NEWSLETTER OF THE HONG KONG COLLEGE OF PATHOLOGISTS

PATHOLOGUE

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

THE HONG KONG COLLEGE OF PATHOLOGISTS
明理 達醫
SCIENTIA ILLUMINAT MEDICINAM
香港病理學專科學院

VOLUME 27, ISSUE 1 JUNE 2018

Message from the President

The Year of 2018 would be a year of celebration as our College has had a very good start!

After months of deliberation and negotiation in the Genetics and Genomics Taskforce, the Training and Examinations Committee as well as the College Council, various pathology specialties including Anatomical Pathology, Chemical Pathology, Haematology and Immunology have finally come to a consensus on the draft training programme for Genetic and Genomic Pathology. On 17 January 2018, the College held an Open Forum to introduce the background and the draft training programme to all Fellows and to receive comments and suggestions from them. It turned out to be a success! With the blessings from our Fellows, the Genetic and Genomic Pathology training programme was approved at one of the Hong Kong Academy of Medicine's Council Meetings on 12 April 2018. It would be a 2-year post-fellowship training programme with knowledge-based, cross-college and specialty-based components. This new Genetic and Genomic Pathology programme will be implemented within 24 months of the date of the Academy's approval. To accommodate the changes, the College has also updated all the fellowship training programmes, which again were endorsed at the Academy's Council Meeting on 15 March 2018.

The College has recently established a Young Fellows' Chapter to encourage our younger generations to increase their participation in College activities. During their participation, various generations of Fellows can sit down together and exchange their views and opinions. In addition, one of the Young Fellows, Dr. Elaine Au, would like to share a Topical Update on immune-mediated demyelinating disease.

To celebrate the ILPP(International Liaison of Pathology Presidents) International Pathology Day 2017, and to promote the image of Pathologists to the public, the College organised a workshop at the Prince of Wales Hospital to receive over 100 senior secondary school students to enjoy some interactive laboratory experiments and demonstrations.

Lastly, Dr. NG Wai Fu would like to share his hobby that can make him young and fit!

Dr. CHAN Ho Ming
June 2018

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Please send comments to:
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A Letter to The Honorable Mr. CHAN Han Pan, Chairman of the Bills Committee on Private Healthcare Facilities Bill

We noticed that the Legislative Council is currently discussing the Private Medical Facilities Bill in Hong Kong to regulate the private healthcare industry. The Bill aims to better protect patients' safety and consumer rights, and sets out the requirements, authorities and responsibilities of the licensee and chief medical executive in managing a licensed private healthcare facility. We are deeply disappointed that the Bill does not cover medical laboratories. The existing legislation (Cap. 359A) is of indirect relevance and only targets personnel performing medical laboratory testing. We believe this is suboptimal, outdated and insufficient in protecting the standard of healthcare.

One of the missions of The Hong Kong College of Pathologists is to promote high quality medical laboratory testing in Hong Kong. We believe the Private Healthcare Facilities Bill needs to be enhanced in terms of including mandatory registration and regulation of medical laboratories.

Medical laboratory test results significantly affect patient management. Whether it is a blood test, a microbiology test or a tissue biopsy, accurate laboratory results are one of the most important factors in assuring proper patient management and safety. We strongly believe that all medical laboratories should be registered and regulated, with the approach and procedures similar to other institutions included in the Private Medical Facilities Bill.

We sincerely appeal to the Committee to consider our suggestions, so as to establish an effective regulatory regime and safeguard the quality and safety of medical care in Hong Kong.

Yours sincerely,

Dr. CHAN, Ho Ming

President, The Hong Kong College of Pathologists

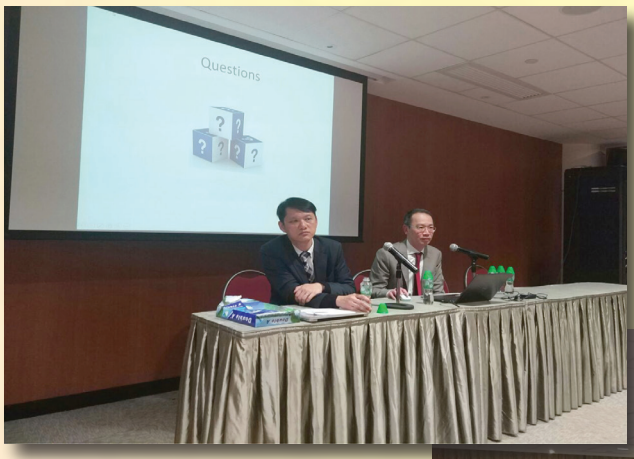
Forum on the Post-Fellowship Programme in Genetic and Genomic Pathology (17 January 2018)

A forum was held in James Kung Meeting Room, Hong Kong Academy of Medicine Jockey Club Building in the evening on 17 January 2018, to discuss the proposed new post-Fellowship programme in Genetic and Genomic Pathology.

Our College President, Dr. CHAN Ho Ming, and Training and Examinations Committee (TEC) Chairman, Dr. CHAN Chak Lam, Alexander, co-chaired the forum. There were about 40 participants, including Immediate Past President, Prof. Annie CHEUNG, Councillors, TEC members, members of the Taskforce on Training for Genetics and Genomics, as well as stakeholders from various disciplines. Participants were from the Hospital Authority, the universities and private hospitals.

After a brief introduction about the background in the development of this programme, and the subsequent requirement for endorsement by the College and the Academy, the key elements of the proposed training programme in Genetic and Genomic Pathology were presented.

Participants actively engaged in the discussion. A few important aspects were thoroughly discussed, including the content of the training programme and the training opportunities for trainees/Fellows. The possibility of practising right and credentialling related to the Genetic and Genomic Pathology Fellowship status, as well as cross-discipline practice among Fellows in Genetic and Genomic Pathology had also been deliberated. It was emphasized that the introduction of this training programme aimed to uphold the uniqueness of our (pathologists') role in laboratory medicine.



▲ *College President, Dr. CHAN Ho Ming (left) and Training and Examinations Committee Chairman, Dr. CHAN Chak Lam, Alexander (right), co-chaired the forum, answering enquiries from the floor.*

The floor also enquired about the "grandfathering" criteria for Fellowship in Genetic and Genomic Pathology. Our proposed criteria and the Academy's timeline requirement for First Fellow admission were briefly introduced.

Impacts and concerns in different aspects were discussed and addressed in the forum.

▶ *Fellows and trainees participated in the Genetic and Genomic Pathology forum.*

The Young Fellows' Chapter

The Hong Kong College of Pathologists' (The College) Young Fellows' Chapter was established in December 2017. Any Fellow from any discipline of pathology who is within ten years of being awarded Fellowship by The College is considered a Young Fellow.

The Young Fellows' Chapter serves to consider matters delegated to it by The College Council and to provide feedback and comments on issues relevant to Young Fellows. It acts as a platform for communication between Young Fellows and The College Council and thus enables the views expressed by Young Fellows to be reflected to The College Council. It aims to promote Young Fellows' engagement and involvement in The College.

▲ *Gathering of some members of the Young Fellows' Chapter: from left to right, Dr. IP Ka Ling, Rosalina, Dr. LI Hiu Lui, Dr. CHEUNG Yu Ying, Ingrid , Dr. CHEONG Renee Constance Yue-kew, Dr. LEUNG Ying Kit, Dr. MAK Siu Ming, Dr. AU Yuen Ling, Elaine.*

The Governing Council of the Young Fellows' Chapter consists of representatives from a wide range of pathology subspecialties. The Chairman, Vice-Chairman and Secretary are elected by representatives that form the Governing Council of the Young Fellows' Chapter.

Fellows and Members are welcome to approach representatives in Young Fellows' Chapter for matters related to Young Fellows. Young Fellows of The College are also encouraged to approach representatives in their discipline to voice any opinions and comments to The College.

Please feel free to contact representatives as below:

Capacity in the Young Fellows' Chapter	Name	Discipline
Chairman	Dr. MAK Siu Ming	Anatomical Pathology
Vice-Chairman	Dr. IP Ka Ling, Rosalina	Haematology
Secretary	Dr. CHEONG Renee Constance Yue-Kew	Anatomical Pathology
Member	Dr. AU Yuen Ling, Elaine	Immunology
Member	Dr. CHEUNG Ingrid Yu Ying	Clinical Microbiology & Infection
Member	Dr. CHONGYeow Kuan	Chemical Pathology
Member	Dr. FOO Ka Chung	Forensic Pathology
Member	Dr. LEUNG Ying Kit	Anatomical Pathology
Member	Dr. LI Hiu Lui	Anatomical Pathology

The 13th Trainee Presentation Session

▲ *Dr. Derek HUNG delivering his presentation entitled 'Use of microtitre well model to demonstrate the efficacy of cranberry extract in inhibiting biofilm formation' at the 13th Trainee Presentation Session.*

The 13th Trainee Presentation Session was successfully completed in the afternoon on 25th November 2017. The Session provides a wonderful platform for our trainees to present their research findings. Four fellows from different disciplines were invited to be judges: Dr. Amy CHAN (Anatomical Pathology, Prince of Wales Hospital), Dr. Rosalina IP (Hematology, Pamela Youde Nethersole Eastern Hospital), Dr. David LUNG (Clinical Microbiology & Infection, Tuen Mun Hospital), and Dr. Chloe MAK (Chemical Pathology, Princess Margaret Hospital). The number of participants is continuously kept high and this year, a total of 11 trainees from different subspecialties actively participated the Trainee Presentation Session in the form of oral presentation.

I would like to congratulate all the participants for their excellent job and impressive presentation. On behalf of the Education Committee, I would also like to express our grateful appreciation to our invited judges and helpers for assisting with the Trainee Presentation Session.

The best presentation was awarded to Dr. Derek Hung (Clinical Microbiology & Infection, Queen Mary Hospital). He presented his study on "Use of microtitre well model to demonstrate the efficacy of cranberry extract in inhibiting biofilm formation". The abstract of his study was:

Biofilm formation by bacteria in human body poses great therapeutic challenge. The bacteria within biofilm have low metabolic rate and the matrix prevents effective antibiotics penetration. Cranberry extract was found in the literature to inhibit biofilm formation, and has good efficacy to prevent recurrence of urinary tract infection.

In order to demonstrate the effect of cranberry extract on biofilm inhibition, an experimental model which is cost-effective and accessible to clinical laboratory has to be devised. An in-house protocol using 96-wells microtitre plate model is formulated based on the existing literature, modified according to the existing laboratory technical apparatus. Single colony of an ATCC strain Pseudomonas aeruginosa is cultured overnight in trypticase soy broth. The broth is then diluted by 10-fold. 200 μL of the diluted broth is inoculated into each of the 48 wells of the microtitre plate. Half of them are supplemented with 20 mg/mL cranberry extract. Each of the remaining 32 wells are inoculated with 200 μL trypticase soy broth, and half of them are supplemented with 20 mg/mL cranberry extract. These 32 wells serve as control.

The plate is incubated in 37°C under aerobic condition for 48 hours. After washing the broth away with phosphate-buffered saline, the biofilm on the plate is stained with 200 μL 5% malachite green. The stain is then washed away, with the adherent stain eluted by acetone. The quantification of the biofilm is performed by photospectrometer and the optical density is compared between wells. It is demonstrated the wells with cranberry extract (OD 1.46) have significantly lower optical density reading as compared to those without

cranberry extract (OD 2.75), and may be evidence that cranberry extract has clinically important role in inhibiting bacterial biofilm. This simple model to quantify biofilm can also be used to compare the effect of different antibiotics in eliminating biofilm forming bacteria.

The study of Dr. Hung did not involve any high-end genetic or genomic techniques. Through his outstanding presentation, the judges and I were impressed by this relatively simple but clinically relevant study. Although large-scale studies with sophisticated research methods are almost the basic requirement for most journals with high impact factor, formulation of clinically meaningful research questions, planning and implementation of the research by oneself are much more important and valuable for a budding researcher.

Dr. Anthony CHAN,
Vice-Chairman, Education Committee

▲ *Some of the participants and judges at the 13th Trainee Presentation Session, from left to right, Dr. Anthony CHAN, Dr. Rocky SHUM, Dr. SZE Kin-ho, Dr. Derek HUNG, Dr. Kelvin HY CHIU, Dr. Amy CHAN, Dr. Rosalina IP, Dr. David LUNG, Dr. Chloe MAK, Dr. Tina YC CHAN, Dr. Tom CC HO, Dr. Nike KC LAU, Dr. Shui-ying CHENG, Dr. Daisy CHU.*

The 26th Annual General Meeting, Conferment Ceremony and T.B. Teoh Foundation Lecture

Annual General Meeting 2017

The 26th Annual General Meeting (AGM) was held after the 13th Trainee Presentation Session on 25th November, 2017. Dr CHAN Ho Ming was elected as the new President, succeeding Prof. CHEUNG Nga Yin, Annie. Dr. CHAN Chak Lam, Alexander was elected as one of the Vice-Presidents to fill the vacancy thus left behind by Dr. CHAN Ho Ming. Dr. WONG Lap Gate, Michael was elected as the Registrar and Dr. CHONG Yeow Kuan was elected as the Honorary Treasurer. Four new Council Members, Dr. CHEONG Renee Constance Yue-kew, Dr. LAI Koon Chi, Christopher, Dr. LEUNG Ying Kit and Dr. LI Hiu Lui, were elected. We would like to take this opportunity to thank the immediate past Council Members Prof. HO Pak Leung, Dr. Yuen Yuet Ping and Dr. Yuen Wah Fun, Nancy for their contribution to the College.

▲ *The Council. Front Row, from left to right: Dr. CHONG Yeow Kuan, Dr. CHAN Chak Lam, Alexander, Prof. CHEUNG Nga Yin, Annie, Dr. CHAN Ho Ming, Dr. SHUM Shui Fung, Bobby, Dr. WONG Lap Gate, Michael, Dr. CHAN Kui Fat. Back row, from left to right: Dr. Lai Koon Chi, Christopher, Dr. LAM Woon Yee, Polly, Dr. MAK Siu Ming, Dr. CHEONG Renee Constance Yue-kew, Dr. LI Hiu Lui, Dr. LO Yee Chi, Janice. Absent with Apologies: Dr. LEUNG Ying Kit, Dr. LEUNG Yuk Yan, Rock.*

Conferment Ceremony

At the Conferment Ceremony, 10 Fellows and 9 Members were admitted to the College. The honorable guests included Prof. Sophia CHAN, Secretary for Food and Health, of the Food and Health Bureau, Hong Kong Special Administrative Region (HKSAR); Professor Gilberto LEUNG, Vice President (Education and Examinations), The Hong Kong Academy of Medicine; Dr. the Honorable Pierre CHAN, Legislative Councillor of the HKSAR; and Dr. Doris TSE, Cluster Chief Executive, Kowloon West Cluster, Hospital Authority. The new College President, Dr. CHAN Ho Ming, shared with the audience the challenges and opportunities that the College is facing in his welcoming speech.

▲ *The College President and some of our officiating guests*

▲ *College President, Dr. CHAN Ho Ming, welcoming distinguished guests and the audience at the Conferment Ceremony.*

▲ *Prof. Gilberto LEUNG addressing new Members, Fellows and the audience.*

▲ *Dr. CHAN Chun Ngai*

▲ *Dr. CHEUNG Sin*

▲ *Dr. LAM Winwhole Larry Ruey Si*

▲ *Dr. SHEA Ka Ho*

▲ *Dr. SRIDHAR Siddharth*

▲ *Dr. YUK Man Ting*

Congratulations to the newly admitted Fellows!

▲ *Group photo of Councillors, guests, new Fellows and new Members after the ceremony.*

T.B.Teoh Foundation Lecture

The 26th T.B. Teoh Foundation Lecture was delivered by Prof. CHIU Wai Kwun, Rossa, Choh-Ming Li Professor of Chemical Pathology and Assistant Dean (Research), The Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital . In her lecture, entitled 'From Prenatal to Cancer assessments: The Power of Precision Diagnostics', Prof. CHIU enlightened the audience on the development of non-invasive prenatal and cancer diagnosis.

▲ *Prof. Rossa CHIU delivering her lecture.*

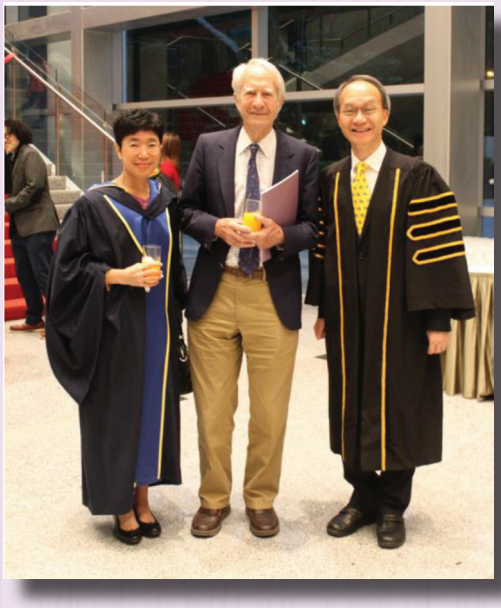
▲ *New Fellow, Dr CHAN Chun Hgai registering with his baby son.*

We would like to thank Dr. CHUNG Ivy Ah-yu for being the Mistress of Ceremonies at the AGM. This year, the College invited two students from the Institute of Vocational Education (IVE), Michael Chan and Janice Chan, to take photos during the Trainee Presentation Session, AGM, Conferment Ceremony and T.B. Teoh Foundation Lecture. We would also like to express our gratitude towards our College Secretary, Ms. Adrienne Yung and Ms. Heidi CHU for their support in organizing the AGM.

▶ *It's a family affair!*

▲ *A joyous occasion for all generations of pathologists.*

▲ *College President Dr. CHAN Ho Ming, and Immediate Past President, Prof. Annie CHEUNG with dignitaries of the ceremony.*



▶ *From left to right, Dr. Janice LO with Dr. John LAWTON, former Professor of Immunology at the University of Hong Kong (HKU), who is visiting from Australia; and Prof. Yu-lung LAU, President of the Hong Kong College of Paediatricians.*

THE HONG KONG COLLEGE OF PATHOLOGISTS:

TOPICAL UPDATE

Volume 13, Issue 1 January 2018

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

Editorial note: *NMOSD is an immune mediated demyelinating disease. Though its clinical presentation may overlap with multiple sclerosis, distinguishing these two entities is important in view of differences in treatment. Anti-NMO antibodies play a crucial role in the workup and diagnosis of NMOSD. In this review, Dr Elaine Au provided an overview of the NMOSD condition and the use of anti-NMO antibody assays. We welcome any feedback or suggestions. Please direct them to Dr Elaine Au (email: ayl436@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.*

An overview of NMO Spectrum Disorder and the diagnostic utility of anti-NMO antibodies

Dr. Au Yuen Ling Elaine
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Department of Pathology,
Queen Mary Hospital

NMO is an idiopathic immune mediated demyelinating disease that predominantly affects optic nerves and spinal cord. The prevalence range from 0.3 to 4.4 per 100000 people, with Asian and African-American more affected than Caucasian, where multiple sclerosis is more common in the white population [1-5]. The condition has been named as Devic's disease in the past [6], which described a monophasic disorder presenting with simultaneous bilateral optic neuritis and transverse myelitis. With the availability of specific serological marker, antibodies that targeted the water channel aquaporin-4 (AQP4), the clinical and neuroimaging spectrum of NMO disease is broadened. Instead of being a monophasic disorder, NMO antibodies positive patients with recurrent attacks are not uncommonly found. Moreover, the clinical presentations are more variable than the traditional Devic disease. There is no pathognomonic clinical feature of NMO spectrum disorder (NMOSD), though certain clinical presentations are particularly suggestive of the disorder. These include simultaneously bilateral optic neuritis, complete spinal cord syndrome and area postrema clinical syndrome.

Multiple sclerosis is an important differential diagnosis of this condition in view of the overlapping clinical features of these two conditions. In NMOSD, optic neuritis tends to be more severe, more often with simultaneous bilateral involvement or sequential in rapid succession, compare to multiple sclerosis. Complete spinal cord syndrome, with longitudinally extensive transverse myelitis in MRI, is more suggestive of NMOSD than multiple sclerosis. Differentiating NMOSD from other demyelinating disease, i.e. multiple sclerosis is important since the treatment is different. Indeed, some multiple sclerosis therapies may aggravate NMO disorders [7-10].

Diagnostic Criteria

In 2006, the serological marker was first incorporated into the revised NMO diagnostic criteria. In 2007, NMOSD was introduced to include seropositive patients who do not follow the classical monophasic bilateral optic neuritis and transverse myelitis. Lately, the International Panel for NMO Diagnosis (IPND) has further revised the diagnostic criteria [11]. For anti-NMO antibodies positive cases, presenting at least one core

clinical characteristic of the disease is required for diagnosis. Core clinical characteristics include optic neuritis, acute myelitis, area postrema syndrome (episode of otherwise unexplained hiccups or nausea and vomiting), acute brainstem syndrome, narcolepsy or acute diencephalic syndrome with typical Magnetic Resonance Imaging (MRI) lesions and symptomatic cerebral syndrome with typical MRI lesions. On the other hand, more stringent clinical criteria, with additional neuroimaging findings, are required in seronegative patients to fulfill the diagnostic criteria (See appendix).

For the workup of the disease, MRI, cerebral spinal fluid (CSF) exam and serological test for anti-NMO antibodies are important. In some patients, CSF pleocytosis, usually in the form of monocytosis and lymphocytosis, are present. Increased CSF protein levels are noted in 46-75% of cases [12, 13]. Nevertheless, presence of CSF oligoclonal bands is uncommon in NMOSD, and at most transient, in contrast to the presence of persistent CSF oligoclonal bands in the case of multiple sclerosis. Finally, visual evoked potentials, somatosensory evoked potentials and brainstem acoustic evoked potentials examination may also be helpful in the workup.

Clinical course and prognosis

In NMOSD syndromes affecting regions other than optic nerve and spinal cord, not uncommonly patients will relapse with more classical involvement in subsequent attacks. Majority of NMOSD patients suffer from recurrent attacks (80-90%), less frequently monophasic attack (10-20%) [14], while gradual progressive course with neurological deterioration is very rare [15]. Relapses usually occur in clusters, but unpredictable intervals. In the Mayo Clinic series, the second relapse occurred within 1 year in 60% of cases, and within 3 years in 90% of cases [16]. Repeated NMO attacks not uncommonly lead to accumulation of neurological impairment. NMO is associated with more adverse outcome than MS in general[14].

NMOSD has been shown to be frequently associated with other autoimmune disorders, including lupus, Sjogren's syndrome, etc [17-19]. On contrary, NMOSD is not common in rheumatic disease patients.

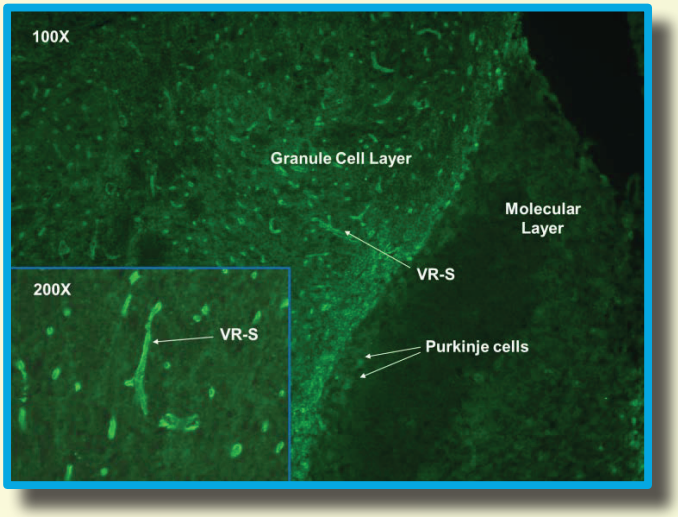
Anti-NMO antibodies

Among the different investigations, NMO antibodies test is central to the workup. Anti-NMO antibodies are pathogenic. The third extracellular loop of AQP4 is the major epitope for the anti-NMO antibodies. Biopsy and autopsy tissue obtained from seropositive patients demonstrate loss of AQP4 immunoreactivity. Perivascular complement activation in actively demyelinating lesions is also happened. In the central nervous system (CNS), AQP4 is expressed at the foot processes of astrocytes, near the basement membranes, in the optic nerve, in a subpopulation of ependymal cells, in hypothalamic nuclei and in the subfornical organ [20,21]. Truncated astrocyte processes or cell loss were found in demyelinating lesions [11]. In rat models, passive transfer of the antibodies leaded to the development of disease [22, 23]. These pathological findings distinguish NMOSD from multiple sclerosis.

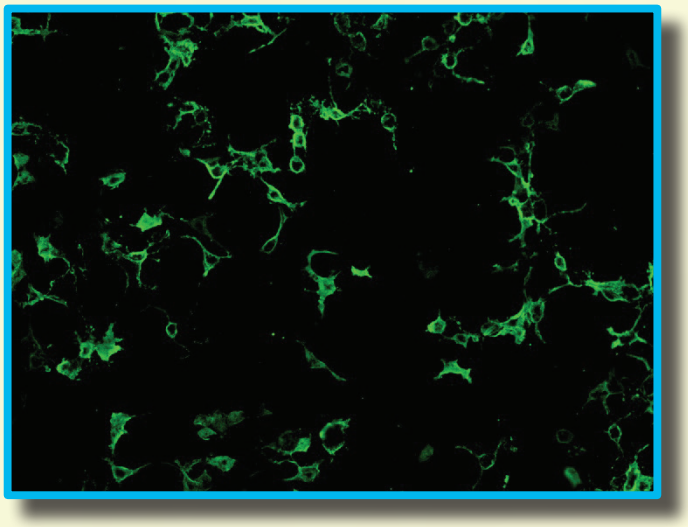
The Anti-NMO antibodies can be detected by indirect immunofluorescence staining on tissue slide using mouse cerebellum tissue section, cell-based assays, radioimmunoprecipitation assays and enzyme-linked immunosorbent assays (ELISA). Overall, cell-based assay is preferred in view of better assay sensitivity and specificity compared to other methods. Ideally, confirmatory testing with one or more techniques is suggested [11], especially in cases with atypical presentation or borderline results are obtained.

In tissue based indirect immunofluorescence test, NMO antibodies positive case is characterized by the binding to structures adjacent to microvasculature, the Virchow-Robin spaces (VRS) and pia mater (Fig.1).

This assay allows the detection of any coexisting anti-neuronal antibodies, which may be important as differential diagnosis and workup. However, the method is observer dependent and subjective. The interpretation of antibody staining may easily be affected by non-specific background staining on the tissue. In some rare occasions, antibodies other than anti-NMO may mimic the staining pattern and lead to false positive results. Moreover, indirect tissue based immunofluorescence test has relative low sensitivity (63-64%) [24-27].



▲ *Figure 1: Mouse cerebellum tissue section stained with anti-NMO antibodies.*



▲ ***Figure 2: HEK 293 cells transfected with AQP-4 gene expression vector and stained positive with anti-NMO antibodies.***

Cell-based assay utilize cell lines such as human embryonic kidney 293 (HEK293) cells or Chinese hamster ovary (CHO) cells that have been transfected with AQP4 gene expression vector, so that expressing much higher level of antigen comparing to normal tissues. Cell lines from different units may use different ratio of the two isoform of AQP4: M1 and M23 in order to obtain optimal antigen presentation. Cell-based assay can be assessed by indirect immunofluorescence staining or flow cytometry. For indirect immunofluorescence cell- based assay, slide with fixed AQP-4 gene transfected cells and non-transfected cells growing on different biochips are placed side by side for comparison. Therefore, false positivity is minimized with the inclusion of control non-transfected cells. A higher expression of antigen in the transfected cells also enhance the assay sensitivity compared to tissue-based indirect immunofluorescence testing. (Fig.2)

Overall, cell-based assay is the recommended assay in view of good sensitivity and specificity (mean sensitivity 76.7% in a pooled analysis; 0.1% false positivity in a multiple sclerosis cohort) [24-27]. Commercial kits for indirect immunofluorescence cell-based assay are available, which facilitate the assay setup in service laboratories. Nevertheless, indirect immunofluorescence method is semi-quantitative and observer dependent.

Protein-based assays, like ELISA and radioimmunoprecipitation assays, in general, have lower sensitivity compared to cell based assays. In addition, ELISA, in particular at low titer, may yield nonspecific results. However, these assays provide quantitative results which may potentially be used for serial monitoring [24].

Though NMO antibody testing in serum is well-established, the diagnostic role of testing the antibody in CSF is controversial. Most of the cases reported in literature are diagnosed by serum test, though there have been rare cases reported that were CSF positive but serum test negative [28,29]. When studying paired CSF and serum samples with antibody indices calculated, intrathecal production of the NMO antibody is rare [24].

NMO antibodies can be present in patients few years before and after the disease presentations. Lately, there is increasing evidence that the antibody titre may reflect disease activity. Elevated antibody levels at relapse and decrease in titre after immunosuppressant treatment has been reported in literature [30-34]. Therefore, serial monitoring may possibly facilitate management and medication adjustment. However, there is no general threshold value for clinical relapse and the absolute level varies with individual patients. Rising level may not predict relapse in all cases. In addition, some methodologies, like indirect immunofluorescence test, only provide semi-quantitative results, and inter-run reproducibility is another issue. Other factors including the frequency of test necessary to achieve meaningful disease status monitoring and the cost involved are also important consideration. Therefore, it remains to be determined whether the marker should be serially monitored for treatment response and disease activity monitoring.

Treatment

The treatment for classical Devic's disease presentation and relapsing NMOSD presentation is no different. High dose steroid is commonly employed as first- line of treatment in acute presentation. Plasma exchange may be considered in treatment refractory cases. Immunomodulatory treatment with interferon β, which is a treatment option in multiple sclerosis, may exacerbate NMOSD disorders. Therefore, differentiating between these two conditions is important. Options of steroid sparing immunosuppressants to consider in NMOSD include azathioprine, methotrexate, mycophenolate mofetil, rituximab, etc [14].

Conclusion

NMOSD is a rare but increasingly recognized condition, which present as an inflammatory and demyelinating autoimmune disorder affecting the central nervous system. With the availability of a serological marker, anti-NMO antibody, the diagnosis and differentiating from related conditions is facilitated. Timely diagnosis and treatment is important for the management of these patients.

NMOSD diagnostic criteria for adult patients

Diagnostic criteria for NMOSD with NMO-IgG

1. At least 1 core clinical characteristic
2. Positive test for NMO-IgG using best available detection method (cell-based assay strongly recommended)
3. Exclusion of alternative diagnoses

Diagnostic criteria for NMOSD without NMO-IgG or NMOSD with unknown NMO-IgG status

1. At least 2 core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
   - At least 1 core clinical characteristic must be optic neuritis , acute myelitis with LETM, or area postrema syndrome
   - Dissemination in space (2 or more different core clinical characteristics)
   - Fulfillment of additional MRI requirements, as applicable
2. Negative tests for NMO-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses

Core clinical characteristics

1. Optic neuritis
2. Acute myelitis
3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting
4. Acute brainstem syndrome
5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions
6. Symptomatic cerebral syndrome with NMOSD-typical brain lesions

Additional MRI requirements for NMOSD without NMO-IgG and NMOSD with unknown NMO-Ig status

1. Acute optic neuritis: require brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm
2. Acute myelitis: requires associated intramedullary MRI lesion extending over >=3 contiguous segments (LETM) OR >=3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis
3. Area postrema syndrome: requires associated dorsal medulla/ area postrema lesions
4. Acute brainstem syndrome: requires associated periependymal brainstem lesions

Neurology 2015;85:177-189

Clinical features and laboratory findings atypical for NMOSD, that need to consider alternative diagnoses

1. Progressive overall clinical course (neurologic deterioration unrelated to attacks: Consider MS)
2. Atypical time to attack nadir: less than 4 hours (consider cord ischemia/ infarction); continual worsening for more than 4 weeks from attack onset (consider sarcoidosis or neoplasm)
3. Partial transverse myelitis, especially when not associated with LETM MRI lesion (consider MS)
4. Presence of CSF oligoclonal bands (oligoclonal bands occur in < 20% of cases of NMO vs > 80% of MS)

Comorbidities associated with neurologic syndromes that mimic NMOSD

1. Sarcoidosis, established or suggestive clinical, radiologic or laboratory findings thereof (e.g. mediastinal adenopathy, fever and night sweats, elevated serum angiotensin converting enzyme or interleukin-2 receptor level)
2. Cancer, established or with suggestive clinical, radiologic or laboratory findings thereof; consider lymphoma or paraneoplastic disease (e.g. collapsing response mediator protein-5 associated optic neuropathy and myelopathy or anti-Ma-associated diencephalic syndrome)
3. Chronic infection, established or with suggestive clinical radiologic, or laboratory findings thereof (e.g. HIV, syphilis)

Neurology 2015;85:177-189

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Out of the Whitecoat:

My Jogging Hobby

by Dr. NG Wai Fu

▲ Dr. NG Wai Fu

I am a latecomer to jogging after the age of 50. It came about incidental to my moving to Kam Tin in 2009 and a decision to accompany a friend to run the 10km race. I could also easily go into scenic jogging trails in the countryside from home which is within a relatively short distance from what became my favorite jogging place of Nam Sang Wai. I soon discovered the merits of jogging. The most wonderful reward is reviving the brain of my youth! I have regained the attentive mind and memory capability of my school days which were long lost. An improvement in cognitive function associated with any sustained aerobic exercise is a well-established fact, and is also supported by MRI studies showing an increase both in the blood flow and volume of grey matter in the brain. The quality of sleep improves very significantly, and the mind and spirit are well-kept in the daytime. I eat considerably more and do not need to worry about my body weight, blood pressure, cholesterol and blood sugar.

My first formal run was a 10km race in 2011, followed by a half-marathon in 2012. I then prepared for a full marathon in 2013. This was really a major undertaking. For the preceding nine months, my daily life was centered on training. I had previously attended a training course for the half-marathon and read books on preparation for the full marathon. I was best prepared for my first two marathons. My peak record of training was attained in December 2012, with a monthly mileage of 350km. Such mileage is considered a requirement for the full marathon, as the peak weekly training mileage should be twice the race distance (i.e. about 80km per week for the full marathon and 40km per week for the half-marathon). The jogging was accompanied by cross-training of mountain (cross-country) running, swimming and gymnastics. Jogging actually involves all the muscles of the body apart from those of the lower limbs. The arm-swing is of equal importance as part of the driving motor, and the core muscles of the body are essential to maintain optimal posture and to provide respiratory support. I managed to complete five full marathons from 2013 to 2015. My personal best result was obtained in the second marathon in 2013 (4 hours 44 minutes).

During these years of training, I would run to work from Kam Tin to Tsuen Wan once a week in the preceding 3 months prior to the marathon. It was impossible to start the run directly from home because I would need to start out before 6am when the road would still be dark. I therefore took public transport from home to the starting point which was about 1km from the hillside of Tai Mo Shan, and started jogging at around 6:45am as the sun rose and the roads became more visible. This also gave me a warm-up run of 1 km before I ascended the mountain along Route Twisk. The run was about 12km in total and I completed it in about 110 minutes, with 5km of uphill running at a slope of 1:10, ascending to 500 meters above ground level. I could then go back to the hospital in time to take a shower before starting the

day's work. This mountain training was soon struck by an unexpected hurdle: the dogs! On the worst occasion, I had to face two dogs approaching me, one on each side! I backed along the road while facing them, but soon landed on the ground. I was very grateful that the dogs did not attack me, although they continued to bark and stare at me. They probably knew that they had already won, seeing the victim fall to the ground. I then searched for methods to defend myself and attended a course to prevent dog attacks, specially designed for civil servants who need to deliver services in rural areas. An umbrella with the colour and pattern of a tiger, and a high-pitched whistle then became essential items in my jogging accessories. On more than one occasion, I managed to deter the approaching dog simply by opening and closing the umbrella continuously without need of the whistle. I am not sure whether the dogs recognize tigers, but it did give me extra confidence! I did however still need to get a lift from passing cars when I heard the warning barks of a mob of dogs on a few occasions. The time I spent jogging up and down Tai Mo Shan, and the encounters with the dogs have since become a special part of my life memories.

Since 2016, I have switched back to half-marathons as one of my knees was giving me warning signals of overuse. As I wanted to continue running, I had to reduce the overall mileage that I did. I still run for most of the year, stopping only for a short period during the hottest summer months. My routine consists of a 7km run in the morning, starting from the Tsuen Wan West Station, along Castle Peak Road to Ting Kau, and then back to the hospital. In order to tackle the progressively tight muscles and tendons, I have also joined Yoga classes in recent years which really help to prolong my running life. My only regret is that so far, I have not joined any races outside of Hong Kong as I am running alone without joining any jogging club for companionship.

I am very grateful to have this unique opportunity to share my experiences with all of you. I consider myself to be quite fortunate to have been able to discover, enjoy and continue jogging. Jogging has transformed me and kept me healthy and energetic. The time and effort spent are well remunerated. Perhaps not everyone is suitable for this type of exercise due to anatomical and personal reasons, but you do not need to run a marathon to see the benefits. Jogging 2-3 times per week for at least 30 minutes would do. It can even be running on a treadmill. A better chance of success is to incorporate the jogging into your daily routine, such as forming part of your trip to/from work. If you have ever thought about jogging, I encourage you to put it into practice and you will soon become addicted to it.

International Pathology Day Workshop 2017

To celebrate the ILPP International Pathology Day in mid-November, and to promote public understanding of pathology and pathologists' work, the College organised the International Pathology Day Workshop 2017 on 12th November, 2017 at Students' Laboratories, 1/F, Day Treatment Block and Children Wards, Prince of Wales Hospital.

Over one hundred senior secondary school students from 37 schools attended the workshop and learnt about pathology and pathologists' work through interactive laboratory experiments and demonstrations, under the guidance of volunteering pathologists and medical students.

Dr. LAI Sai Chak (Chairman of the Professional and General Affairs Committee), Dr. Ingrid CHEUNG, Dr. Elison KAM, Dr. Crystal LAM, Dr. Rock LEUNG, Dr. Garrick LI, Dr. Stanford LI and Dr. Felix WONG took part in in the preparation of the workshop. The Chinese University of Hong Kong kindly allowed us to use the venue.

▲ *College President Professor Annie Cheung explaining pathologists' work to participants of the workshop.*

▲ *Group photo of organisers.*

A tribute to Dr. William Tong

▲ *At the finishing line of the long-distance run outside Whitehall, London in February 2018.*

On 4 May 2018, some of us received the sudden news from the United Kingdom (UK):

"It is with great sadness that we hear of the death of William Tong who died suddenly last Tuesday night. William was a well-known and highly respected senior medical virologist and a personal friend to many colleagues home and abroad who universally found him engaging, friendly, organised and professional. William will be greatly missed. We will particularly miss his smile, his counsel and his expertise in the clinic and the laboratory.

He will be remembered particularly for his dedication to medical education, clinical virology training and as Chief Examiner in Medical Virology for the Royal College of Pathologists."

Dr. William Tong had a close association with many Fellows in the specialty of Clinical Microbiology and Infection, especially those working in virology. All those who know him remember him fondly and many have vivid recollections about him.

William attended secondary school in the St. Joseph's College, and subsequently the Queen's College during matriculation. He was a graduate of the class of MBBS 1983 at the University of Hong Kong (HKU), with distinctions in Pathology, Microbiology, Community Medicine, Obstetrics and Gynaecology. After internship, he was initially trained in paediatrics at the Queen Mary Hospital (QMH), obtaining MRCP at the first attempt. Subsequently, he took up training in virology at the Government Virus Unit in the QMH, under the supervision of Dr. Wai-Kwan Chang.

Prof. Kwok-yung Yuen recalled that when he joined the HKU Department of Microbiology and first met William in around 1988, William told him one day about the very thick Textbook of Human Virology by Robert Belshe: "Since nobody in Hong Kong will read up this big pile of information from DNA to RNA virus and from non-enveloped to enveloped virus, I have the duty to chew up this big book for our patients". Prof. Yuen also remembered that, as a doctor with "super" type A personality, William used to drive a red Italian Alfa Romeo to work at not too slow a speed. Prof. Yuen felt that as a "late comer" to the field of microbiology six years after training in medicine and surgery, he personally benefited a lot from William's coaching, who showed him electron micrographs of viruses, cytopathic effects and even how to set up a checkerboard enzyme immunoassay for tetanus antibodies using tetanus toxoid from the QMH pharmacy as coating antigens.

William subsequently obtained the qualifications of FRCPA in 1990 and MRCPath in 1991. In the same year, he was admitted as a Fellow of our College, and as FHKAM(Pathology) in 1993.

William left Hong Kong in the early 1990s for Newcastle-upon-Tyne to complete his clinical virology training. In 1992, following the very successful interview by Professor Tony Hart, William started his first consultant appointment at the Royal Liverpool University Hospital. His highly impressive career continued with his move from Liverpool to Guy's & St. Thomas' NHS Trust in South London in 2000, finally to the Royal London Hospital in March 2013, as Consultant Virologist at Barts Health NHS Trust in East London.

As can be expected from his brilliant career, William was an avid academic with a passion for the field. He put in much effort in addressing hospital service reforms and in training the next generation of microbiologists and virologists. Throughout the years, he maintained close ties with Hong Kong. He was a visiting scholar at the Microbiology Department of the Chinese University of Hong Kong in 2004, helping to set up and conduct the first programme of the "Certificate Course in Common Viral Infections", with the objective of promoting knowledge on clinical virology among local medical doctors, public health specialists, nursing professionals and research scientists. William served as a member of the Scientific Committee on Infection Control of the Centre for Health Protection in Hong Kong from 2004 to 2010. He also participated in the Hospital Authority Convention in 2013, where he delivered a plenary presentation on "Diagnostic Strategy and Laboratory Preparedness in the Face of Emerging Diseases". Whenever he visited Hong Kong, usually with his wife Pendora and their two daughters Sonia and June to see his parents during Christmas and the New Year, he would gladly give lectures, and get to know trainees in Hong Kong. As an eminent virologist in the UK and subsequently Chair of the Virology Panel of Examiners of the Royal College of Pathologists, his professional guidance, affectionate advice and warm hospitality had benefitted many virology trainees in Hong Kong over the years.

William cared very much for his family. He once confided that he and his family enjoyed UK very much where there are very distinct seasons over the year. Being health conscious, he recently finished his first long distance run in London in February 2018. Despite a very gentle personality, William is a man of principle and would not refrain from speaking up where the situation required.

Microbiologists and virologists in Hong Kong are shocked and deeply saddened by the news of his sudden departure. His legacy will certainly remain with the field of Clinical Microbiology and Infection in Hong Kong.

Contributed by (alphabetical order):
Paul CHAN, Janice LO, Dominic TSANG, Kwok-yung YUEN

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