



## FROM THE CHIEF EDITOR

*Dear Fellows and Members,*

*Molecular biology is becoming the bread-and-butter of pathology in the 21<sup>st</sup> century. For our featured article of this issue, the **Era of Molecular Biology in Diagnostic Pathology**, the Editorial Board has invited Fellows of different subspecialties to provide their views on this subject. The importance of molecular pathology in the current practice of pathology was further explored in the **Message from the President** by Dr. Wing Fung NG. In his message, Dr. NG also highlighted the recent changes in the training requirements for our trainees.*

*In the **Topical Update** from the Education Committee, Dr. Morris TAI discussed on the **Global Standardization of HbA1c**. On a lighter side in the **Out of the Whitecoat** section, **One Pathologist's Passion of Trekking to the High Mountains**, Dr. Harold P.H. YU recollected his fascinating encounter with the mountains and people from different parts of the world.*

*The 18<sup>th</sup> College AGM and the 5<sup>th</sup> Trainee Presentation Session will take place on 7 November, 2009 (Saturday). The **T.B. Teoh Foundation Lecture**, entitled "**Cancer Metabolism: Back to the Future**", will be delivered by Prof. Tak W. MAK from Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada. It will be a good opportunity for us to receive another dose of molecular biology!*

Dr. Alexander C.L. CHAN  
Chief Editor

## Timetable of the 18<sup>th</sup> Annual General Meeting 7<sup>th</sup> November 2009 (Saturday)

Venue:

**HKAM Jockey Club Building, 99 Wong Chuk Hang Road,  
Aberdeen, Hong Kong.**

<b>3:00 p.m. – 5:00 p.m.</b>	<b>The 5<sup>th</sup> Trainee Presentation Session</b>
<b>5:00 p.m. – 5:30 p.m.</b>	<b>Annual General Meeting</b>
<b>5:30 p.m. – 6:00 p.m.</b>	<b>Reception</b>
<b>6:00 p.m. – 7:00 p.m.</b>	<b>Admission of New Fellows and Members</b>
<b>7:00 p.m. – 8:00 p.m.</b>	<b>The 18<sup>th</sup> T. B. TEOH Foundation Lecture: "Cancer Metabolism: Back to the Future" by Prof. Tak W. MAK Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada</b>
<b>8:00 p.m. – 10:00 p.m.</b>	<b>Chinese Banquet Dinner</b>

## INDEX

- 1** From the Chief Editor
- 2** Message from the President
- 3** The 5<sup>th</sup> Trainee Presentation Session
- 3** Book Release: '侯寶璋家族史'
- 4** Featured Article: The Era of Molecular Biology in Diagnostic Pathology
- 12** Out of the Whitecoat: One Pathologist's Passion of Trekking to the High Mountains
- 16** Topical Update: Global Standardization of HbA1c
- 18** Announcements

## THE EDITORIAL BOARD

Dr. CHAN Chak Lam, Alexander  
(Chief Editor)  
Dr. CHEUNG Man Fung,  
Florence  
Dr. LO Yee Chi, Janice  
Dr. LOO Ka Tai  
Dr. POON Wai Ming

(Please send comments to:  
Dr. CHAN Chak Lam Alexander  
(Chief Editor),  
c/o the Department of Pathology,  
Queen Elizabeth Hospital,  
30 Gascoigne Road, Kowloon, H.K.  
E-mail: chancl@ha.org.hk  
Fax: 2385 2455)

# Message from the President

H1N1 human swine influenza was taking possession of the media in the past few months. It greatly affected the clinical practice in hospitals. Similar to the incidence of severe acute respiratory syndrome a few years ago, the work of our Fellows in the development and conduct of the rapid diagnostic tests had tremendous impact in the clinical management of the disease. The battle is going on and we are awaiting the possible evolution of the disease ahead.

In the past one year, there were several medical incidents related to patient identification, or specimen identification. Molecular testing was employed as an important tool for the investigation and confirmation of patient identity. This is just one example showing that molecular testing has gained its increasing importance in the medical field. In fact, molecular testing is playing an important role in different areas of clinical management, including diagnosis, prognostication and therapeutic treatment. How should the College equip her Fellows to face the challenge ahead? Should we develop a diploma course, or a new sub-specialty on molecular pathology? The College should explore the right direction to go.

Furthermore, the College has reviewed the training requirement and has made changes to it when necessity arises. There is a new requirement that the trainee must make two presentations within their 6-year recognized training. The new training requirement should be applied to the trainees who

registered on/after 16 October 2008. This requirement ensures that our future trainee will be better equipped for the career ahead. For Clinical Microbiology and Infection, a written examination is introduced in the fellowship assessment. The Council also clarifies the situation that the College Retired Fellow will not be eligible as examiner for the College examination.

Our Honorary Fellow Mr. M.K. Tan, the Honorary Auditor of the College since its inception, passed away last year. The College is grateful for the valuable professional service he has offered to the College in the past years. More so, Mr. Nicholas Tan, Mr. M.K. Tan's son, is willing to take up the role of Honorary Auditor for the College. On behalf of the College, I would like to thank Mr. Tan for his willingness and continuous support to the College.



Dr. W.F. Ng,  
the President

## THE 5<sup>TH</sup> TRAINEE PRESENTATION SESSION

**T**he 5th Trainee Presentation Session for pathologists in training will be held on the day of the Annual General Meeting on 7 November 2009. This is a good opportunity for trainees to share experience and to practise presentation skills. A prize will be given for the best presentation. The last issue of the College Newsletter (April 2009) has coverage on the 4th Trainee Presentation Session held in 2008, including the event itself, the abstract of the best presentation, and experience sharing by the winning trainee. The Newsletter can be accessed at: <http://www.hkcpath.org/newsletter/Newsletter%2009-1%20final.pdf>

Last year, the College and the Hong Kong Academy of Medicine have endorsed the requirement that all trainees registered on or after 16 October 2008 are required to make two presentations within their six years of recognized training, at least one of which must be at the Trainee Presentation Session or conferences organized by the College. Participating in the Trainee Presentation Session will be an invaluable experience in the training to acquire the aptitude for planning and undertaking scientific studies and projects, and to be able to present the findings in a concise and systematic manner.

Please support this meaningful activity of our College and encourage any trainee to participate. An abstract of not more than 300 words can be forwarded to the College Secretary by e-mail ([hkcpath@hkam.org.hk](mailto:hkcpath@hkam.org.hk)). An acknowledgement email will be issued to confirm receipt. The deadline of submission is 17 October 2009. For any enquiries, please contact Dr. Janice Lo (telephone 2319-8254 or e-mail [janicelo@dh.gov.hk](mailto:janicelo@dh.gov.hk)).

Education Committee

**BOOK  
RELEASE:**

**‘侯寶璋家族史’**



We are glad to learn that after our featured article ‘The Passion of Pathology Runs in the Blood’ was published in March 2007, a book on Prof. HOU Pao-Chang’s family has just been released recently. The book entitled ‘侯寶璋家族史’ was written by Dr. LAU Chi-pang (劉智鵬博士) and Prof. LIU Shu-yong (劉蜀永教授), and was published by Peace Book Co. Ltd. (和平圖書有限公司) (ISBN: 978-962-238-660-0). This work depicts the life of the renowned Prof. Hou and his family, highlighting their contributions to Pathology and Medicine. It will certainly be of interest to pathologists of different generations, especially when you want to relax and take a short break from your stressful daily work.

## The Era of Molecular Biology in Diagnostic Pathology

**The advent of molecular biology has taken diagnostic pathology to new realms. With its development, new standards are being established on various fronts, including assay sensitivity, specificity and turnaround times. Significantly, the application of molecular biology techniques is being embraced by all subspecialties of Pathology. In this featured article, we have invited our fresh generation of Fellows to contribute on this topic. We believe this compilation should be of wide interest to all practising specialists in the field.**

### Clinical Microbiology and Infection

Dr. Rickjason Chi Wai CHAN and  
Dr. May Kin Ping LEE,  
Department of Microbiology,  
Prince of Wales Hospital

Molecular biology has revolutionized all domains of bacterial and viral diagnosis. The diagnosis of infection due to fastidious bacteria has benefited from molecular detection. Its application in detecting fastidious sexually transmitted bacteria like *Neisseria gonorrhoeae* and *Chlamydia trachomatis* has greatly improved the sensitivity of detection compared to culture. It also allows the use of non-invasive specimens like urine and self-collected vaginal swabs which cause less discomfort and embarrassment compared to traditional specimens.

*Molecular biology has revolutionized all domains of bacterial and viral diagnosis.*

For respiratory tract infection, pertussis is another example that molecular methods contribute to enhanced sensitivity and speed in diagnosis. With the recent change in epidemiology, the polymerase chain reaction (PCR) was especially useful to detect atypical infections in adolescents and adults which may present late in their course of illness.

Testing for a panel of respiratory pathogens in multiplex PCR has the potential to improve the

timeliness, sensitivity, and accuracy of diagnosis of community-acquired pneumonia. Molecular techniques have also significantly improved identification of viruses as etiologies agents of many human diseases, such as herpes simplex virus causing encephalitis and norovirus causing gastroenteritis. As a consequence, rapid antiviral and effective infection control measures can be initiated.

Diagnosis of infection by slow growing organisms is also aided by molecular methods. Molecular detection of *Mycobacterium tuberculosis* allows the confirmation of acid-fast bacilli seen on microscopy and it can shorten the confirmation time of suspected tuberculosis even for smear-negative, culture-positive cases.

Broad-range PCR using 16S rRNA followed by nucleotide sequencing is useful in the identification of rare and novel bacteria as well as in detecting pathogens in culture negative infection. Molecular techniques also have played a central role in virus discovery. Examples include discovery of a new human coronavirus responsible for severe acute respiratory syndrome (SARS) and use of cDNA libraries by cloning techniques to identify hepatitis C virus (HCV) and hepatitis E virus.

Molecular techniques allow rapid implementation of diagnostic tests for newly discovered viruses as they can be designed even when only partial nucleic acid sequence information is available. This is valuable when identifying and diagnosing new diseases and emerging pathogens. In April 2009 a global outbreak of human swine influenza (H1N1) came to attention and there has been only about a one-week lag between sequencing

the virus and availability of molecular diagnostic assays.

*Molecular techniques... [are]valuable when identifying and diagnosing new diseases and emerging pathogens.*

Viral load monitoring, genotypic assays and antiviral drug resistance testing by gene sequencing have greatly improved the management of patients chronically infected with the human immunodeficiency virus (HIV), hepatitis B virus, HCV and cytomegalovirus. Moreover, qualitative assays for the detection of blood-borne viruses have increased the safety of blood transfusion and organ transplantation.

## Anatomical Pathology

Dr. Yue CHENG,  
Department of Clinical Pathology,  
Pamela Youde Nethersole Eastern Hospital

Recent advances in molecular genetics and the internet-prompted information highway have led to rapid implementation of genetic testing

from research institutes to bedside laboratories. PCR-based analysis and FISH using formalin-fixed paraffin-embedded tissue can now be done in the histopathology laboratory to detect mutation, deletion, amplification, loss of heterozygosity, hypermethylation, translocation and chromosome ploidy. Surgical pathologists are expected to update themselves on molecular genetic technologies, know how to read and critically assess molecular data in the medical literature, recognize the association between light microscopic morphology and genetic alterations, interact with bioscientists in requesting proper tests, advise on choice of specimens and interpret test results. While some of the molecular testing should only be done in academic centres or specialized laboratories, others can be performed in routine diagnostic laboratories. The application of molecular genetic studies in surgical pathology is wide-ranging and the list of available tests is clearly expanding, as shown by the examples listed below.

*Molecular genetic testing has been rapidly implemented from research institutes to bedside laboratories. The list of available tests is clearly expanding.*

### A. Personalized targeted therapy of tumours

Pre-treatment genetic analysis aims at detecting specific genetic alterations to predict favourable treatment response, maximize treatment efficacy and minimize drug toxicity.

Tumours	Genetic alterations	Methodology for detection	Targeted treatment
Breast cancer	<i>HER2</i> amplification	FISH (more sensitive) and IHC* (c-erb-B2)	Trastuzumab (monoclonal antibody)
Lung cancer (non-small cell lung cancer (NSCLC))	<i>EGFR</i> mutation within exons 18-21	Mutation test kit to detect the 29 most common mutations	TKIs**: gefitinib (Iressa®) and erlotinib (Tarceva®)
Colorectal cancer	<i>KRAS</i> mutation within exons 2-3	Direct DNA sequencing	Favourable response to cetuximab (monoclonal antibody) if <i>KRAS</i> mutation absent
Gastrointestinal stromal tumour	<i>c-KIT</i> mutation in exons 9 and 11	Direct DNA sequencing	Imatinib (Gleevec®)
Renal cell carcinoma	von Hippel-Lindau ( <i>VHL</i> ) gene mutation and activated receptor tyrosine kinase signaling pathway	Mutational analysis of <i>VHL</i> gene or LOH*** for <i>VHL</i> allelic imbalance	Sorafenib (Nexavar®), multitargeted kinase inhibitor and temsirolimus (Torisel®), mTOR inhibitor

\* immunohistochemistry

\*\* tyrosine-kinase inhibitors

\*\*\* loss of heterozygosity

## B. Tumour diagnosis and prognostication

1. Soft tissue tumours: Chromosomal translocation causing production of chimeric proteins, structural abnormalities of chromosomes and gene mutations/deletions are found in some soft tissue sarcomas; in some instances immunostudy can substitute genetic study. Examples include:

Ewing sarcoma/primitive neuroectodermal tumour (PNET)	<i>EWS-FLII</i> or <i>EWS-ERG</i> translocation
Desmoplastic small round cell tumour	<i>EWS-WT1</i> translocation
Synovial sarcoma	<i>SYT-SSX1</i> , <i>SYT-SSX2</i> translocation
Inflammatory myofibroblastic tumour	<i>ALK-RANBP2/TPM3/TPM4</i> translocation
Atypical lipomatous tumour/ well differentiated liposarcoma	Ring or giant marker chromosome
Clear cell sarcoma	<i>EWS-ATF1</i> translocation
Extraskeletal myxoid chondrosarcoma	<i>EWS-CHN</i> , <i>TAF2N-CHN</i>

2. CNS tumours: The differential diagnosis of astrocytic tumours vs. oligodendroglioma, and oligodendroglioma vs. other brain tumours with clear cell changes can be difficult. Information on genetic defects would help.

Oligodendroglioma and anaplastic oligodendroglioma	Co-deletion of 1p/19q with better survival and chemosensitivity to PCV*
Glioblastoma multiforme (GBM)	10q deletion, <i>EGFR</i> gene amplification and <i>MGMT</i> ** hypermethylation; better survival and response to temozolomide and radiation in hypermethylated GBMs

\* procarbazine, lomustine and vincristine

\*\* *O*<sup>6</sup>-methylguanine-DNA methyltransferase

3. Other tumours: Examples are in situ hybridization (ISH) for EBV-encoded RNAs (EBERs) for nasopharyngeal carcinoma, human papilloma virus (HPV) DNA test for triage of ASCUS (atypical squamous cells of undetermined significance) gynaecologic cytology cases, clonality study by PCR of *IGH* (immunoglobulin heavy chain gene) and *TCR* (T cell receptor gene) for lymphoid tumours, *BRCA1*, *BRCA2*, and *APC* gene mutation and DNA mismatch gene alterations for familial cancer syndromes, and *BRAF* mutation for non-HNPCC (hereditary nonpolyposis colorectal cancer) microsatellite instability-high colorectal cancer.

## C. Non-tumour diseases

PCR study can be utilized to detect infectious pathogens, e.g. *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Bartonella henselae* and *Toxoplasma gondii*. Single gene analysis and abnormal trinucleotide repeat are useful in characterizing neuromuscular and neurodegenerative conditions.

## D. Other applications

Molecular genetic studies may be employed to define patient identity in suspected cases of specimen mix-up or floater contamination.

*Molecular genetics is assuming an importance unprecedented in the history of pathology. It is also posing new challenges to surgical pathologists.*

Molecular genetics plays an important role in modern medicine. It is called "next-generation diagnostics" because it provides prognostic factors and treatment guidance in a way unprecedented in the history of pathology. We surgical pathologists, empowered with these cutting-edge technologies, are facing new challenges. Compared with conventional light



microscopy, molecular analysis is less sensitive and specific. Specimen impurity, cross reaction, tumour heterogeneity, genetic polymorphism and error in interpretation are issues that we have to tackle. Correlation with clinical and histologic findings can never be over-emphasized. Currently, genetic analysis is more focused on diseases with straightforward genetic alterations like specific gene mutation and chromosomal translocation, but tumour genetics is often more complicated. High-throughput array analysis, working on multiple genes and specimens, will provide further information on tumour diagnosis, prognosis and treatment, thus enhancing our role in the battle against disease, particularly cancer.

## Immunopathology

Dr. Janette Siu Yin KWOK,  
Division of Transplantation and  
Immunogenetics,  
Department of Pathology and Clinical  
Biochemistry,  
Queen Mary Hospital

Application of molecular biology in the field of immunological pathology has been ever growing for the past thirty years. A number of fundamental discoveries have also helped to enrich its biological science as witnessed by four Nobel Prizes awarded to studies in immunology. Molecular immunology differs from the classic descriptive immunology in terms of its approach to the subject. Molecular immunology focuses on the relationship between the structures that exist in the molecules and their functions in immunology. It also emphasizes the changes in molecular structures of various components of the immune system by its effect on the organism.

The revolution in genetic engineering resulted in huge success in the design of artificial immunoglobulins, receptor proteins and cytokines. Genes of the immune system have been studied both intensively and extensively. The DNA fragment manipulation allows the detailed explanation of their functions. The knockout of the entire gene enhances the mapping of the different roles of the encoded proteins in the functioning of the immune system

inside our human body. All these developments shed light on our better understanding of the finely designed structure of immunological biopolymers and enrich our knowledge of the fundamental biology such as genome functioning and intercellular interactions.

The Nobel Prizes have greatly influenced the development of immunology throughout the twentieth century, leading to great development in the combat against allergic, infectious, autoimmune and immunodeficient diseases and in the increasing success of the human transplant.

In the application for the diagnosis and therapy of allergic diseases, availability of recombinant allergens is considered a major breakthrough. The use of the recombinant allergens per se should obviate the requirement for conventional standardization in the diagnosis and immunotherapy.

The evolution of the germ theory of disease has brought the study of the mechanisms of immunity and the possible conquest of infectious diseases into bloom. Molecular biology applies to all infectious agents, not only to those causing global health problems but also to those affecting developing countries. It studies all aspects of the agents, including their taxonomy, diagnosis, epidemiology and chemotherapy.

The Human Genome Project has provided dramatic explosion of knowledge leading to better appreciation of the mechanisms and gene defects underlying primary immunodeficiency diseases. Distinct gene defects can lead to the same immunologic and clinical phenotype while distinct phenotypes can result from different mutations in the same gene. Furthermore, mutation analysis has gained relevance as a diagnostic tool.

*Molecular biology is important in the study and practice of various fields of immunology including allergic diseases, primary immunodeficiency conditions, autoimmune disorders and transplantation.*



The scan of the whole genome for general polymorphisms associated with disease has identified plentiful new risk genes associated with autoimmune phenotypes. Autoimmune disorders have a complex genetic basis and common genes can be the cause of multiple autoimmune disorders. Also, there exists heterogeneity amongst subphenotypes within a disease as well as across major racial groups. We would expect that it would not take too long to find out the answer regarding the extent of contribution from common variation and multiple rare variants to disease susceptibility.

Last but not least, the application of molecular biology in the field of transplant immunology is immense. The advance in molecular techniques for HLA typing, specialized methods using proteomics and real-time polymerase chain reaction in the areas of tolerance induction and reprogramming of the immune system would continue to bring about improved application in solid organ and bone marrow transplantations. Their contribution on the pathways of antigen presentation and chronic rejection monitoring should not be neglected.

## Haematology

Dr. Michael Lap Gate WONG,  
Department of Pathology (Haematology),  
Tuen Mun Hospital

Molecular tests are now essential in the diagnosis of haematological diseases. The information gathered is important for diagnosis, prognosis and disease monitoring. We shall discuss the role of molecular tests in haematological malignancies, then briefly review its applications in some non-malignant conditions.

In the diagnosis of haematological malignancies, molecular tests are valuable in confirming the findings of morphology and immunophenotypes. However, as some treatments are now able to target the molecular lesion, confirming its presence is also of therapeutic importance. With the advent of tyrosine kinase inhibitors, it is now essential to demonstrate the presence of a Philadelphia (Ph) chromosome or a *BCR-ABL* fusion gene in order to make a diagnosis

of chronic myelogenous leukaemia (CML). FISH or RT-PCR is essential in those cases of CML where the Ph cannot be demonstrated by karyotyping. An equally important role for molecular tests is the demonstration of clonality. This can avoid tedious efforts ruling out reactive causes. The discovery of the *JAK2 V617F* mutation has markedly simplified the diagnosis of myeloproliferative neoplasms. In the past, disease like essential thrombocythaemia (ET) was diagnosed by exclusion, but now we are able to make a positive diagnosis in some cases of ET.

*For haematological diseases, molecular tests can provide important information for diagnosis, prognosis and disease monitoring.*

Molecular tests are also important in providing prognostic information which allows stratification of treatment. Many mutations that are not readily revealed by conventional cytogenetics are prognostically important. Most childhood acute lymphoblastic leukaemia (ALL) treatment protocols stratify treatment according to the presence or absence of *BCR-ABL*, *AF4-MLL* and *TEL-AML1*. As  $t(12;21)(p13;q22)$  is difficult to be detected in routine cytogenetics, FISH or RT-PCR detection of *TEL-AML1* is essential. In contrast to ALL, although molecular prognostic markers are also well recognized in chronic lymphocytic leukaemia (CLL), they are not widely applied. Immunoglobulin heavy chain mutation status and karyotypes like trisomy 12, 13q deletion, 11q deletion and 17p deletion are having a strong impact on the prognosis of CLL. However, owing to the lack of a risk-adapted treatment protocol, current clinical guidelines do not consider these tests as essential.

Minimal residual disease (MRD) monitoring has been relying heavily on molecular methods. However, not all haematological malignancies have a specific gene rearrangement. Furthermore, the persistence of an abnormal transcript is compatible with long term remission in some diseases like acute myeloid leukaemia (AML) with *AML1-ETO*. These have limited the usefulness of PCR in MRD monitoring. CML is one of the

diseases where MRD monitoring is most well established. The disease load in many patients taking tyrosine kinase inhibitors is only detectable by PCR. The IRIS study not only established the role of imatinib in the treatment of CML, but has also set the three log disease load reduction treatment target. This prompted an international effort in standardizing the real time quantitative PCR for *BCR-ABL*. Current clinical guidelines recommend monitoring of MRD in CML every three months.

Molecular tests are also widely applied in non-malignant haematological conditions mainly for the purpose of diagnosis where other modalities are unable to achieve the same result. Multiplex PCR is used for genotyping the common mutations encountered in thalassaemia when electrophoresis and high performance liquid chromatography cannot pinpoint the diagnosis. They are also important tools for prenatal diagnosis where the material for testing is limited. Similarly, a molecular test can allow for a simpler diagnostic procedure where the diagnostic material is difficult to obtain as in using free foetal DNA for genotyping of RhD. In some inherited conditions like prothrombin gene *G20210A* mutation, PCR is the only available method of diagnosis.

The application of molecular biology in diagnostic haematology is not limited to the examples discussed and the possibilities are expanding rapidly. Techniques like gene expression profiling, though still limited for research purposes at the moment, might expand into the field of diagnostic haematology in the future.

## Forensic Pathology

Dr. Ho Wan YING,  
Forensic Pathology Service (NT Division),  
Department of Health

Forensic specialists may use molecular biology tools for diagnostic purposes in the following areas: identification; molecular autopsy with pharmacogenomic test; and determination of cause of death in “negative autopsies”.

## Identification

In the forensic world, we do not usually have fresh uncontaminated specimens for analysis. Instead we are usually dealing with decomposed remains, burnt bodies, tiny fragments of tissues, semen or bloodstains of varying quality and quantity.

Molecular biology tools have strengthened the capability of forensic specialists to characterize biological evidence. The success and widespread acceptance of DNA typing in forensic field is partly due to its sensitivity of detection and ability to analyze minute samples. Notwithstanding the maturity of forensic DNA field, there is still a lot of room for improvements in the future.

“DNA fingerprinting”, which was developed by Professor Alec Jeffreys, has been considered as the greatest breakthrough in forensic science in the last century. Nowadays, instead of using restriction fragment length polymorphism (RFLP) analysis, forensic scientists are frequently using polymerase chain reaction (PCR) based methods coupled with automated fluorescent detection technologies. DNA databases of offender and forensic samples have been established to facilitate criminal investigation in many developed countries. With advanced technology and experience, some institutes have attempted to analyze more difficult trace samples, termed low copy number (LCN).

In the near future, even in the absence of a prime suspect, single-nucleotide polymorphisms (SNPs) that describe phenotypic traits will enable a genetic prediction of morphological features for investigators to identify the perpetrator of a crime. If the sample originator's complexion, facial features and height can be predicted, police investigators will be able to narrow down the number of potential suspects. In addition, the same phenotypic SNPs will be used to identify missing person.

The use of DNA techniques to determine paternity or other family relationships in cases of dispute parentage is another important issue in recent years, with applications in right of abode cases and cases of “swapped babies” in hospitals.



*“DNA fingerprinting” is useful in identifying the originator of a forensic specimen, in describing offender characteristics, in identifying human remains, as well as in settling cases of disputed paternity.*

### **Pharmacogenomics as part of molecular autopsy**

With the emergence of genetic medicine, genetic contributions to drug toxicity can be useful to interpret drug related toxicities and drug-drug interaction in forensic toxicology. Clinically, pharmacogenomic tests will improve the efficacies and safety of drug therapy by the classification of patients according to genotype i.e. to distinguish “responders” from “non-responders” and to minimize drug toxicity by tailoring dosage according to “metabolizer status”. Forensically, knowledge of genetic variations on metabolism of drugs can be applied to postmortem interpretation of toxicological results, to help to reclassify some cases initially believed to be suicides or sudden unexplained deaths, especially in cases of poisoning (e.g. cocaine and methadone) or certain diseases in which long-term medication is essential (e.g. epilepsy, depression, cardiac disease, or diabetes).

### **Determination of cause of death in “negative autopsies”**

Generally speaking, around 5-10% of the autopsies of sudden non-traumatic deaths, especially children and younger adults, remain negative after thorough investigations. Many of the deaths can be explained with advances in molecular biology and DNA technology. Recent studies suggest that the underlying cause of death in many “negative autopsies” is genetic alteration without any morphological marker, and that both heart and liver abnormalities can play a role. Genetically-linked cardiac arrhythmia syndromes, e.g. LQTS syndrome, may be related to gene mutations of *KCNQ1*, *HERG*, *SCN5A*, while genetic forms of liver disease may be associated with mutations that alters the activity of P450 cytochrome system.

Although the ability to identify these “invisible diseases” with postmortem genetic testing has become a reality, the tests are very expensive at this moment. On the other hand, the molecular autopsy can help to determine the cause and manner of death and provide health information to at-risk relatives (i.e. genetic counseling).

*“Molecular Autopsy” is useful in the diagnosis of causes of death without visible morphological alterations e.g. cardiac arrhythmia syndromes including the LQTS syndrome, and in the correct classification of drug-related deaths.*

### **Future development**

The future of molecular biology in forensic fields will be exciting and dynamic. There is still much to be achieved, and developments in molecular biology will be essential to the solving of crimes and the identification of missing persons. Another line of research is focusing on the discovery and understanding of genetics factors influencing lethal disorders with limited knowledge about underlying mechanisms, and the development of new diagnostic tools for molecular autopsy.

There are still a number of gaps that need to be addressed in forensic applications of molecular biology. Further development in the following areas are needed: improving the current limits on typing samples of low quantity and quality; improving the efficiency of sample recovery and extraction; selecting and validating a variety of SNPs for different applications; developing automation for high throughput; developing expert systems for data interpretation.

### **Chemical Pathology**

Dr. Liz Yuet Ping YUEN,  
Department of Pathology,  
Princess Margaret Hospital

The increasing understanding of the molecular basis of human diseases and continuous technological advancement have allowed the



adoption of molecular tests as routine service in clinical laboratories worldwide. There is no exception in Hong Kong. When I first came to work in Princess Margaret Hospital in 2000, molecular tests were not done on a large scale. Over these years, more and more molecular tests have been developed. The chemical pathology laboratories in major public hospitals are currently providing variable numbers of molecular tests serving different clinical purposes.

In chemical pathology laboratories, the major clinical application of molecular tests is in the diagnosis of heritable diseases. The number of causative genes identified for known human disease entities or syndromes is escalating rapidly. Therefore, genetic diagnosis is no longer limited to inborn errors of metabolism, endocrine diseases, developmental disorders and paediatric pathology in general, but has extended to neurogenetics, renal diseases, cardiac diseases, and pharmacogenetics. Results of genetic tests no matter positive or negative can have tremendous impact on the clinical management of patients with heritable diseases. Not only being a definitive diagnostic test, genetic testing can be the only available or feasible investigation in some cases. Examples include the use of genetic tests in the diagnosis of autosomal dominant ataxia syndrome and in the investigation of sudden cardiac death victims.

*Genetic diagnosis is no longer limited to inborn errors of metabolism and developmental disorders, but has extended to neurogenetics, renal diseases, cardiac diseases, and pharmacogenetics. Genetic testing can be the only available investigation in some cases.*

Apart from heritable diseases, molecular tests are also applied to other clinical areas. One successful example is the measurement of plasma Epstein-Barr virus DNA as a tumour marker for nasopharyngeal carcinoma (NPC). This tumour marker is particularly relevant to the local population because the prevalence of NPC is high.

Another area with great development potential is pharmacogenetics and personalized medicine. Analysis of genes which encode for drug-metabolizing enzymes has been proven useful in predicting clinical response and/or risk of adverse events to certain drugs. For example, the allele *HLA-B\*1502* of the human leukocyte antigen gene with a high prevalence in Asians is associated with severe adverse effects to carbamazepine and phenytoin. Testing for *HLA-B\*1502* prior to initiation of carbamazepine and phenytoin therapy has been widely adopted by clinicians in public hospitals.

*Analysis of genes for drug-metabolizing enzymes has been proven useful in predicting clinical response and/or risk of adverse events to certain drugs, most notably anti-epileptics.*

The quality issues of molecular tests, especially those for diagnosis of heritable diseases, are a great concern. In addition to the conventional quality assurance mechanisms, other measures have to be adopted to ensure the quality of genetic tests. Specific areas of concern include patient confidentiality, adequacy of pre-test and post-test counseling, competency of laboratory personnel, and selection and development of new molecular tests. Pathologists play a pivotal role in this regard.

(References available upon request)



# Out of the Whitecoat:

## One Pathologist's Passion of Trekking to the High Mountains

**Dr. Harold P.H. YU,**  
**Department of Pathology (Haematology),**  
**Tseung Kwan O Hospital**



*I am honoured to be invited by the Editorial Board to write about my travel experience. I like to explore the wilderness by trekking or climbing, and enjoy the beauty and tranquility of remote places. Here, I would like to share some of these 'adventures' and photos with colleagues who may have much more travel experience than me.*

### THE HIMALAYAS

As an admirer of mountains, trekking in the Himalaya Range and visiting the base camps of Mt Everest and Mt K2 are just like pilgrimage trips that one has to take at least once in a lifetime. For the visit of Mt Everest base camp, I took the classical trekking route in Nepal which started in Lukla. The flight from Katmandu to Lukla was very memorable because of the spectacular panorama of the Himalaya mountains and the shaky ride in the tiny propeller aircraft.

The trekking experience in Nepal was pleasant as the local people were very friendly and always smiling. They taught me that one can always be cheerful and smile despite living in such a harsh environment.



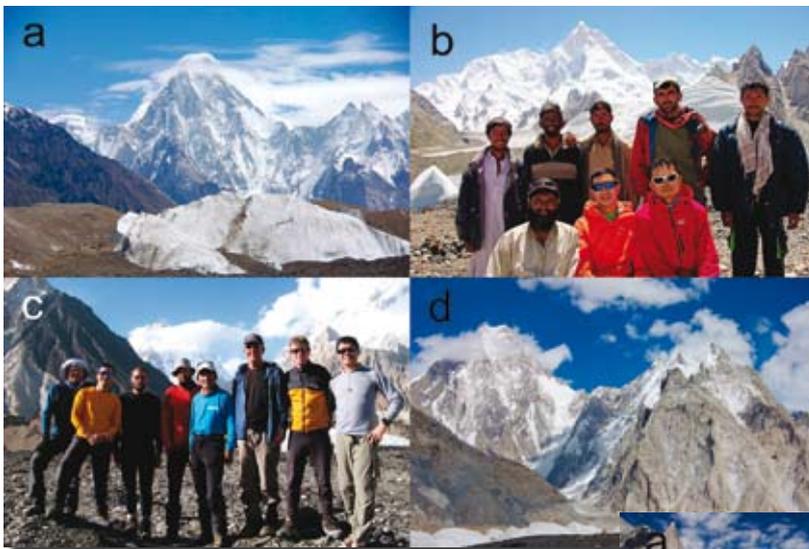
*Fig 1. The Himalayas:*

*a) Early morning in Thyangboche*

*b) Lenticular clouds over Lhotse (8516m) and Nuptse (7879m) indicating high wind speed and deteriorating weather.*

*c) Trekking towards Gorak shep (5100m)*

*d) Views of Khumbu Glacier*



◀ **Fig 2. The Himalayas:**  
 a) Mt Gasherbrum IV (7925m)  
 b) Photo with local guide and porters in front of Mt Masherbrum (7821m)  
 c) Photo with retreating K2 climbers in Concordia (4650m)  
 d) Broad Peak (8047m) at left and Gasherbrums at right

▼ **Fig 3. The Himalayas:**  
 a) Camp site at Concordia with view of K2 (8611m) in the middle  
 b) & c) Views of Upper Baltoro Glacier  
 d) Crossing the Gondogoro La Pass (5600m)

The experience of trekking in Pakistan proved to be much different from that of Nepal because of the inhospitable rugged landscape. The trekking route was in the Karakorum region in Northern Pakistan. It took us 2 weeks to trek up the Baltoro Glacier to K2 base camp, then past the Gondogoro-La (a high mountain pass at 5600m) back to Hushe Valley. This route had unique attractions and challenges that led us to close encounters with many beautiful gigantic mountains, like the Trango Tower, Masherbrum, Gasherbrum, Broad Peak and K2. I also had a chance to talk to the retreating climbers from K2. They gave us the detailed account of a fatal accident which took away 9 climbers' lives after an avalanche near the summit a few days ago. They felt sad for the deaths but also blessed as they had chosen to turn back at a critical moment. This reminded me that one should pay due respect to mountains and nature whenever we venture outside our comfort zone.



**Fig 4. The Alps:**  
 a) & b) Trekkers climbing up the slope to Pigne d'Arolla (3796m) in Switzerland  
 c) Crossing the Glacier du Mont Collon in Switzerland  
 d) View of Mt Matterhorn

## THE ALPS

The Alps in Europe is the birthplace of modern mountaineering, and actually the word 'Alpinism' originated from there. So, it is another 'must go' area for mountain enthusiasts. I have trekked the classical Haute Route in summer time, which is a one-week trekking route from Chamonix (France) to Zermatt (Switzerland). The route passes through the snow-capped high mountain passes and various glaciers, bringing us into close contact with many razor-shaped mountains including the famous Matterhorn. I was amazed by the many keen European climbers and trekkers who venture into the mountains whenever there is a window period of good weather.

## MOROCCO, NORTH AFRICA

It is unusual to associate snow and coldness with Africa, but I had a chance to experience this coincidence during a trip to Morocco. In that trip, I have spared a few days to climb the Mt Jebel Toubkal (at 4167m the highest mountain in North Africa) which is located at the edge of Sahara Desert. It was quite an experience to stand on top of the snow-capped mountain and look towards the endless sand dunes in the desert far away.

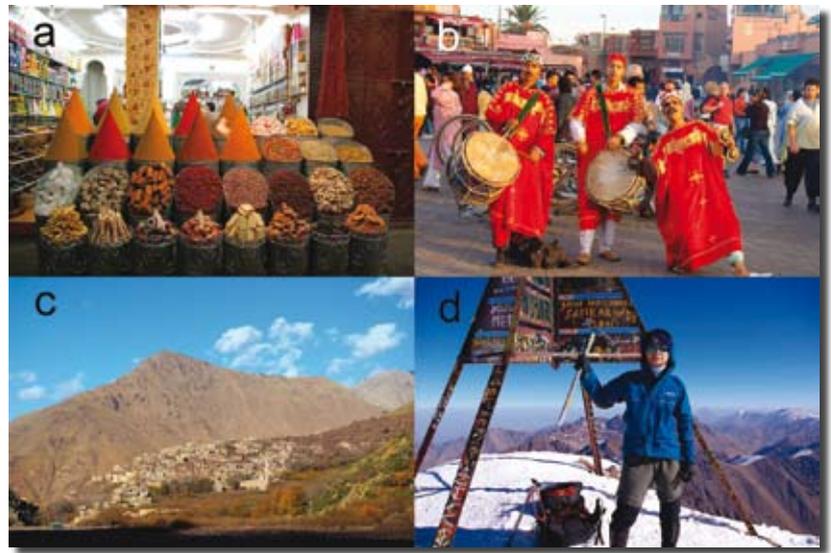


Fig 5. Morocco:

- a) Spice market in Marrakesh, Morocco
- b) Street performers in Djemaa El-Fna Square in Marrakesh
- c) Imlil, a small mountain village which is the starting point for climbing Jebel Toubkal
- d) Summit view of Jebel Toubkal



Fig 6. East Java:

- a) & b) Views of the smoking Kawah Ijen. The crater lake is also called the "green lake" which is 700m across, 200m in depth with the pH level less than 1.0
- c) Pipes connecting with the volcano's vents which will direct sulphur fume down to the ground for collection
- d) Miner carrying the solidified sulphur blocks from the end of smoking pipes

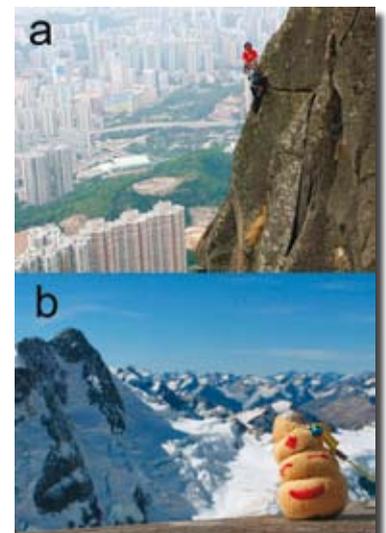
## EAST JAVA, INDONESIA

The trip to East Java of Indonesia has impressed me deeply of the living condition of the local people. I hiked to the Kawah Ijen (宜臻火山口), which is the acidic crater lake of an active volcano where sulphur-containing gases are emitted continuously. Local miners, with minimal protection consisting of just a damp cloth over the mouth and nose, work under the harmful gases. They collect the sulphur blocks and carry them (up to 75kg in weight) down to a chemical factory one mile away. All this hard work only earns them US\$5 per day for a living. Life could be very tough and short-lived for these miners.

Finally, I would like to end with the wisdom borrowed from Edward Whymper, the first to summit Matterhorn in 1865. "Where there's a will there's a way, and we come back to our daily occupations better fitted to fight the battle of life..."

► Fig 7.

- Freedom and passion in the mountains:
- a) Rock climbing in Fei Ngo Shan, HK
- b) Mountaineering in Mt Cook, New Zealand



## EDITOR'S NOTE:

In order to understand how a pathologist, who normally leads a sedentary life, can take up such an adventurous and demanding hobby as mountain-trekking, we asked Dr. Yu several questions which he amiably responded. Here we convey the questions and his answers.

### 1. When and how did you start trekking as a hobby?

I have liked hiking and mountains since I was small. At that time, I lived in Western District of Hong Kong Island and always looked at the Peak from our home down by the waterfront. Whenever there was holiday, I would run up to the Peak with my brothers or alone to train for endurance and explore the area. This became a hobby and enjoyment for me. I only started traveling abroad since the last year in medical school back in 1993. At that time, I did my elective study in a teaching hospital in South India. After that, I did regular 自由行, especially in developing countries which I found more interesting. Then I gradually did more trekking overseas as experience and enthusiasm grew.

### 2. Did you join a special club for coaching and group support?

I am a member of the 岳峰 climbing club. The club organizes climbing activities and training in HK and overseas, like China and Korea. However, the trips that I have written of were not organized by the club. All these were planned by me or friends together. Most of these trekking activities needed some sort of logistic support from local people. For short trekking in Morocco and Indonesia, I hired local guides or drivers after I got there, whereas for the longer trekking in the Himalayas, I had to do more preparation beforehand. For Nepal, I hired a local guide through a Nepalese friend in HK. For the K2 trekking, we asked an adventure company in Pakistan (via internet) to organize a mini-expedition for us as the logistic arrangement was quite complicated. I brought my own personal gear to these trips and the adventure company provided the rest of the gear, like tents, stove, food etc.

### 3. Is physical training required?

As for the question of stamina, I am not particularly strong but I do regular aerobic training, like running and hiking, to keep fit. I guess the passion for exploration and mountains is the driving force behind me to complete the trekking.

### 4. Would you welcome pathologists to share your hobby?

I write to share some of my experience and to show that life can be multifaceted. It was quite common to meet doctors when I was traveling. One of the K2 climbers I met (second right in the photo) was an anaesthetist from USA who helped to treat severe frostbite by giving tissue Plasminogen Activator to the injured climbers during their expedition. I welcome comments or sharing of experience from colleagues if they are interested in this kind of activities.



# TOPICAL UPDATE

## Editorial note:

In this issue of Topical Update, Dr. Morris TAI discussed on the use and standardization of the HbA1c test, an important assay in the management of diabetes mellitus. We welcome any feedback or suggestions. Please direct them to Dr. Janice Lo (e-mail: janice10@dh.gov.hk) 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.

## Volume 4, Issue 1

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

## Global Standardization of HbA1c



**TAI, Morris**  
*Associate Consultant,  
Department of Pathology and Clinical Biochemistry,  
Queen Mary Hospital*

### Introduction

The prevalence of diabetes mellitus (DM) has been increasing in recent years and DM is now a global epidemic. Haemoglobin A1c (HbA1c) plays an important role in the management of DM as the vast majority of outcome studies on diabetic complications are based on it. The most famous of such studies, which demonstrated the relationship of HbA1c to diabetic complications, are the Diabetes Control and Complications Trial (DCCT) & the United Kingdom Prospective Diabetes Study (UKPDS). HbA1c is formed via a posttranslational nonenzymatic attachment of glucose to haemoglobin in an irreversible fashion. In strict chemical terms, the molecular structure of HbA1c is  $\beta$ -N-(1-deoxy)-fructosyl-haemoglobin and it serves as an indicator of glycaemic control over the preceding 2- to 3- month period.

*The heterogeneity of methodology necessitated test standardization.*

There are a great number of analytical methods used in the measurement of HbA1c. More than 20 methods were in clinical use as reported in the year 2004. The heterogeneity of methodology eventually generated concerns about comparability and usability of HbA1c, especially when patients' data were to be compared with study results. The call for test standardization was therefore

critical. Various standardization programmes have been carried out since the 1990s. The National Glycohaemoglobin Standardization Program (NGSP) and the International Federation of Clinical Chemistry (IFCC) are the two most important international standardization programmes while local ones such as Japan Diabetes Society/Japanese Society for Clinical Chemistry (JDS/JSCC) and Mono-S have been adopted in Japan and Sweden respectively.

### The standardization programmes

The NGSP was initiated by the American Association of Clinical Chemistry in July 1996 aiming at harmonization of HbA1c methods so that HbA1c results generated from different methods could be aligned to the ones employed in the DCCT & the UKPDS. Designated comparison methods, but not a primary reference method, is the standardization method used in NGSP, as well as JDS/JSCC and Mono-S.

The HbA1c standardization working group of IFCC was formed in 1994. They adopted a totally different approach. They prepared pure standards of Hb and HbA1c, which were subsequently digested with endopeptidase. The glycosylated and non-glycosylated N-terminal hexapeptides were then separated by reversed phase high-performance liquid chromatography (HPLC) followed by identification and quantification by capillary electrophoresis or electrospray ionization mass spectrometry (ESI-MS). This method is

highly specific - only the compounds matching the eluent time in HPLC and mass spectrum in ESI-MS are detected as Hb and HbA1c. Because of the high specificity, the IFCC HbA1c values are lower than the NGSP values by about 2%. Correlation studies demonstrated that NGSP and IFCC results are highly correlated and the results are interchangeable by a master equation ( $\text{HbA1c-NGSP} = 0.915(\text{HbA1c-IFCC}) + 2.15\%$ ). Equations converting IFCC values to either JDS- or Mono S- equivalents are also available.

*A consensus statement enumerating recommendations on reference system and results reporting was published.*

Following these developments, a meeting was held in Milan 2007 and a consensus statement was published jointly by American Diabetes Association (ADA), European Association for the Study of Diabetes (EASD), IFCC and International Diabetes Federation (IDF). The five recommendations were:

1. HbA1c test results should be standardized worldwide, including the reference system and results reporting.
2. The new IFCC reference system for HbA1c represents the only valid anchor to implement standardization of the measurement.
3. HbA1c results are to be reported worldwide in IFCC units (mmol/mol) and derived NGSP units (%), using the IFCC-NGSP master equation.
4. If the ongoing "average plasma glucose study" fulfils its a priori-specified criteria, an A1c-derived average glucose (ADAG) value calculated from the A1c result will also be reported as an interpretation of the A1c results.
5. Glycaemic goals appearing in clinical guidelines should be expressed in IFCC units (i.e. mmol/mol), derived NGSP units (i.e. %), and as ADAG values (i.e. mg/dl or mmol/L).

Concerning point 4, the correlation study was finished and published in August 2008; the results support the notion between HbA1c levels and ADAG for both type 1 and type 2 DM.

### **Impact on management of DM**

The new standardized IFCC-HbA1c result is not trouble-free at all. It has been criticized that patients & health care professionals may be confused and be falsely reassured by the seemingly lower IFCC values (in %). The introduction of ADAG and the use of the unit mmol/mol

for IFCC-HbA1c may solve this problem and certainly more time is required for the clinicians and patients getting used to the new reporting format. As NGSP methods were used in previous studies, comparison of new data with historical ones requires conversion by master equation and this creates substantial inconvenience.

*The resolution of the standardization issue has allowed the use of HbA1c for screening and diagnosis of DM.*

Currently screening and diagnosis of DM rely on two tests, fasting plasma glucose and oral glucose tolerance test. The former suffers from inadequate sensitivities while the latter is cumbersome and is infrequently used in clinical settings. Fasting is required in both tests and repeated testing is necessary to establish the diagnosis. Ever since the invention of glycated haemoglobin, it has been suggested to be used as a tool for diagnosis of DM. In fact, the glycation of haemoglobin may be more accurately reflecting the pathogenesis of the complications associated with prolonged hyperglycaemia toxicity in which toxic advanced glycation end products are involved. Furthermore fasting is not necessary if the test is done for screening and short-term life style changes do not affect the HbA1c level at all. However the use of HbA1c as screening and diagnosing tools was rejected in the current ADA recommendations, which were made a decade ago, largely because HbA1c was considered at that time to be inadequately standardized and insensitive. The resolution of the standardization issue has allowed the use of HbA1c for diagnosis of DM. An expert panel recently published new diagnostic guidelines, recommending an HbA1c screening cutoff of 6% as a threshold for close follow-up, and a diagnostic cutoff of 6.5%. This recommendation improves the investigation flow as diagnosis of DM can be made after a single blood collection for HbA1c and fasting glucose as the simultaneous glucose result may support the diagnosis of DM.

### **Summary**

HbA1c is the cornerstone of diabetes care. It is widely used as a treatment goal and to predict the risk of development of complications in DM patients. Various standardization programmes have been carried out in the last 15 years and results obtained by different methods are interchangeable by master equations. It is agreed that the measurement should be standardized against the IFCC method, which detects the "true" HbA1c. NGSP values will not be abandoned as it is aligned to most large DM studies.

ADAG values may provide more comprehensible results to patients. Future reports may contain more than one of these measured and derived values.

## References

1. Consensus Committee. Consensus statement on the worldwide standardization of the hemoglobin A1C measurement: the American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation. *Diabetes Care*. 2007 Sep;30(9):2399-400.
2. Geistanger A, Arends S, Berding C, Hoshino T, Jeppsson JO, Little R, Siebelder C, Weykamp C; IFCC Working Group on Standardization of Hemoglobin A1c. Statistical methods for monitoring the relationship between the IFCC reference measurement procedure for hemoglobin A1c and the designated comparison methods in the United States, Japan, and Sweden. *Clin Chem*. 2008 Aug;54(8):1379-85.
3. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; A1c-Derived Average Glucose Study Group. Translating the A1c assay into estimated average glucose values. *Diabetes Care*. 2008 Aug;31(8):1473-8.
4. Saudek CD, Herman WH, Sacks DB, Bergenstal RM, Edelman D, Davidson MB. A new look at screening and diagnosing diabetes mellitus. *J Clin Endocrinol Metab*. 2008 Jul;93(7):2447-53.
5. Weykamp C, John WG, Mosca A, Hoshino T, Little R, Jeppsson JO, Goodall I, Miedema K, Myers G, Reinauer H, Sacks DB, Slingerland R, Siebelder C. The IFCC Reference Measurement System for HbA1c: a 6-year progress report. *Clin Chem*. 2008 Feb;54(2):240-8.

## NOTICE ON CPD FROM THE HONG KONG REGIONAL COUNCILLOR, RCPA

Fellows of the Hong Kong College of Pathologists (HKCPath) who are also Fellows of the Royal College of Pathologists of Australasia (RCPA) may be aware that the RCPA has recognized the Continuing Medical Education/Continuous Professional Development (CME/CPD) Scheme of HKCPath as equivalent provided that quality assurance (Category C) meets the minimum of 10 hours.

When the annual RCPA subscription reminder comes together with the personal information sheet, RCPA Fellows should tick the box that indicates that they take part in another College's CPD.

To streamline the process, Fellows have 3 options for returning their annual Continuing Professional Development Program (CPDP) documentation to RCPA:

1. Fill in the actual hours online and submit. With regards for Category C (quality assurance) this may include biopsy, grand round or Clinicopathological Conference (CPC) meetings with clinicians which are part of quality assurance or audit in which Hong Kong Fellows have actively reviewed the material beforehand. For instance, with Anatomical Pathologists or Haematologists the CPD is interpreted as passive (i.e. just attending a grand round) for A2, B30 is the time you spend in preparing for the meeting (i.e. personal time) and C59 the actual formal review session which you have with the clinicians.
2. They can type in "Hong Kong College" or "Hong Kong Path" on the line on the RCPA website saying they participate in another program ('Other recognised program - Please enter the name of the institution'). If they do this they should NOT put any numbers into the other boxes, otherwise they will get back a computer generated letter with incomplete hours.
3. Do nothing online and send the annual Hong Kong CME/CPD documentation to RCPA by hard copy (or scan it in and send it in by email).

If RCPA Fellows require a certificate from RCPA then they should enter the above information as well as entering hours of CPD pertaining to RCPA requirements. If no hours are entered then the RCPA database will show that the Fellow participates in the Hong Kong program only and hence will NOT receive a certificate from RCPA. If a Fellow in Hong Kong wants documentation from RCPA saying they participate in "another recognised program" it is not a problem for the RCPA to provide them with such a document.

*Dr. John NICHOLLS  
Regional Councillor, Hong Kong  
The Royal College of Pathologists of Australasia*

## **ADOPTING NEW COLLEGE REGULATIONS (2007) FOR ANATOMICAL PATHOLOGY TRAINEES**

According to the College policy, existing Anatomical Pathology trainees adopting the new regulations (2007) should adopt the entire training programme stipulated in the new training regulations, and must fulfil all training requirements stipulated therein and at the same time demonstrate the required skills with competence during an assessment.

Existing trainees still in basic training are allowed to adopt the new training regulations, while trainees *already* in the higher training are not eligible to adopt the new regulations. Eligible trainees should submit the request to the Training and Examinations Committee (TEC) for approval at least six months before the completion of Membership.

In the 2007 regulations, the total number of autopsies required at the time of fellowship examination is 120 (instead of 150). There is a requirement that the candidates should gain knowledge in modern-day laboratory and mortuary management practice, as stipulated in the regulations. How the modern-day laboratory and mortuary management practice is examined will be decided by the examiners. This can be in the form of questions in the written or oral examination.

*Training and Examinations Committee*

## **POLICY ON INTERRUPTION OF TRAINING DUE TO LONG LEAVE**

Trainee shall report any long leave more than 90 continuous calendar days to the Training and Examinations Committee (TEC) as soon as possible and not later than the deadline of the Annual Report submission. The whole period of such leave may not be counted as recognized training. The effective date of the policy on interruption of training due to long leave is 1st June 2009. Such leave taken after 1st June 2009 may be deducted from the effective training period.

*Training and Examinations Committee*

## **RIGHTS AND PRIVILEGES OF RETIRED FELLOWS OF THE COLLEGE**

The rights and privileges of Retired Fellows of the College have recently been discussed by the Council. Retired Fellows are Fellows, Overseas Fellows or Founder Fellows who applied for retired status with the College and recorded in the College Registry. The Council has endorsed that the rights and privileges of a Retired Fellow shall be the same as a full Fellow except the followings:

- (1) A Retired Fellow can enjoy a reduced annual subscription rate at HK\$100.
- (2) A Retired Fellow is not eligible for new appointment as examiner for College Examination. However, if a Fellow changes his/her status to Retired Fellow during the term of appointment as examiner, he/she can complete that appointment term as examiner.
- (3) A Retired Fellow shall pay up the balance of the normal annual subscription rate if he/she administers CME/CPD activities via College. The annual subscription rate for various categories of Fellow is listed below.

As a result, the College fees have been adjusted:

- (1) For Founder Fellows, Fellows and Overseas Fellows applied for Retired Fellow Status with the College as recorded in the College Registry, the annual subscription would be HK\$1,000 before 1st of November 2006. Afterwards, only the nominal annual subscription of HK\$100 would be applied.
- (2) If Retired Fellow administers his/her CME/CPD activities via the College, an administrative fee representing the balance of the Annual Subscriptions between Full and Retired Fellows will apply.

*Application form for Retired Fellow Status can be downloaded from the College website at [www.hkcpath.org](http://www.hkcpath.org)*

# TIPS TO FACILITATE CONTINUING MEDICAL EDUCATION/ CONTINUOUS PROFESSIONAL DEVELOPMENT (CME/CPD) ANNUAL RETURN

## Prepare relevant documents

- College CME/CPD Scheme, 2008 version
- Regular CME/CPD activities preapproval lists of various specialties
- Current version of CME/CPD Annual Return Form
- The above documents are available in our College Website <[www.hkcpath.org](http://www.hkcpath.org)>.

## Compiling information in the Annual Return Form

1. Please use the latest Official CME/CPD Annual Return Form, (hard & soft copies will be sent to all Fellows annually), since the College standard return form would be submitted to the Academy for processing. Using old forms or other formats will definitely delay the whole process.
2. A major portion of Fellows' CME/CPD activities will be captured by the HKAM iCME/CPD system, which would be listed in the appropriate categories in the Annual Return Form. The scores may not reflect activities in the last 3 months of the cycle as it takes time to enter points into the system. Please do not duplicate the activities already recorded by iCME/CPD system.
3. E-mail submission of Annual Return Form in Microsoft Excel format is highly preferred as it facilitates further computation. If sent by hard copy, Fellows are suggested to fill in the return form by typewriting or handwriting in block letters.
4. There are 10 categories of CME/CPD activities for Fellows to participate in, with details listed in Part 5 of the 2008 CME/CPD Scheme.
5. For most categories, Fellows should fill in the details listed in the Annual Return Form. A few notes are listed to facilitate the process:
  - a. Self study (SS), *CME/CPD Scheme 2008, item 5.1*
    - All articles of indexed journals are approved self study material.
  - b. Passive participation (PP) and Active participation (AP), *items 5.2 & 5.3*
    - Regular education programmes held in various institutes could be found in Regular Activity Preapproval Lists.
    - The "title of activity" in the Annual Return Form refers the "title" used in application for preapproval. For instance, if you attended the regular "Department Seminar" in "Institute X" on the topic of "Advances in Thyroid Cancer", the "title of activity" should be "Department Seminar of Institute X".
  - c. Publication and Research (PR), *item 5.4*
    - "The first page of the publication" is required for documentation. Alternatively, Fellows could provide the correct URL that links directly to the "NCBI PubMed Index" or the "e-Journal of the particular publication" as proof.
  - d. Conducting Examination (EX), *item 5.10*
    - A maximum of 2 CME/CPD points would be granted to the Examiners of a College Approved Specialist Examination, even if the examiner was involved in multiple parts of that examination.

## Submission of the Annual Return Form

- Fellows are encouraged to use soft copy sent by e-mail for submission.
- After compiling the Annual Return Form, please send it to any one of the following:
  - E-mail: [hkcpath@hkam.org.hk](mailto:hkcpath@hkam.org.hk)
  - Fax: 2871 8755
  - Address: Room 606, Hong Kong Academy of Medicine Building,  
99 Wong Chuk Hang Road, Aberdeen, Hong Kong
- Please **do not** send the Form to the Education Committee secretary through any means.

*Education Committee*