HONG KONG COLLEGE OF PHYSICIANS
香港內科醫學院
Sapientia et Humanitas

SYNAPSE

Hong Kong College of Physicians **April 2002**

Room 801, Hong Kong Academy of Medicine Jockey Club Building,
99 Wong Chuk Hang Road, Aberdeen, Hong Kong
Tel: 2871 8766 Fax: 2556 9047
email: hkcp@netvigator.com
College Web site: www.hkcp.org

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Smallpox vaccine production in open yard of the animal house, Old Pathological Institute. (winter 1962)(Feature story of smallpox Vaccine at the back.)

(Photos and information courtesy of the Hong Kong Museum of Medical Sciences)

Contents

Special Article

PACES: The new MRCP Clinical Examination

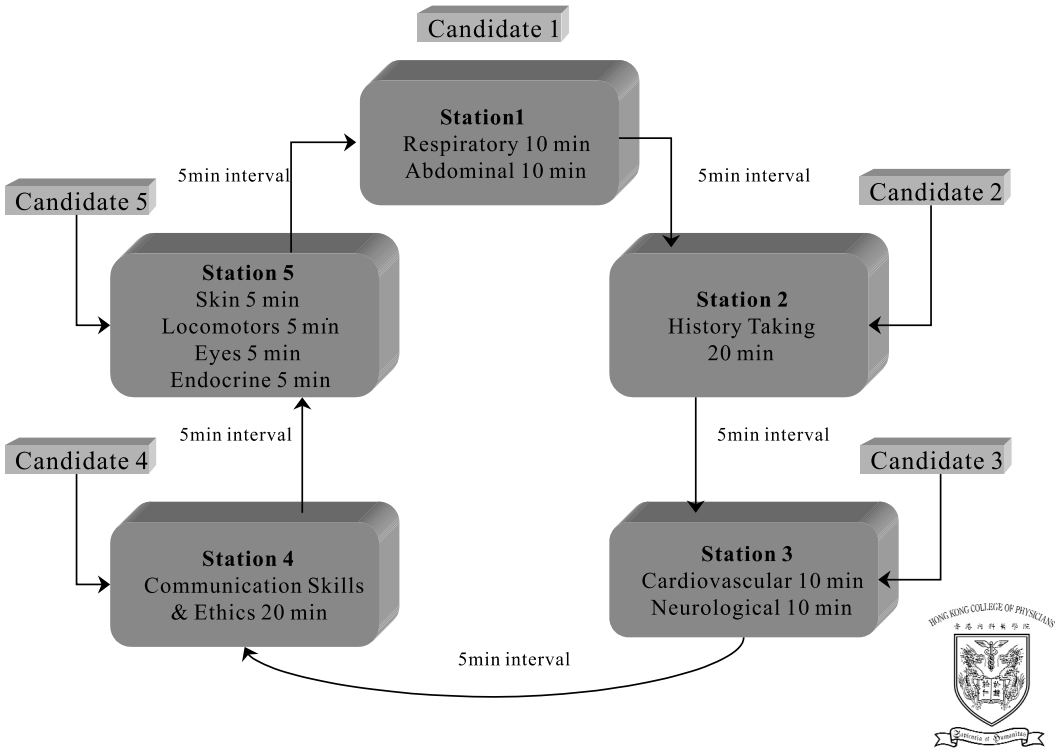
The MRCP examination has been conducted in Hong Kong since 1985. After the College was inaugurated in 1986, it has been sponsoring the same examination until 1994, when the examination took on a new format, that of a Joint MRCP/HKCP Intermediate Examination. Passing the examination is a pre-requisite for admission to Higher Physician Training. Traditionally it took the form of Part I (Written) and Part II (Written and Clinical) sections. The Clinical section used to be composed of a long case (1 hour plus 20 minutes of examination), several short cases (30 minutes) and a viva (20 minutes). To improve and update the examination, the MRCP (UK) Policy Committee has started an extensive review some years ago, and has revised the examination format in 2001.

This revision takes several phases: the content of the Part II Written Section was progressively modified since February 2001, with multiple choice questions (MCQ) requiring a selection of "best of five" answers replacing the previous free-text response to the case scenarios. The scope of the Part I examination also become widened, to include clinical knowledge as well as immunology and molecular biology, in addition to the traditional pathophysiological basis of clinical medicine. The clinical section, named PRACTICAL ASSESSMENT OF CLINICAL EXAMINATION SKILLS, or PACES, replaced the previous Part II Clinical Examination in June 2001, and becomes the Part III of the MRCP examination. Finally, to enable candidates to be tested over a wider scope of knowledge, Part I and Part II (both Written) will be changed in May 2002, from the current one paper examination to a two-paper examination (2 1/2 hour each, making a total of five hours per examination), by which time the metamorphosis will be complete. Because our College is holding our Intermediate Examination jointly with the MRCP, Basic Physician Trainees will have to write the new format of the examination in exactly the same manner as those of the United Kingdom.

In the June 2000 issue of Synapse, Prof WK Lam, Chairman of the Examination Committee, has detailed the format of the new PACES, which is summarised again below.

There are three Clinical Stations in which a candidate examines a total of eight patients, and two "talking" stations which tests his/her history-taking, communication skills and basic understanding of medical ethics. There are only 16 real patients and four patients or patient surrogates on each day, and candidates examine, or talk with, alternate patients/surrogates as they go through the three carousels.

The Carousel of PACES Stations



There is thus better uniformity in the scenarios in PACES: on each day eight candidates with examine all group A patients/surrogates, while seven will be tested in all group B patients/surrogates. Instructions are clear and the actual mark sheets are made known to both examiners and candidates many months beforehand, so that both can prepare themselves for the big change. Each of a pair of examiners marks on his/her own mark sheet, making a total of 14 mark sheets with a maximum score of 4 x 14 (56). The examiners have to mark independently without any discussions among themselves, reducing another source of potential bias. Each candidate will be examined by 10 examiners instead of the previous four. PACES can thus be considered a fairer and more transparent test of the candidates' clinical skills. In-depth assessment of knowledge is usually impossible within the time allotted, but this should have been amply tested in the 10-hour Part I & II MCQS! On the other hand, candidates must finish their physical examination within 6-7 minutes in each clinical station, to allow some time to demonstrate their skills in interpreting clinical data and in the general approach to clinical problems, on which they will also be marked.

In preparation for this change, Dr E Beck, Senior Examiner of the February 2000 clinical examination, helped QMH to organise a mock 2-station (the "talking" station) PACES after the examination, using medical students as surrogates. A 20-minute demonstration video made by Dr Beck and Prof J Dacre was also shown, followed by in-depth discussions on the implications for the candidates, the examiners as well as the examination centre. The local examiners expressed doubts and misgiving on the idea, not least the problem of language. Another PACES demonstration was conducted at PWH after the October 2000 Clinical Examination by Prof GM Besser. A final full 5-station one-round mock PACES examination was conducted for 60 local examiners, trainers and trainees, at PYNEH after the February 2001 Clinical Examination under Dr J Bath. The demonstration video was again shown, and explanatory notes and mark sheets were distributed one week beforehand to assist comprehension and clarification of all relevant issues.

The world's first PACES took place on 9-11 June 2001 in Singapore. The College was able to send a delegation of observers to that examination, consisting of the President and the three host examiners of the October 2001 PACES locally. The UK Examiners included Drs Eric Beck (Senior Examiner) and Stefan Slater. Dr Slater was subsequently co-senior examiner with Prof M Besser in our own October 2001 PACES. There were 39 candidates in 21/2 days in three centres (15 + 15 + 9 candidates respectively). The 5-station cycles ran smoothly, and time-keeping was good. Singaporean surrogate patients for Stations 2 and 4 were nursing staff/officers and technicians. They acted and spoke English very well, and on their return the Hong Kong examiners put surrogate training high on their agenda. Most examiners used the full range of marks from "1" to "4". 15/39 candidates obtained 42 marks or above, which was, according to the UK examiners, a sign that PACES was entirely comparable to the old MRCP examination.

The experience gained in Singapore was put to good use in the Joint HA-HKCP Mock PACES held in September 2001 in four hospitals under the directorship of Dr ML Szeto. Drs E Beck and C Hind were the invited examiners, who helped our candidates find their feet, so to speak, with using English in the slightly artificial situations of Stations 2 and 4. Their unanimous final comment, however, was that that candidates must improve their communication skills rather than English, which might have allayed some of our concerns about language.

The College then decided to conduct 5-day PACES for 75 candidates each time. Priority is given to those candidates who will attempt their third PACES within two years of passing the written examination, followed by the more 'senior" candidates in terms of years after first medical qualification. All other applications are accepted on a first-come-first-served basis. The first local PACES was held in QMH, PWH and PYNEH in October 2001. It went quite smoothly, which is not surprising given the time and effort spent in preparation. To everyone's relief, 36/72 (50%) passed, comparing very well indeed to the 38% of the February 2001 "old" examination. In the two PACES held worldwide in 2001, 41 was used as the pass mark instead of the planned 42 in order to move closely approximate the passing rate with that of the "old" examination. The MRCP office expects examiners and candidates to get used to the new examination in time, such that enhanced performance on all sides will allow the scheduled pass mark of 42 to come into effect. A summary of the territory's MRCP record is tabled below.

Year - Part I	No. of candidates	Pass
1/94	154	65(42%)
3/94	107	20(19%)
1/95	175	32(18%)
3/95	114	45(39%)
1/96	159	53(33%)
3/96	141	46(33%)
1/97	132	40(30%)
3/97	111	48(43%)
1/98	114	50(44%)
3/98	111	37(33%)
1/99	169	50(30%)
3/99	162	48(30%)
1/00	188	38(20%)
3/00	143	45(31%)
1/01	143	35(24%)
3/01	97	29(30%)

Year -Part II	No. of candidates	Pass (Written)	Pass (Clinical)	Overall Pass
94/1	77	60(78%)	29(48%)	38%
94/3	89	73(82%)	33(45%)	37%
95/1	82	70(85%)	37(53%)	45%
95/3	88	67(76%)	39(58%)	44%
96/1	77	59(77%)	33(56%)	43%
96/3	96	76(79%)	38(50%)	39%
97/1	93	67(72%)	32(48%)	34%
97/3	92	58(63%)	29(50%)	32%
98/1	89	61(68%)	24(39%)	27%
98/3	100	70(70%)	22(31%)	22%
99/1	102	59(58%)	18(31%)	18%
99/3	116	68(59%)	37(54%)	32%
00/1	109	68(61%)	28(41%)	26%
00/3	120	81(68%)	43(53%)	36%
01/1	115	65(57%)	25(38%)	22%

To ensure that candidates from all hospitals are well-prepared for the February 2002 examination, the President held a personal briefing on PACES at the Academy of Medicine Building on 19 January 2002, followed by mock examinations again for 24 candidates in Stations 2 & 4 by 12 local examiners. After that, all new examination centres (KWH, RH and UCH) held one or two carousel mock PACES for their cluster's candidates. Examination centres for PACES face major changes and high administrative demands. Now that all centres have gained some experience, candidates can rest assured that examinations will be conducted to a meticulous and uniform standard, and that their own performance will not be affected whichever centre they are assigned to.

The feedback of all 2002 mock PACES is uniformly encouraging. Candidates must, however, remember that it is the Clinical Stations which are crucial to passing the examination. Of 14 mark sheets per candidate, 10 are for Clinical Stations, with eight for Stations 1 & 3. Stations 2 & 4 Score a maximum of 4 x 4 marks only our of a total maximum of 56. After repeated mock examinations, it would not be difficult to achieve passing grades in these two Stations. The very fact that "talking" Stations are being included in the examination has already alerted everyone to the importance of communicating skills, and candidates (and trainers and examiners) are improving quite significantly on this score. But PACES, after all, is a test of the practical clinical examination skills, and a good physician cannot forego accurate (and graceful) physical examination, as well as the ability to present and discuss clinical data logically and succinctly.aSo there are no tricks to PACES, just simple honest clinical and communicating skills, the ability to think on one's feet based on one's background knowledge, and a bit of luck!

L Yam
Member
Examination Committee

Council News

Call for Research Papers for Distinguished Research Paper Award for Young Clinicians

Please be informed that competition for the captioned Award is now open to all young College Fellows and Members, who are under the age of 40 on the deadline date of 15 June 2002 for submission of application. The criteria and application procedures are listed below for your reference.

1. The Hong Kong College of Physicians has established a Distinguished Research Paper Award for Young Investigators, with the objective of promoting outstanding research in medicine by young clinicians of the College.

2. The prize shall be known as the Hong Kong College of Physicians "Distinguished Research Award for Young Investigators" (hereafter referred to "the Award").

3. Competition for the Award shall be open to young Members and Fellows of the College who are aged 40 years or below on the deadline date for submission of application.

4. Up to five Awards of HK$5,000.00 each shall be presented annually to the first authors of best research papers published in the field of medicine in the previous year.

5. Eligible Members and Fellows are invited annually in June to enter into the competition. Each competitor is requested to submit only one first-authored original research paper each time. The paper must be already published in peer-reviewed journal not more than 12 months before the deadline for submission of application. Papers accepted for publication but still in press are not acceptable.

6. All applications must reach the College Secretariat before the deadline and should contain a covering letter, a electronic version and five copies of the paper.

7. The Research Committee shall appoint an Award Subcommittee to assess each year's submissions. This Subcommittee may also seek advice from local or overseas experts where necessary.

8. The Award Subcommittee shall determine the criteria for selection. They may include scientific excellence, local relevance, clinical application and impact factor of the journal.

9. Recipients of the Award may be invited to present their paper in an open meeting organized by the College.

New additions to the Specialist Register

The Medical Council of Hong Kong has accepted three medical specialties, namely Rehabilitation, Palliative Medicine and Clinical Pharmacology and Therapeutics to be included in the Specialist Register.

A Step Towards Mutual Recognition of Postgraduate Training Worldwide

A meeting of the International Association of College and Academy Presidents (IACAP), in conjunction with the Presidents and Masters of Surgical Colleges and Academies, was held on the 6th November 2001 in London. A working group, of which our President is a member, has been established towards achieving mutual recognition of training worldwide. The working group has already issued a template form to gather information on current training programmes to all Colleges and will report at the next IACAP meeting in Adelaide, Australia on 9 May 2002.

Specialty Board Corner

New Format for Exit Assessment

1. Marking of Individual Scores in Clinical Viva -

*(Implementation date: **May/June 2002**)*

The New Exit Assessment format consists of two panels, each comprising a pair of examiners asking two out of four aspects of questions for 30 minutes (15 minutes per section): dissertation viva, clinical problems, EBM/local/ethics and data/interpretation. There will thus be four examiners for clinical viva, who have to score the candidate's performance independently. The examiners have to discuss the questions before the Exit Assessment to ensure that there are no repetitions for any candidate, while as far as possible the same questions are used for each round. The Assessment Board should convene a meeting at the end of the Exit Assessment, to decide on recommending successful completion of training or extension of a specified period of targeted training before further assessment.

All examiners will continue to use the new scoring system of 0-10 scale. In the new system, two appraisers will continue to mark the dissertation out of a total of 20 marks. When such scoring yields one failure and one pass, a third examiner will be required to read the dissertation. The total marks given by the three examiners will then be multiplied by a factor of 2/3 to obtain the Dissertation Appraisal Score. Together with the other 20 marks for the dissertation viva, the final maximum dissertation score remains at 40. The pass mark for the dissertation is 20, or 50% of the maximum of 40. Because there would now be six scores in the clinical viva with a maximum of 10 marks each, the total clinical viva score becomes 60. The pass mark for the clinical viva is 30, or 50% of the maximum of 60. The maximum marks of 40 (dissertation) plus 60 (clinical viva) makes up a total of 100. There is no need for any conversion of marks, and again 50% (score of 50) will be the pass mark.

Another major difference from the previous Exit Assessment format, other than the new pairing of examiners and specification of assessment topics, is that there would now be a heavier bias towards clinical viva: the score becomes 60 marks while previously it was 50 marks. For candidates to compensate for bare failure in one section, the dissertation score must reach a minimum of 18 out of 40, and the clinical viva score must reach a minimum of 27 out of 60 (ie 90% of the minimum passing marks of 20 and 30 respectively).

To recapitulate, the final score is calculated as follows:

Dissertation score (maximum 40)	Summation of two individual examiners' score, or (summation of three individual examiners' score x 2/3)
Clinical viva score (maximum 60)	Summation of three individual Panel members' scores (maximum 20 each)
Exit Assessment score (maximum 100)	Dissertation Score + Clinical Viva Score
Pass Mark	50
Pull up marks	Dissertation 18 Clinical Viva 27

2. Dissertation Writing *(Implementation date: **December 2002**)*

From the December 2002 Exit Assessment onwards, the College will only require a minimum of one dissertation before a trainee is accredited as specialist. In general, AIM training aims at broad-based training in the knowledge and skills pertaining to multiple systems and the logical approach to complex medical problems, whereas dissertation writing aims at testing the candidate's ability to demonstrate in-depth knowledge in, and to perform critical analysis of specific segments of the literature. For candidates undertaking concurrent training in AIM and a specialty, therefore, the dissertation should be written in the specialty rather than in AIM. In the same context, trainees who undertake concurrent training in Geriatrics and another specialty should also write their dissertations in the specialty. Only AIM trainees who are trained in a single specialty would therefore be required to write their dissertation in AIM.

Candidates who do not have to write dissertations are to be examined on one clinical area for 15 minutes by the first panel, and for the usual 30 minutes by the second panel. The maximum score of 60 in the Clinical Viva will be converted to 100 to reach the final Exit Assessment score. If the Converted Score turns out to be a non-integral value, it will be transformed into the closest integer, e.g. any mark higher than 31 but lower than 31.5 will be counted as 31; whereas any mark from 31.5 to 32 will be counted as 32.

11 March 2002

Eligibility for College Trainers

According to present criteria, all doctors who are Fellows of the HKCP can become trainers if they are able to organize the required programmes in the appropriate facilities.

With effect from July 2002, only College Fellows who possess two years of relevant post-Fellowship experience can apply to become trainers in the respective specialties, unless there are objections from the Board in question. Trainers who have already been recognized by your Board on or before 30 June 2002 will continue to maintain their trainer status after 1 July 2002.

Scientific Section

Abstract of the Sir David Todd Lecture

Immunogenetics of IgA Nephropathy- Insights into its Pathogenesis and Progression

Philip K.T. LI

Department of Medicine and Therapeutics, Prince of Wales Hospital, Chinese University of Hong Kong

Introduction

Mesangial IgA nephropathy (IgAN) is the commonest cause of primary glomerulonephritis in the world. It affects all racial groups with different frequencies and accounts for 30-35% of all primary glomerulonephritis in southern Chinese living in Hong Kong (1-3). Up to 30% of patients can progress to end-stage renal failure (ESRD) in 10 years (3,4). IgAN probably accounts for at least 10% of all renal failure patients requiring dialysis in Hong Kong (1).

Clinical Features of IgA Nephropathy

Our recent cohort from 1987 to 1996 with 168 Chinese patients with IgAN showed a female preponderance (M: F = 1:1.5) with an average age of 32.9 years (4). 28% were hypertensive. 47 of 136 patients (34.6%) had family history of hypertension. A high histologic grade was associated with hypertension at presentation, family history of hypertension, a higher serum creatinine, total cholesterol and 24-hour urine protein excretion, and a lower serum albumin level. The renal survival was 92.0% at 1 year, 87.5% at 5 years and 81.8% at 10 years. Hypertension at presentation, family history of hypertension, renal impairment at presentation, proteinuria > 1g/day, and histologic grading are independent predictors of renal survival (4).

Pathogenesis of IgA Nephropathy

Although the exact pathogenesis of IgAN remains unknown, patients with IgAN have disturbances of cellular and humoral immunity with altered cytokine production (5,6). T cell activation is thus considered to be important and this involves the T cell receptors that can only recognize antigenic peptides bound to the Major Histocompatibility Complex (MHC) molecules (7,8,9).

Immunogenetics of IgA Nephropathy: Pathogenesis and Progression

Candidate disease genes for IgAN can be broadly classified into MHC and non-MHC genes. For glomerular diseases, we always need to consider genetics factors in 2 aspects: contributing to the development of the disease and affecting the progression leading to renal failure (7).

MHC class II genes: We previously studied a group of Caucasoid IgAN patients and found that HLA DQw7 was found in 71% of the IgAN patients compared with 27.8% in control with a RR of 6.17 (11). A Chinese family with 8 members having 3 suffering from IgAN allowed us to study the MHC class II genes using RFLP. The 3 affected siblings shared the same DR and DQ pattern with homozygous DR12, DQw7, DQα1b (10). This interesting family led us to study further the MHC class II genes in 73 Chinese patients with IgAN (12). In short, the frequency of DQα2 allele (a good prognostic gene) was found to be significantly lower in patients with chronic renal failure (14.3%) when compared with patients with normal renal function (40.4%). The DQA2 U allele (a poor prognostic gene) was found to be significantly higher in patients with chronic renal failure (66.7%) compared with patients with normal renal functions (26.9%). We found that the presence of this U allele has a significantly worse renal function with a higher percentage of patients reaching end stage renal failure (12).

T cell receptor genes: As mentioned earlier, T cell receptor (TCR) plays a key role in T cell stimulation. TCR consists of two chains - alpha (α) and beta (β) chains bound by disulphide bonds and associated with CD3 complex in the membrane of T lymphocytes. Each chain has a variable (V) and a constant (C) region that can undergo DNA rearrangement to generate receptor diversity (13). A 7kb C-α *Taq 1* fragment is found in 32 of 53 patients (60.3%) compared with 26 of 67 controls (38.8%). We confirmed that the TCR C-α gene is associated with IgAN and may be important in causing the disease (13).

Transforming growth factor-(1 (TGF-(1) gene: TGF-β1 is known to be a major regulator in extracellular matrix molecule

production (eg. collagens, fibronectin and proteoglycans) and is involved in the process of glomerulosclerosis. The treatment with antagonists of TGF-beta prevented the development of glomerulosclerosis (14). We previously demonstrated that CD4+ T cells from IgA nephritic patients expressed a higher level of TGF-beta mRNA than that of healthy controls (14). It is also a critical IgA isotype switching factor (15,16). Recently, several TGF-β1 gene polymorphisms have been identified and among these the +869(T→C) [codon 10 (leucine→proline)] gene polymorphism of the TGF-β1 gene correlates with TGF-β1 expression. We recently found that the presence of C allele (CC/CT) is associated with increased risk of IgAN compared with controls. This suggests that TGF-(1 may play a role in determining susceptibility to the development of IgAN, possibly through its effect on the switching and augmentation of IgA expression.

Conclusions

Immunogenetic studies are important in determining disease susceptibility and protection genes as well as the genes that will affect the severity and prognosis of IgA nephropathy. This is useful in the understanding of the pathogenesis of the nephritis. Cytokine gene study will allow us to find out any significant effect of the cytokine and help us to assess the potential role of anti-cytokines. We recently looked at the natural history of "Early" IgAN in clinical (mild hematuria and minimal proteinuria with normotension and normal renal function at presentation) and pathological (low grade lesions) aspects and found that actually 44% of them will progress (17). The presence of a genetic marker will help, in addition to clinical and histological indicators, to identify a poor prognostic group of IgAN patients so as to select them for early intervention or treatment. This will hopefully prevent the progression of disease in these poor risk patients and reduce the number of patients reaching end stage renal failure requiring the costly dialysis (18). This may be useful in managing patients with recurrent IgAN in renal transplant allografts (19).

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Abstracts of the Best Dissertation Awards

Best Dissertation Award (Gold)

Role of *H. pylori* infection in Gastroesophageal reflux disease: Facts and Controversies.

Justin WU
Department of Medicine & Therapeutics, Prince of Wales Hospital

The role of *Helicobacter pylori* infection in gastroesophageal reflux disease (GERD) is one of the most controversial topics of gastroenterology in recent years. Epidemiologic trends and recent cohort studies revealed a negative association between these two conditions. Owing to its effect on gastric acid physiology, *H. pylori* is postulated to have protective role against GERD, and the pattern of gastritis plays a determining role in the clinical outcome of *H. pylori* infection as well as its contribution to pathogenesis of GERD.

Compared to Western population, there is a stronger negative association between *H. pylori* and GERD in Chinese population [1]. This is an echo of the phenomenon that GERD is much less common and severe in Asian countries, where *H. pylori* is highly prevalent [2]. This protective effect is not only limited to non-reflux population because similar inverse relationship has also been observed between *H. pylori* and severity of GERD [3]. *H. pylori* infected GERD patients have milder reflux disease. Multivariate analysis reveals that *H. pylori* is the only independent factor that shows negative correlation with severity of GERD. The absence of *H. pylori* in all patients with reflux complications such as Barrett's esophagus and adenocarcinoma of esophagus further supports a protective role of *H. pylori* against severe reflux disease.

This protective effect is probably attributed to inflammation of acid-secreting mucosa induced by *H. pylori*, which suppresses gastric acid secretion. Furthermore, ammonia produced by *H. pylori* provides buffering effect against gastric acid. These two processes lead to reduction in gastroesophageal reflux. High prevalence of cagA positive *H. pylori* strain contributes to more severe gastritis and profound gastric acid suppression in Chinese population, which provides more effective protection against GERD compared to Western population.

The reason why *H. pylori* fails to protect against GERD in some patients is probably due to different patterns of gastritis between GERD patients and asymptomatic population. GERD is characterized by a pattern of *H. pylori*-related gastritis that is distinct from other *H. pylori* associated diseases. GERD patients have antral-predominant gastritis with very mild inflammation at cardia, where bacterial colonization is also sparse [4,5]. The acid secreting mucosa at corpus is relatively spared and there is little gastric acid suppression. The close proximity between cardia and distal esophagus makes ammonia generated by bacteria at cardia a particularly important buffer compared to other parts of stomach. As a result, lack of severe corpus gastritis and dense bacterial colonization at cardia leads to ineffective protection against GERD in these patients even though they are infected by *H. pylori*.

Apart from different pattern of gastritis, esophageal motility dysfunction also plays an important role in pathogenesis of GERD among patients with *H. pylori* infection. They have more severe esophageal motility dysfunction such as lax lower esophageal sphincter and weaker peristaltic contractions [6]. Defective anti-reflux barrier and impaired esophageal acid clearance may overwhelm the protective effect of *H. pylori* gastritis and results in esophagitis.

Current evidence shows that severity of GERD is not exacerbated by *H. pylori* eradication in majority of patients, although modest increase in esophageal acid exposure has been observed in some patients given anti-helicobacter therapy [7]. Yet, the significance of *H. pylori* eradication and long-term consequence of persistent *H. pylori* infection in management of GERD are still uncertain. *H. pylori* infection may have therapeutic benefit during initial treatment of reflux esophagitis through augmentation of acid-suppressant but its long-term benefit may be counterbalanced by its controversial role of accelerating atrophic gastritis after chronic proton pump inhibitor therapy.

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Best Dissertation Award (Silver)

P-glycoprotein and multidrug resistance *(MDR)* gene expression in epilepsy

Patrick Kwok Leung KWAN
Dept. of Medicine, United Christian Hospital

Background

Hippocampal sclerosis (HS) is one of the commonest aetiologies of drug-resistant epilepsy. Over-expression of the drug transporter P-glycoprotein (P-gp) confers chemoresistance in certain cancers. P-gp extrudes a wide range of xenobiotics out of cells and is present in cerebral capillaries where it contributes to the integrity of the blood-brain barrier. It is encoded by the *MDR1* gene in man and the *mdr1a* and *1b* isoforms in rodents. It was hypothesised that over-expression of the *MDR* gene may play a role in the pathophysiology of refractory epilepsy by limiting antiepileptic drug (AED) access to the epileptic focus.

Methods

A range of single-dose AEDs were administered to *mdr1a* knockout mice, which lack cerebrovascular P-gp, and their brain levels measured. Regional P-gp expression was determined in the normal rat brain by measuring *mdr1* mRNA concentrations. The effects of experimental seizures on the expression of *mdr1* were determined in the brains of genetically epilepsy-prone rats (GEPRs). Temporal lobe tissues resected from patients with refractory epilepsy due to HS were examined for the extent of *MDR1* gene expression.

Results

Phenytoin, carbamazepine and topiramate reached higher levels in the brains of *mdr1a* knock-out mice than in wild-type mice ($p<0.05$), suggesting they are substrates for P-gp. The hippocampus of rats expressed both *mdr1* isoforms, while other brain regions expressed *mdr1a* only. *Mdr1a* expression in the midbrain and cortex was higher in GEPRs subject to an audiogenic seizure compared with unstimulated, seizure-free controls. Significant *MDR1* expression was observed in resected tissues from patients with HS.

Conclusion

MDR gene expression may be relevant to the pharmacoresistance of HS. This mechanism may also play a role in other aetiologies of refractory epilepsy.

Abstracts of Update lectures

Interpretation of Randomized Controlled Trials: Facts and Fallacies

Cheuk Chun SZETO
Department of Medicine & Therapeutics, Prince of Wales Hospital

There are two major aspects that one should pay attention to when interpreting clinical trials: the design of the study, and the method of data presentation. The aim of a clinical trial must be clarified before one can decide whether the design of a trial is appropriate. It is a common error to design a superiority trial but conclude as an equivalence trial. The result is usually inadequate statistical power.

Clinicians can easily grasp the process and conduction of a clinical trial by going through the CONSORT flow chart, which is a necessary component for a paper to be published in many prestigious journals. It is, however, important to note the type of outcome measures chosen. Although the major or primary outcome measure should really be the focus of a trial, many clinical trials use multiple secondary outcomes and comparisons to "fish" a positive result. For diseases that hard clinical outcome is difficult to achieve, surrogate measures are commonly, and sometimes inappropriately, used. Furthermore, the duration of follow up should be adequate for the particular outcomes chosen.

The method of data analysis and presentation is another important loophole. In general, there are two types of analysis for clinical trials: Intention-to-treat analysis is the analysis of outcomes for individuals based on the treatment arm to which they were randomized, rather than which treatment they actually received and whether they completed the study. This is in contrast to evaluable patient analysis, of which outcome evaluation is based on treatment actually received.

Many clinical trials nowadays perform multiple interim analysis and subgroup analysis. Investigators often focus on the positive results and sometimes distort the whole picture of the trial. In addition, many investigators, especially those with pharmaceutical background, present the result of clinical trials in relative risk reduction, which may exaggerate the benefit of a treatment. It is always useful to determine the absolute risk reduction, number needed to treat and cost-effectiveness of a new treatment. Many prestigious journals include an editorial comment after an original article to address these important issues.

What can a practising clinician do? First, one should carefully select respectable journals. When reading a paper, it is important to define the aim of it and focus on absolute benefit of the major outcome. It is, in fact, often useful to read the editorial comments after the paper. For busy clinicians, with the rapid advance in medical informatics and increasing desire of people to publish paper, one may have to rely on textbook teaching and expert advice.

Mega-trials: Strengths and Limitations

Kenneth Ka Hing LAM
Department of Medicine, Pamela Youde Nethersole Eastern Hospital

The term Mega-trial (MT) is often used to describe a randomized controlled trial (RCT) which recruits more than one thousand patients with the aim of studying the effect of a therapeutic intervention. The evolution of MTs is both demand and industry driven. In the first place, there is always the need to establish benefit of new therapies over existing therapy. However, the margin of benefit (treatment effect) becomes progressively smaller as a number of useful therapies have already been established for a given disease. A RCT on a new therapy with only modest treatment effect expected will then need a large sample size so as to achieve a reasonable power. In the second place, pharmaceutical companies are eager to support trials that establish efficacy of their products

that have potentially large markets, even though MTs would be required.

MTs are based on a pragmatic trial philosophy. In order to recruit a large sample size from multiple centres at more containable costs, eligibility criteria have to be broad; trial design is often simple; treatment regimens are uncomplicated; clinical monitoring and adjunctive care are often unrestrictive; and data collection is often streamlined and focused on clinical outcome.

There is no doubt that MTs have the power in detecting moderate treatment effects. This is well exemplified by GISSI-I[1], a MT that confirmed the benefit of use of streptokinase (SK) in acute myocardial infarction (AMI). MTs can also reliably detect synergistic effect of therapies with moderate treatment effect. This is illustrated by ISIS-2[2], a MT that confirmed the additive benefit of SK on aspirin in AMI. Positive results from MTs normally have significant impact on clinical practice. The use of tissue plasminogen activator (tPA) instead of SK in AMI (GUSTO-I[3]); the use of angiotensin converting enzyme inhibitors in post-AMI patients (ISIS-4[4]); and the use of beta-blockers in systolic heart failure (MERIT-HF[5]) are good examples. The implication from the widespread adoption of confirmed therapies is that a large number of patients suffering from diseases with both high incidences and mortality rates can be saved. Results from MTs can be more readily generalized because of the wider spectrum of patients studied and the "closer to real-life" management that these patients received. MTs are also invaluable in the reliability of data they provide for outcome assessment and resource utilization, which form the basis for cost-effectiveness analysis.

On the other hand, MTs are expensive, and cannot be conducted without pharmaceutical support, and therefore their influence. It is always assumed that conclusions drawn from MTs are reliable. However, this has been questioned by Furukawa et al [6] who discovered a lower than expected congruence rate among MTs addressing the same issue, and who concluded that "findings should lead to a healthy reduction in confidence in generalization from MTs", and that "there is simply no substitute for hard, clear thinking about the results of each study (MT)". Moreover, efficacy of a therapy may be falsely low in a MT due to a) presence of null-bias: when patients receive non-trial treatment which replicates effect of the therapy under test, or when patients' characteristics are not rigorously defined, and b) failure to achieve maximum treatment effect by not addressing fully the underlying mechanisms of therapy. These phenomena could well explain, at least in part, why oral mononitrate and intravenous magnesium did not show any significant effects on outcome in AMI patients recruited in the ISIS-4 trial. The road leading to establishment of superiority of tPA over SK in treating AMI patients shows us that MTs do not serve an explanatory or exploratory role, but instead require input from experimental models and exploratory human studies. A positive MT may also confer a false impression of generalizability, particularly when subgroup differences are not clearly discernible for more in-depth analysis. In fact, post-hoc subgroup analyses are often unreliable, as they may either overemphasize or underestimate treatment effect differences between subgroups. In GISSI-I, for instance, SK was found to be beneficial only to patients without prior MI. This was subsequently disproved by other MTs. Finally, it is important to remember that MTs only provide statistical answers to treatment effect differences, but then clinical relevance of such differences should always be examined.

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Evidence-based medicine and its applications in clinical management

Matthew Ng
Department of Medicine, Tung Wah Hospital

Evidence-based medicine is the care of patients using the best available evidence from the results of research to guide clinical decision-making.

DEFINING THE QUESTION

Clinicians in their practices need answers to many questions like : Is the finding abnormal? What is the risk factor for the disease? What is the pathogenesis? How effective (and harmful) is treatment? How effective (and harmful) are preventive interventions? The question must be defined before searching for the answer. Research can only answer specific questions, one at a time.

ACCESS TO INFORMATION

Information is relatively easy to come by in the electronic age. The sheer volume of easily accessed information creates a new challenge: finding the best available answers to specific questions amidst all the other information, an activity known as "knowledge management". The searching and sorting must be delegated to maintain a comprehensive surveillance on new developments in internal medicine. Among the options are:

"Evidence-Based Medicine" (http://ebm.bmjjournals.com/)

"Best Evidence" (American College of physician Journal Club + Evidence-Based Medicine)

"Clinical Evidence Online" (OVID)

"Cochrane Database of Systematic Reviews" (OVID)

"Clinical practice guidelines" (http://www.guideline.gov)

JUDGING THE CREDIBILITY OF RESEARCH RESULTS

Clinicians should have the ability to do an in-depth analysis of research articles that are especially important to their practice and those that are controversial. They should be in a position to experience the power, independence, and enjoyment of critically analyzing articles on their own or with colleagues in a local journal club.

APPLYING RESULTS TO THE CARE OF PATIENTS

Even after efforts to obtain research results that match the individual patient as closely as possible, the evidence must be interpreted in relation to the individual patient. Evidence-based medicine is not intended to replace clinical judgment. Each individual patient will be cared for with the best research evidence as a benchmark, but with care tailored to their individual circumstances - genetic makeup, past and concurrent illnesses, health-related behaviors, and personal preferences.

References

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Diary

May 18, 2002 (Saturday)

"Scientific Symposium on Recent Advances in Management of Nephropathies"
organised by Hong Kong Society of Nephrology. HKCP CME accredited
Venue : Concord Room, Renaissance Harbour View Hotel Time: 1:45pm to 6pm
Registration (Free) : Contact Ms Charlene Cheung (Tel: 2105 4873, Fax: 2895 5157)

Opening Remarks:	Richard Yu & Philip K.T. Li
1. Lupus Nephritis	Edmund J Lewis
2. Vasculitis and Glomerulonephritis	Philip K.T. Li
3. Chronicity Based Grading for Nephropathies: one system for all	FM Lai
4. Ischemic Nephropathy: What's the right approach?	Julia B Lewis
5. IgA Nephropathy	KN Lai
6. Membranous Nephropathy & Focal Segmental Glomerulosclerosis	T M Chan
7. Diabetic Nephropathy	Edmund J Lewis
8. Hypertensive Nephropathy - The AASK results	Julia B Lewis

26-27 October 2002 (Saturday & Sunday)

Combined Annual General Meeting & Joint Scientific Meeting.
Details to be announced later.

9-10 November 2002 (Saturday & Sunday)

"Minimally Invasive Medicine"
1st Intercollegiate Scientific Meeting organised by Hong Kong College of Physicians, College of Surgeons of Hong Kong, Hong Kong College of Otorhinolaryngologists and Hong Kong College of Radiologists.
Venue : Hong Kong Academy of Medicine
Registration : conference secretariat tel : 2871 8787 email confdept@hkam.org.hk
Sessions on

* Acute Renal Failure
* Liver Tumour
* Bronchogenic Carcinoma
* Sinusitis
* Obstructive Sleep Apnoea
* Aortic aneurysm
* Coronary Artery Disease
* Colorectal Tumours

Examination and Results

Pass list of Joint MRCP/HKCP Intermediate Examination Part II (PACES) Oct 01

Chan Ching Kit
Chan Chun Man, Jones
Cheung Wai Ching
Cheung Yuet Chow
Chui Pui Yuk
Kwong Kai Yan
Lai Koon Chi, Christopher
Lam Chung Mei, Jamie
Lau Yuen Fun, Emmy
Lee Ka Lai
Lee Joo Shium, Thomas
Lee Yee Ace
Leung Tsi Mei, Violet
Liang Ka Shing
Liu Hor Ming
Lo Chi Wai
Lo Yi Tat
Pang Sai Yau
Shing Kam Kwok, Donald
Shum Nam Chu
Sim Pui Yin, Joycelyn
So Yui Chi
Tse Wai Choi, Eric
Tsui Yee Tuen
Wat Zee Man
Wong Chi Kwan
Wong Chit Wai
Wong Pui Ming
Wong Wai Ming
Wong Wai Shan
Wong Wing Hang
Woo Wai Shan, Sandy
Yau See Yun, Joyce
Yiu Kwok Hing
Yu Chung Kwan, Cellina
Yu Kin Chap

Exit Assessment Pass List for December 2001

Advanced Internal Medicine
Chan Koon Ho
Choi Kin Wing
Fung Tang Tat, Konrad
Ho Chung Man
Leung Chi Man
Leung Chung Ping
Leung Yat Yee, Natalie
Liu Sung Yu, Herman
Ma Hon Ming
So Kit Ying, Loletta
Wong Che Keung
Wong Sze Ho, Sunny
Yim Cheuk Wan

Critical Care Medicine
Chiu Alexander
Chow Fu Loi
Lau Lee Sung
Lee Wai Chuen
Leung Yuen Wah, Winnie
So Sheung On
Tsang Hin Hung

Cardiology
Wong Wai Lun

Endocrinology, Diabetes & Metabolism
Chung Chun Hoi
Ozaki Risa
Tong Chun Yip, Peter

Haematology & Haematological Oncology
Kho Chi Shan, Bonnie

Nephrology
Chu Kwok Hong
Lo Hok King, Stanley

Dates of the Joint MRCP(UK)/HKCP Intermediate Examination

Part 1	May 2002
Part II Written	July 2002
PACES	21-25 October 2002

For the written examination, the new format of the timetable is as follows;

14:30	Candidates report to Examination centre
15:30 - 18:00	First paper of Part I/ Part II
18:00 - 19:00	Dinner break
19:00 - 21:30	Second paper of Part I/ Part II

Once In, No Way Out !

Author: Dr. Ray Chan Chun Chung

HKCP College Tie

These attractive ties bearing the College emblem can now be purchased from the HKCP *(telephone 2871 8766)* for only $100 each.

Obituaries

Eulogy for Professor Gerald Choa

Professor Gerald Hugh Choa
His Life and His Work
Eulogy Delivered by Prof. Arthur K.C. Li
10 December 2001

We are gathered here this morning to remember Gerald Hugh Choa. We all had the good fortune to have met him, known him, worked with him, but now that we have lost him, we are bound by the same desire and indeed the same need to mourn our loss, and to pay him our last respects.

Prof. Choa was born in Hong Kong on the 21st day of March 1921, to a father who was a compradore in a Dutch Bank. The youngest son in the family, he and his five elder sisters - Agnes, Molly, Daisy, Phyllis, and Leatrice, received private tuition at home during their childhood years. It was in Wah Yan College on Hong Kong Island that he acquired his secondary schooling, and was converted to Catholicism. All his life he remained a devout Catholic. All his life the selflessness of the Christian missionaries impressed him much more than the trade of his father. His own life was one of giving and service, in much the same natural and low-key manner as the Jesuit fathers who taught him.

A brilliant student, he won a place to read medicine at The University of Hong Kong . From that point onwards, his life became inextricably linked with medicine. He graduated from the University in 1946, obtained his MD in 1960, and acquired in the following 14 years a string of further qualifications from prestigious medical institutions in the United Kingdom.

In the early fifties, he was teaching at The University of Hong Kong as a Lecturer in Medicine. There in its teaching hospital, Queen Mary Hospital, he met Peggy Leong, a medical social worker, who later became his beloved wife and partner for life. At the prompting of his department head, he joined the Medical and Health Department of the Hong Kong Government in 1956, being the first Chinese to be appointed to the position of Specialist in Medicine at Queen Mary Hospital, a post akin to a full professorship in academia. And in this position, the young Gerald Choa rose quickly through the ranks and was handpicked by the then Director of Medical and Health to be groomed as his successor.

The decision to give up practising medicine and to take up administration was a difficult one, for he was such a good doctor and enjoyed so much looking after his patients. But he never regretted the decision he made.

Prof. Choa assumed the Directorship of the Medical and Health Department in 1970. In the six years that followed, he demonstrated his flair for administrative medicine and made monumental contributions towards the improvement of local medical and health services. His colleagues well remembered how he introduced Methadone detoxication to treat drug addiction, how he designed a new role for the government in family planning, and how he launched geriatric and community nursing services for Hong Kong people. They remembered how, in 1975, he arranged for the new Princess Margaret Hospital to be turned almost overnight into a temporary shelter for the Vietnamese boat people after their unexpected arrival in the waters of Hong Kong.

His colleagues also had a vivid memory of the smooth running of all the meetings he chaired--how he had everything under control, never allowing a single word, a single minute to be wasted over unnecessary argument and debate. Prof. Choa proved himself a director of the highest distinction, having impressed his colleagues with his sagacious leadership, his boundless energy, and his superb efficiency.

It was in late 1975, some 20 years after he had joined the government, that academia once again beckoned. This time it was The Chinese University of Hong Kong, which was to set up a new medical school. The then Vice-Chancellor, Dr. Choh-ming Li, approached him in person and convinced him that his service as the founding Dean was indispensable for the new medical school.

So from 1976 onwards, a long and close association with The Chinese University began, which spanned a quarter of a century, extending well beyond his retirement from the University in 1987. He had served as founding Dean of Medicine, Professor

of Administrative Medicine, and Pro-Vice-Chancellor. And until last Monday, he was honorary adviser to the Vice-Chancellor, and member of the University Council.

It was during these 25 years that we at The Chinese University came to know the Prof. Choa that we knew.

A man of just average physique, he stood tall among us all.

The awe he inspired and the respect he commanded from other chair professors in the new medical school was legendary. It was not so much because he was the founding dean, who was in charge of the recruitment of senior professors from across the world; it was rather because Prof. Choa had an aura of authority around him, he had the charisma of a natural leader, and the shrewdness and tenacity required for the formidable task of building a medical school from scratch. Those early years were difficult years, but he was a tower of strength, the mastermind behind everything: from course structure to curriculum, from budgeting to the general design, planning and facilities of a teaching hospital. Under his Deanship, the Prince of Wales Hospital in Sha Tin became operational in 1984, and the first batch of medical students graduated from the Chinese University in 1986.

It was Prof. Choa who started in the Chinese University the tradition of Inaugural Lectures by the chair professors. I remember how, at the very first lecture, we all expected a glowing introduction of the professor. Instead, Prof. Choa, as Dean, merely announced: 'I call upon the Professor of Physiology to deliver his inaugural lecture'. Short, sharp, and to the point. No nonsense, just get the thing done. Such was his style so much admired and so very well remembered.

It was also he who established the practice of convening faculty board meetings after office hours at 5.00 p.m., so that none would complain the meetings were interfering with their classes or their clinical duties. Five o'clock sharp, and Prof. Choa would demonstrate once again how efficiently meetings should be conducted. Prof. Choa did not need to argue or debate contentious issues; just one look from him and one was put in one's place.

Returning to academia gave him the opportunity to practise medicine again, his true lifelong passion. He held a Consultant post at the University's Health Centre, and old-timers on the campus would tell you how popular and well-loved Prof. Choa was in the clinic. His patients ranged from amahs in the pantry to senior administrators, college heads, and vice-chancellors, and they all got the same high quality medical treatment and meticulous care. Rank was utterly irrelevant in Prof. Choa' s concept of patient-doctor relationship.

Those who might have been a little daunted by the sombre and brisk Gerald Choa in his office would take to him instantly in the clinic. As patients, they would be moved by his gentleness, they would get to feel his genuine concern for their will-being, they would see a genial Prof. Choa, they would benefit from his superb clinical acumen. It is no surprise that the nurses who worked closely with him always admire him the most.

Across the campus in different offices, those who knew him well would tell you that once the flame of friendship was kindled, you would feel Prof. Choa's great warmth. His peers had found in him a trusting and loyal friend, who was always ready to go the extra mile to help them out. Those more junior in rank and his own subordinates had found in him a wise counseller, a benevolent mentor, a kindly father figure. They all say: 'You've got to know him first, then you'll love him.' What he had fostered were lifelong, lasting relationships. Today, in this hall, all his old friends, his mentees, his numerous 'sons and daughters' have come to show their grief. We all miss you, Prof. Choa.

And then of course he was dearly loved and respected by his students. Just last June he was celebrating the 20th anniversary of the Faculty of Medicine with all the alumni of the Medical School. You should have seen how he was cheered and applauded when he was invited to go onto the stage for a toast in his capacity as the founding dean. He had set extremely high standards for his students and he painstakingly made available to them the best possible education and training. He had every reason to be proud of the achievements of the medical school he founded. And we are better doctors, administrators, and human beings for having known him and worked with him.

Prof. Choa had combined three distinctive and equally illustrious careers in one life--those of physician-clinician, public servant, and medical educationalist cum administrator. For his distinguished service to the community, he was made a CBE in 1972. He was

awarded an honorary degree of Doctor of Laws in 1987 and then an emeritus professorship in 1988 by The Chinese University. He was also among the first to become an Honorary University Fellow of the University of Hong Kong in 1995.

Yet Prof. Choa was always modest and understating about his achievements. He tended to regard them as nothing more than the call of duty. He was just doing his job, he would say, in a most matter-of-fact manner. Just as he would not make glowing introductions of the chair professors who were to deliver their inaugural lectures, he shied away from praises for himself. He once told the writer of his citation for the degree conferment ceremony that two lines would suffice for him. And if he could, he would probably complain that this eulogy is far too long. But, Prof. Choa, I feel duty-bound to sing all the praises you deserve, to express all the respect and affection we have for you. There is no reason why I should allow you to be short-changed this time, this last time. So bear with me, Prof. Choa, even if this doesn't suit your style.

Yet give me another hour, it would still be insufficient to cover all that he quietly did for the infirm, the needy, and the sick, for whom he had a particularly soft spot. His long association on a personal capacity with the good work of the Action Committee Against Narcotics, the Mental Health Association of Hong Kong, and the Hong Kong Anti-Tuberculosis, Chest, and Heart Diseases Association bespoke his lifelong concerns. His close involvement in the charitable work of the Council of Caritas-Hong Kong reflected the true humanitarian that he was.

Making his life useful to others was so important to him that retirement meant only different channels of rendering service. Before his own health started to fail him about three years ago, he was engrossed in the work of a private clinic in Central, and prior to that, he had been in charge of a medical health assessment unit he helped found in a private hospital.

And until his very last days, he was fully supportive of the work and activities of The Chinese University of Hong Kong, giving us his shrewd advice on various Council committees, attending university functions which had a special meaning for him. The last time I saw him on campus was less than a month ago, celebrating with his old friends and indeed his fans the opening of our newly renovated Health Centre, a place where he once tended to the health of so many of his colleagues and their families, and a place which he opened some 30 years ago as Director of Medical and Health Department. And I was congratulating myself on my good fortune in having Prof. Choa agreed to continue to be my honorary adviser for another two years.

How we will all miss him.

While he was a most efficient workaholic in the office, Prof. Choa never brought his work or his worries home. Home was the private sanctuary he shared with Mrs. Choa, to whom he had been happily wedded for over 40 years. There he sought her lively companionship and regained his peace of mind. To relax, he loved listening to music, going to concerts occasionally if he could afford the time. He was also an avid reader, his favorite subjects being history and biography, in particular the history of western medicine in Hong Kong and mainland China, and the biographies of those related to that subject. It is not generally known that he was a historian and writer himself. He was the author of *The Life and Times of Sir Kai Ho Kai*, a biography of the first Hong Kong Chinese to qualify in medicine. His other book, *Heal the Sick*, tells the story of the Protestant medical missionaries in China.

Whether Prof. Choa had plans to write or publish any other book we have no way of finding out now. What we know is that his was a life dedicated to medicine and medical related services, with complete disregard for worldly fame or earthly riches, in much the same selfless spirit of a Christian medical missionary.

In the early hours of a Monday morning on the 3rd of December 2001, Prof. Choa passed away peacefully at home, during sleep. As we reflect on his life and mourn his passing, we seek solace in the thought that he was taken away at his most peaceful and tranquil time, having led a life so rich, so full, so generous.

We extend our condolences to his loving wife Mrs. Peggy Choa, to his beloved sisters, and to all his nieces and nephews who are here with us to pay our last tributes. Prof. Choa has departed, having dutifully completed his earthly commitments. We give thanks for what he has done for us. We give thanks for having shared his wonderful life and warm friendship. Dear mentor and friend, may you rest in peace. We shall always remember you in our hearts. We shall look forward to seeing you again in dreams that we dreamt together.

Professor Gerald Choa - Epilogue

The Hong Kong College of Physicians and her Council mourned with deep sadness the passing away of Professor Gerald Hugh Choa a former Vice President and founding father of the College. Professor Choa had a distinguished career and life-long devotion to medicine. From 1956 to 1970 he was the Medical Specialist in the Government Medical Unit, Queen Mary Hospital. He was a clinician par excellence whose clinical judgment and diagnostic skill had no equal. From 1970 to 1975 he served the Government as the Director of Medical and Health Service. During this tenure he demonstrated his skill and talent as an administrator. He introduced a series of reforms, which still continue to this day. From 1976 to 1987 he returned to the academia - a career he so much cherished - to be the Founding Dean of the Faculty of Medicine of the Chinese University of Hong Kong. The legacy of his achievement stand proud in the Medical School of the Chinese University whose undergraduate teaching and research is ranked as equal to any international school of medicine.

In the formative years of the founding of the Hong Kong College of Physicians he played a vital if not essential role. Originally the Memorandum and Articles of Association was drafted under "The Association of Physicians". It was thought that the name of Hong Kong College of Physicians at that juncture was not appropriate. On the evening of inauguration on the 15th October 1986 at the Jockey Club in Happy Valley Professor Choa made an eloquent plea for the establishment of a proper professional body and hence the College name came into existence at the very last minute to everybody's delight and relief. His wisdom, his authority, his charisma and his stature as Pro-Vice Chancellor of the Chinese University carried the day.

During the College's history from infancy to adolescence and then into maturity, Professor Choa had been very active as a Vice President from 1986 to 1988, Council Member from 1991 to 1993 and re-elected as Vice-President from 1993 to 1995. He was the generous anonymous donor in establishing the AJS McFadzean Lecture/Oration in memory of his mentor and the Sir David Todd Lecture on Sir David's retirement from the College as the Founding President. The College had always relied on him in controversial issue to be the judge. His opinion and advice had always been fair, firm, deliberating with wisdom and compassion and we are always indebted to him for guiding us in those formative years. He will be remembered by generations of Council Members for his contribution to post-graduate training. His contribution to both the community and academia was duly recognized by the last Colonial Government when the Commander of British Empire was bestowed on him in 1972.

Here we have a most exceptional and distinguished member of the medical profession who had devoted his whole life to medical education, service to the community-at-large and healing of the sick whose passing away was not even acknowledged by the present Administration. It was indeed with great sadness to find that no official representative nor any word of condolence was sent by this Administration to bid farewell to a devoted citizen who had done and achieved so much for the community.

Prof. Richard Yu
President
Hong Kong College of Physicians

Events

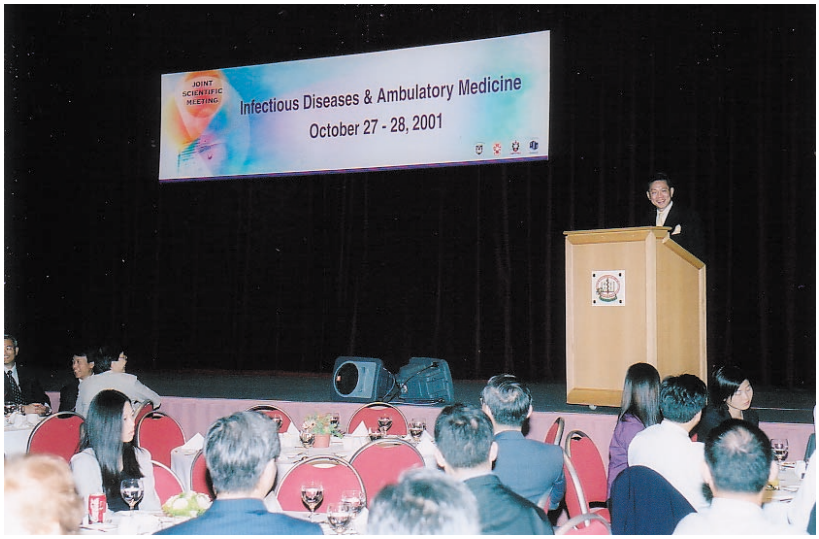
Report on the Joint Scientific Meeting organised by the Hong Kong College of Physicians, Hong Kong College of Family Physicians, Hong Kong College of Pathologists and Hong Kong College of Paediatricians.

27-28th October 2001. The Hong Kong Academy of Medicine, Jockey club building.

The above meeting turned out to be most successful and was very well attended. 23 speakers contributed to the meeting including 5 from overseas. The total number of registered delegates was 595. Infectious disease was the theme for first day of the conference and several areas were addressed including respiratory tract infection, infection in immuno-compromised patients and miscellaneous infection. On day 2, wide range of issues concerning ambulatory medicine were discussed including allergic and functional disorders, hypertension, hyperlipidemia and common problems in family medicine. Three interesting cases were presented and discussed during the interactive session whereby audiences participated by the use of a wireless voting system.

During the opening ceremony, speeches were delivered by three colleges presidents (Prof. Richard Yu, Prof. Nai Kong Leung and Dr. Donald Li) and Hong Kong College of Pathology representative (Dr. Chris Tse). Dr. EK Yeoh and Dr. CH Leong also addressed the audiences. The Sir David Todd lecture entitled " Immunogenetics of IgA Nephropathy-insights into its pathogenesis and progression" was given by Dr. Philip Li. Dr. Li was introduced by the late Prof. Gerald Choa. Sadly, this turned out to be one of Prof. Choa's last public appearance. The award ceremony took place during the dinner banquet and was presented by our president to the awards recipients. Dr. Philip Li was honored with the Sir David Todd medal and the Best Dissertation awards were given to Dr. Justin Wu (Gold) and Dr. KL Kwan (Silver).

The Sir David Todd lecturer, Dr Philip Li, is photographed with Professor Richard Yu (left) and the late Professor Gerald Choa (right).



Dr EK Yeoh, the Secretary of Health and Welfare, is addressing the audience before lunch.

Dr Wu Che Yuen, Justin, is presented with the Best Thesis Award (Gold) from Professor Richard Yu.

Professor Richard Yu is presenting the Best Thesis Award (Silver) to Dr Kwan Kwok Leung, Patrick.

Dr Stephen Foo (L-1), Dr Carolyn Kng (L-2), Prof Russell Scott (L-4), Prof Richard Yu (L-5), Prof. Mark E. Cooper (L-6), Prof Joseph Sung (L-7), Dr Henry CM Yu (L-8) after a symposium in the Scientific Meeting.

Cocktail reception for Fellows of RCP (London) to meet Prof. Sir George Alberti

A cocktail reception for Fellows of Royal College of Physicians, London was hosted by the HKCP on the 23 November 2001. The guest of honour, Prof Sir George Alberti, President of the RCP (London) met with over 30 fellows, including the late Prof Gerald Choa, at the reception held at the Hong Kong Club. The event was a great success, being a notable and delightful occasion for Fellows and old friends to meet together.

The Respectables

Prof. TK Chan, Prof. Sir George Alberti, Prof. Gerald Choa, Prof. Richard Yu, Prof. Rosie Young, Prof. Sir David Todd (from left to right)

Visit by Prof Carol Black

Prof Richard Yu is photographed here with Prof Carol Black, the then Vice President of RCP(London), at a welcome dinner held in her honour on the 4/1/02. Prof Black was recently elected as the new President of the RCP(London). The College would like to congratulate Prof. Black.

Visit by Prof Neil Douglas

Prof Neil Douglas, the Vice President of the RCP (Edinburgh) was in Hong Kong recently where he met with Edinburgh Fellows and our College Fellows on the 9/4/02. There were useful discussions on the use of guidelines such as the Scottish Intercollegiate Guidelines Network (SIGN) as well as the issue of Senior Medical Officers and Associate Consultants in Hong Kong being granted the FRCP(Edinburgh). Pictured here is the Council with Prof Douglas.

Feature Story

Smallpox Vaccine Production in Hong Kong.

The first report of Smallpox in China occurred in the reign of Chien Wu (49 AD). His army was fighting the 'barbarians' at Nanyang in the South West when a large number of soldiers, including General Ma Yuan succumbed. The disease may have been present in the Middle East and Asia for centuries. In Egypt, the mummified head of the Pharaoh Ramases V dated 1160 BC showed signs of smallpox. The first authentic description was made by the great physician, Ko-Hung (281-932 AD), in his 'Chou Hou Pei Chi Fang'.

Smallpox has changed the course of China's history. The Ch'ing emperor Shun Chi died of it in 1661 AD, but his son K'ang Hsi, Emperor from 1661 - 1722 AD, was more fortunate. He caught the disease but survived. A hundred years later Emperor T'ung-Chi died of the infection in 1875 AD, at the age of 18, opening the way for the Empress Dowager Ci-Xi to take power.

Hong Kong did not escape this deadly scourge. There are reports of hundreds of victims in the 1940s, immediately after the Second World War when refugees flooded into Hong Kong. Older clinicians amongst us will recall administering smallpox vaccines. Clinicians of even greater seniority will recall attending patients suffering from this deadly disease, for which there was no specific treatment.

William W.T.Cheung did more than most to end this scourge of humanity. He joined the Pathological Institute, now the Museum of Medical Sciences, in 1952 and was for many years the senior medical technologist involved in the production of smallpox vaccine in Hong Kong. He has been the source of much of the information in this account, derived from his own experience, and from historical information held at the museum.

Production of vaccine started some years after the inception of the Bacteriological Institute in 1906, and continued till 1973 when production was transferred to the new Institute of Immunology on Victoria Road.The methodology strictly complied with WHO requirements, and the British Therapeutic Substances Act. After the Second World War, production of smallpox vaccine in Hong Kong was restarted by a Mr A.E.P. Grimmo who had been trained at the Lister Institute of Preventive Medicine at Elstree near London. He had worked in Shanghai from 1946-48. The initial vaccinia seed came from the Lister Institute.

A stable near the main building was large enough to hold the many animals required to produce vaccines. 24 to 36 water-buffalo calves were used for smallpox production each year. The ideal animal was male, 12 months old, maximum age 20 months - after which the skin was too thick. In Hong Kong the production was limited to the cold, dry, winter months.

For the purpose of the scarification procedure the calf was brought to stand beside a heavy wooden 'operating table' to which it was tied by hemp ropes. The table was then tilted from the vertical to the horizontal, bringing the calf to lie on its left side. The uppermost hind leg was then tethered in such a way that the legs were wide apart, exposing the softest skin of the lower abdomen for the procedure. The abdomen was washed, shaved, and sterilised. The sterile area was then scarified with a multi-pointed instrument that left a parallel line of furrows on the skin. The vaccinia was inoculated on this scarified area. The abdomen was covered by a sterile white cotton apron and the animal was returned to the isolation stall in the animal house. The whole process took about two hours.

The sterile apron was changed every day. The calf was monitored for temperature, if there was a successful 'take' going up to 103-105 F (normal 100F) on the fifth and sixth days. On the sixth day the animal would be retied to the operating table killed, and exsanguinated to provide a bloodless field for harvesting specimens. The skin would be prepared as before to clear any bacterial contaminants, and the smallpox crusts, or 'pulp' would be scraped off using a metal instrument shaped like a shovel called a Volkmann Spoon. A good harvest would result in 500-600 Gms of pulp. The pulp was cleared of fragments of hair and skin, diluted with 1% phenol in sterile water then homogenised in an instrument called a Silverson Omnimixer, temperature control being maintained by an ice-bath.

A Triturator rendered the pulp into even finer particles and the resultant fluid was filtered through sterile gauze, before being mixed with more 1% phenol in water and incubated at 22 C. for 24 hours. A toxicity test was done by growing a sample of the final vaccine product on a culture medium, and taking a sample of the growth to inoculate two guinea-pigs. The test was successful if the guinea-pig survived a week without loss of weight. A potency test involved incubating an inoculum of diluted vaccine for 48 hours on chick chorio-allantoic membrane. Once the specimen had passed all its tests it was mixed with 1 part of glycerol, which was antiseptic and had a low freezing point, and stored at -20 C. At which temperature it could be kept potent for several years. Before use, the vaccine had to undergo a repeat of the egg pock count potency test to satisfy WHO standards.

To rejuvenate the seed vaccine to be used for production of a fresh batch of vaccine it was necessary to make a fresh culture using rabbit hosts. The rabbit's skin, (scarified and sterilised as described for the calf scarification), was inoculated with the seed vaccine, harvesting being carried out after five days of incubation. After the standard toxicity and potency tests this new culture could now be used to vaccinate buffalo calves to produce another batch of vaccine. The number of animals used for the production of one batch of vaccine, about 12,000 mls, from the initial vaccinia seed to the final product was:-

Four rabbits for vaccinia seed production
Six buffalo calves
Twelve guinea-pigs for toxicity testing
Eighteen mice for testing abnormal toxicity of phenol
Six rabbits for potency tests of vaccine (for comparison with the pock count potency test carried out on chick chorio-allantoic membrane culture).

This was high volume production. 1 ml of fluid provided sufficient vaccine for 30 vaccinations, so one batch of 12 litres of vaccine fluid was enough for 360,000 vaccinations. Four to six batches of vaccine were produced each year. This was more than enough to vaccinate one third of the population of Hong Kong every three years. Vaccines were exported to Manila and India, WHO regional centres, and to Macau.

Today, at the Museum of Medical Sciences, can still be seen the instruments used to process the smallpox pulp, and even more unique, the wooden 'operating table' on which the young buffalo lay, for our benefit, and the ultimate benefit of mankind. The last reported case of Smallpox was in Somalia in October 1977. This was remarkable news, as recently as 1974-75 there had been 2826 cases reported from India, with a 20% death rate. The World Health Assembly in 1980 declared that Smallpox had been eradicated. Despite this fact, the U.S.A. and Russia have stocks of Smallpox with which they have been recently producing vaccine stockpiles in case of germ warfare attack.

We can only hope that there is never the need for the vaccine to be used.

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John Mackay