HONG KONG COLLEGE OF PHYSICIANS

SYNAPSE

SPECIAL ISSUE

CELEBRATING

HONG KONG COLLEGE OF PHYSICIANS
香港內科醫學院

Sapientia et Humanitas

30 YEARS
1986 — 2016

OCTOBER 2016

Contents

SYNAPSE
(SPECIAL ISSUE)

October 2016

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Foreword

Sir David Todd
Founding President,
Hong Kong College
of Physicians

This special edition of *Synapse* celebrates the 30th Anniversary of the Hong Kong College of Physicians which is to be congratulated as time has enhanced its image and stature. The College Officers, Fellows, Members, Colleagues, and Friends both local and overseas and Benefactors have all contributed to its achievements and we are indebted to them one and all. May the College continue to succeed in its mission and rise to even greater heights in the decades to come.

It is only five years since our Silver Anniversary but much has happened in Hong Kong. Anti-establishment demonstrations and social unrest have split the community. There is a tug of war between 'idealism' and 'realism'. Let us hope good sense will prevail. In these times, members of our profession, young and old, should uphold professionalism even more conscientiously and not be distracted from our primary calling.

On a brighter note the College published its magnum opus '*Sapientia et Humanitas* – A History of Medicine in Hong Kong' in its Silver Anniversary year; and the gem, 'Centenary Tribute to AJS McFadzean', followed in 2015. Both are eminently readable.

Synapse first appeared in 1992 with SC Tso as editor. Many distinguished Fellows have been editors with Carolyn PL Kng holding the record of over seven years. All along John Mackay has been an invaluable advisor. Richard Yu has added colour with his photographic art. They and their colleagues are to be thanked and applauded for transforming a newsletter into a magazine of stature. For some time now it has featured special articles of scientific and professional interest, Council news, specialty updates, postgraduate training information, notice of examinations and the results and the ever interesting Profile Doctor. So far nothing Rosie Young would consider 'juicy' has appeared in its pages. The present issue has some special features which include greetings from Government, overseas Academies and sister Colleges and a notable contribution from our President. It brings the activities of the 17 specialty boards up to date and contains recent news of Fellows and Members. Long may *Synapse* continue to enlighten and to entertain.

Preface

Patrick C.K. Li
President, Hong Kong College of Physicians

Sapientia et Humanitas – The essence of physician training and practice

As the Hong Kong College of Physicians celebrates her 30th anniversary, we can proudly reflect on our achievements in setting a high standard for physician training and practice in our community. Recognising the increasing complexity of modern medical practice, our College was among the first to lay down the framework for specialisation. Our College now encompasses 17 different specialties with well-developed training programme and clearly defined criteria for specialist accreditation. The curriculum of each individual specialty has evolved over time to incorporate new advances in diagnostics and therapeutics, stipulate experience necessary for attainment of competence in technical procedures, and encourage exposure to other relevant specialties to broaden the professional horizon. While continuously enhancing the standard for training, the College has been mindful of the practicalities in implementation and possible hardship faced by the trainees. Successful implementation of the comprehensive training and accreditation framework has only been possible through the strong leadership of our Council over the past 30 years, tireless effort of our standing Committees and Specialty Boards, unfailing support from our Trainers and Fellows, and back up by our loyal and efficient Secretariat. As reflected in the articles in this issue of *Synapse*, the Specialty Boards are all poised to embrace the important new advances that will change our professional practice in the coming decades.

Our College has all along recognised the equal importance of the breadth as well as the depth of medical knowledge in fostering holistic patient care. It has been visionary for our earlier Councils to establish a higher physician training programme in Advanced Internal

Medicine alongside those of the specialties. Recognising the complex comorbidities among our elderly patients and the risk of fragmentation of care with over-specialisation, our College introduced in October 2010 the mandatory requirement that all specialty trainees (with the exception of Dermatology and Venereology) will have to undertake dual training with a broad-based specialty (either Advanced Internal Medicine or Geriatrics). In addition, with effect from July 2012, only specialists who have also been accredited in a broad-based specialty will be appointed as trainer by our College. Our dual training programme has been favourably commented on by many overseas physician colleges which are struggling to maintain a balanced supply of generalists versus specialists.

The reflection of the important milestones in the past 30 years of our College's history by our Senior Advisor in this issue of *Synapse* highlights the importance of our training programme to evolve with the changing healthcare needs of our population. Looking ahead to the coming decades, our College will face many challenges in our endeavour to maintain the standard of internal medicine training and practice. The traditional textbooks and didactic mode of teaching are no longer sufficient to cater for the rapid pace of advances in medical knowledge. The future generations of physicians will need to be able to master the electronic media and web-based resources to access up-to-date medical evidence and maintain lifelong learning. With increased sophistication of therapeutic interventions and requirement for seamless teamwork in delivery of complex medical care, there will be more widespread adoption of artificial intelligence and virtual reality for simulation training. In anticipation of growing emphasis on patient safety, our College will need to develop a framework for credentialing and maintenance of competence in invasive procedures not only during training but throughout the entire professional career. We should also prepare for the rising public expectation for the standard for medical care which will go beyond continuing medical education and continuous professional development to ultimately a system for periodic recertification for all registered medical practitioners.

Of equal if not greater importance to excellence in knowledge and skills is the humanistic aspect of medical practice, namely ethical standard and professionalism. We shall need to prepare the future generations of physicians for the evolving doctor-patient relationship with easier access to medical information and even consultation via the internet as well as increased expectation on safety and accountability. On the other hand, they should strive to maintain their professional standard while coping with the drive for cost saving and enhanced efficiency by the funding organisations. There will also be challenges in appropriately harnessing novel therapeutic options made possible by medical advances such as

gene-based diagnostics and therapy as well as personalised medicine. The Government is yet to formulate a sustainable service and financing model that will cater for the needs of an ageing population and physicians should be actively engaged in the planning process. The above issues need to be considered in the context of changes in the value system of our younger generation. Teaching of professionalism has never been easy and opportunity for role-modelling is increasingly constrained by the heavy workload that compromises trainer-trainee contact time. We shall need to work together to develop a model for instilling in our trainees a high ethical standard, the ability for critical analysis of complex moral issues and a strong sense of social responsibility.

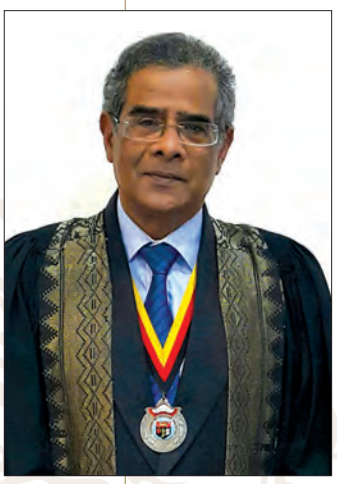
The challenging tasks ahead call for strong leadership from our future College Council and concerted effort of our Fellows. Our Founding President has described briefly in his Foreword the history of *Synapse*. As a neurologist, I cannot resist remarking on the name of our College Newsletter. Synapses serve the important function of transmission of signals from one nerve cell to another within the nervous system. Signal transmission across a synapse is always unidirectional. However, the human brain has evolved into a complex organ with highly sophisticated functional potentials through an intricate network of synapses that give directions and feedbacks among the myriads of nerve cells in the nervous system. In order for our College to excel in its mission of raising the standard in the science and art of internal medicine practice, we cannot rely on one-way communication from our College to our Fellows through *Synapse*, but shall need active contributions and feedback from all our Fellows, especially our younger generation of physicians, to shape the future of our profession.

Congratulatory Messages

Since its inception in 1986, the Hong Kong College of Physicians has stood by its vision and made significant contributions to the advancement of internal medicine in Hong Kong, including setting the standard of practice, providing quality training and continuing professional development, as well as promoting research in medicine and collaboration with overseas partners. Today, its membership counts more than 1 500 Fellows in seventeen specialties with over 200 Members. I commend the College for its outstanding achievements in nurturing talented physicians as well as physician trainers, while advancing medicine and patient care for the benefit of our community.

My warmest congratulations to the College on its 30th anniversary and I wish it continued success in the years ahead.

Dr. KO Wing-man, BBS, JP
Secretary for Food and Health
Food and Health Bureau



Patron: His Royal Highness, Sultan of Perak, Sultan Nazrin Muizzuddin Shah

ACADEMY OF MEDICINE OF MALAYSIA

9th June 2016

Dr Patrick Li Chung Ki
President
Hong Kong College of Physicians

Dear Dr Patrick Li

I would like to congratulate the Hong Kong College of Physicians (HKCP) which is celebrating its 30th anniversary in October 2016 and am happy to pen this message for the special anniversary issue of Synapse, the College newsletter.

With its untiring efforts and dedicated officers, the HKCP has continued to fulfil its role as a statutory body responsible for overseeing physician training and setting the standard of internal medicine practice in Hong Kong.

May I wish the HKCP a wonderful 30th anniversary with more achievements and progress to come.

Yours sincerely

Prof Dato' Dr P Kandasami
Master
Academy of Medicine of Malaysia

ACADEMY OF MEDICINE
SINGAPORE

On behalf of the Council of the Academy of Medicine, Singapore, I would like to record my heartiest congratulations to the Hong Kong College of Physicians on the occasion of its 30th anniversary.

Since its foundation in 1986, the Hong Kong College of Physicians has been playing an important role in upholding the standard of physicians training and practice in Hong Kong as well as providing professional inputs to the Government on its public health initiatives. With the complexity in medicine and the high cost of technology, its role has never been more relevant and important. The Academy also enjoys a close relationship with the College, which continues to flourish and further strengthened with their participation in the bi-annual Singapore-Malaysia Congresses of Medicine, in which the Hong Kong Academy of Medicine is a participating partner.

Once again, I would like to congratulate the Council and Fellows of the Hong Kong College of Physicians on reaching this milestone, and look forward to maintain this link of kinship and close ties between both professional bodies.

Dr S R E Sayampanathan
Master
Academy of Medicine, Singapore

COLLEGE OF PHYSICIANS, SINGAPORE

CONGRATULATORY MESSAGE TO THE HONG KONG COLLEGE OF PHYSICIANS ON ITS 30TH ANNIVERSARY

On behalf of the Council of the College of Physicians, Singapore, it gives me great pleasure in congratulating the Hong Kong College of Physicians on its 30th Anniversary.

The Hong Kong College of Physicians has been overseeing the physician training and responsible for setting the standard of internal medicine standards. The leadership and structured training programs provided by College has led to the large pool of internationally recognized physicians and the high standards of local medical care. Over the years the Hong Kong College of Physicians has demonstrated its commitments to uphold the highest standards of professional competence.

We have had the opportunity to welcome the Hong Kong College of Physicians through the bi-annual Singapore-Malaysia Congress of Medicine. We sincerely hope that the Hong Kong College of Physicians will continue its success and that our two colleges will continue to maintain our close relationship. We will continue to collaborate and look forward to further developing our relationship in the future.

Once again, many congratulations to the Hong Kong College of Physicians on their 30th Anniversary.

Dr Chan Choong Meng
President
College of Physicians, Singapore

RACP
Specialists. Together
EDUCATE ADVOCATE INNOVATE

From the President

14 June 2016

30th Anniversary of the Hong Kong College of Physicians

Members of the Board, Fellows and staff of The Royal Australasian College of Physicians (RACP), join with me in congratulating the President, Council, Members, trainees and staff of the Hong Kong College of Physicians on the occasion of your 30th Anniversary. The RACP has witnessed the growth and development of the Hong Kong College of Physicians from small beginnings to the respected establishment of education and learning that it is today.

The RACP is proud of its close association and collaboration with the Hong Kong College of Physicians over many years through the exchange of ideas and practices. The Hong Kong College of Physicians' reputation for excellence is well-recognised in the region and internationally. I am sure the activities and events surrounding the Academic Sessions in October 2016 will highlight, recognise and reflect the achievement of excellence synonymous with the Hong Kong College of Physicians.

Once again, congratulations to the Hong Kong College of Physicians' on this 30th anniversary of achievement, collaboration and excellence.

Catherine Yelland

Dr Catherine Yelland PSM FRACP
President
The Royal Australasian College of Physicians

Royal College of Physicians

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Dr Li Chung Ki Patrick
President
Hong Kong College of Physicians
Room 603 HKAM Jockey Club Building
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Aberdeen, Hong Kong

October 2016

Message from the President of the Royal College of Physicians of London

I am delighted to join with many other people around the world to congratulate the Hong Kong College of Physicians, and its President, Fellows and Members, on the celebration of their 30th Anniversary.

Doctors and the professional institutions of our countries have close and enduring bonds. Those bonds have been forged by our shared heritage in medicine, in education and in practice, and in academic medicine. They are invigorated by the many personal exchanges we have enjoyed over the years, and they have been made even stronger during the formative years of this established and admired Institute, which I am sure will, with all that it stands for, continue to grow and flourish as it has during the thirty years you celebrate today.

Jane Dacre

Professor Jane Dacre MD, PRCP
President
Royal College of Physicians

Royal College *of*
Physicians *of* Edinburgh

Representing physicians, maintaining standards.

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It gives me great pleasure in conveying this message on the occasion of the 30th anniversary of the Hong Kong College of Physicians. The Hong Kong College can be justly proud of its enviable record in providing professional support and high quality postgraduate education for doctors at all stages of their careers.

I look forward to this year's congress with great interest and anticipation. The Royal College of Physicians of Edinburgh is proud of its very close and long association with Hong Kong and I am honoured to have been invited to attend this prestigious event. We wish you every success for the future.

With kind regards
Yours sincerely

Professor Derek Bell MD FRCPE
President

ROYAL COLLEGE
OF PHYSICIANS AND SURGEONS OF CANADA
COLLÈGE ROYAL
DES MÉDECINS ET CHIRURGIENS DU CANADA

royalcollege.ca • collegeroyal.ca

June 16, 2016

Dr. Li Chung Ki Patrick
President
Hong Kong College of Physicians
Room 603, Hong Kong Academy of Medicine
99 Wong Chuk Hang Road, Aberdeen, Hong Kong

Dear President Li

On behalf of the Royal College of Physicians and Surgeons of Canada, I would like to extend my heartfelt congratulations to the Hong Kong College of Physicians. You have accomplished a great deal in your 30-year history, and I'm sure your college will reach new milestones in the years ahead.

We applaud your efforts in education, assessment, professional standards and research – work that is essential to advancing medicine and quality patient care. From one college to another, we thank you for the important service you provide to your physicians and health system, as well as your college's contributions to the international postgraduate medical education community.

Warmest regards

Kevin Imrie, MD, FRCPC, FACP, FRCPI (hon)
President

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

From the President

June 2016

To the President and Council
Hong Kong College of Physicians

I am delighted to send the good wishes and congratulations of the Royal College of Physicians and Surgeons of Glasgow to the Hong Kong College of Physicians on the occasion of its 30th Anniversary.

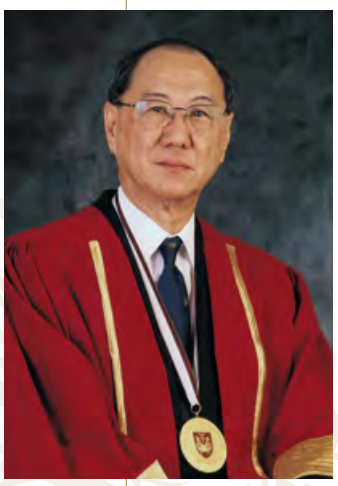
These milestones are important and provide an opportunity to step back, consider all that has been achieved and plan ahead. Medical practice has become increasingly demanding over the last three decades and the Colleges are vital as professional organisations to provide the strategic resources for Fellows and Members to thrive in this challenging environment. We cherish the links and the opportunity for collaborative working with your College and indeed recall the long association between our cities. Early on, this was perhaps best represented by the work of a Glasgow graduate, Professor Alexander J S McFadzean, who became a very significant figure in the development of medical knowledge, training and research in Hong Kong.

As your College continues to play its role in the provision and direction of training, as it interacts with the government in developing initiatives for the future, we stand with you. Our common interest and duty to support and sustain the highest possible standards in healthcare remains a set of important shared objectives. We look forward to continuing to interact and to share experience with you in the years ahead.

With very best wishes from your friends here in Glasgow.

Yours sincerely

Professor David J Galloway, PRCPSG
President



Richard Yu
Senior Advisor, Hong Kong College of Physicians

HKCP – Celebrating Thirty Years in the Pursuit of Excellence

I am proud and privileged to have witnessed and participated in the growth and advancement of the College over the past 30 years.

The first 25 years — from infancy to adolescence to maturity — was well-documented in the HKCP 25th Anniversary Monograph – *Sapientia et Humanitas*.

Here, I wish to recount a few areas and events in our history, areas and events of enormous significance which shaped the path by which the College has traversed 30 years with *elan* and achievement. My tale is one of dynamics and upward progress, of an evolution which was necessarily rapid under the rapidly changing paradigm of science and art in the practice of medicine.

In the early 1990s, the Education and Accreditation Committee was endowed with a mandate to integrate the traditionally separate streams and departments of Medicine and Geriatrics. This was on the sage advice of EK Yeoh, who was Vice-President and Chairman of the Education and Accreditation Committee at the time he was appointed Chief of the Hospital Authority. Of particular importance was a vision of a rapidly ageing population in Hong Kong. The rationale and objective of the integration was to ensure that geriatricians and their trainees would be capable of managing the acute medical problems which can be projected to increasingly occur in the ageing population. Its success is clear from the fact that Geriatrics is now on par with Advanced Internal Medicine as a broad-based specialty. Not only is the new generation of geriatricians as competent as general physicians, they are now beginning to further specialize in other subspecialties — Cardiology, Endocrinology, Diabetes and Metabolism, and Gastroenterology-Hepatology — to name a few.

Because of the dearth of grandfather specialists, the Specialty in Infectious Disease began as a subcommittee under Advanced Internal Medicine. The practice and its training guidelines were still in the 'dark ages'. A fundamental and radical departure from the traditional approach then took place — mandatory training in Microbiology as the backbone of infectious disease. This initiative was initially met with antagonism and objection on the part of many microbiologists, with some archaic physicians thrown in for good measure. However, with perseverance, commitment, and strong belief in the proper direction — I mention in particular Prof KY Yuen and Dr Robert Collins (who was President of the Hong Kong College of Pathologists in the 2002) — a set of new guidelines was adopted by both Colleges in a landmark collaboration. Soon after, other specialties also entered into the collaborative training with the College of Pathologists — Haematology with Laboratory Haematology, Endocrinology with Clinical Biochemistry and Rheumatology with Immunology. Trainees in these specialties now command a fundamental understanding of the diseases they are to manage.

Changing demographics, shifts in the distribution towards higher ages and an absolutely older population have combined to bring about a change in the structure of the specialties. The College now boasts 17 Specialty Boards. Over 30 years, there has been a progressive increase in the number of specialists in Infectious Disease, Rehabilitation, and Medical Oncology — the latter to meet an alarming increase in cancer among the aged. Rehabilitative Medicine, Infectious Disease, and Medical Oncology are now independent Boards.

Technological change has supplied the physician with a greater number of more efficient tools to manage disease. *Pari passu*, the College is busy updating guidelines in its training manual: a 6th Edition will be published by the end of this year.

To ensure fairness, transparency and accountability, the Examination Committee has introduced new format of assessment for Higher Physician Trainees in both Advanced Internal Medicine and the specialties. In December 2011, the two Annual Assessments have been replaced by one Interim Assessment during Higher Physician training. This change aimed to reduce anxiety on the part of Higher Physician trainees who were required to face six examinations during professional training. From June 2005, a formally-structured and standardized format was introduced in the Exit Assessment in three sections — Acute, Chronic and Ethics Scenario questions. From June 2013, to pass overall candidates must achieve pass marks in aggregated score in Acute and Chronic Sections. Beginning in December 2016, the Interim Assessment format will be re-

structured to more effectively assess the candidate's clinical, diagnostic and management process and data and imaging interpretation. Two questions based on lectures given in the Annual Scientific Meeting of the College, Hong Kong Medical Forum of the HKU Department of Medicine, and Advances in Medicine, CUHK Department of Medicine and Therapeutics will now appear. Remaining unchanged are the two case reports, which seek to develop the trainee's ability in analyzing and preparing case history, management, and literature review.

A Self-Learning Tool has been introduced as part of training for both Basic and Higher Physician Trainees. It is a compulsory web-based requirement which must be completed before eligibility for Interim and Exit Assessment. This change ensures that trainees would possess broad and deep knowledge exposure to complexity in medical diseases and risk management.

In the past 30 years, the College has grown into a multi-faceted institution, serving a total of 1,740 Fellows with continuing increase in the number of trainees to provide cutting edge healthcare of international standard to the community. The Education and Accreditation Committee, Examination Committee, and the 17 Specialty Boards have assumed heavy and increasing burden of work and responsibilities. All the Board Chairmen and Members have served with purpose and dedication, commitment and distinction, a happy fact for which I am very proud and grateful. Last but not the least, the College Secretariat has performed above and beyond the call of duty. In this, Gloria Ng — HKCP's *passepartout* and walking encyclopedia — has borne the blunt with grace and humour.

Our College in her 30 years is still young. That it has achieved international repute in so short a time has filled me with great pride. This happy event is due in large part to unstinting dedication and effort on the part of all Consultants, Fellows, and Professors in the Hospital Authority and the two Academic Departments of the Hong Kong and Chinese Universities.

To all the Chairmen and Committee Members, the Secretariat, and to all Fellows of the College, I offer my grateful thanks. My cup runneth over …

HKCP Council, 1988

HKCP Council, 2015-2016

Past and present Presidents of the HKCP

Advanced Internal Medicine

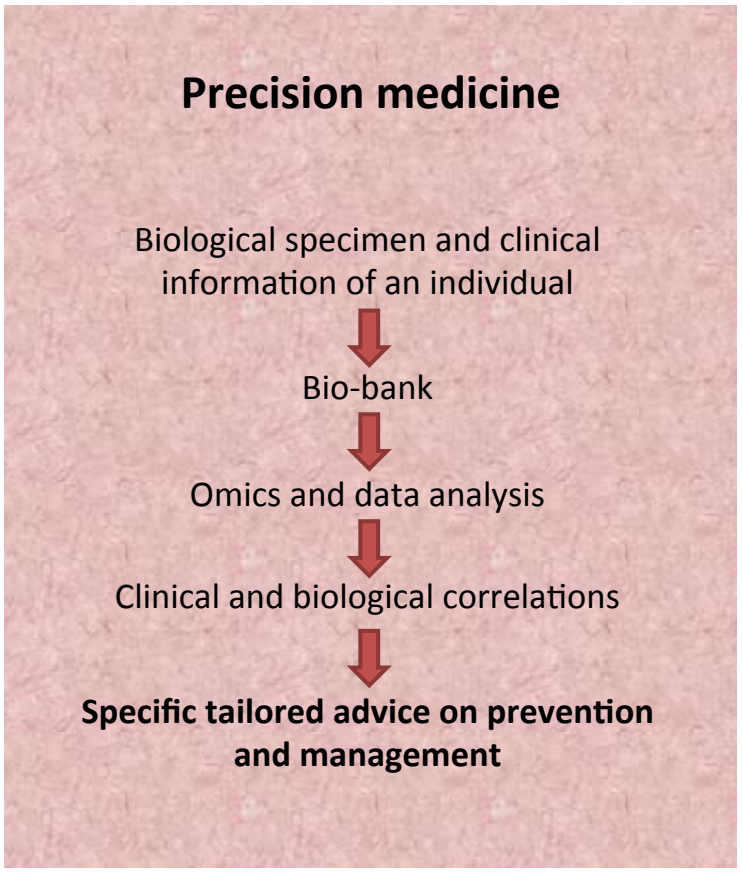
Precision Medicine

JONAS H.M. YEUNG

Since the establishment of advanced internal medicine (AIM) as an integral component of higher physician training (HPT) in 1996, we have seen major developments in the training programme and accreditation process.

With the objective of acquiring all-round competence as physicians, trainees are required to have experience in handling medical problems in centres offering obstetrics and acute surgical services (2009 onwards). In October 2010, AIM (as well as geriatrics) became a broad-based specialty forming a mandatory part of the HPT programme (excluding dermatology and venereology).

Since the first exit assessment in June 1998, there have been evolutionary changes in the examination format, essentially pioneering HPT programmes. In June 2005, a structured format was adopted for the exit assessment, with standardized questions in three sections: acute, chronic and ethics problems, aiming at comprehensiveness of assessment, control of quality and consistency of questions, while maintaining confidentiality. In December 2011, a single interim assessment (30-minute viva) replaced the first and second annual assessments (20 minutes each). Medical knowledge covered at Hong Kong College of Physicians (HKCP) annual scientific meetings is tested. Completion of a web-based 'self-learning tool' has become a compulsory requirement before a candidate is eligible for interim and exit assessments. Starting from June 2013, in the exit assessment, candidates must obtain pass marks in their aggregate score in



the acute and chronic medicine sections, in order to secure an overall pass. And from December 2016, the interim assessment will also adopt a structured format, testing diagnostic processes and management of medical diseases, as well as data and image interpretation. All these form a solid foundation for physicians after completion of training, enabling them to be fully prepared in taking up new professional skills and advancement.

Indeed, rapid developments in molecular medicine and biotechnology have led a startling speed to great advances in diagnostics and therapies for patients. These involve all branches of internal medicine. On the patient side, each individual is unique and deserves individualized appropriate management, not simply in the humanistic sense, but for strong reasons of biological individuality. These form the basis of precision medicine, which takes into consideration the genetic and molecular landscape of an individual, allied with clinical and environmental information, to decide on the best preventive and management strategies.

Precision medicine is not new, but was brought to wider attention when the European Union in 2012 established the 'European Alliance for Personalized Medicine', and the United States in 2015 proposed the 'Precision Medicine Initiative'. Since then, views have been expressed highlighting possible over-

expectations on the part of the public, the complexity of the processes, and potential implications as regards the ethical as well as socio-economic dimensions. Whatever the perspectives, developments leading to precision medicine are now under way, with cumulating scientific findings based on collaborative work worldwide, including Hong Kong. The impact on clinical practice cannot be ignored.

Precision medicine includes, after informed consent, obtaining biological specimens (such as serum) of an individual, using high throughput 'omic' technologies (genomics, transcriptomics, proteomics, etc.), and comparing them with data from the bio-bank, with analysis and clinical-biological correlation (Figure). The responsible physician then uses the findings to discuss appropriate preventive measures (if high risk and before having the diseases) with the individual and best benefit-versus-risk treatment proposals, with shared decision-making by the individual and physician. Bio-banks must be under strict regulatory control. Clinical researchers in Hong Kong are currently working with major academic institutions in the United Kingdom, Europe and North America on the addition of local Asian data.

Among the relevant data that influence treatment choices and dosages, information from pharmacogenomics can give useful direction, which provides a genetic explanation why effective outcomes in well-designed large clinical trials may not be replicable with every patient. A seminal study by Masellis et al (*Brain* 2016;139:2050-62) has identified the specific single nucleotide polymorphisms of the dopamine D2 receptor gene that account for the improvement effect of rasagiline in patients with early Parkinson's disease. This has led to views that the future design of drug trials as regards recruitment, as well as analysis of data, will need to include genotypes. Indeed the use of bioinformatics in precision medicine has commenced in oncology, most notably in treatment planning.

In conclusion, continual advancements in molecular biology and technology have provided guiding evidence for physicians in giving advice on prevention and management tailored to individuals, aiming at improved effectiveness. These can be viewed as modern clinical tools added to the core traditional principles of good clinical practice, the doctor-patient relationship, and medical ethics.

Cardiology

New Advances in Cardiology

KWOK-KEUNG CHAN

There are major innovative advances that will greatly change clinical practice in the field of cardiology, namely, the leadless pacemaker, transcatheter aortic valve implantation (TAVI), and the bioresorbable stent.

The basic design of cardiac pacemakers has remained relatively unchanged over the past fifty years: a pulse generator connected to one or more transvenous leads. The transvenous lead is usually considered the weakest link in the conventional pacemaker system, as the insertion of a transvenous lead can result in both acute and chronic complications. Besides, the creation of a subcutaneous pocket carries some risk of local complications, such as haematoma and erosion.

A self-contained, leadless, single-chamber right ventricular pacemaker represents a novel breakthrough technology. The leadless pacemaker integrates the pulse generator and sensing/pacing electrodes into a single unit and is implanted into the right ventricle by a special delivery catheter through the femoral vein. The leadless pacemaker is small (about 1 cc) but its battery life is comparable to that of a transvenous pacemaker. The current generation of leadless pacemakers can only provide single-chamber right ventricular pacing, but the next generation of multichamber pacing systems is already in development.

TAVI has been developed as a treatment option for patients with severe aortic valve stenosis and contraindications to surgical aortic valve replacement or high surgical risk. The transcatheter aortic valve prosthesis can be balloon-expandable or

self-expandable. There are various implantation access routes, including femoral (the most common), transapical, subclavian, and direct aortic. Non-invasive imaging is crucial in assessment of the aortic annulus for prosthesis sizing. The durability of the transcatheter aortic prosthesis seems adequate for elderly patients with limited life expectancy. But if younger patients are considered for TAVI, durability remains a concern. We are now seeing rapid developments in prosthetic designs, sizes, and delivery systems. These advancements may provide further insights into the use of TAVI in lower-risk patients in the future.

Metallic drug-eluting stents in percutaneous coronary intervention have been found to reduce acute vessel occlusion and restenosis. However, a permanent metallic stent embedded in a coronary artery has long-term disadvantages, leading to vascular inflammation, stent thrombosis, and impaired coronary vasomotion. The current bioresorbable stent is made from poly-L-latide and is hydrolyzed into water and carbon dioxide inside the body. Bioresorbable stents offer the mechanical scaffolding and the drug-eluting capabilities just as regular metallic stents. But they are completely absorbed over the following few years, allowing for restoration of vessel-wall vasomotion and physiology. The lactic acid–based stent has relatively thick stent struts and a large crossing profile. So there are certain limitations in treating complex coronary lesions, for example left main lesions, bifurcation lesions, and heavily calcified lesions. We can look forward to more long-term clinical data in the coming years.

With the introduction of innovative interventional procedures, the provision of medical services requires new skills and knowledge. There is a need to establish a formal process to verify the credentials of health care professionals and to define the scope of practice. In the Hospital Authority (HA), a two-tier system oversees the development of credentialing: the Central Credentialing Committee and the Cluster Credentialing Committee. The Central Credentialing Committee is entrusted with steering corporate development and endorsing credentialing activities. The HA has a partnership and liaison relationship with professional bodies such as the Hong Kong Academy of Medicine (HKAM) and the respective colleges. The Central Credentialing Committee communicates with the HKAM at various stages of the credentialing activities review to align the professional requirements. The members of the Cardiology Specialty Board provide input on the qualifications, professional training credentialing guidelines, and clinical experience of operators, and on defining the scope of practice at different centres. The first batch of credentialed procedures, including TAVI, was endorsed by the Central Credentialing Committee in December 2015.

There are 258 Fellows (135 in HA and 123 in the private sector), and 19 trainees under the Specialty Board of Cardiology.

Clinical Pharmacology and Therapeutics

Developments in Clinical Pharmacology

BERNARD M.Y. CHEUNG

Clinical pharmacology is about the use of drugs in man. The discipline is both broad and specialized (Box), and covers the full spectrum of drugs for human use, from the development of new drugs and testing them in clinical trials, to the post-marketing monitoring of drug utilization and detection of adverse effects, toxicity, and interactions. It provides the tools for selecting drugs and developing guidelines on the basis of risk-benefit and cost-benefit. Increasingly, genetic and genomic analysis is used to predict therapeutic benefit and adverse effects. Clinical pharmacologists treat not only individual patients but also deal with the effectiveness and safety of drugs at the population level.

The modern practice of medicine is based on evidence derived from large clinical trials and meta-analyses. Clinical pharmacology is therefore the discipline underpinning the approval of new drugs. However, large Phase III trials are extremely expensive and so there is a trend towards well-conducted Phase I trials that enable early decisions on the development of new drugs. To date Hong Kong has two dedicated Phase I clinical trial centres: at the Prince of Wales Hospital and Queen Mary Hospital. These purpose-built units are equipped and staffed to conduct first-in-man trials in patients and normal volunteers. In August 2016, these two units were accredited by the China Food and Drug Administration, making them the first accredited Phase I units in the whole of China. These facilities are also suitable for studies of bioavailability and bioequivalence, for which there is

Roles of clinical pharmacology

- Drug development
- Clinical trials
- Evaluation of drug efficacy, safety, and cost-effectiveness
- Pharmacoepidemiology and monitoring of drug use
- Pharmacovigilance
- Pharmacogenetics and pharmacogenomics
- Clinical toxicology
- Undergraduate and postgraduate teaching
- Summarizing evidence and producing guidelines
- Pharmacoeconomics
- Drug policy

a large demand in China and Hong Kong because of the tighter regulation of generic drugs.

The concept that drugs are harmful until proven otherwise should also be extended to traditional, herbal, and alternative medicines. Such drugs can be evaluated by randomized double-blind controlled trials, meta-analysis, pharmacovigilance, and pharmacoeconomics. Such critical evaluation is particularly important when there are firm beliefs about their efficacy and safety.

Clinical trials do not necessarily reflect real-world clinical practice, nor do they have the power to detect rare adverse effects. Information gained from pharmacoepidemiology and pharmacovigilance is as important as the evidence base derived from clinical trials. Adverse drug reaction is a major reason for medical consultations and admissions, yet drug toxicity and drug-drug interactions are neglected areas in a world fixated on blood tests and scans. As the cost of genotyping falls, clinical pharmacologists will have molecular tools to refine their diagnosis. There are already DNA chips that can predict beneficial or adverse responses to certain drugs. This growing and specialized area, often called precision medicine, calls for input from clinical pharmacologists.

Up to now, there are eight Fellows and two trainees in clinical pharmacology in the College. There is a worldwide shortage of clinical pharmacologists because hospitals want clinicians in busy specialties. Yet, from the viewpoint of a health system such as the Hospital Authority of Hong Kong, the money saved and harm prevented by treating patients appropriately will pay for the employment of clinical pharmacologists many times over.

Clinical pharmacologists can also help to run clinical toxicology services in hospitals. While acute poisonings are managed initially in accident and emergency departments, medical departments look after patients needing hospitalization, intensive care, and follow-up. Subacute and chronic poisoning are managed in a toxicology clinic. To provide a better toxicology service, the Poisons Treatment Centre was set up at the Prince of Wales Hospital, and a multidisciplinary clinical toxicology service was initiated at Queen Mary Hospital. Clinical toxicology is a key component in the training programme in clinical pharmacology and there is currently a plan to launch a training programme in clinical toxicology under the Subcommittee in Clinical Pharmacology and Therapeutics in the College.

Clinical pharmacology is a small specialty at present, but with the development of pharmacogenomics, Phase I clinical trials units, and clinical toxicology, it is now a growing and exciting specialty.

Critical Care Medicine

Critical Care Medicine: Making Steady Progress

WAI-MING CHAN

In the field of critical care medicine (CCM), major improvements have been seen in the survival rate of some common syndromes in intensive care units (ICUs), including acute respiratory distress syndrome (ARDS) and septic shock. The improvements largely stem from enhancement of evidenced-based practices in ICUs, by distinguishing effective against ineffective treatment strategies. Evidence-based medicine will guide the development of CCM in the foreseeable future, and we will enjoy the benefit of refined tools in haemodynamics monitoring and in support of respiratory failure and circulatory failure. Meanwhile we are seeing constant improvements in hardware and equipment, for example, smart ventilators are now available that can adjust ventilation to specific physiological targets in patients, thus achieving earlier weaning from ventilators. It is also anticipated that extracorporeal treatment will have an impact in some areas, such as the use of extracorporeal membrane oxygenation (ECMO) in circulatory support and after cardiac arrest, the use of various blood-purification devices, and extracorporeal elimination of carbon dioxide. Blood purification devices to remove endotoxins are now being used in clinical trials and might modulate the outcome of patients with septic shock. With the use of ECMO in the settings of cardiac arrest, survival with good neurological outcomes can be achieved in around one-third of patients.

Technological improvements are likely to facilitate and enhance personalized medicine in the ICU, as most ICUs now

are moving towards digital collection of patient data. In the era of Big Data, more precise delineation of clinical syndromes and better prognosis could be possible. Thus, we might be able to achieve better phenotypic classification of sepsis and ARDS, and thus individualized therapy.

There is an increasing need for specialists to handle the expanding range of services now being delivered by CCM but, at the same time, there is an increasing difficulty in recruiting trainees into CCM training. Over the past few years, the Board has worked towards greater collaboration with other medical specialties, such as cardiology, respiratory medicine, and nephrology, such that trainees will be trained up to a standard enabling them to collaborate with other specialists in meeting their need to support critically ill patients through their own specialty. On the other hand, in view of the increasing complexity of the case mix in ICUs, the Board has also endeavoured to increase the exposure of trainees to the ICU by extending their accredited training within ICUs. Thus, the training programme has been extended both in breadth and depth, balancing the quality of training with the expectations of the trainees. With these sustained effects, there has been steady growth in the number of both Fellows and higher trainees, now some 94 and nine respectively. Of the 15 Hospital Authority ICUs, ten are now managed by CCM Fellows.

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Dermatology and Venereology

The Emergence of Biologic Agents for Psoriasis

HENRY H.F. HO

The emergence of biologic agents for psoriasis in the past ten years and the prospect of more biologics emerging has changed the management concept for patients with psoriasis and posed challenges for dermatologists who are taking care of patients with the condition.

Before the emergence of biologic agents, with the limited capacity of topical and conventional systemic treatments (methotrexate, cyclosporin, acitretin) and phototherapy, health care workers and patients alike settled for a less-than-ideal treatment effect. With the greater potency of emerged biologic agents—the tumour necrosis factor alpha inhibitors (etanercept, infliximab, adalimumab), the interleukin-12/interleukin-23 inhibitor (ustekinumab), and an interleukin-17 inhibitor (secukinumab)—better control of moderate and severe psoriasis is now achievable. As a result the principles of management have been revised and treatment consensus re-written. It should be mandatory for health care providers to address these changes and adjust their practice. The changes are:

The need to grade the severity of psoriasis and tailor the treatment according to the severity as well as the response to initial treatment. An algorithm has been implemented to guide the initial treatment and to adjust within a time frame of 16 to 24 weeks if improvement is not satisfactory.

The treatment target needs to be set and set high: if the Psoriasis Area and Severity Index (PASI) score is to be employed for severity grading, PASI 75 (improvement of PASI score by 75%) is

the target, especially for moderate-to-severe psoriasis. A more recent trend is an even higher target of PASI 90, which is a result of both the potency of newer biologic agents and the patient's wish for clearance of their disease.

While grading of severity is important as a guide to treatment, dermatologists need to recognize, firstly, the limitations of the grading system (the commonest employed is the PASI); secondly, the heterogeneity of psoriasis (e.g., some patients have more facial involvement while others have genital or nail involvement); thirdly, that the impact of psoriasis varies between patients with a similar severity. Each patient has to be managed individually, and tools to assess the impact on particular patients (e.g., Dermatology Life Quality Index, DLQI) need to be employed.

While dermatologists' primary interest is managing the skin condition in patients with psoriasis, in parallel with the emergence of biologics, there is now a better understanding of psoriasis as a multi-system condition, with up to 30% of psoriasis patients developing psoriatic arthritis (PsA) and a significant proportion having comorbidities, especially of the cardiovascular system. Dermatologists have the responsibility of taking care not only of the patient's skin, but the patient as a whole, with at least the knowledge and skills to spot the early signs of PsA and comorbidities and be prepared to refer to the appropriate specialist.

The challenge is enormous, though well justified, and entails a paradigm shift from a targetless single treatment set for all to a targeted individualized treatment plan, all of which is time consuming. Dermatologists need to be prepared to undertake this.

At the same time, despite the excitement over the emergence of biologics, dermatologists need to be vigilant: we should not forget the lesson of efalizumab, which was approved for moderate-to-severe psoriasis in 2003. In 2009, after over 46,000 patients were exposed, the drug was withdrawn from the market after three confirmed cases and one suspected case of progressive multifocal leukoencephalopathy were reported.

In recent years more emphasis has been placed on procedural dermatology training: from diagnostic procedures, such as patch test, scrapping, and microscopy for fungal elements, to therapeutic procedures, including skin surgery and phototherapy. Trainees are encouraged to seize the opportunity to practise, while training institutes are required to adjust so as to facilitate procedural dermatology training. Of special note is dermoscopy: all clinics in training institutes are now equipped with at least one dermoscope; trainee dermatologists are encouraged to carry their own dermoscopes with them all the time; and dermoscopy images have been incorporated into interim and exit assessments.

The specialty in dermatology and venereology accepts its training programme members of the Hong Kong College of Physicians (HKCP) who have successfully completed their basic physician training. As stipulated in the Guidelines in Postgraduate Training in Internal Medicine (5th Edition, 2011), training in dermatology is a single specialty training not requiring dual training together with a broad-based specialty. Some 108 HKCP Fellows are now in the specialty in dermatology and venereology, of which 20 are serving in the Department of Health and two in the Hospital Authority. Currently there are 11 trainers in the Social Hygiene Service, which is an accredited training institute for dermatology and venereology, with ten trainees undergoing training. The other accredited training institute currently in function is in the Prince of Wales Hospital, with one trainee under the supervision of one trainer.

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Endocrinology, Diabetes and Metabolism

A Journey in Dissection: From Genotype to Phenotype

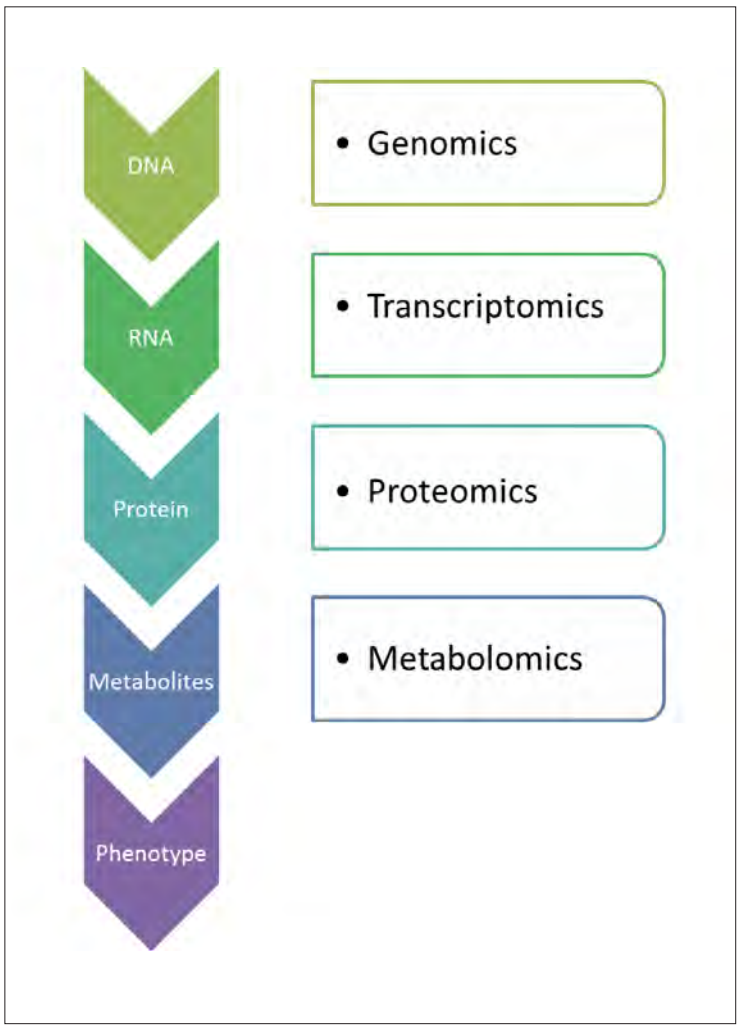
JENNY Y.Y. LEUNG

The field of endocrinology and metabolism is a relatively young science, and thus endowed with the enthusiasm and infinite potential of the young. It was first launched in the early 1960s, when the advent of immunoassays enabled the measurement of small molecules in our bodies, leading to the discovery of hormones. Endocrinology hastened its pace of development as genetic engineering enabled the production of man-made hormones, thus providing various new avenues of treatment. The most recent newcomers in this field were the parathyroid hormone, now being used for treatment of hypoparathyroidism, and the GLP-1 analogues, for the treatment of diabetes and obesity.

In the next few decades, the coming of age of the 'omics' and 'LEWAS', made possible by bioinformatics based on advanced computing technologies, will transform the field again, by greatly broadening our understanding of the impact and role of factors that thus far cannot be measured, due to the interactions with multiple factors and their effects that develop and evolve over a period of time. This will enable us to better predict disease at its early stage and deliver treatment in a personalized and multi-targeted manner.

Under the 'omics' are grouped genomics, transcriptomics, metabolomics, proteomics, lipidomics, microbiomics, and so on, each studying a complex set of biological molecules that share an overlapping and integrated set of functions.

From genotype to phenotype



To highlight a few areas, genome-wide association studies (GWAS) enable the comparison of the genetic sequence and allele frequency in the human genome for each single nucleotide polymorphism in a hypothesis-free way. For example, 185 loci associated with obesity traits have been identified in large-scale GWAS and 13 loci were associated with extreme and/or early-onset obesity. While GWAS are limited by its inability to take into account the interactions and the component of time, LEWAS has begun to add value. LEWAS (with the 'L' standing for 'longitudinal', the 'E' for 'environment, exposure, or epigenetics', and 'WAS' for 'wide association study') has added the dimension of time to our understanding of disease by testing at multiple time-points, thus providing an insight into the development and progression of diseases.

'Metabolomics', which involves the simultaneous comprehensive characterization of metabolites in the biological system,

represents the fingerprint of cellular metabolism. In particular, the metabolic-fingerprinting approach will help to identify new and unknown pathophysiological pathways of diseases. For example, elevated levels of branched-chain amino acids (leucine, isoleucine, and valine) or α-hydroxybutyric acid have been demonstrated in those who will develop type 2 diabetes mellitus nearly a decade ahead of the overt disease.

And the study of omics is not limited to the cells of an individual. We live in symbiosis with multiple organisms. The gut microbiota comprise 10 to 100 trillion microbes and play a crucial role in maintaining homeostasis. From the study of 'microbiomes', we have learned that obesity is associated with our gut microbiota and can be transmitted by transplant of the particular microbiome. Modulation of gut microbiota could be used as therapeutic target for treatment of diseases.

At the moment there are around 107 registered endocrinologists in Hong Kong. Of these some 56 are accredited higher-physician trainers, responsible for the training and supervision of 15 higher-physician trainees. Our latest training structure requires trainees to have practical experience in common endocrine assays in a hospital chemical pathology laboratory, and we are delighted to have experienced chemical pathologists as our honorary trainers at a number of hospitals. We also require trainees to be equipped to provide multi-disciplinary pituitary care. We encourage trainees and young Fellows to undergo basic and clinical research, either locally or overseas. Over the years, the dissertation topics of our trainees have covered a wide range of topics, from diabetes and thyroid diseases to adrenal, pituitary, reproductive, and metabolic bone diseases. Research from clinical, genetic, or basic science areas in the specialty has been awarded 'best thesis' recognition in recent years.

We look forward with excitement and anticipation to this interesting voyage into the unknown in the coming decade.

Gastroenterology and Hepatology

New Developments in Gastroenterology and Hepatology

MICHAEL K.K. LI

Our improved understanding of the key steps in the pathogenic mechanisms of liver and gastrointestinal (GI) diseases and recent progress in endoscopy technologies and techniques have led to many therapeutic breakthroughs.

Both chronic hepatitis B (CHB) and C (CHC) infections are the major public health concerns affecting hundreds of millions of people worldwide. For more than 25 years, treatment of CHC infection remained interferon-based with new drug discovery being hampered by the failure to develop a tissue-culture model for the hepatitis C virus (HCV). This hurdle was overcome in 2005 with the establishment of a robust HCV infection system that enabled molecular insights into the HCV life cycle and host-virus interactions. This knowledge fostered the discovery of direct-acting antivirals (DAAs) that target viral products at various steps in the viral life cycle and host-targeted agents (HTAs) that inhibit the host protein that contributes to viral replication. Now by using a combination of DAAs, the viral eradication rate can be as high as 100%, even in difficult-to-treat conditions such as cirrhosis, decompensated diseases, and post-organ transplantation. With a preventive vaccine still to be developed, these highly effective drug combinations are playing a crucial role in controlling HCV infection.

Due to the persistence of intrahepatic covalently closed circular DNA (cccDNA), eradication of the hepatitis B virus is not possible with the current treatment. Various DAAs and

HTAs that target the viral functions (inhibition of the priming of reverse transcription, core allosteric modulators, small interfering RNA [siRNA], cccDNA inhibitors, HBsAg release inhibitors) or the host functions (viral entry inhibition, induction of apoptosis of infected cell, immune response restoration) are undergoing Phase I and II studies. It is conceivable that these new drugs could eliminate the intrahepatic cccDNA and that we could envisage a complete cure for CHB in the near future.

Anti-tumour necrosis factors-α (anti-TNFα) have revolutionized the therapeutic approach to inflammatory bowel disease (IBD). Yet, this treatment is associated with loss of response in more than 30% of patients. New biologics that can be directed at different pathogenic mechanisms (integrin antagonist, interleukin antibodies, JAK kinase inhibitors) have been discovered and some have shown promising results in anti-TNFα failure patients. Cost affordability is a major concern for both anti-TNFα and the new treatments. Biosimilars are therefore being produced as lower-cost alternatives. Although they have been approved for use in Europe and Korea, more research is needed to assess their efficacy, immunogenicity, pharmacokinetics, and safety in IBD patients.

Our horizons in GI endoscopy are expanding rapidly. Much effort has been made to improve the endoscopic image by features such as high definition, high magnification, image enhancement, wider viewing angle, and laser endomicroscopy. These new endoscopes now play an important role in detection, classification, and diagnosis of early neoplastic GI lesions. The hurdle in diagnosing and treating small bowel disease has been overcome by the use of wireless capsule endoscopy and balloon-assisted enteroscopy. The application of interventional endoscopic ultrasonography continues to evolve. Patients requiring drainage of pancreatic/abdominal fluid collections, biliary decompression, local pancreatic cancer treatment, and celiac plexus neurolysis can be treated with this less-invasive option. Sophisticated procedures such as endoscopic submucosal dissection, peroral endoscopic myotomy, and submucosal tunneling endoscopic resection are becoming feasible alternatives to surgical intervention for early cancerous GI lesions.

Since the inception of gastroenterology and hepatology (G&H) specialty training under the Hong Kong College of Physicians, as at July 2016, 143 trainees have completed their training and passed the exit assessment. Currently we have 183 registered specialists, 71 trainers, and 25 trainees in this specialty. To meet increasing expectations regarding the competence of GI endoscopists, the Board has taken the initiative to enhance our basic and advanced GI endoscopy training (Figure).

Enhancement of basic and advanced GI endoscopy training

(1) Simulation training

With the approval of the Education and Accreditation Committee, the Board successfully organized a pilot simulation training course on basic endoscopic procedures for trainees in year 2015/16. The Board will work out the possibility of integration of simulation training into the core specialty training programme.

(2) Advanced GI endoscopy training programme

This is a two-year post-Fellowship training programme provided by accredited training institutions under the supervision of trainers acknowledged by the Board. There will be continuous assessment during and at the end of the training period. Fellows who pass the assessment will be issued with a certificate serving as a credential to facilitate granting of clinical privilege by their institutions. All invasive GI endoscopic procedures in Hospital Authority hospitals will require credentialing in the future.

Given the rapid evolvement in knowledge, techniques, and technologies in G&H, the Board has an important role to play in upholding training standards with the goal of delivering high-quality patient care.

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Geriatric Medicine

Geriatric Medicine in the Next Decade

CHRISTOPHER C.M. LUM

Geriatric medicine (GM) is branch of internal medicine concerned with the clinical, preventative, remedial, and social aspects of illness in old age. Older persons (or patients) are characterized by their progressive reduction in homeostatic capacity and individual variability in physiological parameters, as well as markers of organ function. Comorbidities, multi-morbidities, or manifestations uncommon in the young are typical in older patients. Dimensions or severity of morbidities in each older individual are likely to differ. Current standardization of diagnostic and therapeutic algorithms largely based on younger populations (typically age <70 years) or single disease/organ model have limitations in their applicability to older patients. Increasing researches have now moved age cut-off to <75 or <80 years as inclusion criteria instead of <70 years, or exclusively use older subjects (e.g., blood pressure lowering among patients age >75 or >80 years) as sampling frame. We will thus see more evidence-based guidelines tailored for older patients in coming decade.

With increasing heterogeneity among older patients, we are going to see more individualized or personalized medicine based on biological rather than chronological age. Because of different risk/benefit considerations, an 85-year-old fit patient with diabetes mellitus will require tighter control of the glucose level than a 75-year-old diabetic patient suffering vascular dementia. Within the wide range of heterogeneity, we are developing tool(s) for frailty assessment as surrogate measurements

in estimating bodily reserves which, in turn, guide the focus of care (e.g., whether to aim for primary/secondary prevention, or symptomatic relief/end-of-life care only). Research is now underway into different tools and their applicability in clinical practice.

Despite the advancements in medicine from other specialties or sub-specialties that delay senescence, ageing is inevitable unless of course one dies in middle age! With an increasing ageing population and complexity of conditions (pathologies or functional reserves), it is highly likely that hospital-based practice will serve an increasing number of older patients in all specialties except paediatrics and obstetrics. Evidence is accumulating that geriatrics medicine input, in terms of prehabilitation, peri-procedural assessment and optimization, and aftercare, improves patient outcomes. Instead of being a 'black box', there are increasing details (e.g., the prescription of prehabilitation) on which Fellows or future trainees need to acquire knowledge and skills. In this regard, inter-specialty collaboration, such as geri-orthopaedics, geri-surgery, geri-oncology, geriatrics-psychogeriatrics, geriatrics-family physician, is developing and we envisage better care of our senior citizens as a result of this collaboration.

Besides collaborations with-out (other specialties), GM will collaborate and share more with-in (other medical specialties). With changing demographies and successes in delaying progression of a disease, organ specialty colleagues are seeing more older patients with the same disease than before (e.g., advanced stages of Parkinson's disease). We will learn of advancements in basic science, patho-physiology, and technical skills and management from other specialties, while GM will share its knowledge and skills in the area in the context of older patients as stated above. The same collaboration and sharing applies equally to other trans-organ specialties, such as rehabilitation medicine and palliative medicine, and GM takes pride in the early development of this in light of patient care needs. Future training will see more cross-specialty learning.

With an ageing demographic, all clinicians should have basic training in understanding the uniqueness of older patients, and how they differ from the young in clinical assessment and management. This should start early at undergraduate level. Although both teaching universities have academic geriatricians, there are only three at present and this falls seriously short of requirements. With the population demand, more research and undergraduate teaching sessions are required. It is envisaged that more academic geriatrician posts will be put in place in order to meet population demand.

The Hong Kong College of Physicians displayed some foresight and vision concerning the rapidly ageing population in

early 1990s, giving the Education and Accreditation Committee a mandate to integrate their traditionally separate departments of medicine and geriatrics into a single department in public hospitals in the late 1990s. This was to ensure that geriatricians and their trainees had the necessary training and experience in managing acute medical problems. As of June 2016, we have 192 Fellows and 13 higher physician trainees in GM. Besides, all higher physician trainees, irrespective of advanced internal medicine or specialty training, have an exposure to advanced internal medicine. However, there is still a need to increase training posts and training centres to cope with population demand.

GM is growing fast in knowledge, skills, and development. It is one of the most cognitively challenging specialties. To quote a renowned geriatrician, one has to 'know something of everything, and everything of something'. It is a specialty that an 'expert generalist' and one who treasures person-centred care should choose.

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Haematology and Haematological Oncology

What Lies Ahead in Haematology?

ALBERT K.W. LIE

A look at the latest developments in haematology can provide some appreciation of likely changes in the near future.

Diagnostics

Proper clinical management of haematological malignancy is firmly rooted in diagnostic accuracy. In addition to standard cytogenetic and molecular tests for acute and chronic leukaemias, gene expression profiling and next-generation sequencing technologies better stratify risk factors and impact on intervention. The update of the World Health Organization classification of haematological malignancies due later this year will facilitate better treatment choice and clinical trial design.

Targeted agents

The recent successes in treating chronic myeloid leukaemia with tyrosine kinase inhibitors have prompted development of other targeted agents. Ruxolitinib, a Janus kinase inhibitor, already in clinical use, demonstrates significant clinical benefits in myeloproliferative neoplasms. Quizartinib, directed against multiple kinases, including FMS-related tyrosine kinase, is used in trials for treating relapsed or refractory acute myeloblastic leukaemia. Newer proteasome inhibitors, carfilzomib and ixazomib, have demonstrated significant efficacy in multiple myeloma (MM) patients failing the first-generation agent, bortezomib.

Monoclonal antibodies

Similarly, success with rituximab has led to the development of a novel anti-CD20 monoclonal antibody, obinutuzumab. Clinical results are very promising, especially in the treatment of indolent B-cell malignancy. Daratumumab (anti-CD38) and elotuzumab (anti-CD319) are approved in the United States for the treatment of advanced MM.

Besides directing against specific antigens expressed on tumour cells, a new class of monoclonal antibodies (e.g., nivolumab and pembrolizumab), termed immune checkpoint inhibitors, inhibit PD-1 protein expressed on normal T, B, and NK cells. This results in enhanced cytotoxic T-cell–mediated tumour-cell apoptosis. Early results show dramatic responses in certain types of lymphoma.

A third anti-cancer mechanism with monoclonal antibody is demonstrated by blinatumomab, a bi-specific T-cell engager (BiTE). It targets both CD19 expressed in B-cell malignancy (e.g., acute lymphoblastic leukaemia [ALL]) and CD3 expressed on T cells, linking the tumour cells and T cells together and effecting in cytotoxic T-cell–mediated tumour cell kill.

Other than for malignancy, eculizumab (anti-C5) is now an established treatment for paroxysmal nocturnal haemoglobinuria, pending introduction into the local scene.

Cell therapy

In recent years, worldwide use of haploidentical donors in haematopoietic stem cell transplantation (HSCT) greatly minimizes the hurdles in searching for an HLA-matched donor. Clinical outcomes comparable to HLA-matched siblings or unrelated donors are expected.

A novel form of cell therapy uses genetically engineered chimeric antigen receptor T cells (CAR-T cells). Autologous T cells harvested from patients are modified using a lentiviral vector with specificity for CD19 coupled with T-cell signalling domain. Reinfused CAR-T cells would then target CD19-expressing ALL cells. Preliminary results in refractory ALL are very encouraging, with a high remission rate and lasting effects.

Importantly, gene therapy is now becoming a reality. In a clinical trial, patients with β thalassaemia major received HSCT with modified autologous haemopoietic stem cells containing an engineered β globin gene. Subsequent transfusion independence has been maintained for over a year.

Training

Laboratory training has always been an important component in haematology. With the advancement of diagnostics mentioned above, laboratory exposure continues to be indispensable. Attachments at the Hong Kong Red Cross Blood Transfusion

Service also provide background training for the increasingly important area of patient-blood management.

In the last few years, expansion of autologous HSCT to all Hospital Authority clusters has not only helped to improve patient service but also enhanced training exposure to the basics in cell therapy. Nonetheless, clinical attachment at an allogeneic HSCT centre remains essential to complete training. Overseas attachment at centres with more sophisticated cell-therapy programmes is to be encouraged to meet further advancements in the field.

Conclusion

Long-term outcomes of some of the treatments mentioned above are being eagerly awaited. Currently, we have 61 Fellows and ten trainees under the Specialty Board of Haematology and Haematological Oncology. Truly exciting times in haematology await us and much work remains to be done.

Infectious Disease

The Endless War Against the Challenges of Emerging Infectious Diseases and Antimicrobial Resistance

NELSON L.S. LEE

Over the last two decades the medical profession has been continuously challenged by emerging viral diseases, such as novel coronaviruses (e.g., SARS, MERS), avian and pandemic influenza viruses (e.g., H5N1, H7N9, H5N6, $H1N1_{pdm09}$), viral haemorrhagic fever (e.g., Ebola virus), and vector-borne infections (e.g., West-Nile, Zika), as well as the rapid development of antimicrobial resistance (e.g., MRSA, VRE, ESBL, CRE, MDRA) [Figure]. Such viruses are commonly of zoonotic origin (e.g., bats, poultry, swine, camels, primates) and have adapted for efficient human-to-human transmission, thus creating the potential to cause epidemics. Morbidity and mortality are high among immunologically naïve humans, while treatment and vaccines are often unavailable to assist in outbreak control. Social and economic disruption can be enormous. Widespread, multidrug resistance among the common bacterial pathogens has greatly limited treatment options, leading to adverse clinical outcomes and increased health care costs. 'Untreatable' infections are increasingly reported. Better surveillance, newer diagnostic tools, novel treatments, and enhanced vaccines with rapid production are imperative in meeting the future challenges.

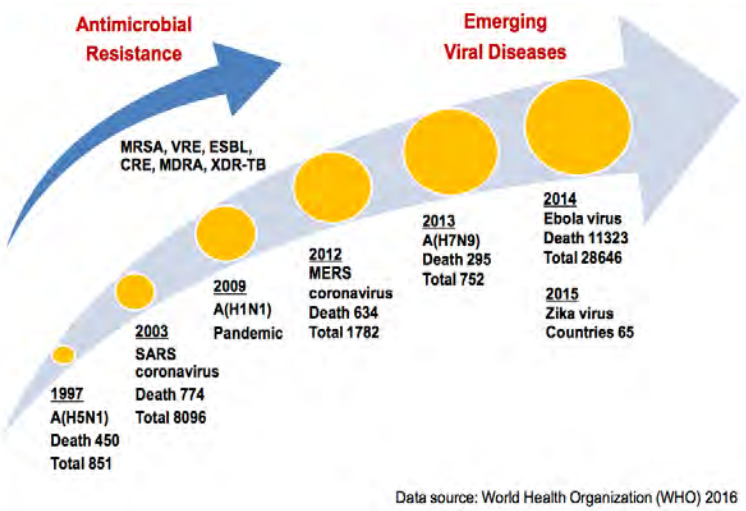
Enhanced, extended surveillance efforts at the 'human-animal interface', and research on virus evolution, genetic reassortment, and adaption for human infection and sustained transmission are necessary to improve our understanding of these natural events, paving ways to limit their future occur-

rence. Elucidating the role of extensive antibiotic consumption in the animal industry in driving the rapid development of antimicrobial resistance may lead to its successful control. At the community level, pathogen-directed and syndromal surveillance systems using the latest informatics technologies and social media can provide early warning signals and real-time data on evolving epidemics/pandemics.

Molecular diagnostics have largely replaced conventional culture or antigen tests in detecting viral infections because of their high sensitivity, specificity, and rapid turn-around time. Multiplex polymerase chain reaction (PCR) assays which detect a panel of respiratory viruses (e.g., influenza, RSV, coronavirus, and rhinovirus, plus selected bacteria in some systems) and molecular-based 'point-of-care' tests are starting to revolutionize patient management. Together with advances in biomarkers (e.g., procalcitonin, myxoma resistance protein-1) and transcriptional signature analyses that help to differentiate viral from bacterial infections, curbing unnecessary antibiotics prescription becomes possible. Next-generation sequencing and other advanced techniques are accelerating the discovery of novel viruses. Newer PCR assays for bacterial pathogens and their resistant genes (e.g., MRSA/mecA) may streamline antimicrobial therapies in future.

There is an urgent need to develop newer-generation, novel, and broad-spectrum antivirals against the proliferation of emerging infections. Recent examples include anti-influenza intravenous (e.g., peramivir) or long-acting inhalational (e.g., laninamivir) neuraminidase-inhibitors, sialidase fusion-protein, polymerase-inhibitors; anti-RSV fusion-inhibitors; anti-coronavirus protease inhibitors; and polymerase inhibitors that target

Major emerging viral diseases and antimicrobial-resistant bacterial infections in the last two decades



Data source: World Health Organization (WHO) 2016

Abbreviations: CRE = carbapenem-resistant Enterobacteriaceae; ESBL = extended-spectrum beta-lactamase producers; MDRA = multidrug-resistant *Acinetobacter baumannii*; MERS = Middle East respiratory syndrome; MRSA = methicillin-resistant *Staphylococcus aureus*; SARS = severe acute respiratory syndrome; VRE = vancomycin-resistant *Enterococcus*; XDR-TB = extensively drug-resistant tuberculosis

multiple RNA viruses (e.g., favipiravir inhibits influenza/flavi-/entero-/Ebola viruses). 'Immune-based' therapies (e.g., interferons, monoclonal antibodies) are being evaluated in coronavirus and influenza infections, showing promise. New antibacterials designed to address specific resistant mechanisms are in the pipeline (e.g., ceftaroline, ceftobiprole, dalbavancin; ceftazidime-avibactam, ceftolozane-tazobactam). For prevention, cell-based or recombinant vaccines may allow surge production capacity during epidemics; adjuvants or intradermal administration can amplify immunogenicity. The search for a 'universal' influenza vaccine, which offers cross-protection and cellular immunity against evolving virus strains, remains the Holy Grail for scientists. Clinical trials of these next-generation vaccines are already underway.

To meet these challenges, the Hong Kong College of Physicians has played a pivotal role in the professional training of clinical infectious disease specialists. In 2002, in collaboration with the Specialty Board in Microbiology, Hong Kong College of Pathologists, a leading-edge, well-rounded programme was initiated. Presented in distinct modules, the core programme covers all the major areas, including emerging and communicable diseases, principles and practices of infection control, clinical and laboratory microbiology (mandatory), tropical and travel medicine, serious infections in immunocompetent and immunocompromised hosts, HIV/AIDS, complicated tuberculosis, clinical epidemiology, and public health. Starting with a few pioneers, the specialty has grown rapidly to have more than 30 fully accredited Fellows and 14 experienced trainers, and established its specialty board in 2013.

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Medical Oncology

Cancer Immunotherapy: The Fifth Element

EDWIN P. HUI

In 2013, *Science* magazine named cancer immunotherapy the breakthrough of the year. It is forecast that immunotherapy will become the treatment backbone in 60% of cancer types during the next decade.

The concept that the immune system has a role in controlling cancer is not new. Cancer immunotherapy was born in 1891, when William Coley began injecting bacteria into a patient's tumour in the hope of triggering an immune response to the infection that would also attack the tumour. Recognizing the huge success of vaccines in preventing infectious diseases, cancer researchers have also tested multiple vaccines made up of inactivated tumour cells, with the hope of activating the immune system against the cancer. But evidence of clinical responses to these approaches has been mostly anecdotal.

Knowledge of immune regulation has led to the testing of recombinant cytokines, such as interferons and interleukin-2, in activating the immune system against cancer. With these agents, tumour responses became more reproducible and sometimes durable, but these were still infrequent (achieved in <5% of patients) and occurred in few rare cancer types, such as melanoma and renal cell carcinoma.

The power of the immune system is tightly regulated by checkpoints to prevent misfire. One of the first checkpoint proteins exploited for cancer therapy is cytotoxic T-lymphocyte associated antigen 4 (CTLA-4), which functions to dampen T-cell immunity. Another important checkpoint is the programmed

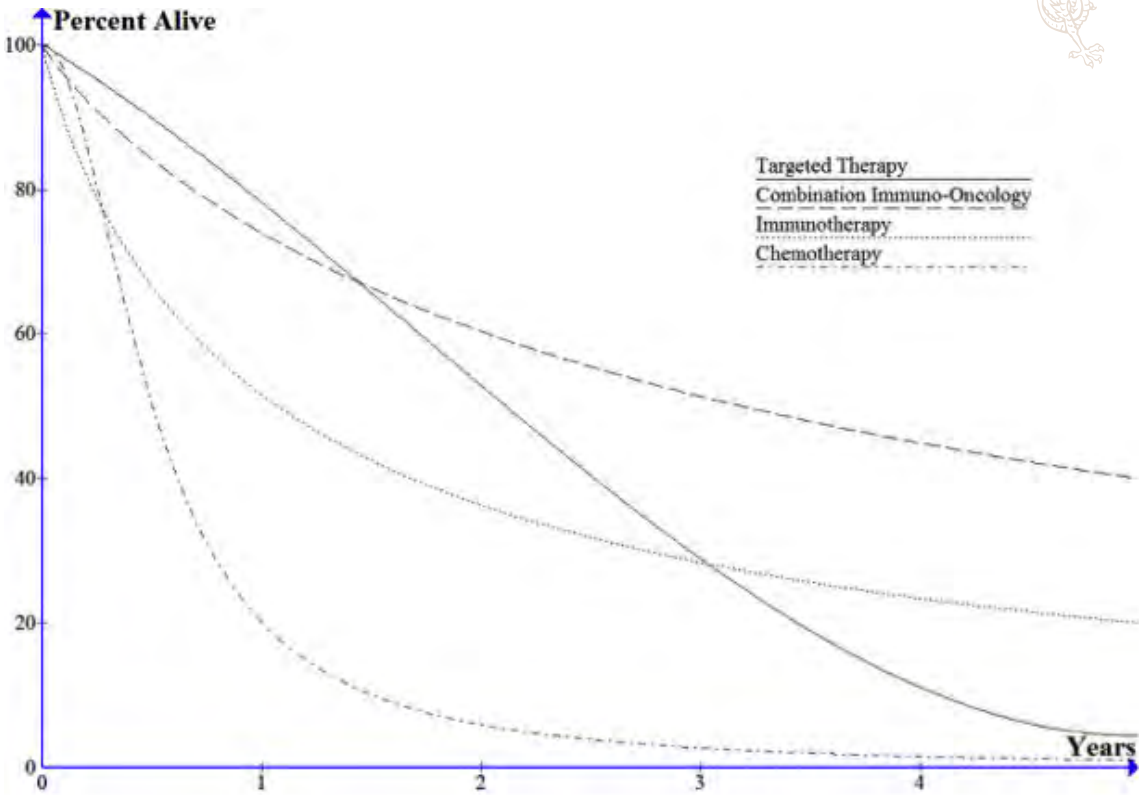
death (PD)-1/PD ligand (L)-1 axis. PD-1 is expressed mostly on activated T cells, while PD-L1 and PD-L2 are expressed in inflamed tissue and some tumour cells. Interaction of PD-1/PD-L1 results in T-cell anergy and loss of effector function, which is recognized as a major mechanism of immune escape by cancer.

Immune checkpoint inhibition is now the most exciting advance made in cancer treatment history. Immunotherapy has now joined surgery, radiation therapy, chemotherapy, and targeted therapy, as the fifth modality of cancer treatment. Blockading CTLA-4 was the first treatment to improve overall survival in patients with metastatic melanoma. In 2016, antibodies blocking PD-1 or PD-L1 are in clinical development for the treatment of more than 30 cancer types, and some have already gained approval for the treatment of metastatic melanoma, lung cancer, renal cell carcinoma, Hodgkin's lymphoma, and bladder cancer. Combining CTLA-4 and PD-1 blockade provides even higher response rates than either approach alone in patients with advanced melanoma, highlighting the potential of combination immuno-oncology to push the limits of what the immune system can achieve (Figure). Another immunotherapy approach that is likely to grow in the coming years is adoptive T-cell therapy, which involves removing a patient's T-cells, genetically modifying them in the laboratory, and then returning them to the patient to fight cancer.

As we push the limits of cancer immunotherapy, we will face the inevitable risk of autoimmune side-effects. By learning how to optimally combine immune checkpoint modulators, we should be able to unleash the full potential of immuno-oncology.

Changes in training curriculum and accreditation framework

In order to provide broad-based higher physician training to better manage the increasing complexity of systemic cancer treatment in the ageing population with multiple medical comorbidities, all medical oncology trainees are required to undertake either advanced internal medicine (AIM) or geriatric medicine (GM) as one of their dual specialty trainings, with AIM/GM training to be taken either concurrently or sequentially with medical oncology.



Overall survival rate with the immunotherapy approach, as compared to chemotherapy and targeted therapy, in advanced cancer, illustrating the curative potential of immuno-oncology

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Nephrology

New Developments Influencing Clinical Practice in Nephrology over the Next Decade

SING-LEUNG LUI

This article summarizes important developments in diabetic nephropathy, immunoglobulin A (IgA) nephropathy, membranous nephropathy, and autosomal dominant polycystic kidney disease (ADPKD), as well as advancements in stem-cell therapy that will influence clinical practices in the coming decade. Recent changes in the training framework of our specialty will also be highlighted.

The incidence of diabetes mellitus is increasing globally, and diabetic nephropathy has become the most common cause of end-stage renal disease (ESRD) in many developed countries, including our locality. Despite optimization of blood glucose and blood pressure control, together with blockade of the renin angiotensin system (RAS) using angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, many patients with diabetic nephropathy still progress to ESRD. A number of emerging therapeutic options, such as aldosterone antagonists, endothelin inhibitors, and chemokine receptor blockers, used in combination with RAS blockade, are currently being evaluated in clinical trials. The findings of these trials could well be translated into new treatment strategies for patients with diabetic nephropathy in the near future.

IgA nephropathy is the most common form of primary glomerulonephritis worldwide, and is an important cause of ESRD. The existing treatment for IgA nephropathy is not entirely satisfactory and the role of immunosuppressive treatment remains to be clarified. A number of large, prospective multi-centre ran-

domized trials, such as the STOP IgAN and TESTING studies, are currently under way and will provide definite data on the usefulness of corticosteroids in the treatment of IgA nephropathy. Genome-wide association studies in patients with IgA nephropathy have identified new genetic susceptibility loci that might allow the development of new treatment options specific to the underlying pathogenic process.

In 2009, the M-type phospholipase A2 receptor 1 (PLA2R) was identified as the main target antigen in primary membranous nephropathy, which represents a major breakthrough in understanding the pathogenesis of the disease. Assays for circulatory PLA2R antibodies are becoming widely available in diagnosing primary membranous nephropathy and monitoring response to treatment. Recent advances in bioanalytical technologies have helped to identify genomic, proteomic, and metabolic biomarkers in various chronic kidney diseases that could be of diagnostic and prognostic value. We can anticipate that some of these biomarkers might eventually reach clinical application.

ADPKD is the most common inherited kidney disorder and an important cause of chronic kidney disease (CKD). Until recently, there has been no specific disease-modifying agent that is of proven value to prevent or delay the progression of ADPKD. Tolvaptan, a highly selective vasopressin V2 receptor antagonist, has emerged as a promising disease-modifying agent and has been shown to significantly reduce growth in total kidney size and retard renal function decline in patients with ADPKD. Tolvaptan has been approved for use in ADPKD patients with CKD stage 1-3 in Europe and Canada. Octreotide, a long-acting somatostatin analogue, is currently undergoing clinical trials and preliminary results indicated that it can slow renal cyst growth in ADPKD.

Recent advances in stem-cell therapy and regenerative medicine are providing opportunities to develop novel treatments for patients with CKD. Exciting research is being carried out to evaluate the therapeutic potential of mesenchymal stem cells in acute kidney injury and CKD, particularly in diabetic nephropathy. The advent of 3D bio-printing technology and recent developments in induced pluripotent stem cells, as well as kidney organoid cultures, raise hopes that the generation of functional kidneys *ex vivo* for use in kidney transplantation may soon become a reality.

In response to the rapid developments in the field of nephrology, a number of changes have been implemented in the training and accreditation framework of our specialty in recent years. Our trainees are required to understand the principles and practice of continuous renal replacement therapy in the treatment of acute kidney injury and nocturnal home haemodialysis and on-line haemodiafiltration in the management of ESRD.

They have to acquire experience in managing renal complications during pregnancy by working in a hospital that provides an obstetrics service for at least three months during the course of their nephrology training. They are also expected to be competent in providing rehabilitation and palliative care services to patients with CKD. Currently, we have 135 Fellows and 13 trainees under the Specialty Board of Nephrology.

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Neurology

Thirty Years in Neurology

PING-WING NG, TAK-HONG TSOI

The past three decades have seen tremendous advances in neurology diagnostics and therapeutics. We would like to highlight a few aspects in this special issue of *Synapse* to mark the 30th anniversary of the Hong Kong College of Physicians.

Stroke

Cerebrovascular disease is a major cause of death and the commonest cause of permanent disability among adults. Intravenous thrombolysis has been established as a standard therapy for acute ischaemic stroke and is now available in all regional hospitals in Hong Kong. Evidence has emerged of the benefits of endovascular thrombectomy for acute major cerebral artery occlusion, and a proper triage and transfer protocol is needed for eligible patients to receive this therapy during the hyperacute phase. Stroke is a heterogeneous disorder and the formulation of a multimodal imaging protocol will allow better triage of patients so that they receive the appropriate mode of revascularization. As regards the prevention aspect, the development of specific antidotes to thrombin/factor Xa inhibitors will enhance the use of the newer generation of oral anticoagulants in embolic stroke prevention for non-valvular atrial fibrillation patients. The use of robotics has improved the rehabilitation result of many stroke patients, while a new strategy to increase neuroplasticity through transcranial electrical/magnetic stim-

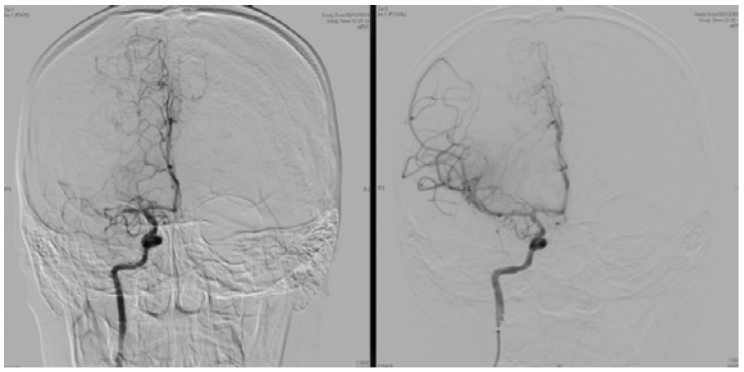
ulation is under evaluation to further augment the functional outcomes.

Cognitive impairment

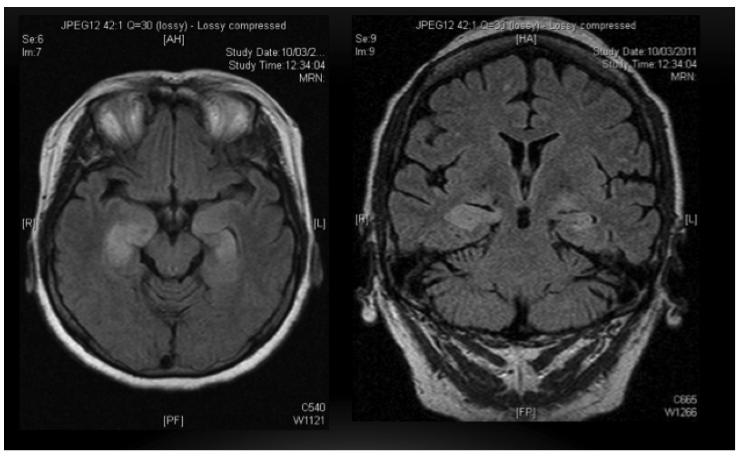
With the ageing population, the prevalence of Alzheimer's disease (AD) is rising rapidly and is a major social and economic burden for society. Immunotherapy clinical trials with active Abeta peptide vaccination at the turn of the century failed to reproduce the beneficial effects seen in the mice model and resulted in serious meningoencephalitis complications among human subjects. Passive immunotherapy using antibodies against Abeta, though safe, did not improve the cognitive outcomes in patients with mild-to-moderate AD. It is now clear that the pathophysiology of AD starts years before the symptomatic stage and thus it is too late to start treatment in patients with memory symptoms. The use of new biomarkers including functional imaging and cerebrospinal fluid (CSF) biochemistry has allowed the detection of amyloid accumulation before plaque formation. The results of several clinical trials employing anti-amyloid monoclonal antibodies to treat AD in the pre-symptomatic stage will be available in the next one or two years and these may alter our management of this neurodegenerative disorder.

Neuroinflammatory disorders

The prevalence of multiple sclerosis (MS) is increasing in Asia. The new magnetic resonance imaging (MRI) modalities have not only facilitated early MS diagnosis but also allowed its use as a biomarker for disease process monitoring and prognosis prediction. Interferon β1a/β1b and glatiramer acetate are first-generation disease-modifying therapies (DMTs) in standard use locally. The treatment repertoire of second-generation DMTs is expanding rapidly beyond natalizumab, fingolimod, dimethyl fumarate, and teriflunomide. Alemtuzumab is the latest humanized recombinant monoclonal antibody approved for the management of relapsing-remitting MS. In addition a number of biologics are in the pipeline pending approval. Over the next few years we will also see whether the escalation-therapy policy of advancing treatment intensity according to disease response will be replaced by the more aggressive strategy of starting highly effective therapy right from the start. The latter approach tries to stop the conversion of MS progression by suppressing the inflammatory process earlier. The prevalence of neuromyelitis optica spectrum disorders is higher among Chinese patients with neuroinflammatory disorders. The pathology has a predilection for the optic nerve and spinal cord. The wider use of MRI and the discovery of antiaquaporin-4/antimyelin oli-



Endovascular intervention for right-middle cerebral-artery occlusion



MRI FLAIR scan of a patient with anti-VGKC Ab encephalitis

godendrocyte glycoprotein antibodies have improved its diagnosis but we still have much to explore in terms of its underlying pathological mechanism and treatments.

Autoimmune encephalitis

The advances in immunomolecular diagnostics have identified autoimmune limbic encephalitis associated with neuronal antibodies. The typical presentation is combinations of subacute onset of cognitive impairment, neuropsychiatric disturbances, seizures, movement disorders, and autonomic symptoms. Some patients may have severe refractory status epilepticus or rapidly progressive cognitive decline. Early recognition of the neuroinflammatory features and prompt immunotherapy is associated with better therapeutic responses. The definite diagnosis, however, will often depend on the presence of a specific neuronal antibody in the serum or CSF, which may cause a short delay. The development of a clinical algorithm using a syndromic diagnostic approach with conventional neurological assessments and laboratory tests would help in clinical diagnosis and treatment initiation at an earlier stage.

Conclusion

Molecular and genetic technologies have led to tremendous advances in the diagnosis of neurological disorders. With further research into pathophysiological mechanisms, it is hoped that this situation can be translated into improved therapeutics and prognoses in the near future.

The Neurology Specialty Board

Since the Neurology Specialty Board was founded in 1996, nearly 100 neurologists have been accredited after undertaking the structural training programme. The first neurology exit examination was conducted in 1999. Regular reviews of the training programme and training centres have been conducted to ensure that they are in line with the College's policy and directive and to uphold professional standards. In its latest revised form, the training programme has recognized experience in innovative, specialized skills, such as deep-brain stimulation, epilepsy surgery, hyperacute stroke treatment, and endovascular intervention. From 2003 onwards, it has been mandatory for all trainees to be the primary case–doctor of neurology patients admitted to designated neurology beds during the core training period. The Board also works in collaboration with professional societies to provide seminars, teach-in courses, and workshops for trainees. All newly accredited neurologists are invited to present their dissertations to the annual scientific meeting of the Hong Kong Neurological Society and since 2004 a prize has been awarded for the best paper each year.

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Palliative Medicine

Recent Developments in Palliative Medicine

KIN-SANG CHAN

Palliative care for advanced cancer is well established in Hong Kong with two-thirds of cancer deaths covered by palliative care. And since 2010, palliative care has also been systematically extended to patients suffering from advanced non-cancer diseases in Hong Kong.

Palliative care has become an established option of treatment for patients with end-stage renal failure (ESRF) whom for various reasons decline renal replacement therapy. In 2015, a cohort review performed by the Central Committee on Palliative Care of the Hospital Authority indicated that 44% of patients who died from ESRF had received palliative care. A local randomized controlled study has demonstrated that an enhanced psychosocial support programme for patients with chronic kidney failure and their caregivers has resulted in an early significant reduction in caregiver burden and anxiety. Apart from ESRF, palliative care services are also extended to patients with advanced chronic obstructive pulmonary disease, heart failure, and neurodegenerative conditions such as motor neuron disease. A multi-disciplinary palliative care clinic has been established to provide evidence-based non-pharmacological management of breathlessness in patients with advanced lung diseases through therapeutic interventions provided by nurses and physiotherapists. A local randomized controlled study further demonstrated the effectiveness of post-discharge transitional palliative care, delivered at home, in reducing re-admissions and improving symptom control among patients

with end-stage heart failure. A collaborative approach between palliative care teams and the respective specialist teams is becoming an established model of care for patients entering the palliative care phase of a disease.

Advanced care planning (ACP) is not just an integral part of palliative care, but also that of chronic disease management, and is becoming more important as the population ages. Healthcare decisions on life-sustaining treatments can be discussed in advance when a patient is mentally competent and with the participation of the family. Preliminary results of a local randomized controlled study on advanced non-cancer diseases showed that a structured ACP programme enhanced the discussion and decision making of ACP. Meanwhile, care for terminally ill elders in residential care homes has been launched with the collaboration of geriatric outreach teams and palliative care teams.

Although deaths in Hong Kong are highly hospitalized, palliative home care remains a core service in palliative care. The Cochrane review in 2013 demonstrated clear evidence that home palliative care increases the possibilities for home death and reduces the symptom burden, in particular for patients with cancer; and locally, a single-arm study on an eight-week palliative home-care programme has been shown to be effective in improving patients' quality of life, reducing readmissions, and promoting decision-making in ACP. Despite multiple barriers to home death in Hong Kong, small-scale collaboration with hospital-at-home programmes has successfully supported patients at home during their last days, with the death procedure streamlined at accident and emergency departments in order to relieve the family from the burden of a coroner referral.

Enhancement of psychosocial care in palliative care has been mediated through risk stratification, the use of local validated screening tools in identifying high-risk patients and family members, providing evidence-based interventions through a stepped-care model, and the provision of structured bereavement support. Evaluation of enhanced psychological care in palliative care units has shown improved coverage and enhanced intensity of interventions, with improved psychological outcomes among the family members.

After three decades of palliative care, addressing patient's existential and spiritual distress is still a challenge. Local studies of the patient's dignity model and its assessment have been explored in order to address the existential distress of the dying. The essence of hope was explored amidst apparent hopelessness.

Since the development of palliative medicine in 1998, there are 28 Fellows in palliative medicine and currently seven higher physician trainees. To address new developments in palliative medicine in the coming years, the components of palliative care

for advanced non-cancer diseases in different settings, disease management, and evidence-based practices are being enhanced in the training guidelines for palliative medicine. There is a definite need for more palliative medicine physicians in Hong Kong in order to meet the needs of an ageing population, the rising incidence of chronic disease, and cancer.

New developments influencing future clinical practices

- Evidence-based palliative care for patients with advanced non-cancer diseases
- Collaborative model between palliative care team and respective specialist team
- Advanced care planning and care for terminally ill elders in residential care homes
- Evidenced-based home care and support for dying at home
- Psychosocial stepped-care model and structural bereavement care
- Contextual existential and spiritual care

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Rehabilitation

The Most Important Developments to Influence Clinical Practice in Rehabilitation Medicine in the Next Decade

KWOK-PUI LEUNG

As a reflection to the growth and development of this relatively new specialty, rehabilitation medicine has been recognized as an independent specialty of the Hong Kong College of Physicians since October 2012. Currently, there are 55 Fellows and three trainees. Rehabilitation Fellows are required to go through at least 24 months of core training in various branches of rehabilitation medicine with particular weights in neurological, cardiopulmonary, geriatric, musculoskeletal, and spinal rehabilitation. In recent years, the Rehabilitation Specialty Board has placed greater emphasis on the acquisition of interventional and diagnostic skills among new trainees and existing trainers, such as nerve or motor-point block and botulinum toxin injection for spasticity; therapeutic and diagnostic uses of ultrasound in muscle and joint diseases; endoscopy in management of swallowing dysfunction; among others. Numerous workshops have been arranged in collaboration with other medical specialties to achieve these purposes. In 2012, the Board conducted a territory-wide inspection of all accredited training centres in Hong Kong to make sure the training provided, in terms of both hardware and software, was up to standard. The Board will perform similar exercises in future to strive for the highest possible quality of training.

Rehabilitation medicine is a broad specialty dealing with the functional restoration of various defective organ systems. This article will limit its scope to neurologically damaged patients,

for example patients after stroke, traumatic brain injury, and similar events. Rehabilitation always identifies itself using a biopsychosocial approach. With the recent leaps and bounds in science and technology, I would say, nowadays and in future, rehabilitation is better described as a specialty using a bio-psycho-socio and technological approach to deal with various health conditions.

With advancements and innovations in robotic and computer technologies, we are going to see their unprecedented impacts on neurological rehabilitation, not only to lessen the impairments through intensive training but also as a direct replacement or compensation for lost functions. Contrary to the traditional belief that an adult brain is almost fixed, unalterable, and unable to regenerate, the last 20 odd years of neuroscience research have persuaded us to move away from the concept that the brain is static and hardwired. We now recognize that the brain is very dynamic, and that neuroplasticity is a fundamental property of the human brain that can be harnessed to create new neural pathways for recovery. In some areas of the brain, new neurons can actually re-grow. Training up the brain is the main focus of newer rehabilitation strategies. Constant practice is the crucial factor in recovery of function. In particular, the amount and frequency of practice, task specificity, motivation, and feedback are of vital importance. Techniques that continually stress specifically the desired outcome of functional limb use are preferred.

Robotic devices are above all appealing in neurological rehabilitation for delivering well-defined repetitive exercises in a consistent and prescriptive fashion. Currently, devices for both upper and lower limbs are available. In fact, robotic systems not only can produce simple and repetitive stereotyped movement patterns but also can generate more complex, controlled multisensory stimulation for patients. Robots can be engaging and enhance human experiences. Robotic devices can be used by patients with severe paresis and those who cannot complete conventional movement therapy without assistance. Fewer personnel are required for same amount of training, a factor which certainly can alleviate problems of therapist shortage and high costing. Moreover, work-related injuries among therapists can be minimized.

Another area of application for robotic devices is the replacement of permanently lost functions in the neurologically infirm; a good example is found in patients with spinal cord injury who are rendered paraplegic. ReWalk is a powered exoskeleton system designed specially to restore bipedal mobility in this group of patients. Subjects are able to stand and walk independently with crutches after a period of training. Stair climbing is also

possible with this powered exoskeleton and is undoubtedly more welcome than a wheelchair for short-distance manoeuvring.

When humanoid robots become more affordable, I also predict there will be wider use of these robots to solve everyday household problems in caring for the neurologically impaired, such as assisting paretic patients transferring to and from bed or toilet, doing household chores, activating an alarm system in case of emergencies, and so on. This will surely reduce the institutionalization rate for the disabled and further reduce the strain on caregivers.

In conclusion, clinical needs will drive the growth and development of new interventions. And in view of the rapidly increasing demands from our ageing population, technological innovations should be encouraged using a team where clinicians, patients, and engineers can all collaborate and work together.

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Respiratory Medicine

The Most Important New Developments in Respiratory Medicine Influencing Clinical Practice in the Next Decade

MO-LIN WONG

Developments in respiratory medicine will continue to be as thrilling as ever over the next ten years, and a 500-word essay cannot do justice to the trends in recent breakthroughs.

The use of biologics is the centerpiece of change: it also opens doors to personalized medicine. Blockage of IL5 or IL13 in severe eosinophilic asthma is a prime example. Soon there will be an increased use of antibodies and antagonists to block or modify disease mechanisms and metabolic pathways. CXCR2 antagonists and kinase inhibitors are such new hopefuls in asthma, chronic obstructive pulmonary disease, pulmonary hypertension, and idiopathic pulmonary fibrosis.

In lung cancer, screening will not be based on low-dose computed tomography alone; instead, stratification will incorporate the use of biomarkers such as circulating microRNA as liquid-biopsy. The identification of microRNA in bronchial and nasal brushings will also be crucial in genomic classification for diagnosis and management. Regarding treatment, targeted therapies are currently available or being developed for subsets of patients with adenocarcinoma, such as those harbouring ALK or EGFR mutations, and there will be greater use of these treatments in squamous cell carcinoma. Nanotechnology is also on the horizon for better tumour-drug delivery.

There is much excitement in tuberculosis (TB) research too. Non-sputum diagnosis will be the way forward and the new

three-gene test developed in the laboratory at Stanford University has been a major breakthrough. Unlike skin-prick tests and interferon assays, an ordinary blood sample can be used to accurately identify active TB and distinguish it from latent TB or BCG effect. The test is also applicable to children and HIV patients.

After the dearth in discoveries of new TB drugs over the last 40 years, bedaquiline, a diarylquinoline which offers greater bactericidal effects than isoniazid and rifampicin, is finally bringing new hope. The drug received fast-track approval in the US in 2012 and the World Health Organization has already issued interim guidelines on its use in multidrug-resistant TB.

New methods allowing better use of borderline donor organs, management of ischaemic reperfusion, and prevention of chronic graft dysfunction will transform the landscape of lung transplants. Its momentum is palpable with the recent encouraging news from Texas on the use of ex-vivo lung perfusion to evaluate and recondition the lungs; currently more than 70% of potential donor lungs are deemed unusable.

Intense activity is also seen in interventional pulmonology. The technique can be applied in airways, mediastinum, or pleural spaces for diagnosis, staging, and management. Notably, the judicious use of bronchial thermoplasty can now be added to our armory in the treatment of severe asthma.

In sleep apnoea, a phenotypic approach sheds new light. Based on the four traits identified, that is, upper-airway collapsibility, pharyngeal dilator response, respiratory arousal threshold, and loop gain, tailor-made treatments will be available, such as hypnotics in low-arousal thresholds and reduction of high-loop gain with oxygen or acetazolamide. Novel therapies such as oral pressure therapy and pacemakers are also being investigated.

Last but not least, advances in imaging and technology will bring new rays of hope. The latter can empower patients through the use of the web and smartphones, and this will mark a new era in disease monitoring.

To embrace the immense training challenges that follow, the Respiratory Specialty Board has made successive revisions to our training guidelines over the past 30 years with more emphasis on ethics, interventional pulmonology, surgical management, and sleep medicine. Soon, we will expand the section on procedural sedation in our new training guidelines. Trainees are requested to study the related document newly released under the auspices of the local professional societies. They are encouraged to join various simulation or interventional workshops and sleep medicine courses, when we actively partner with various stakeholders, including local professional societies and the Hos-

pital Authority, to create training opportunities for them. As of April 2016, there are 191 Fellows in respiratory medicine. With the accreditation of Pok Oi Hospital as a new training centre in 2015, we now have 90 trainers in 22 sites mentoring 16 trainees throughout the territory.

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Rheumatology / Immunology and Allergy

Prevention and Cure of Rheumatoid Arthritis in the Coming Decade: Is It Possible?

LAI-SHAN TAM

Rheumatoid arthritis (RA) is traditionally regarded as a life-long disease that cannot be cured and where patients require life-long immune modulation to control the inflammatory process and prevent damage. However, the treatment of early RA should now be aiming at remission and taking it for granted that targeted approaches are the best way to achieve this. Indeed, remission in RA occurs more frequently now than ever before. Registries/observational studies have demonstrated that 50% of patients with early RA were in disease activity score 28 remission five years after disease onset and 65% in low disease activity, especially in countries with easy access to synthetic and biologic disease-modifying anti-rheumatic drugs (DMARDs).

Nowadays, we believe that DMARDs debulk inflammation in patients with RA, shifting them from high, moderate, or low disease activity into remission. There are different states of remission: immunological remission, characterized by an immunological reset and seroconversion with respect to auto-antibodies, which is rare; imaging/serologic remission (I/SR), resembling true absence of inflammation (synovitis) measured by either imaging (magnetic resonance imaging osteitis and synovitis, or ultrasound synovitis) or serum biomarkers; and simple clinical remission (CR), indicating the virtual absence of signs and symptoms in the joints. These states may differ considerably in their likelihood to relapse, with immunological

remission having the highest chance of a cure, followed by I/SR and CR.

Data suggest that early remission can be achieved with biologics and that less radiographic progression occurs. One area of growing consensus is that early achievement of remission in milder patients does allow withdrawal of biologics if these are used in the first instance. Investigators are addressing the possibility of curing RA and are developing structured DMARD-tapering strategies to achieve a cure. Anti-cyclic citrullinated antibody (ACPA) negativity and presence of 'deep' remission, such as the absence of ultrasound synovitis and/or normal serum markers of inflammation, are associated with a higher likelihood of achieving drug-free remission and hopefully can guide us in selecting patients in whom a cure can be the ultimate goal.

RA-related systemic autoimmunity and inflammation occur long before clinical arthritis. There is growing evidence that initiating events may occur at mucosal surfaces, including the periodontium, lung, and gut and may be influenced by the local microbiome. For potential preventive strategies to be feasible, it is important that individuals at high risk for RA development can be readily identified from the general population. Ongoing studies focusing on multiple biomarkers in prospective cohorts of at-risk individuals enable risk prediction in different at-risk phenotypes. RA prevention using immunomodulation is currently being investigated in individuals at high risk of RA development. If these studies are successful, targeted intervention in these subgroups may represent a new 'window of opportunity' in RA and ultimately lead to a therapeutic shift towards the prevention of this common autoimmune disease.

Our specialty has grown significantly since 1994 when biologics first became available, with a total number of 80 Fellows and nine trainees at present. For training, all acute hospitals except North District Hospital are accredited training centres. In order to equip our future rheumatologists, our board has already been working closely for the past few years with the Hong Kong Society of Rheumatology in order to facilitate and encourage musculoskeletal ultrasound training. We have also updated the training guidelines for immunology and allergy and we are pleased to welcome our first trainee in this field. We are confident that, over the next decade, rheumatologists and clinical immunologists can all work closely together so that curing rheumatic disease can be more than just a dream.

Honorary Fellowship

1 Sir Lee Quo Wei (1996) **(deceased)**
2 Mr Peter Mark (1996) **(deceased)**
3 Sister Gabriel O' Mahony (1996) **(deceased)**
4 Professor John Vallance-Owen (1996) **(deceased)**
5 Professor Sir David Todd (1997)
6 Professor Rosie Young (1997)
7 Professor Gerald Choa (1998) **(deceased)**
8 The Right Hon the Lord Turnberg (1999)
9 Professor Li Lei Shi (2000) **(deceased)**
10 Professor Kan Yuet Wai (2000)
11 Professor Chan Nap Yee, Vivian (2001)
12 Professor Chan Kwong Fai, Laurence (2002)
13 Professor Chew Chin Hin (2002)
14 Dr Lo Ka Shui (2002)
15 The late Dr Cheng Ha Yan (Posthumous) (2003)
16 The late Dr Tse Yuen Man (Posthumous) (2003)
17 Professor Chan Tai Kwong (2004)
18 Professor Leong Che Hung (2004)
19 Professor Yeoh Eng Kiong (2004)
20 Professor Zhong Nan Shan (2004)
21 Professor Tsui Lap Chee (2005)
22 Dr Liu Lit Chung, Vincent (2005)
23 Professor Yu Yue Hong Richard (2008)
24 Professor Sir Neil Douglas (2009)
25 Professor Sir Ian Gilmore (2011)
26 Professor Lai Kar Neng (2011)
27 Professor Lam Wah Kit (2011)
28 Dr Neil Dewhurst (2012)
29 Dr Yam Yin Chun, Loretta (2013)
30 Professor Sung Jao Yiu, Joseph (2015)
31 Dr John F Mackay (2015)
32 Professor Matthew Ng (2015)
33 Professor Dame Carol Black (2016)
34 Dr Li Chun Sang (2016)
35 Dr Tse Tak Fu (2016)
36 Professor Peter William Mathieson (2016)

Winners of the Best Thesis Award (Gold Medal)

Year	Name of winners	Title of dissertation
2000	Dr Wong Yuk Hwa, Teresa	Genetics in type 2 diabetic nephropathy
2001	Dr Wu Che Yuen, Justin	The role of *Helicobacter pylori* infection in pathogenesis and management of gastroesophageal reflux disease
2002	Dr Tso Wai Kwan, Annette	Obesity – current understanding and recent advances
2003	Dr Wong Siu Ming, Raymond	Non-myeloablative stem cell transplantation – a study of non-myeloablative matched unrelated donor transplant in patients over 55 years old with hematological malignancies and a literature review of the biological basis and indications of non-myeloablative transplant
2004	Dr Ma Shing Yan	Liver graft-versus-host disease (GVHD) after haematopoietic stem cell transplantation (HSCT): diagnosis, pattern and prognosis
2005	Dr Tse Wai Choi, Eric	Potential role of Lmo4 in the pathogenesis of Lmo2-induced T-cell acute lymphoblastic leukaemia
2006	Dr Wong Wai Sun	Nonalcoholic fatty liver in Hong Kong Chinese
2007	Dr Chan Lam	Inactivation of secreted Wnt antagonists (WIF1 and SFRPs) in nasopharyngeal carcinoma: epigenetic perspective
2008	Dr Yuen Ka Yan, Catherine	Detection of subclinical synovitis in patients with rheumatoid arthritis in clinical remission
2009	Dr Chan Kwok Ying	Quality of life in Chinese patients with advanced gynaecological cancers and its clinical correlates
2010	Dr Lau Yuk Lun, Alexander	Good collateral circulation predicts better outcome in patients with intracranial large artery occlusive disease
2011	Dr Chan Tuen Ching	Continuous use of antipsychotics and its association with mortality and hospitalizations in institutionalized older people with behavioral and psychological symptoms of dementia (BPSD): an 18-month inter-specialty prospective cohort study
2012	Dr Chan Wai Chung	Assessment of liver fibrosis with transient elastography (TE) and non-invasive clinical formulae in patients treated with methotrexate for psoriatic arthropathy and rheumatoid arthritis
2013	Dr Lee Chi Ho	A clinical and genetic study of subjects with phaeochromocytomas & paragangliomas in Hong Kong
2014	Dr Ng Siew Chien	Prospective study into the risk of colorectal neoplasms in asymptomatic individuals with a family history of advanced adenomas
2015	Dr Cheung Ka Shing	Relationship between hepatocellular carcinoma development and serum viral markers in patients with undetectable serum HBV DNA level while on nucleos(t)ide analogues
2016	Dr Mak Yin Fung, Ingrid	The use of salivary cortisol and cortisone during low dose corticotropin stimulation test in the diagnosis of adrenal insufficiency – a local study


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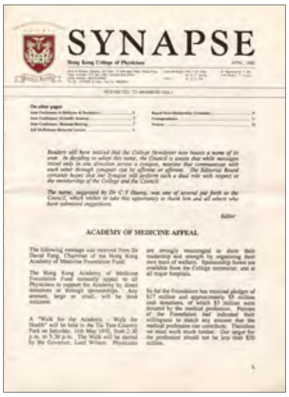
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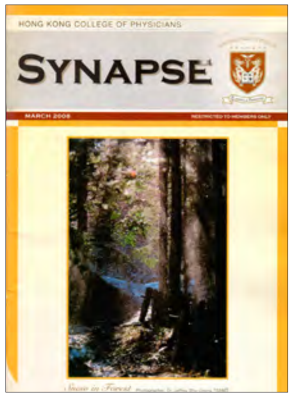
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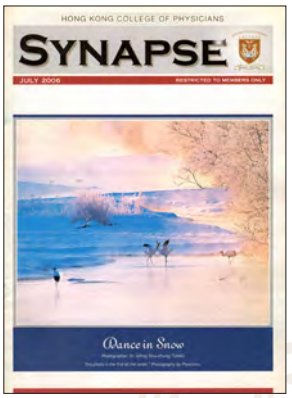
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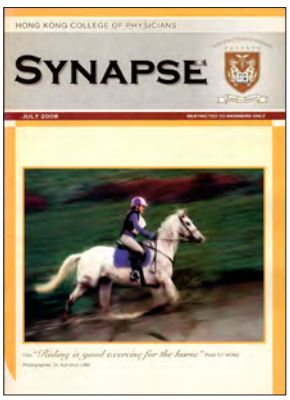
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