# NEWSLETTER OF THE HONG KONG COLLEGE OF PATHOLOGISTS

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



This year is the 25th Anniversary of The Hong Kong College of Pathologists. Since the establishment, the most important mission of our College is to safeguard the quality of training, so as to ensure high standard of pathology service to our patients.

November is the time when new Fellows and Members are admitted to the College. On behalf of the College, I would like to extend my sincere welcome to all new Fellows and Members to the family of The Hong Kong College of Pathologists. This is a moment of celebration for the new milestone. After overcoming years of serious training and prevailing the challenge of examinations, our Fellows are now qualified specialists in Pathology who are consultants to bedside doctors. This is also a moment of gratitude. Trainers in Hong Kong should be proud of our tradition of selfless contribution to training. Our trainees and our new Fellows should thank your trainers for their tireless supervision. Of course, you should also thank your family for their unfailing support.

It is now increasingly known that pathologists play a pivotal role in the prevention, diagnosis, and treatment of diseases. The continuously changing clinical scenario and widening scope of knowledge need our vigilant attention to adaptation of training. Due to the increasing use of genetics and genomics in modern pathology, our College is preparing for the establishment of a post-specialty fellowship in Genetic and Genomic Pathology.

To ensure provision of safe service, long term planning of manpower and new services in pathology is important. The Academy and our College will hopefully play a more active role in the future.

To let our community understand our work, the College has been reaching out. With President as representative, our College has expressed views in task forces and specialist panels on health issues. In liaison with the international pathology community on International Pathology Day, a two days' workshop has been organized in November for the public and secondary school students. With our sincere and persistent effort, we should be able to break the barrier surrounding our profession and communicate better with the public and health professionals.

Let me express our thanks to Fellows and friends for the continuous support of the College. We sincerely welcome active participation from our new Fellows to strengthen the profession and to better serve the community.



Professor CHEUNG Nga Yin, Annie November 2016





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# President's activities



President (standing) at the Fellowship Conferment Ceremony, Hong Kong College of Community Medicine.



President (second from right) at the kick off ceremony of Globe-athon Hong Kong 2016.

## We are pleased to announce that the following candidates have passed the Fellowship Assessment or Membership Examination. Congratulations!!

CHAK Pui Kwan	(Fellowship Assessment – Anatomical Pathology)	
CHEUNG Tin Yan Elaine	(Fellowship Assessment – Anatomical Pathology)	
LOK King Fung	(Fellowship Assessment – Anatomical Pathology)	
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LEE Wai Kwan	(Membership Examination – Anatomical Pathology)	
SHEA Ka Ho	(Membership Examination – Anatomical Pathology)	
TSE Victoria Pui Wai	(Membership Examination – Anatomical Pathology)	

#### For all trainees in Anatomical Pathology:

The Training and Examinations Committee (TEC) would like to reiterate that trainees in Anatomical Pathology are required to report 2,500 cases of histopathology, 60 cases of autopsy and 800 cases of cytology before they shall be accepted for Membership Examination. Eligibility to examination is subject to TEC and Council endorsement.



▲ Examiners in Chemical Pathology: Front row (left to right): Dr MAK Wing Lai Tony, Dr SHEK Chi Chung Anthony (Chief Examiner), Dr Penelope COATES (External Examiner), Dr CHAN Ho Ming, Dr Sidney TAM. Back row (left to right): Dr POON Wing Tat, Dr MAK Miu Chloe, Dr CHAN On Kei Angel, Dr YUEN Yuet Ping, Dr TAI Hok Leung Morris.



Examiners in Anatomical Pathology: Front row (left to right): Dr NG Wing Fung, Dr Sanjiv MANEK (External Examiner), Prof. KHOO Ui Soon (Chief Examiner), Dr LEE Kam Cheong. Back row (left to right): Dr LEUNG Chung Ying, Dr IP Pun Ching, Philip, Prof. TO Ka Fai, Dr NG Wai Fu.



**Examiners in Clinical Microbiology and Infection:** From left to right: Dr Bone TANG, Dr QUE Tak Lun, Prof. Malik PEIRIS, Dr Kitty FUNG, Dr Janice LO, Dr Dominic TSANG, Prof. Robert NORTON (External Examiner), Prof. HO Pak Leung (Chief Examiner), Dr Cindy TSE, Dr TO Wing Kin, Dr Rickjason CHAN, Dr Rodney LEE.

#### 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:** In this topical update, Dr Chloe Mak reviews the history and development of newborn screening, in particular for Hong Kong. Both benefits and limitations of expanded newborn screening were discussed. The latest pilot screening programme, as stipulated in the Policy Address by Chief Executive, was also illustrated. We welcome any feedback or suggestions. Please direct them to Dr. Sammy Chen (e-mail: chenpls@ ha.org.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.

#### Newborn Screening: Past, Present and the Future



**Dr MAK Miu Chloe** Department of Pathology Princess Margaret Hospital

#### Introduction

Newborn screening (NBS) is one of the most successful public health programs in the 20<sup>th</sup> century. In fact, the idea of mass screening was totally new to the society before 1960's. When Dr Ivar Asbjørn Følling discovered the disease phenylketonuria (PKU) leading to mental retardation in many children <sup>[1]</sup> and Dr Robert Guthrie invented a simple and reliable screening test using bacterial inhibition test for blood phenylalanine <sup>[2]</sup> together with the understanding of disease pathogenesis and effective treatment to prevent mental retardation initiated during early asymptomatic phase [3], the proposal of NBS was born. However, criticisms were vigorously received over the uncertainties of disease nature, assay validity and long-term treatment effectiveness. To begin with, NBS for PKU was tested as a pilot service in Massachusetts in 1962 [4]. World Health Organization (WHO) issued two landmark reports about population screening: "The Principles and Practice of Screening for Disease" [5] and "The WHO Scientific Group on Screening for Inborn Errors of Metabolism (IEM), Geneva''<sup>[6]</sup>. The latter report elaborates more on screening for IEM.

After the success of PKU screening in preventing mental retardation, the legislation for mandatory screening was made in 1975 in USA. More disorders were added to the panel, such as congenital hypothyroidism (incidence I

in 2,200) in 1976, congenital toxoplasmosis (1 in 27,800) in 1986, hemoglobinopathies (1 in 2,900) and congenital adrenal hyperplasia (1 in 19,200) in 1990, biotinidase deficiency (1 in 42,000) in 1992, medium-chain acyl-CoA dehydrogenase deficiency (1 in 21,000) and cystic fibrosis (1 in 2,900) in 1999 in the New England Newborn Screening Program of the University of Massachusetts Medical School <sup>[7]</sup>. The Centers for Disease Control and Prevention (CDC) launched the Quality Assurance Program for NBS laboratories in 1978 and now more than 200 laboratories worldwide has participated.

The first wave of NBS started in other countries soon, such as Canada in 1963, Singapore in 1965, Japan in 1967, Australia in 1967, Portugal in 1979, while in other Asian areas NBS was mostly initiated after 1980s: Mainland China, Hong Kong, India, Malaysia and Taiwan in 1980s; Bangladesh, Indonesia, South Korea, Philippines and Thailand in 1990s; Mongolia, Myanmar, Palau, Pakistan, Sri Lanka and Vietnam in 2000s <sup>[8-10]</sup>. The approach adopted was one-testone-disease and the panel was limited to a few conditions usually including PKU, congenital hypothyroidism, maple syrup urine disease, homocystinuria, galactosemia, cystic fibrosis and/or congenital adrenal hyperplasia.

#### **Classifications of IEM**

- I. Disorders of amino acid and peptide metabolism
- 2. Disorders of carbohydrate metabolism
- 3. Disorders of fatty acid and ketone body metabolism
- 4. Disorders of energy metabolism
- 5. Disorders in the metabolism of purines, pyrimidines and nucleotides
- 6. Disorders of the metabolism of sterols
- 7. Disorders of porphyrin and haem metabolism
- 8. Disorders of lipid and lipoprotein metabolism
- 9. Congenital disorders of glycosylation and other disorders of protein modification
- 10. Lysosomal disorders
- 11. Peroxisomal disorders
- 12. Disorders of neurotransmitter metabolism
- Disorders in the metabolism of vitamins and (non-protein) cofactors
- 14. Disorders in the metabolism of trace elements and metals
- 15. Disorders and variants in the metabolism of xenobiotics

http://www.ssiem.org/centralstore/resources/ SSIEMClassificationIEM2011.pdf

#### Expanded Newborn Screening for Inborn Errors of Metabolism

IEM is a huge group of clinically and genetically heterogeneous metabolic disorders (Table 1). There are more than 1,000 diseases mainly affecting children. The cumulative incidence was reported up to 1 in 800 <sup>[11, 12]</sup>. Some IEM are amenable to timely treatment with good prognosis. Traditionally, the diagnosis replies on one or more tests for one disease. However, the advent of tandem mass spectrometry (TMS) applications in amino acids and acylcarnitines detection enables the one-test-manydiseases breakthrough in NBS for IEM <sup>[13-15]</sup>.TMS accurately identifies analytes by their fingerprint molecular mass-tocharge ratios with commendable specificity and sensitivity. Table 2: Advantages and Disadvantages of TMS Applications in NBS

### Advantages and Disadvantages of TMS Applications in NBS

#### Advantages

- I. Detection of multiple analytes in the same analytical run
- 2. Small blood volume required (0.3 mL whole blood)
- 3. Fast analytical time about two minutes per sample
- 4. High throughput capacity
- 5. Accurate identification of molecular compounds by their fingerprint mass-tocharge ratios
- 6. Highly sensitive and specific with low false positive rate
- 7. Availability of commercial kits for acylcarnitines and amino acids

#### Disadvantages

- I. High capital cost
- 2. Skillful expertise
- 3. Lack of full automation

It only requires 0.3 mL whole blood to test for more than 30 diseases in a single dried blood spot. The analytical time takes about two minutes for one sample allowing a highvolume throughput with rapid turnaround time in a NBS setting. Table 2 shows the advantages and disadvantages of TMS applications in NBS.

In 1998, the New South Wales Newborn Screening Program was the first centre to implement expanded NBS based on electrospray ionization TMS <sup>[16]</sup>. In the next year, the New England Newborn Screening Program introduced an optional metabolic panel for 19 IEM <sup>[7]</sup>. Twenty IEM patients were identified after 2.5 years screening of 200,000 newborns <sup>[17]</sup>. The prospective study showed that screened patients had shorter hospitalization and required less extra parental care. There was no significant difference in parental stress among NBS screened true positive, false positive results and normal control groups. In the same year, Germany started its extended screening with an unrestricted approach and since 2005 streamlined into  Table 3: Screening Panel of Government-initiated Pilot Study

#### Screening Panel of Government-initiated Pilot Study

#### Disorders of Amino Acids

Classical phenylketonuria

6-pyruvoyl-tetrahydropterin synthase deficiency

Argininosuccinic acidemia

Maple syrup urine disease

Citrullinemia type I

Citrullinemia type II

Tyrosinemia Type I

Homocystinuria

#### Disorders of Organic Acids

Multiple carboxylase deficiency

Glutaric acidemia type I

Methylmalonic acidemia

Propionic acidemia

Isovaleric acidemia

3-hydroxy-3-methylglutaryl-CoA lyase deficiency

Beta-ketothiolase deficiency

#### Disorders of Fatty Acid Oxidation

Carnitine uptake deficiency

Carnitine-acylcarnitine translocase deficiency

Carnitine palmitoyltransferase II deficiency

Medium-chain acyl-CoA dehydrogenase deficiency

Very long-chain acyl-CoA dehydrogenase deficiency

Glutaric acidemia type II

#### Others

Congenital adrenal hyperplasia

Biotinidase deficiency

Classic galactosemia

10 conditions <sup>[18]</sup>. Japan piloted TMS-based NBS from 1997 to 2007 with screening of 606,380 babies <sup>[19]</sup> and 65 IEM patients were identified with overall incidence of 1 in 9,330. Mainland China piloted TMS based NBS in Shanghai from 2003 to 2007 with 116,000 newborns screened <sup>[20].</sup> Twenty patients were positive for six IEM with mainly PKU, maple syrup urine disease, methylmalonic acidemia and propionic acidemia. The overall incidence of IEM was I in 5,800. There were significant differences in the disease spectrum between northern and southern Chinese<sup>[21]</sup>. For example, classical PKU with phenylalanine hydroxylase deficiency accounts for the majority of PKU in northern Chinese, whereas, 6-pyruvovyl-tetrahydropterin synthase deficiency was much more common among southern Chinese. There were around 1,300 new cases of PKU screened in China each year. Glucose-6-phosphate dehydrogenase (G6PD) deficiency was very prevalent in Guangzhou with incidence of I in 28 but not in Northern Chinese <sup>[22]</sup>. In addition to expanded NBS in some advanced provinces covering more than 30 IEM, congenital hypothyroidism and PKU are mandatorily screened throughout the whole mainland stipulated in the law of maternal and infant health (launched in 1994) and its action program (launched in 2000) <sup>[22]</sup>.

The International Atomic Energy Agency had devoted a total of \$6.7 million USD to assist developing countries developing the infrastructure for NBS, in particular for congenital hypothyroidism <sup>[23]</sup>. In 2008, the Working Group of the Asia Pacific Society for Human Genetics on Consolidating Newborn Screening Efforts in the Asia Pacific Region was formed with representatives from 11 countries, viz. Bangladesh, China, India, Indonesia, Laos, Mongolia, Pakistan, Palau, Philippines, Sri Lanka and Vietnam. <sup>[24]</sup>.

In 2006, the American College of Medical Genetics (ACMG) announced a consensus statement to standardize the NBS panel and decision matrix with recommendations of a core panel of 29 disorders and 25 additional secondary targets disorders <sup>[25]</sup>. It also provides the act sheets and confirmatory algorithms on each condition (http://www. ncbi.nlm.nih.gov/books/NBK55827/).

Wilson-Jungner criteria have been recently revisited in the context of genomic and modern medicine. The emphasis has been shifted towards more on the benefits to the affected baby and the family from early diagnosis and the availability of a satisfactory medical system for subsequent patient management <sup>[26]</sup>. Whether curative treatment is available or not, this is not a mandatory pre-requisite for NBS implementation.

Table 4: Outcome comparison between screened and unscreened IEM patients

Outcome comparison between screened and unscreened IEM patients				
Wilcken et al. <sup>[56]</sup>	Screening more than two million babies	The handicap rate I in 74,074 in the clinical group versus I in 232,558 in NBS group		
Boneh et al. <sup>[57]</sup>	Six babies with glutaric acidemia type I detected by NBS	These patients benefited from mild protein restriction and carnitine supplement. All patients except one had normal cognitive and gross motor development, versus in unscreened patients with glutaric acidemia type I leads to acute encephalopathy and debilitating dyskinetic dystonia.		
Klose et al. <sup>[58]</sup>	57 patients clinically diagnosed with organic acidemias and fatty acid oxidation defects	Sixty-three percent of these patients presented within the first year of life and 54% suffered from acute metabolic crises with eight deaths. Majority of these metabolic crises (93.5%) and death (87.5%) could have been prevented by expanded NBS and early treatment.		
Schulze et al. <sup>[44]</sup>	250,000 neonates for 23 metabolic diseases and 106 patients with positive screening results followed for 42 months	Seventy patients received proper treatment and remained asymptomatic. Six patients developed symptoms and three died. Nine patients presented earlier than the availability of screening results. Overall, I in 4,100 babies benefited from the early screening and subsequent treatment.		
Cipriano et al. <sup>[59]</sup>	Decision-analytic model analyzing 21 diseases taking into account of the disease severity, analytical sensitivity and specificity, need of confirmatory tests, specialist management, start-up and operating costs, hospital-related costs and potential deflation of future costs and benefits.	Bundling PKU together with 14 diseases was the most cost-effective strategy with \$70,000 Canadian dollars per life-year gain.		
Seymour et al. <sup>[60]</sup>	Systemic reviews published by the Health Technology Assessment in United Kingdom	Recommended screening for PKU, biotinidase deficiency, congenital adrenal hyperplasia, MCADD and glutaric acidemia type I.		
Pollitt et al <sup>[61]</sup>	Systemic reviews published by the Health Technology Assessment in United Kingdom	Considered screening as many conditions as possible with the emphasis on the benefits of early diagnosis to the patients and the family. The availability of effective treatment was not a compulsory pre-requisite.		

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#### (continued from page 8)

Filiano et al. <sup>[62]</sup>	Cost-benefit study	The lifetime costs for one cerebral palsy patient from infancy to 65 years old were \$167,000 to \$1 million USD as at 1998. The costs included medical charges, developmental services, special education and lost wages. Projected yearly savings of \$36,600,000 (USD as at 1998) could be achieved through expanded NBS. The saving was twice of the incremental cost for NBS.
Couce et al. <sup>[63]</sup>	10-year clinical follow-up of 137 IEM patients picked up by expanded NBS	The incidence was I in 2,060 newborns. With the long-term management, death rate was only 2.92% and majority of the survivors (95.5%) were asymptomatic after a mean observation of 54 months.
Linder et al. <sup>[64]</sup>	373 IEM patients detected from a cohort of 1,084,195 newborns studying the efficacy and outcome of 10-year experience in expanded NBS	Presymptomatic diagnosis and treatment of other IEM achieved the same clinical benefits as in PKU.

#### **Newborn Screening in Hong Kong**

In Hong Kong, two metabolic conditions have been screened on a population basis namely congenital hypothyroidism and G6PD deficiency since March 1984 under the Neonatal Screening Unit of Clinical Genetic Service, Department of Health. The local incidence of CH is about 1 in 2,500, while that of G6PD deficiency is 4.5% in male and 0.3% in female newborn <sup>[27]</sup>. The program significantly lowered the mortality and morbidity. Apart from antenatal education through the Maternity and Child Health Centres, the Department of Health also provides follow-up and counselling to affected families.

The third was neonatal hearing screening. Language development is significantly improved if the hearing loss is treated before the age of 6 months. A local feasibility study was performed in 1999 screening 1,064 infants with an incidence of permanent deafness I in 355 <sup>[28]</sup>. A two-stage age 4 of 10 program was implemented in all Hospital Authority hospitals with maternity service since 2007 <sup>[29]</sup>.

In 2008, a Coroner inquest was called into the acute death of a 14-year-old boy with a postmortem genetic diagnosis of glutaric acidemia type II (multiple acyl-CoA dehydrogenase deficiency) <sup>[30]</sup>. The Coroner's report recommended that "the Department of Health, the Hospital

Authority, the Faculty of Medicine of various universities and others concerned should carry out a feasibility study to see whether universal check may be carried out on all newborn babies for congenital metabolism defect'' (http://www.judiciary. gov.hk/en/publications/coroner\_report\_july08.pdf).

In 2012, the University of Hong Kong conducted the first territory-wide pilot study funded by the SK Yee Medical Fund Foundation (http://hub.hku.hk/cris/project/ hkugrant107939).The study tested the feasibility of expanded NBS in public hospitals with an OPathPed model <sup>[31]</sup>. In 2013, a private NBS for IEM service commenced in the Chinese University of Hong Kong, sponsored by Joshua Hellmann Foundation for Orphan Disease (http://www.obg.cuhk.edu.hk/ fetal-medicine/fetal-medicine-services/jhf-newborn-metabolicscreening-program/).

In 2015, the Policy Address by the Chief Executive announced that a working group was established between the Department of Health and Hospital Authority to study the feasibility and logistics of expanded NBS for IEM in the public healthcare system (http://www.info.gov.hk/gia/ general/201501/14/P201501140477.htm).

The feasibility study in the form of a pilot study was officially initiated on 1 October 2015 and lasts for 18 months,

Figure 1. Education materials of the Government-initiated Pilot Study



testing in two public hospitals with the collaboration between the Department of Health and the Hospital Authority. The aim of this pilot study is to demonstrate the feasibility of implementing NBS for IEM while developing and optimising education on IEM to public and healthcare professional, the screening tests, laboratory algorithms, clinical management and follow-up algorithms and programme evaluation. Twenty four conditions are included (Table 3). Educational materials were distributed to public and healthcare professionals (figure I). A video was broadcasted in antenatal clinics and postnatal wards (Cantonese: https://youtu.be/RHKINOGZkDs; Mandarin: https://youtu.be/MLLxJf7RvEQ and English version: https:// youtu.be/JPPFfzUavGQ).

#### Pros and Cons of Expanded Newborn Screening

NBS for IEM enables early diagnosis and treatment, prevents morbidity and mortality, avoids unnecessary investigations, alleviates family's anxiety, predicts prognosis and providesvaluable information for family planning and genetic counselling. In addition, some maternal diseases with treatment implications can also be detected during NBS, such as primary carnitine deficiency, PKU and vitamin B12 deficiency. The storage of DBS on a population scale can be a valuable asset in quality assurance, biomedical researches and forensic investigations.

NBS is shown to be cost-effective. Although randomized clinical trial on clinical utility and cost-effectiveness is difficult due to the rarity of individual IEM, cost-effectiveness in PKU <sup>[32-34]</sup>, congenital hypothyroidism <sup>[35-37]</sup> and MCADD <sup>[34, 38, 39]</sup> were well documented. Table 4 shows some examples of studies on the outcome comparison between screened and unscreened patients.

There are also limitations in expanded NBS. First, because of the short history of expanded NBS developed only in the last two decades, long-term evaluation is still lacking. Recently, the Southeastern Newborn Screening Genetics Collaborative and the Public Health Informatics Institute collaborated to address the long-term issue through international effort. Second, patients with early symptom onset before release of NBS result would not benefit. False negative can happen to patients with mild or atypical presentation or use of non-standardized cutoff values and testing strategies. Third, since TMS allows one-testmultiple-diseases, some diseases which are not required by the program would also be unravelled. Conditions which are benign or with doubtful pathological significance may be identified, for examples, 3-methylcrotonyl-CoA carboxylase deficiency and short-chain acyl-CoA dehydrogenase deficiency. Detection and disclosure of carrier status such as in sickle cell disease and cystic fibrosis may create confusion to the parents <sup>[40, 41]</sup>. Fourth, although screening is available and even mandatory in some countries, treatment is not and not all screened positive children received proper treatment. Some treatments require special drugs and milk formulae. The clinical follow-up system may not be as well established as the screening program. Fifth, NBS results can be false positive or inconclusive. The overall sensitivity and specificity of TMS-based NBS is already commendable more than 99% with false positive rate from 0.07% to 0.33%, positive predictive values from 8% to 18% [20, <sup>42-46]</sup>. False positive may lead to unnecessary hospitalizations and parental anxiety [47]. Measures such as better education and communication, algorithmic interpretation rules and two-tier testing system, can be implemented to reduce false positive rates and potential adverse effects.

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#### Conclusion

NBS represents the highest volume of genetic testing. It is more than a test and it requires a comprehensive healthcare system from pre-analytical, analytical to post-analytical phase involving expertise from public health, healthcare management, clinical, pathology and information technology. The field of NBS and IEM is still expanding. More disorders are under evaluation and covered such as severe combined immunodeficiency [48,49] and X-linked adrenoleucodystrophy [50]. Various different or new technologies are applied to enhance the diagnostic performance, increase throughput, allow more automation and decrease costs [51-54]. Although a genomic approach for NBS is technically feasible, it entails a lot of difficult technical, clinical, social and ethical issues with hazards more than good <sup>[55].</sup> On the other hand, using SNP array approach to detect a large panel of well-known pathogenic mutations on a wide spectrum of disorders would be more pragmatic. Expanded NBS is shown to be economically valid with significant reduction in critical care and chronic medical care expenditures. Last but not the least, NBS saves lives.

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#### **Contribution by Professor Dennis LO Recognised as "Nobel Class"**

Professor Yuk Ming Dennis LO, Li Ka Shing Professor of Medicine and Professor of Chemical Pathology of The Chinese University of Hong Kong, and Honorary Fellow of the College, has recently won two major research awards.

He won the inaugural Future Science Prize -- Life Science Prize for his seminal work on non-invasive prenatal testing. This prize is worth one million US dollars and it has been regarded by many commentators as China's version of the Nobel Prize.

Professor Lo has also been named a 2016 Thomson Reuters Citation Laureate in Chemistry. Clarivate Analytics, formerly part of Thomson Reuters, uses citation statistics of publications to quantify the influence and impact that a scientist makes. The Laureates are recognised "to have demonstrated themselves, by their contributions and citation records, to be "of Nobel class" and worthy of future Nobel recognition". Since 2002, 39 of the Citation Laureates have gone on to win a Nobel Prize.

Professor Lo is grateful for such recognitions and thanks his research team for joining hands with him for the last 19 years for pushing forward the field of molecular diagnostics.



Professor Yuk Ming Dennis LO.

# Out of the Whitecoat:

# Pipa under the Moonlight in Xunyang

#### by Cycles POON



#### **Editorial Notes:**

Dr Cycles Poon of the Department of Pathology, United Christian Hospital is a keen pipa player and a Tang poem lover. In this issue she shares her two passions with us, and discusses the popular traditional Chinese music piece "Spring, River, Flowers, Moon, Night" with two related Tang poems. As any translation will do the poets and their masterpieces injustice – we have great difficulty choosing the best translations just for the titles –, we are publishing this article in Chinese as per Dr Poon's original submission, with an English abstract.

#### Abstract

The author narrates the literary association of a masterpiece of Chinese pipa music, 春江花月夜 ("Spring, River, Flowers, Moon, Night", sometimes known as "Spring River in the Flowery Moonlight"). There were two famous poems about pipa written in the Tang Dynasty (A.D. 618-907). One was written by ZHANG Ruo Xu (張若虛) (A.D. 660-720) and was by the same name as the musical piece. The other one was written by BAI Juyi (白居易) (A.D. 772–846) and was called 琵琶行 ("Pipa Xing" or "Song of the Pipa Player"), which describes the poet's encounter with a lady pipa player when both the poet and the musician were at the trough of their lives. The instrument pipa, the melody, the poets, the poems, readers and music-lovers all interact and resonate with sentiments across the barrier of history and time.



The pipa is a four-stringed Chinese musical instrument, belonging to the plucked of instruments. category sometimes called the Chinese lute. The instrument has a pear-shaped wooden body with a varying number of frets ranging from 12 to 26. It has been played for almost two thousand years in China. (Source: Wikipedia)



潘雪冰

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2 -	

這是中樂古曲「潯陽夜月」主旋律的簡譜,驟看你也許會摸不著頭腦。然而如果你有聽過由唐 滌生先生編劇、編曲,任劍輝和白雪仙女士領銜演出的殿堂級粵劇「紫釵記」的主題曲「劍合釵圓」 ,隨著主角李十郎唱出心聲「霧月夜抱泣落紅,險些破碎了燈釵夢,喚魂句,頻頻喚句卿須記取再重 逢…」,那優美的曲調便會油然在耳奏起。

「潯陽夜月」,又名「春江花月夜」,是一首著名的琵琶傳統大套文曲,旋律優美流暢,明清時 代便已在江南一帶廣泛流傳。全曲有九段,各有小題,如歌如畫,繪畫出夕陽映江面、月出東山、風 迴曲水、欸乃歸舟的境界。全曲由慢漸快,由弱至強,表現波浪層湧,由遠而近的意境。最後歸舟遠 去,萬籟俱寂,春江夜空月輪高掛,幽靜安詳,音已靜而意未窮。

上世紀經唐滌生先生和其他專劇編曲家採用,配上劇情和曲詞,令這曲為嶺南人、廣東人更加熟 悉和鍾愛。相關的劇目,也更為膾炙人口。

話說回來,潯陽位於今天的江西省九江市,這裡和琵琶有很久遠的緣份。中唐時期的大詩人白居 易(772-846A.D.)曾被貶官,左遷九江郡司馬(816A.D.)。他在任期間,在潯陽江頭夜送客,遇到一位琵 琶樂師。一位是淪落風塵、歷盡滄桑、年老色衰的江湖女子;另一位是仕途失意、謫居臥病的才子, 大家都感懷身世,惺惺相惜。白居易的名作「琵琶行」就是記敘這次不凡的相遇,讓讀者在千年之 後,如身歷其境,親聞其音。

詩人對琵琶指法的描述準確而生動,對音色的欣賞和領悟出神入化。「輕攏慢撚抹複挑,初為 《霓裳》後《六幺》。大弦嘈嘈如急雨,小弦切切如私語。嘈嘈切切錯雜彈,大珠小珠落玉盤…」。 最有意思的,也是今人常愛引用的:「同是天涯淪落人,相逢何必曾相識。」大家萍水相逢,卻付出



Song of Pipa at Xunyang (潯陽琵琶). Qiu Ying (仇英, ca. 1494-1552), Ming Dynasty (1368-1644). Album leaf, ink and colour on silk, 33.8 x 41.4 cm, Palace Museum, Beijing

最深的交流:「莫辭更坐彈一曲,為君翻作琵琶行。感我此言良久立,卻坐促弦弦轉急。 淒淒不似向前聲,滿座重聞皆掩泣。座中泣下誰最多?江州司馬青衫濕。」

人生感悟,因「春江花月夜」之名而更上層樓。初唐詩人張若虛(660-720A.D.),江蘇 揚州人,曾任衰州兵曹。開元初年,與賀知章等人共稱「吳中四士」馳名京都。他傳世只 得兩詩,而「春江花月夜」被譽為「孤篇蓋全唐」的傑作。此詩共三十六句,重現了江南 春夜的景色,如同明月照耀下的萬里長江畫卷,媲美清明上河圖。「春江潮水連海平,海 上明月共潮生。…江天一色無纖塵,皎皎空中孤月輪。」閨中人、客旅的情懷:「此時相 望不相開,願逐月華流照君。」江水、月華,真的可以紓解相思掛念嗎?然而這詩的文學 價值的高峯,在於詩人哲人式的「問天」遐想。「江畔何人初見月?江月何年初照人?人生 代代無窮已,江月年年祇相似。不知江月待何人,但見長江送流水。」詩人處身這優美的 月夜,出人意表地提出這哲學性,至為深邃的問題。面對歷史長河,人生如滾滾東逝的長 江,無從把握,不許勾留。

一把琵琶,一關樂章,讓我們聯想起詩人對琵琶和音樂的精彩入微描述;又擴闊了 我們對歷史、生命、大江東去、天地悠悠的境界。詩人、音樂家和後人,縱橫時空相交、 相知、共鳴於春、江、花、月、夜的美景中;相忘於磅礴卻滄桑的歷史長河裡。

白居易

元和十年,予左遷九江郡司馬。明年秋,送客湓浦口。聞舟中夜彈琵琶者,聽其音,錚錚然有京都聲;問其 人,本長安倡女。嘗學琵琶於穆、曹二善才。年長色衰,委身為賈人婦。遂命酒使快彈數曲,曲罷憫然。自 敘少小時歡樂事,今漂泊憔悴,轉徙於江湖間。予出官二年,恬然自安;感斯人言,是夕始覺有遷謫意。因 為長句,歌以贈之。凡六百一十二言,命曰《琵琶行》。

潯陽江頭夜送客,楓葉荻花秋瑟瑟。主人下馬客在船,舉酒欲飲無管弦。醉不成歡慘將別,別時茫茫江浸月。 忽聞水上琵琶聲,主人忘歸客不發。尋聲暗問彈者誰?琵琶聲停欲語遲。移船相近邀相見,添酒回燈重開宴。 千呼萬喚始出來,猶抱琵琶半遮面。轉軸撥弦三兩聲,未成曲調先有情。弦弦掩抑聲聲思,似訴平生不得志。 低眉信手續續彈,說盡心中無限事。輕攏慢撚抹複挑,初為《霓裳》後《六幺》。大弦嘈嘈如急雨,小弦切切如私語。 嘈嘈切切錯雜彈,大珠小珠落玉盤。間關鶯語花底滑,幽咽泉流水下灘。水泉冷澀弦凝絕,凝絕不通聲漸歇。 別有幽愁暗恨生,此時無聲勝有聲。銀瓶乍破水漿迸,鐵騎突出刀槍鳴。曲終收撥當心畫,四弦一聲如裂帛。 東船西舫悄無言,唯見江心秋月白。沉吟放撥插弦中,整頓衣裳起斂容。自言本是京城女,家在蝦蟆陵下住。 十三學得琵琶成,名屬教坊第一部。曲罷常教善才服,妝成每被秋娘爐。五陵年少爭纏頭,一曲紅消不知數。 鈿頭銀篦擊節碎,血色羅裙翻酒汙。今年歡笑複明年,秋月春風等閑度。弟走從軍阿姨死,暮去朝來顏色故。 門前冷落車馬稀,老大嫁作商人婦。商人重利輕別離,前月浮梁買茶去。去來江口守空船,繞艙明月江水寒。 夜深忽夢少年事,夢啼妝淚紅闌干。我聞琵琶已歎息,又聞此語重唧唧。同是天涯淪落人,相逢何必曾相識。 我從去年辭帝京,謫居臥病潯陽城。潯陽地僻無音樂,終歲不聞絲竹聲。住近湓江地低濕,黃蘆苦竹繞宅生。 其間旦暮聞何物?杜鵑啼血猿哀鳴。春江花朝秋月夜,往往取酒還獨傾。豈無山歌與姑笛?嘔啞嘲哳難為聽。 今夜聞君琵琶語,如聽仙樂耳暫明。莫辭更坐彈一曲,為君翻作琵琶行。感我此言良久立,卻坐促弦弦轉急。 淒淒不似向前聲,滿座重聞皆掩泣。座中泣下誰最多?江州司馬青衫濕。



張若虛

春江潮水連海平,海上明月共潮生。灩灩隨波千萬里,何處春江無月明!江流宛轉遶芳甸,月照花林皆似霰。 空裏流霜不覺飛,汀上白沙看不見。江天一色無纖塵,皎皎空中孤月輪。江畔何人初見月?江月何年初照人? 人生代代無窮已,江月年年祇相似。不知江月待何人,但見長江送流水。白雲一片去悠悠,青楓浦上不勝愁。 誰家今夜扁舟子?何處相思明月樓?可憐樓上月徘徊,應照離人妝鏡臺。玉戶簾中卷不去,擣衣砧上拂還來。 此時相望不相聞,願逐月華流照君。鴻雁長飛光不度,魚龍潛躍水成文。昨夜閑潭夢落花,可憐春半不還家。 江水流春去欲盡,江潭落月復西斜。斜月沉沉藏海霧。碣石瀟湘無限路。不知乘月幾人歸,落月搖情滿江樹。

#### 1. CMIE/CPD ANNUAL BELFUBN 2016

To align our practice to the regulations laid down by the Hong Kong Academy of Medicine, the Education Committee will call CME/CPD annual return early on 3rd October 2016 this year. The deadline of submission will be advanced to 5th January 2017.

Nil return is NOT required if the CME/CPD requirement is already fulfilled. Fellows should submit CME/CPD annual returns if:

i) there are CME/CPD activities to update or report, and/or

ii) based on existing iCMECPD record, the CME/CPD requirement is not yet fulfilled.

The CME/CPD Annual Return Form can also be downloaded from the "Downloads" area of the College webpage (http://www.hkcpath.org/).

#### 2. CNIE/CIPD PIBOLALE

The Education Committee will no longer include individual Fellow's personal CME/CPD profile in the call-for-annual return notice starting this year. Fellows are required to login to the iCMECPD website (http://www.icmecpd.hk/) to check their own CME/CPD records.

#### 3. "ATTENDANCE BECOBD FOB INDIVIDUAL FELLOW"

To avoid the 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 http://www.hkcpath.org/resources/downloads.



Visit our homepage at: www.hkcpath.org **Dr YIP Chi-pang (葉志鵬醫生)**, retired Consultant Forensic Pathologist who has been known to many forensic pathologists affectionately as "YIP Sir", passed away peacefully on 6 June 2016 at St. Teresa Hospital, Kowloon, Hong Kong. Dr. YIP was born on 13 May 1947. He graduated from the Wah Yan College, Kowloon in 1963, and the Faculty of Medicine of The University of Hong Kong in 1970. He joined the Forensic Pathology Service of the Government of Hong Kong in 1971 and served for 31 years as a Forensic Pathologist till his retirement in 2001. Dr YIP was the Consultant Forensic Pathologist i/c from 1988 to 1995.

# enge

#### **OBITUARY**:

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DR YIP CHI-PANG (葉志鵬醫生)

### Programme of the 25th Annual General Meeting

## 26 November 2016, Saturday

#### Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong

1:00 p.m. – 4:30 p.m.	The 12th Trainee Presentation Session
5:00 p.m. – 5:45 p.m.	The 25th Annual General Meeting
5:45 p.m. – 6:00 p.m.	Reception
6:00 p.m. – 6:50 p.m.	Conferment Ceremony
	Admission of New Fellows and Members and Presentation of Fellowship and Membership Certificates
	Conclusion of Conferment Ceremony
6:50 p.m. – 7:00 p.m	Group Photo of Stage Party
7:00 p.m. – 8:00 p.m.	The 25th T. B. Teoh Foundation Lecture: "Digital Workflow in Anatomical Pathology – On Track to Patient Safety and Beyond" Dr. LEE Kam Cheong Consultant Pathologist Department of Pathology Princess Margaret Hospital Hong Kong
8:00 p.m. – 10:00 p.m.	Chinese Banquet Dinner