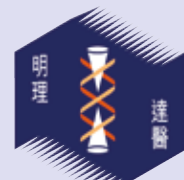


PATHOLOGUE

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



SCIENTIA ILLUMINAT MEDICINAM
香港病理學專科學院

VOLUME 23, ISSUE 1 MAY 2014

Message from the President

First of all, I wish to extend my warmest welcome to all newly admitted Fellows and Members to the family of The Hong Kong College of Pathologists.

Pathology has evolved into a field combining clinical interpretation and application of advanced laboratory techniques. It is estimated nearly 70% of clinical decision is related to medical laboratory test results.

To address the increased expectation of the community, not just patients and relatives, we have to get well prepared. Nowadays, our responsibilities are not confined to diagnosing infection or malignancy efficiently and finding causes of sufferings or death accurately. From a few cells or drops of blood, we need to predict prognosis and guide the use of personalized medicine, to trace the routes of infection, to dissect genetic basis of disease, and to decide whether a person can receive organ from a donor.

To meet the needs of the present and future, the curriculum needs to be updated continuously. Three months' training on molecular pathology has been incorporated into structured training programme of the College.

As consultants to bedside doctors, we also need to let the public understand our work. Since 2013, the College has been working with the Academy on a series of media events to promote public understanding on the training and contribution of our specialties. The International Liaison of Pathology Presidents has announced 5 November 2014 (Wednesday) to be the International Pathology Day in 2014 to enhance interaction between the pathology profession and the public.

As illustrated by the two reports in this newsletter on the College's media actions on the

DR Beauty Treatment Centre incident and the "direct-to-consumer" genetic testing event, the College has been firm and clear in highlighting our views.

Indeed, the views of the College are important to health of the public. Our College representatives have participated in Colorectal Cancer Screening Pilot Programme Task Force and expressed our professional views on biochemical and anatomical pathology tests, which are crucial to the success of the programme. Through the Academy, we have also contributed our suggestions to the Review on Hospital Authority. Our College representative nominated to the Hong Kong Accreditation Service will continue to contribute to enhancement of medical laboratory service in Hong Kong.

I would like to share my vision with you: The Hong Kong College of Pathologists will continue to foster future generations of compassionate pathologists with high professional standard and confidence in joining forces with bedside clinical colleagues of various disciplines to enhance health of our community.

In the future, I also hope that new generation of Fellows will be active to participate and contribute to the work of the College. Your opinions and comments, through email (anycheun@pathology.hku.hk) or phone call 2255-4876, are most welcome.

Prof. CHEUNG Nga Yin, Annie
The President
May 2014



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Please send comments to:
Dr. LAI Sai Chak
(Chief Editor),
Address: Forensic Pathologists'
Office, 6/F Arsenal House West
Wing, Police Headquarters, Arsenal
Street, Wanchai, Hong Kong.
E-mail: sc_lai@dh.gov.hk
Phone: 2860 2461
Fax: 2804 1714

The 22nd Annual General Meeting 2013 and the 22nd T.B. Teoh Foundation Lecture

The 22nd Annual General Meeting (AGM) was held after the 9th Trainee Presentation Session on 30th November, 2013. Prof. CHEUNG Nga Yin Annie, was elected as the new President, succeeding Dr. SUEN Wang Ming Michael. Dr. CHAN Ho Ming was elected as one of the Vice-Presidents to fill the vacancy thus left behind by Prof. CHEUNG. Three new Council Members, Prof. HO Pak Leung, Dr. YUEN Wah Fun Nancy and Dr. YUEN Yuet Ping were elected. We would like to take this opportunity to thank the immediate past Council Members Dr. NG Wing Fung, Dr. LO Yee Chi Janice and Dr. QUE Tak Lun for their contribution to the College.

► *Prof. CHEUNG Nga Yin Annie, President, receiving the College Medallion from Dr. SUEN Wang Ming Michael, immediate Past President. Also on stage were Dr. CHAN Chak Lam Alexander, Registrar, (2nd from left) and Dr. CHAN Kui Fat, Honorary Treasurer (left).*

▼ *The College Council.*





▲ *Guests of honour; Council members, and newly admitted Fellows and Members posing for a group photo after the Conferment Ceremony.*

In the Conferment Ceremony, 9 Fellows and 13 Members were admitted to the College. The honourable guests included Dr. Li Kwok Tung Donald (President of the Hong Kong Academy of Medicine) and Dr. Hon. LEUNG Ka Lau (Member of the Legislative Council of Hong Kong, Medical Functional Constituency). The new College President Prof. CHEUNG Nga Yin Annie shared with the audience the opportunities and threats the College is facing.

▼ *New Fellows receiving certificates from the President*





The 22nd T.B. Teoh Foundation Lecture was delivered by Dr. WONG Kit Fai, Chief of Service and Consultant Haematologist, Department of Pathology, Queen Elizabeth Hospital. In the lecture titled "Chromosomes and Genes: from Bedside to Bench-top", Dr. WONG enlightened the audience on genetic diagnosis in haematological diseases. The guests, senior fellows, new fellows and members enjoyed the subsequent Chinese banquet dinner.

We would like to thank Professor CHIU Wai Kwun Rossa for being the Mistress of Ceremonies in the AGM. We thank Dr. CHUNG Ah Yu Ivy and Dr. CHONG Yeow Kuan Calvin for taking photos during the Trainee Presentation Session, AGM, Conferment Ceremony, T.B. Teoh Foundation Lecture and the dinner. We would also like to express our gratitude towards our College Secretary, Ms. Adrienne YUNG, as well as Ms. Maizie CHAN and Ms. Heidi CHU, for their continuous support in organizing the AGM.

► *Dr. WONG Kit Fai, the 22nd TB Teoh Lecturer, addressing the audience.*

▼ *Pathologists enjoying themselves at the banquet after the AGM.*



**The 23rd Annual General Meeting will be held on
29 November 2014 (Saturday).
Please mark your diaries!**

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THE 9th TRAINEE PRESENTATION SESSION

The 9th Trainee Presentation Session was successfully held on 30th November 2013. Four senior Fellows formed the Judges Panel. They were (in the picture below from left to right) Dr. Jason CC SO, Haematology, Queen Mary Hospital; Dr. Polly WY LAM, Anatomical Pathology, Queen Elizabeth Hospital; Dr. Susanna KP LAU, Clinical Microbiology & Infection, Queen Mary Hospital and Prof. Ching Wan LAM, Chemical Pathology, Queen Mary Hospital.

There were a total of 12 participants from across the disciplines. The number of participants reached a record high this year. This is very encouraging but at the same time poses a challenge to the Education Committee (EC). The Trainee Presentation Session is held on the day of the College's Annual General Meeting in the HKAM Building. Its duration is restricted by the availability of venue and judges. The EC will consider capping the maximum number of participants so that the event can be completed within a period of 3 to 4 hours and each participant can be given adequate time for presentation. The EC will discuss this issue in the coming meetings. The decision will be announced as soon as possible.

Dr. Liz YP YUEN

Organiser, 9th Trainee Presentation Session



▲ Panel of judges



▲ *Organisers, Judges and Participants of the 9th Trainee Presentation Session*

The Winner's Abstract

Detection of germline TP53 mutation in paediatric patients with double cancers

Dr. Pui Kwan CHAK

Anatomical & Cellular Pathology, Prince of Wales Hospital

Abstract

Germline TP53 mutation is the hallmark of Li-Fraumeni Syndrome. The affected individual has positive family cancer history and is predisposed to a wide variety of early-onset cancers. However, germline TP53 mutation can also be detected in cancer patients without a positive family history or not fulfilling the criteria of classical Li-Fraumeni Syndrome. The National Comprehensive Cancer Network has issued the updated guidelines for germline TP53 mutation screening. The guideline acknowledges the expanding spectrum of phenotypes that may be associated with germline TP53 mutation. However, the prevalence of germline TP53 in pediatric patients with double cancers but without apparent positive family history is uncertain. In the present study, we investigated 6 such patients for the germline TP53 mutation by direct sequencing. We detected 3 out of 6 patients harbouring germline TP53 mutation. The results suggested that paediatric patients with double cancers, but without positive family history are also at risk of germline TP53 mutation. Such finding has important implication in familial counseling and patient management. The observation further expands the phenotypes that may be associated with germline TP53 mutation.



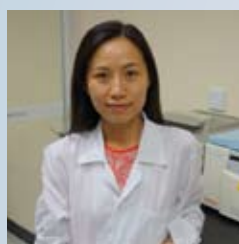
▲ *Dr. Pui Kwan CHAK (left) receiving the winner's trophy from Dr. Janice YC LO (outgoing Chairman of Education Committee) at the AGM.*

TOPICAL UPDATE

Volume 9, Issue 1 January 2014

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

Editorial note: Congenital hypothyroidism is the most common endocrine disease in infants. Through early identification and treatment of affected patients, delays in cognitive and motor development can be effectively prevented. In this topical update, Dr. Liz Yuen reviews the aetiology and shares recent advances in understanding the molecular basis of congenital hypothyroidism. Genetic diagnosis and counselling can be provided to affected families regarding prognosis and recurrence risk. We welcome any feedback or suggestions. Please direct them to Dr. Poon Wing Tat (e-mail: poonwt@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.



Dr. YUEN Yuet Ping
Department of Chemical Pathology
Prince of Wales Hospital

Thyroid Dyshormonogenesis

CH ----- Congenital hypothyroidism	TG ----- Thyroglobulin
PIOD ----- Partial iodide organification defect	TIOD ----- Total iodide organification defect
T3 ----- 3,5,3'-Tri-iodothyronine	TPO ----- Thyroid peroxidase
T4 ----- 3,5,3',5'-Tetra-iodothyronine or thyroxine	TSH ----- Thyroid stimulating hormone

Introduction

Congenital hypothyroidism (CH) is an important preventable cause of mental retardation. To prevent irreversible brain damages caused by hypothyroidism, sufficient doses of thyroxine should be started within a few weeks after birth.⁽¹⁾ Since neonates with CH have no obvious or minimal clinical manifestations, biochemical screening in the newborn period has become the best public health strategy for early detection of affected neonates. In Hong Kong, a territory-wide screening programme for CH was started in 1984.⁽²⁾ Cord blood samples are collected immediately after birth for measurement of thyroid stimulating hormone (TSH) by a single laboratory dedicated for newborn screening. The incidence of CH in Hong Kong was reported to be 1 in 2,404, which is comparable to that in other populations.⁽²⁻⁶⁾

Causes of congenital hypothyroidism

The aetiologies of CH are summarized in Table 1.⁽⁷⁾ Approximately 80 - 85% of CH are caused by thyroid

dysgenesis, which is a group of congenital disorders of thyroid gland development or migration. Affected patients may have complete thyroid gland aplasia, hypoplasia or ectopic glands. The large majority of thyroid dysgenesis cases are sporadic and only about 5% has a genetic basis.^(8,9) Thyroid dyshormonogenesis describes a group of inherited disorders which affect the biochemical pathway of thyroid hormone synthesis. These disorders collectively account for 10 - 15% of CH cases. Approximately 1/4 of patients with CH in Hong Kong have some forms of thyroid dyshormonogenesis.⁽¹⁰⁾ Some neonates detected by newborn screening program have transient instead of permanent CH. Although this subgroup of patients does not require life-long thyroid hormone replacement, early identification and treatment in early years of life is equally important.⁽¹¹⁾ The time course of recovery of the hypothalamic-pituitary-thyroid axis in patients with transient CH depends on the underlying cause. Although most of the transient CH are due to acquired conditions such as iodine deficiency or maternal transfer of autoantibodies, a few genetic causes have been described.^(11,12)

Primary congenital hypothyroidism

- Thyroid dysgenesis (ectopic, aplasia, hypoplasia)
- Thyroid dyshormonogenesis
- Resistance to TSH binding or signaling

Secondary congenital hypothyroidism

- Isolated TSH deficiency
- Congenital hypopituitarism

Peripheral congenital hypothyroidism

- Thyroid hormone transport defect
- Thyroid hormone metabolism defect
- Thyroid hormone resistance

Transient congenital hypothyroidism

- Prematurity
- Maternal or neonatal excess iodine exposure
- Maternal or neonatal iodine deficiency
- Maternal antithyroid drugs
- Maternal TSH-receptor blocking antibodies (TRB-Ab)
- Thyroid dyshormonogenesis caused by DUOX2 or DUOXA2 mutations
- Congenital hepatic haemangiomas
- Protein-losing nephrosis

▲ *Table 1. Aetiology of congenital hypothyroidism (modified from reference 7)*

Thyroid dyshormonogenesis describes a group of inherited disorders which affect the biochemical pathway of thyroid hormone synthesis. These disorders collectively account for 10 - 15% of CH cases.

Biochemistry of thyroid hormone synthesis and their defects

The basic components required for thyroid hormone synthesis are specific tyrosyl residues on thyroglobulin (TG, encoded by the TG gene) and iodine. Iodide ions in the circulation are taken up by the thyroid gland via the sodium-iodide symporter (NIS, encoded by the SLC5A5 gene) located at the basolateral membrane of the thyroid follicular cells. The iodide ions are then concentrated in the colloid by passing through the pendrin protein (encoded by the SLC26A4 gene) on the apical side of the follicular cell membrane. Inside the follicular lumen (i.e. colloid), iodide ions are first oxidized to iodine radicals and then incorporated to tyrosyl residues on TG to form moniodotyrosine (MIT) or di-iodotyrosine (DIT). Coupling of one MIT and one DIT or two DITs forms the final active thyroid hormones 3,5,3'-triiodothyronine (T3) and 3,5,3',5'-tetraiodothyronine (T4), respectively. The iodide organification and iodotyrosine coupling steps are catalyzed by the enzyme thyroid peroxidase (TPO, encoded by the TPO gene) in the presence of hydrogen peroxide

which acts as the ultimate electron acceptor. The thyroid hydrogen peroxide-generating system is composed of two dual oxidase enzymes DUOX1 and DUOX2 (encoded by the DUOX1 and DUOX2 genes, respectively) and their corresponding maturation factors DUOXA1 and DUOXA2 (encoded by the DUOXA1 and DUOXA2 genes, respectively). DUOX2 is preferentially expressed in human thyroid tissue.⁽¹³⁾ Subsequent evidence demonstrated that DUOX2/DUOXA2 is the predominant enzyme system in the thyroid while the exact role of DUOX1/DUOXA1 in the thyroid remains unknown.⁽¹¹⁾ Under TSH stimulation, TG is endocytosed into the follicular cells and metabolized by lysosomal enzymes. This process releases T4 and T3, which diffuse through cellular membrane and enter the thyroidal circulation. Iodide ions bound to DIT and MIT are recycled by the enzyme iodotyrosine deiodinase (encoded by the IYD gene) for further thyroid hormone synthesis.

Defects in any component of the above described thyroid hormone synthetic pathway can cause thyroid dyshormonogenesis (Table 2).⁽¹⁴⁾ Except the case of NIS defect caused by SLC5A5 mutations, patients with thyroid dyshormonogenesis are characterized by a large orthotopic thyroid gland with increased radionuclide uptake.⁽⁷⁾ Perchlorate discharge test, which involves the administration of radioactive iodine followed by perchlorate and serial monitoring of radioactivity of the thyroid gland, is the conventional method used to sub-classify patients with thyroid dyshormonogenesis. In normal subjects, less than 10% of the radioactive iodine is discharged after the administration of perchlorate. Patients with TPO mutations are characterized by a rapid and almost complete release of radioactive iodide in perchlorate discharge test (i.e. total iodide organification defect, TIOD). Both TIOD and partial iodide organification defect (PIOD) have been described in patients with DUOX2 mutations.⁽¹¹⁾ Defects in SLC26A4 (Pendred syndrome) and DUOXA2 are associated with PIOD.⁽¹¹⁾

In the following parts, more details about the 5 nonsyndromic forms of thyroid dyshormonogenesis will be described, i.e. sodiumiodide symporter defect caused by SLC5A5 mutations, thyroglobulin deficiency caused by TG mutations, thyroid peroxidase deficiency caused by TPO mutations, hydrogen peroxide-generation defect caused by DUOX2 or DUOXA2 mutations and iodotyrosine deiodinase deficiency caused by IYD mutations. Readers may refer to the recent reviews by Choi et al. and Bizhanova and Kopp for details about the molecular basis of Pendred syndrome and its association with hypothyroidism.^(15,16)

Perchlorate discharge test, which involves the administration of radioactive iodine followed by perchlorate and serial monitoring of radioactivity of the thyroid gland, is the conventional method used to sub-classify patients with thyroid dyshormonogenesis.

Sodium-iodide symporter

The first case of CH caused by a homozygous mutation in the SLC5A5 gene, which encodes the sodium iodide symporter (NIS), was described in 1997.⁽¹⁷⁾ Patients with NIS defect are characterized by a normal orthotopic thyroid gland with no to minimal radionuclide uptake. Therefore, if ultrasonography is not routinely performed, these patients can be easily misdiagnosed to have thyroid aplasia. The phenotypes of NIS defects are broad with some patients present at birth while others present during childhood or even in adulthood.^(18,19) Therefore, patients with NIS defects may not be detected by newborn screening. Iodine supply is a known factor which influences the clinical manifestations of patients with NIS defects. Iodide supplement is as effective as thyroxine replacement in treating these patients.⁽¹⁹⁾

Patients with NIS defect are characterized by a normal orthotopic thyroid gland with no to minimal radionuclide uptake.

Thyroid peroxidase deficiency

Thyroid peroxidase (TPO) is the enzyme which catalyses the iodination of tyrosyl residues on TG and the coupling of iodotyrosines to form thyroid hormones. TPO mutations account for approximately 40% of thyroid dyshormonogenesis in various populations.⁽²⁰⁻²²⁾ Previous studies in Taiwanese patients showed that TPO defect was the most common form of thyroid dyshormonogenesis and many patients were either homozygous or heterozygous for the insertion mutation c.2268dupT.^(22,23) Haplotype analysis in eight patients who were homozygous for c.2268dupT strongly suggested that it was a founder mutation in Taiwan.⁽²²⁾ In addition, heterozygosity for c.2268dupT have been demonstrated to be an important susceptibility factor in Taiwanese patients with transient CH.⁽²⁴⁾

Thyroglobulin deficiency

Thyroglobulin (TG) is the most abundant protein

in the matrix of thyroid follicles. It provides tyrosyl residues for synthesis of thyroid hormones and serves as a reservoir of thyroid hormones. Therefore, mutations in the TG gene that result in defective synthesis or metabolism of TG can lead to CH.^(25,26) Previous studies in Taiwanese patients showed that TG defects accounted for 38% of thyroid dyshormonogenesis.^(22,27) Patients with TG defects have an orthotopic thyroid gland with normal to raised radionuclide uptake and very low serum TG concentrations. To obtain meaningful result, sample for TG measurement should be collected before commencement of thyroxine replacement.

Defects in the generation of hydrogen peroxide DUOX2

Mutation in DUOX2 is now a well-known cause of CH.^(11,28) However, the exact genotype-phenotype correlation, especially the relation between the severity of hypothyroidism and number of DUOX2 mutations, remains unresolved. The first report that described DUOX2 mutations in patients with CH were published in 2002 by a group from the Netherlands.⁽²⁸⁾ Among 45 patients with permanent CH and TIOD, one was found to harbour homozygous DUOX2 mutations. In addition, in 3 out of 8 patients with transient CH and PIOD, heterozygous DUOX2 mutations were identified. All four DUOX2 mutations described in this study were predicted to create premature stop codons and abolish the hydrogen peroxide-generating domain of the DUOX2 enzyme. This group of investigators for the first time demonstrate a genetic basis for transient CH and postulates that affected patients only develop biochemical and clinical abnormalities at periods of high thyroxine requirement e.g. early infancy, puberty and pregnancy. Therefore, they suggest that long-term follow-up of patients with monoallelic DUOX2 mutations may be necessary as these patients are prone to develop recurrent hypothyroidism later in life.⁽²⁸⁾

Subsequent studies showed that the inheritance patterns of DUOX2 mutations is more complex than that proposed by previous studies.^(11,29,30) In 2008, Maruo and co-workers described biallelic DUOX2 mutations in eight Japanese patients (2 familial and 2 sporadic) with transient CH. In particular, a family with 4 affected siblings affected by transient CH were found to be compound heterozygous for 2 DUOX2 frameshift mutations (p.L479SfsX2 and p.K628RfsX10). Both mutations were predicted to result in total loss of DUOX2 activity. Some degree of intrafamilial phenotypic variation was also observed in this family. The youngest affected sibling had elevated TSH but normal free T4 at initial evaluation. His TSH gradually returned to normal at 2 months of age without any thyroxine

supplementation. Furthermore, the only unaffected sibling with heterozygous p.L479SfsX2 mutation had normal TSH in newborn screening and did not develop transient CH.

The natural course and severity of hypothyroidism not only depends on the number DUOX2 mutations present in the genome, other genetic (e.g. DUOX1) and environmental factors (e.g. supply of iodine) may also play a role.

Based on the reported cases with DUOX2 mutations, it is obvious that the genotype-phenotype correlation is not straightforward. Patients with biallelic DUOX2 mutations may develop either permanent or transient CH, while patients with monoallelic DUOX2 mutations may or may not develop hypothyroidism in the neonatal period. The natural course and severity of hypothyroidism not only depends on the number DUOX2 mutations present in the genome, other genetic (e.g. DUOX1) and environmental factors (e.g. supply of iodine) may also play a role.^(11,31)

DUOXA2

Dual oxidase maturation factor 2 (DUOXA2) plays a crucial role in the maturation and translocation of DUOX2 from the endoplasmic reticulum to the plasma membrane.⁽³²⁾ DUOXA2 was first described as a cause of CH in 2008.⁽³³⁾ In this study, 10 Caucasian patients and one Chinese patient with CH and PIOD were recruited. Interestingly, only in the Chinese patient but not the Caucasian patients, a homozygous nonsense DUOXA2 mutation p.Tyr246* was detected. Follow-up study of this Chinese patient at 7 years of age, one month after cessation of thyroxine replacement, showed a slight elevation of TSH (5.0 mU/L, reference range 0.4 – 4.0) and normal free T4. Further studies detected one heterozygous carrier of p.Tyr246* among 92 Chinese controls, and none in 89 Caucasians and 41 Japanese controls.⁽³³⁾ Results of this study demonstrated that biallelic DUOXA2 mutations is a cause of mild CH. They also suggested that p.Tyr246* in the DUOXA2 gene was a common mutation among the Chinese population. A recent study from the Mainland China found one out of 47 CH patients with compound heterozygous DUOXA2 mutations, and one of the detected mutation was p.Tyr246*.⁽³⁴⁾ This result provides further evidence that DUOXA2 mutations, p.Tyr246* in particular, is relatively common among the Chinese population.

There is evidence that the DUOXA2 mutations, p.Tyr246* in particular, is relatively common among the Chinese population.

Iodotyrosine deiodinase deficiency

Iodotyrosine deiodinase is the enzyme responsible for recycling of intra-thyroidal iodide from MIT and DIT. The clinical severity of iodotyrosine deiodinase deficiency is highly heterogeneous, but in contrast to other thyroid dyshormonogenesis, affected patients are typically missed by newborn screening.⁽³⁵⁾ Therefore, a significant proportion of affected patients were identified late and thus developed mental and growth retardation. Iodotyrosine deiodinase is encoded by the IYD gene and the first report of IYD mutations in hypothyroid patients was published in 2008.⁽³⁶⁾ Although most reported cases appear to inherit the disease in an autosomal recessive manner, patients carrying heterozygous IYD mutations, who developed goiter and hypothyroidism, have also been described.⁽³⁷⁾ Therefore, it is speculated that the phenotypes of iodotyrosine deiodinase deficiency are influenced by environmental factors (e.g. iodine supply) and possibly other genetic factors. The biochemical hallmark of iodotyrosine deiodinase deficiency is an excessive excretion of MIT and DIT in urine. In some instances, this may be the only clue to diagnosis.⁽³⁸⁾ However, this biochemical test is not readily available in local laboratories.

The phenotypes of iodotyrosine deiodinase deficiency are influenced by environmental factors (e.g. iodine supply) and possibly other genetic factors.

Conclusion

Congenital hypothyroidism is the most common endocrine disease in infants. Like other developed countries, Hong Kong has a well-structured newborn screening programme in place with over 99% coverage.⁽²⁾ Through early identification and treatment of affected patients, delays in cognitive and motor development can be effectively prevented. However, little clinical attention is paid to the aetiology of CH despite all the recent advances in molecular biology. In most paediatric centers, other than confirmatory serum TSH and free T4 concentrations, only

minimal additional investigation (e.g. thyroid radionuclide scan) is done to delineate the underlying cause of CH.

Recent advances in molecular biology have greatly improved our knowledge and understanding on each individual form of thyroid dysmorphogenesis. With a genetic diagnosis, precise counselling can be provided to affected families regarding prognosis and recurrence risk.⁽³⁹⁾

With a genetic diagnosis, precise counselling can be provided to affected families regarding prognosis and recurrence risk.

In particular, female patients with DUOX2 mutations may be at risk of recurrent hypothyroidism during pregnancy, which requires thyroxine replacement to prevent adverse neurodevelopmental outcome in the fetus. In addition, some forms of thyroid dysmorphogenesis such as NIS defect and iodotyrosine deiodinase deficiency may

be beneficial to iodide supplementation. Furthermore, a genetic diagnosis facilitates the identification of asymptomatic family members who are at risk of developing hypothyroidism later in life.

Addition of thyroid ultrasonography and measurement of TG into the local routine evaluation protocol of neonates with abnormal newborn screening results helps stratify them for appropriate genetic testing. Previous studies have shown that several hot spot mutations are present in the Chinese population, e.g. c.2268dupT in the TPO gene and p.Tyr246* in the DUOX2 gene. Further studies are required to confirm whether the local Chinese patients with CH share a similar genetic basis.

Studies have shown that several hot spot mutations are present in the Chinese population, e.g. c.2268dupT in the TPO gene and p.Tyr246* in the DUOX2 gene.

Gene	Protein product	Chromosomal locus	Defects	Perchlorate discharge test
SLC5A5	Sodium-iodide symporter	19p13.11	Iodide trapping defect	Normal
SLC26A4	Pendrin	7q22.3	Defect in apical iodide efflux / Pendred syndrome	PIOD
TG	Thyroglobulin	8q24.22	Defect in synthesis of thyroglobulin	PIOD
TPO	Thyroid peroxidase	2p25.3	Defect in thyroid peroxidase activity	TIOD
DUOX2	Dual oxidase 2	15q21.1	Defect in hydrogen peroxide generation	PIOD or TIOD
DUOX2	Dual oxidase maturation factor 2	15q21.1	Defect in hydrogen peroxide generation	PIOD
IYD	Iodotyrosine deiodinase	6q25.1	Defect in recycling of intrathyroidal iodide	Normal

▲ Table 2. Genes associated with thyroid dysmorphogenesis

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College Takes the Lead in Public Issues

College urges LEGCO to strengthen regulation on medical laboratories

In response to the DR Beauty Treatment Centre incident in 2012, the Hong Kong Government formed a Steering Committee on Review of the Regulation of Private Healthcare Facilities. There are several working groups under this Steering Committee, and the Working Group on Differentiation between Medical Procedures and Beauty Services recently published their report which was discussed in the LEGCO Panel on Health Services Special Meeting on 23 December 2013. Our College was invited to express our view. A letter was sent to the panel and Dr. WONG Lap Gate, Michael represented the College in the meeting. The College expressed concern on the omission of recommendations on regulating medical laboratories by the Working Group, and the laxity of regulation on medical laboratories in many respects at the moment. The College reiterated the importance of stipulating the role of pathologists in the operation of a medical laboratory and urged the Panel to take a closer look at the need to strengthen regulation on medical laboratories along this line. The College's view has been reported by media. The webcast of the meeting is accessible at <http://goo.gl/YchKJx>.

College cautions the public against “direct-to-consumer” genetic testing

In November 2013, US Food and Drug Administration (FDA) stopped a Google funded company called 23andMe from providing direct-to-consumer genetic testing. Previously consumers just needed to spit their saliva into a container and mail it back to 23andMe, and they could download the results from the company website. In February 2014, the China Food and Drug Administration (CFDA) and the National Health and Family Planning Commission (NHFPC) also jointly issued an administrative notice that regulatory clearance and approval must be obtained before such genetic testing services are launched, marketed or put to clinical uses. The notice further ordered that all existing service which has not been approved be stopped immediately. In response to these two events, the College issued a press release statement on 21 March 2014 warning the public that direct-to-consumer testing services are potentially dangerous and they should seek advice from doctors experienced in genetic counselling and testing. The College also advised doctors to request genetic testing from properly accredited laboratories with pathologists of the appropriate specialties, and urged the Food and Health Bureau to seriously consider regulating direct-to-consumer genetic testing and related laboratories. Dr. MA Shiu Kwan, Edmond, representing the College, was interviewed by several media agencies.

Out of the Whitecoat:

Bridge

by Dr. LO Yee Chi Janice, Public Health Laboratory Services Branch, CHP, DH.

I am nowhere near being proficient in playing bridge. I am just addicted to the game, to the extent that I take leave from work one morning each week to play.

I first came across the game when I was a first year medical student, when bridge was one of the events in the Medic Festival. According to the regulations of the Festival, just by enrolling one pair of players in the game, one point would be awarded to the Class. It was the first time that I ever played bridge, and it was already in the setting of a competition! Well,

my partner did give me a basic crash course beforehand. I was glad our pair did not come last! Since that time, I did not have any opportunity to play bridge. Fast forward 25 years, I rediscovered the game in a local club setting, and since then I have been totally fascinated, now in my third year of playing. Playing bridge demands concentration, observation, memory, collaboration, analytical power, and decision making under the pressure of time – virtually a simulation of life itself.

The game of bridge requires four players comprising two pairs, oneself and partner sitting opposite each other, and another pair of opponents in partnership. The game consists of two main sequential parts: bidding and playing. Although there are strict rules for the game, and also established conventions during both bidding and playing, there are at the same time endless flexibility, demanding logical deductions to give best results for the partnership.

Bidding

Each player, holding 13 cards, needs to carefully assess one's cards, or "hand", with the aim of each player participating in the bidding process to arrive at a contract for the partnership in the best suit (spades, hearts, diamonds or clubs) and level (taking as many "tricks", out of a total of 13 in each game, as possible). The bidding process enables exchange of information between each pair of partners, while in the process, opponents will also be able obtain information to assist in their own bidding. Even when one player has very good cards, the partner may have a dismal hand, and it might be futile to bid to high levels. On the

Card	High Card Points
Ace	Four
King	Three
Queen	Two
Jack	One
Ten to two	Zero

▲ Table 1



▲ The club where I rediscovered bridge

other hand, when both partners have strong hands, it is essential to reach the most optimal contract by effective communication during the bidding process, such that opportunities for bonus scores by making "game" (nine to eleven tricks depending on the suit) or even "slam" (twelve to thirteen tricks) will not be missed. Occasionally, very weak hand in terms of the number of high cards (see Table 1 for the most widely

used convention) between the partnership might still make “game”, when the distribution of cards in the suits is favourable. In life, it is not uncommon to forget that we have partners and that we are not lone players. We need to communicate to bring out the best for the common good. Furthermore, we should make comprehensive considerations using available information to take calculated risks, in order not to miss opportunities that come our way

Playing

After the contract is reached, the playing starts. The first card is played, or “led”, by the defender sitting to the left of the declarer of the contract. The declarer’s partner is the “dummy”, who, after the first card is led, lays down the cards for all to see, while all the playing is done by the declarer on behalf of the pair. Leading the optimum card by the defender is often instrumental in either enabling or preventing the declarer to or from making the contract. All the information observed during the bidding needs to be carefully analysed when deciding on the lead card, especially length or shortage of any suit in the declarer’s and in one’s partner’s hand. Each trick comprises four cards in one round of play, and is “taken” by the player with the highest card of the suit led by the first player. Each player is mandated to “follow suit” if one has cards in the led suit. In a contract with a “trump suit”, in case any player does not have any card in the led non-trump suit, one can play a card in the trump suit, which wins over cards in all other suits, or one can “discard” a card in another non-trump suit. During playing, there are numerous considerations: whether to play a high card to win the trick or to “duck” and hold up a high card till later tricks, to trump or to discard when one does not have any card in the led suit, what card to lead next when one has won a trick, etc. All these decisions are made based on the cards that have already been played so far, and what cards are believed to be left in opponents’ and partner’s hand. Memory and keen observation are called into play to make the best decision. There are many analogies to daily life and work. Refraining from immediate gain might lead to future benefits such as collaboration opportunities and improved relationships. Taking one suboptimal step may lead to regrettable chain reactions of events.

Afterthoughts

In bridge, like life, the variations are endless, such that there is no room for rigid application of fixed rules. Even the expert among experts is continuing to learn and encounter new hands, let alone myself as a semi-novice. Nevertheless, bridge is also a game of probability and chance, and not purely depending on skill. Ultimately, the requirement for intense concentration during bridge playing enables me to cast all worries of life aside for a few hours a week. The exhilaration of playing is the antidote to life stress, and hence reason for my addiction!



▲ The author (facing camera) playing bridge

Fellows' Laurels

Professor Dennis Lo receives King Faisal International Prize



▲ *Prof. Dennis Lo receiving the King Faisal International Prize for Medicine for 2014 from His Royal Highness Prince Salman bin Abdulaziz Al Saud, Crown Prince of Saudi Arabia.*

Professor Dennis Lo of The Chinese University of Hong Kong has just received the King Faisal International Prize (<http://www.kff.com/EN01/KFIP/KFIPIndex.html>) for Medicine for 2014. This is a prestigious annual award sponsored by King Faisal Foundation presented to “dedicated men and women whose contributions make a positive difference”. The foundation awards prizes in five categories: Service to Islam, Islamic Studies, Arabic Language and Literature, Science, and Medicine. Professor Lo was awarded the prize for his contribution to non-invasive prenatal diagnosis.

Professor Annie Cheung awarded Croucher Senior Medical Research Fellowship

The Croucher Foundation held the presentation ceremony of its prestigious Research Fellowships 2014/15 on April 3, 2014. Professor Cheung Nga Yin Annie, President of the HKCPath, was awarded the “Croucher Senior Medical Research Fellowship”. Professor Annie Cheung has made significant contributions to gynaecological research. Her research areas include oncogenic signal pathways and stem cell transcription factors in ovarian and endometrial cancers as well as gestational trophoblastic disease. Professor Cheung aims at investigating further the role of NANOG to combat against chemoresistance and enhance the survival of ovarian cancer patients. The Croucher Senior Research Fellowships scheme is awarded to local academics that have excelled in scientific research work.



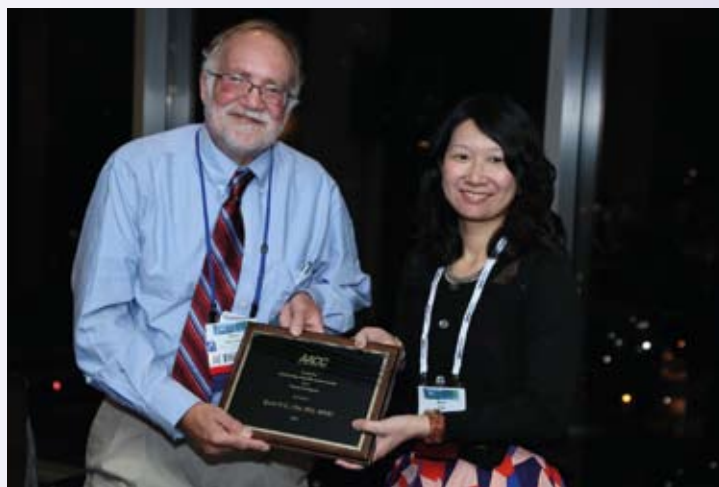
▲ *Prof. Cheung Nga Yin Annie receiving the award from Mrs Carrie Lam Cheng Yuet-Ngor, Chief Secretary for Administration of the HKSAR Government.*

Double honours for Professor Rossa Chiu

Professor Rossa Chiu, Department of Chemical Pathology, Chinese University of Hong Kong received the Science & Technology Award for Chinese Youth and the Outstanding Scientific Achievements by a Young Investigator from the American Association for Clinical Chemistry (AACC) in 2013.

The conferment ceremony of the Science & Technology Award for Chinese Youth took place at the Great Hall of the People in Beijing on 16 December 2013. Professor Chiu was awarded for her work in non-invasive prenatal diagnosis. The award is jointly organized by the Organization Department of the Communist Party of China, the Ministry of Human Resources and Social Security, and the China Association for Science and Technology, and recognizes young science and technology talent who made contributions to economic and social progress, and innovation in science and technology.

Professor Chiu is the first ever scientist from an Asian institution to receive the Award for Outstanding Scientific Achievements by a Young Investigator from the American Association for Clinical Chemistry (AACC), which recognizes her significant contributions on non-invasive prenatal diagnosis. The award was set up in 1976, with one awardee each year, to recognize the exceptional scientific achievements early in his or her career.



▲ Professor Rossa Chiu received the Science & Technology Award for Chinese Youth (left) and the Outstanding Scientific Achievements by a Young Investigator from the American Association for Clinical Chemistry (right).

EXAMINATION DATE:

College examination (written) for all disciplines will be held on
7-July-2014 (Monday).

PLEASE MARK YOU DIARIES!

Announcement from the Education Committee

CME/CPD Annual Return goes green

With effect from the 2014 – 2016 CME/CPD cycle, we will adopt a GO-GREEN POLICY for calling CME/CPD Annual Returns.

At the end of each cycle-year, we will call for CME/CPD Annual Returns by both email and post.

The email will contain:

1. A Fellow's iCMECPD Summary, which is generated from the iCMECPD database maintained by the Hong Kong Academy of Medicine.
2. The CME/CPD Annual Return Form.

The post will contain the iCMECPD Summary only. The CME/CPD Annual Return Form can be downloaded from the "Downloads" area of the College webpage (<http://www.hkcpath.org/>). Fellows are highly encouraged to return the completed CME/CPD Annual Return Form to the College Secretary by email (hkcpath@hkam.org.hk). If there is any problem in getting a softcopy of the CME/CPD Annual Return Form, please contact the College Secretary by email (hkcpath@hkam.org.hk).

It is the responsibility of a Fellow to update the College his/her email address and postal address whenever it is changed. To update your contact details, please contact the Registrar of the College.

Reminders on CME/CPD Annual Return

1. Fellows can use the CME/CPD Annual Return Form:
 - a. To update "Participation as an attendee" (PP) and "Chairing/Presenting at FCAA" (AP) activities that are not captured by the iCMECPD database.
 - b. To report CME/CPD activities of the non-PP/AP categories, e.g. "Self Study" (SS) and "Publications and Development of CME/CPD or Knowledge-Translation Material" (PB).
2. Fellows should submit their CME/CPD Annual Return Forms year by year. E.g. CME/CPD activities completed in year 2013 should be submitted using the CME/CPD Annual Return Form 2013. If the CME/CPD Annual Return Form 2014 is used to report CME/CPD activities completed in year 2013, this would be considered a late return and the Fellow will be charged an administrative fee of HK\$500. The College will not process late CME/CPD Annual Return Forms until the administrative fee is received.
3. Fellows are not required to submit the CME/CPD Annual Return Form if:
 - a. There is nothing to update or report, and

- b. The CME/CPD requirement is fulfilled (based on the iCMECPD Summary generated from the iCMECPD database).
4. If a Fellow decides to submit a CME/CPD Annual Return Form, it must be done before the deadline stated in our announcement. If CME/CPD Annual Return Forms are received beyond the deadline, the Fellows will be charged an administrative fee of HK\$500. The College will not process late CME/CPD Annual Return Forms until the administrative fee is received.
5. Fellows are advised to monitor their CME/CPD points in the iCMECPD database, which is accessible through the Hong Kong Academy of Medicine webpage (<http://www.icmecpd.hk/>).
6. To ensure effective communication, Fellows are reminded to update the Registrar of the College of their contact postal and email addresses whenever there are changes.

NEW College CME/CPD Scheme for 2014-2016 CME/CPD Cycle

The new College CME/CPD Scheme for 2014 – 2016 CME/CPD Cycle is now available for download in the College webpage (<http://www.hkcpath.org/>).

We highlight some important changes here for your easy reference. The revisions were made in accordance with the new guidelines from the Hong Kong Academy of Medicine.

1. “Undergraduate and Postgraduate Teaching” (UT) (5.4) was introduced as a new category of CME/CPD activities. Pre-approved undergraduate and postgraduate teaching may be accepted as a form of CME/CPD, subject to a quality assurance process. 1 CME/CPD point will be awarded per session of undergraduate and postgraduate teaching, irrespective of duration. A maximum of 5 CME/CPD points in each three-year cycle may be accredited for UT.
2. The category “Quality Assurance, Audits, and Activities for Improvement of Patient/Medical Care” (QA) was split into two categories: “Quality Assurance and Audits” (QA), and “Activities for Improvement of Patient/Medical Care” (IC).
3. For “Quality Assurance and Audits” (QA) (5.8), Fellows are strongly recommended to accrue at least 5 CME/CPD points in each three-year cycle.
4. For “Activities for Improvement of Patient/Medical Care” (IC) (5.9), up to one CME/CPD point is awarded for each hour of participation in College pre-approved learning/activities that enhances the ability to practice medicine both as an individual doctor and as part of the health care team eventually leading to improvement of patient management and medical care, e.g. clinical and other skills, laboratory learning, simulator and virtual reality learning, patient safety enhancement programme. A maximum of 10 CME/CPD points in each three-year cycle may be accredited for IC.
5. The maximum points in each 3-year cycle for the category “Research and Development of New Technologies and Services” (RD) (5.6) was revised from 20 to 10 points.

Announcement from the Training and Examinations Committee

TRAINING REQUIREMENT REGARDING PRESENTATIONS IN CONFERENCES (This requirement is mandatory and applies to all trainees of all disciplines registered on or after 16 October 2008.)

Trainees are required to make two presentations, which can be either on-stage or poster presentation, within their six years of recognised training. The presentation should be at local or overseas conference endorsed by the Training and Examinations Committee of the College. At least one of the presentations must be at the Trainee Presentation Sessions or conferences organised by the College.

The non-College organised meetings for trainee presentations can be:

Educational activities arranged by (a) organisers pre-approved by the Education Committee (refer to Category A, CME/CPD Pre-approval list 1, Education Committee, The Hong Kong College of Pathologists at http://www.hkcpath.org/CME/Preapproval%20List_1.20140307.pdf) or (b) the following:

For trainee in Anatomical Pathology only

- Divisions of International Academy of Pathology (IAP), including Hong Kong division (HKIAP)
- Hong Kong Society of Cytology (HKSC) (Annual General Meeting only)
- Japanese Society of Pathology

For trainee in Chemical Pathology only

- Hong Kong Society of Clinical Chemistry (HKSCC)

For trainee in Clinical Microbiology & Infection only

- Asia Pacific Foundation for Infectious Diseases, Asia

For trainee in Immunology only
Immunology (International)

- American College of Allergy, Asthma and Immunology
- American Society of Clinical Pathology
- Association for Molecular Pathology
- Australasian Society for Immunology
- British Society for Allergy and Clinical Immunology
- Canadian Society for Immunology
- Canadian Society of Allergy and Clinical Immunology
- College of American Pathologists
- European Federation of Immunological Societies
- International Histocompatibility and Immunogenetics Workshop
- International Society for Cellular Therapy
- International Society for Stem Cell Research
- International Union of Immunological Societies
- Pan American Group for Immunodeficiencies
- New Zealand Society of Immunology

Immunology (Local)

- Hong Kong Society of Immunology
- Hong Kong Society of Histocompatibility and Immunogenetics

For trainee in Haematology only
Haematology (International)

- American College of Medical Genetics and Genomics
- American Society of Clinical Pathology
- Association for Molecular Pathology
- Australasian Society of Thrombosis and Haemostasis
- College of American Pathologists
- Cord Blood Symposium
- European Society of Human Genetics
- International Society for Cellular Therapy
- International Society for Stem Cell Research
- International Society of Haematology Asia-Pacific Division
- International Society of Laboratory Haematology
- World Congress of World Federation of Haemophilia

Haematology (Local)

- Hong Kong Society of Haematology
- Hong Kong Association of Blood Transfusion and Haematology

Presentations in occasions other than the aforementioned meetings require approval by the Training and Examinations Committee.