responsibilities, he was also vice-president and then president of the Royal College of Pathologists from 1996 to 1999 and Chairman of the Academy of Medical Royal Colleges from 1998 – 2000. In the same



 Fig.2 Roddy with his wife Marjory during an interlude in their golfing tour in Cambodia. (Photo kindly supplied by Dr Marjory MacSween)

year, he was knighted for his services to medicine and pathology. In 2007 he was awarded the degree of DSc by his Alma Mater.

My first encounter with Roddy was during the period when he was Senior Lecturer under Prof. Anderson and I was attached to the department for training for the MRCPath finals at the end of 1974. I happened to be assigned to the surgical pathology team when Roddy was heading the team. I quickly realized that he was one of those rare individuals whom everyone recognized were "going places", but at the same time, were also genuinely popular and respected among their peers and colleagues. As everyone who knew him would agree, he was a warmhearted person who was sincere, helpful and considerate to all those he came into contact with, and his great passion for life and for his work was inspiring. During the time that I am describing, he was further developing his studies on



Fig.3 A photo taken of Roddy during a visit to Hong Kong in 1992, together with a number of those who received training in his department.

the immunological aspects of liver disease in partnership with Professor Anderson and other colleagues, and indeed that period was the era of immunology, something which Professor John Anderson as Head of Department was encouraging us to explore. Pathologists were coming to realize the importance of T and B-lymphocytes and learning how to identify them, but the era of applying monoclonal antibodies and molecular pathology to everyday practice had not arrived yet. Roddy used to rush in and out of the reporting room trying to juggle his time between surgical pathology reports and teaching and research.



But this became one of the greatest lessons for me because I learnt how important it was for academic pathologists to develop and sharpen their skills in diagnostic histopathology while at the same time adapting the newest scientific advances to the study of disease. It is this unique combination of skills that make them special.

Roddy was of course to become 'a giant in liver pathology and leader in the pathology field' as attested to by one of his mentees, and herself a leader in liver pathology research in Hong Kong, Professor Irene Ng. Roddy had rapidly built up his international reputation through his many publications, including the classic textbook 'Pathology of the Liver" edited by him together with Peter Anthony and Peter Scheuer. It is a fitting tribute that the latest edition of this book has come out under the title: MacSween's Pathology of the Liver.

Dr Tsui Man Shan, another Hong Kong hepatopathologist has this to say: "Roddy is a kind, humble scholar and devoted to educate the new generations of liver pathologists. I still remember vividly his friendly encouragement words on the few occasions we lectured together.....In his memorial is the manner in which he



Fig.4 Roddy and Marjory with friends during their visit to Hong Kong in connection with the International IAP Congress of 1994.

set a standard for our generation of liver pathologists: to form a close knit, friendly, collegial community, energized and maintained not only by the excitement of science and medicine, but also by the joys to be found in the finer aspects of life, culture and art outside of our laboratories."

Indeed Roddy's legacy stretches far beyond liver pathology alone, even though that is substantial already. He never neglected his wider responsibilities including pathology teaching for medical students. He edited and revised Muir's Textbook of Pathology and also encouraged those of us in Hong Kong

who were preparing a local pathology textbook for our students entitled: Topics in Pathology for Hong Kong by writing a preface for the book. He was enthusiastic in promoting the profession of pathology as a whole, whether as President of the Royal College of Pathologists or by more direct training of junior pathologists, or through editorship of journals like Histopathology or his work with the International Academy of Pathology. More than 20 anatomical pathologists from Hong Kong have visited the Department of Pathology at Western Infirmary, Glasgow for training, either as part of their preparation for the MRCPath examinations, or after the examinations to further their training in specific areas. They have not only benefitted from the skills learnt, but also from the generous sharing with Glasgow colleagues in matters both cultural and professional. All have been personally touched by the warm welcome and hospitality shown by so many members of the department, not least the professor himself. Many of these former trainees have held or are now holding senior responsible positions in the delivery of pathology service in Hong Kong and elsewhere (see Fig. 3 for a sample). There is probably no other overseas Pathology department that have done so much for promoting Hong Kong Pathology as the Department headed by Prof. Roddy MacSween and his predecessor Prof. John Anderson, and we hope



MacSween and his predecessor Prof. John Anderson, and we hope to pay our debt of gratitude in a small way by acknowledging their great contribution in this article.

As Dr Tsui mentioned, Roddy also encouraged us by example to appreciate many 'finer aspects of life, culture and art outside our laboratories." Even though he had so much on his plate, he seemed to be able to always find time to enjoy himself and participate in non-professional activities. It would be nice to learn the secret of how he does this, but I suspect that the warm support from Marjory in all his endeavours has quite a lot to do with it. Both Marjory and himself were keen golfers at a competitive level, and as the photo shows (see Fig 2), golfing took them to many countries in the world and to make many friends. Roddy was always mindful of his Gaelic heritage, and was proud to share it with others. He was the President of his local Burns Club, which celebrates the Scottish poet Robert Burns, and also Chairman of the charity Tenovus Scotland; there are many other public duties of his that we do not have room to mention here.

We are grateful for people like Professor Roddy MacSween who through their work, their friendship and their example have made our lives richer in so many ways. As Prof. Irene Ng says, "with his radiant and warm personality, [Roddy] had been an impressive role model. He is sorely missed but the fond memories of him will stay with us always."



Fig.5 Prof. MacSween with Dr Tsui Man Shan at a liver meeting in San Francisco in 2009. (Photo kindly supplied by Dr Tsui).

1. CAVIL CNIE/CPD ANNUAL REFURN AT AN EARLIER TIME

Starting this year (3rd year of the current 2014 – 2016 cycle), <u>the Education Committee</u> <u>will call CME/CPD annual return in early October</u>. The deadline of submission will also be advanced to the first week of January. This is to align our practice to the regulations laid down by the Hong Kong Academy of Medicine.

Fellows are reminded that mandatory update or nil return is not required in the 1st and 2nd cycle years. Fellows should submit annual return only if there are CME/CPD activities to update or report, and /or based on existing iCMECPD record the CME/CPD requirement is not yet fulfilled. In the 3rd cycle year, mandatory update or nil return is not required if the CME/CPD requirement is already fulfilled.

2. CNIE/CPD PIBOLALE

In previous years, the Education Committee will include individual Fellow's CME/CPD profile in the call-for-annual return notice. Fellows may notice a few weeks' gap between our downloaded CME/CPD profiles and the actual CME/CPD points captured in the online system. As a result, Fellows may submit activities that were not shown in the downloaded CME/CPD profiles, but were actually captured in the computer system. With the maturation of the online iCMECPD system, Fellows can now monitor and review their CME/CPD records by logging in to the iCMECPD website (http://www.icmecpd.hk/). To save Fellows' time in the annual return process, Fellows are encouraged to check their most up-to-date CME/CPD records in the iCMECPD website and the Education Committee will no longer include individual Fellow's CME/CPD profile in the call-for-annual return notice starting this year.

8. "AVITMENIDANCE BECORD FOR INDIVIDUAL MELIOW"

To avoid a last minute rush, Fellows are encouraged to make use of the "Attendance Record for Individual Fellow" to report their CME/CPD activities (e.g. Self Study and Publications) to the Education Committee soon after completion of the CME/CPD activities. The forms can be found at <u>http://www.hkcpath.org/resources/downloads</u>.