

HONG KONG PHARMACEUTICAL JOURNAL

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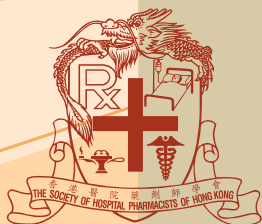
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(2 CE Units)*

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References: 1. Data on File, MSD Hong Kong. 2. Hong Kong Product Circular (JANUVIA, MSD). 3. Goldstein BJ, Feinglos MN, Luchford JK, et al; for the Sitagliptin D36 Study Group. Effect of initial combination of sitagliptin, a dipeptidyl peptidase-4 inhibitor, and metformin on glycemic control in patients with type 2 diabetes. *Diabetes Care*. 2007;30:1979-1987. 4. Hong Kong Product Circular (JANUMET, MSD).



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The Hong Kong Pharmaceutical Journal is a journal of the pharmacists, for the pharmacists and by the pharmacists. Submissions are welcome for the following sections:

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- Society Activities
- Drug & Therapeutics
- Pharmaceutical Technology
- Herbal Medicines & Nutraceuticals
- New Products

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There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The Editorial Committee may make editorial changes to the articles but major amendments will be communicated with the authors prior to publishing.

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For any queries on submission, please feel free to contact the Editorial Committee through mail or by the e-mail address.

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“Not all problems will find an immediate solution or answer. Scientific explorations with the right tools, however, will eventually get closer to it”

Although 2008 has been an eventful year to say the least - it is difficult to sum up the thousands of stories in just a few words, whether they were sad or joyful, cruel or lovely, a failure or a success. To local pharmacists, one thing that did happen last year was the annual Conference that took place on November 1-2 at AsiaWorld Expo. The conference was a big success. I believe everyone will agree with me as you see the joyful faces on every participant in the photos printed in the recapture report written by the Chairlady of the organizing committee (page 114-115). Besides the happy times, every participant in the conference certainly learned some new things.

Scientifically or technologically, there were many breakthroughs and achievements, particularly in the field of life sciences, amongst the international community in the year 2008.

Life, whether big or tiny when it is compared to the Universe, is small in term of size. These two different things, however, share the same characteristics; i.e. both are complex systems. For several thousand years, medical practitioners and philosophers were curious and puzzled by life. They adopted different approaches to reveal how life works and functions. Some even attempt to provide answers to explain the underlying principles so that it becomes possible to keep life indefinitely. In order to reveal what life is and to understand how it works, some good instruments and methodologies are required. An article published in pages 99 to 103 of this issue is about the top ten innovations of the year for life science, biomedical and pharmacological research. It outlines what sort of breakthroughs scientists accomplished and what kind of impacts they might have on healthcare practices and research in the long run. Because contemporary discovery of new drugs relies heavily on in-depth study of life with an interdisciplinary approach, the report is informative to all pharmacists.

The Chinese people are probably amongst a few human races that have developed their own holistic approach to prevent and treat a wide range of diseases by using medicinal herbs (MH) or by other alternative medical practices. During its five thousand year history, Chinese people have

accumulated a large pool of theories and experiences on the applications of herbs in their daily maintenance of health. A WHO study and a Taiwan survey also indicate that over 70% of the world population in developing countries apply MH for curing illness.⁽¹⁻³⁾ With the increasing use of MH, questions arise concerning their safety, regulation, efficacy and mode of action. The widespread use of MH has been connected to a number of adverse effects resulting in nephropathy, acute hepatitis, coma and fever. Unlike Western drugs, which are heavily standardized and regulated, MH has not been subject to scientific scrutiny and regulatory control.⁽⁴⁻⁶⁾ A few recent reports,⁽⁷⁻⁹⁾ including the latest study conducted by a group of scientists in the University of East London,⁽¹⁰⁾ reveal that the quality of herbal medications varied widely (see News in this issue). This partially explains why many attempts to integrate MH into the world of real drugs end with little success. Fortunately, our government has realized the importance of standardization and safety of our commodities and started to do some things about it in recent years and that is why the second volume of HKCMMS was launched even though it is a small step forwards.

Meanwhile, a mission driven proposal has been raised and submitted to the SAR Government by the Modernized Chinese Medicine International Association (MCMIA) (refer to p. 104 - 112 for details). In brief, the organization urges the HK SAR Government to honor a promise that was proclaimed by the former Chief Executive ten years ago to shape Hong Kong as an International Centre for Chinese Medicine. In order to achieve the seven objectives that they have proposed, the organization suggests the government should marshal sufficient public and private resources to nurture its realization and not simply give lip-service to the idea. This editorial does agree with their view and strongly believes that there is no such policy of non-intervention in this world except differences in degree of intervention. The US government has been selling their free trade ideas all the time yet they are also simultaneously practicing a small business assistance scheme for their

own citizens in the last few decades. Another proof is the latest efforts by the Federal Government in the United States and the British Government in the UK to rescue their banking and manufacturing sectors in the recent financial tsunami even though they have been promoting non intervention in markets all the time. Therefore, our political leaders should awaken and learn from all the wrong policies of the past. Whatever is good for our nation and for our whole society; the government has the obligation to take the lead, such as signing agreements for us with other countries (refer to news on Natural Health Products) or introducing policies to promote the establishment and maturation of an International Centre for Chinese Medicine. Likewise, the establishment of an advisory board of suitable and capable professionals is equally important. To this point, I will leave it to the reader to explore how good the MCMIA's proposal is and everyone is encouraged to give your comment to the organization or even to the SAR Government.

References

1. Farnsworth NR, Akerele O, Bingle AS, Soejarto DD, Guo Z (1985). Medicinal Plants in Therapy. Bulletin of the World Health Organization, 63(6):965-981.
2. Elder NC, Gillcrist A, Minz R (1997). Use of alternative health care by family practice patients. Arch. Fam. Med. 6:181-184.
3. Chen FP, Chen TJ, Kung YY, Chen YC, Chou LF, Chen FJ, Hwang SJ (2007). Use frequency of traditional Chinese medicines in Taiwan. BMC Health Services Research 7:26 (DOI:10.1186/1472-6963-7-26).
4. Cheung HY (1999). Scientific evaluation and quality assurance of herbal medicine. HK Pharm. J, 8(2);55-57.
5. Lord GM, Tagore R, Cook T, Gower P, Pusey CD (1999). Chinese herbal remedy linked to kidney failure. Lancet 354(9191):481-482.
6. Makino T, Hishida A, Goda Y, Mizukami H. (2008). Comparison of the major flavonoid content of *S. baicalensis*, *S. lateriflora*, and their commercial products. Nat Med (Tokyo) 62(3):294-299.
7. Osowski S, et al (2000). Pharmaceutical comparability of different therapeutic Echinacea preparations. Res. Compl. Nat. Classical Med. 7:294-300.
8. Kressmann S et al (2002). Pharmaceutical quality of different Ginkgo biloba brands. J. Pharm. Pharmacol. 54:661-669.
9. Ge Lin (2008). Quality assurance of TCM herbs relies on reproducibility of their safety and efficacy. IICMCM Conference Handbook, p 19. venue: HK Convention & Exhibition Centre, 15-16 August.
10. Gao J, Sanchez-Medina A, Pendry BA, Hughes MJ, Webb GP, Corcoran O. (2008). Validation of a HPLC method for flavonoid biomarkers in skullcap (*Scutellaria*) and its use to illustrate wide variability in the quality of commercial tinctures. J Pharm. Pharm. Sci. 11(1):77-87.

Cheung Hon-Young, BPharm, PhD, LFIBA
Managing Editor
31th December, 2008

New Research Indicates Commercial Herbal Medicines Vary Widely in Quality

Date: April 9, 2008

Commercially available herbal medicines vary widely in quality and in the concentration of their active ingredients, according to a research report published in the April issue of the Journal of Pharmacy and Pharmaceutical Sciences by a team from the University of East London (UEL). In their paper entitled "Validation of a HPLC method for flavonoid biomarkers in skullcap (*Scutellaria*) and its use to illustrate wide variability in the quality of commercial tinctures" the authors Jiayu Gao et al concluded that the wide variability between undermines the practice of scientific herbal medicine and makes accurate scientific assessment difficult.

Skullcap is a powerful medicinal herb. The genus *Scutellaria* consists of over 350 species worldwide and has been

used by many cultures to treat a variety of medical conditions, including anxiety, nervous disorders, liver disease and cancers. The UEL team conducted a number of tests to compare the flavonoid biomarker content of eleven commercial tinctures derived from the two most commonly-used species, *S. lateriflora* (American skullcap) and *S. baicalensis* (Chinese skullcap). They found that commercial tinctures of both *Scutellaria* species vary widely in the drug-to-extract ratio (ranging from 1:1 to 1:5) and alcohol concentration (25 – 70%), depending on the manufacturer. Thus, for the herbalist there is no guarantee or measure of either quality or efficacy from the products currently available. They suggested this variation could help to explain the variable efficacy of herbal medicines used in clinical practice and also the variation in

the reported activity of herbal medicines and dietary supplements in clinical trials and in assays of pharmacological activity.

Dr Olivia Corcoran, lead researcher and head of Forensic Science at UEL, said: "Wide variability in the biomarker content of herbal preparations undermines the practice of herbal medicine itself. There is an urgent need for products to be labeled with accurate assessment of the content of agreed biomarkers. "Without such labeling, it is extremely difficult to assess the effects of herbal medicines, many of which are known to be useless in low doses and dangerous in high concentrations".

Source of News:
www.uel.ac.uk/news/press_releases/releases/herbal.htm

Completion of Research Works on the Quality and Safety Standards for another 28 Herbs in Hong Kong

Date: December 1, 2008

On December 1, 2008, Department of Health (DH) of the Hong Kong SAR Government officially launched the publication of the Second volume of Hong Kong Chinese Materia Medica Standards (HKCMM). Meanwhile, it was announced that the research work

on the quality and safety standards for another 28 Chinese herbal medicines commonly used in Hong Kong has been completed under the HKCMM project which was launched in 2001. Altogether 60 herbs have already been characterized with efforts input from

local universities which in turn were monitored by a Scientific Committee from local experts as well as by an International Advisory Board from other countries.

Source of News: DH TCMD/6-20/20

New Recommendation from DH for the Use of Medulla Junci (燈心草)

Date: December 1, 2008

In a press released on December 1, Mr Robert Law, a government officer from DH, recommended Hong Kong people to change the traditional practices of using medulla junci (*Juncus effuses* L.) for the treatment of fidgetiness, insomnia, oliguria,

urination problems etc. It was told that in Hong Kong the whole plant of Medulla Junci (Figure 1) has been sold everywhere. But it was found that active ingredient in the stem pith (Figure 2) was significantly higher than that of the whole plant. Results of

other indicators suggested only the stem pith is effective. Based on the scientific findings, International Advisory Board (IAB) members considered that the medicinal part of Medulla Junci should be restricted to its "stem pith" and not the whole plant. Taking into

account the recommendation of the IAB and with a view to enhancing the quality control of Chinese herbal medicines in Hong Kong, DH urge people to observe and comply with the new requirements as set out in the Chinese Medicine Ordinance whenever purchasing, accepting, retailing and dispensing Medulla Junci.

Source of News: DH TCMD/6-20/20

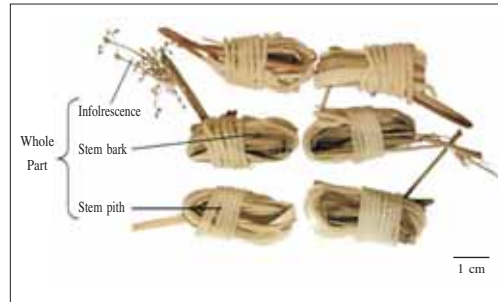


Figure 1. Whole plant of Medulla Junci.

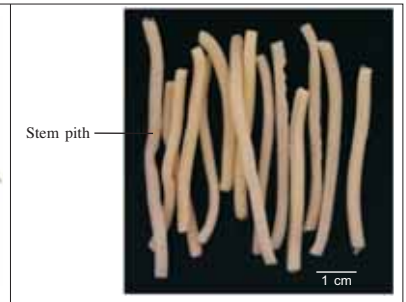


Figure 2. Stem pith of Medulla Junci.

Hong Kong Department of Health and Canada Signed Agreement on Natural Health Products

Date: December 5, 2008

The health authorities of Hong Kong and Canada signed "Plan of Action for Regulatory Co-operation on Natural Health Products (NHP)" to further enhance their co-operation in the regulation of NHP on December 5, 2008. NHP include vitamins, minerals and traditional Chinese medicines.

The document was signed by the Director of Health of Hong Kong, Dr P Y Lam, and the Assistant Deputy Minister of the Health Products and Food Branch of Health Canada, Ms Meena Ballantyne, to establish formal mechanisms for joint co-operation and exchange of information on NHP between the two places. It

came into immediate effect and will be reviewed before expiry of the four-year term. The plan of action is formulated to establish a clear framework for communication, maintaining ongoing dialogue, developing mechanisms for joint collaboration and exchange of relevant information on NHP between Hong Kong and Canada. It will enhance the safety, quality and efficacy of NHP and strengthen reciprocal knowledge, understanding and updates of regulatory frameworks of the two places.

"The signing of the action plan will formulate our working relationship and I

have confidence that the synergies we achieve will certainly go a long way safeguarding and promoting the health of people of Canada and Hong Kong," Dr Lam said. Under the plan of action, the areas of co-operation between Hong Kong and Canada include: (1) exchange of information such as monographs, pharmacopoeia, standards, guidelines, terminology of natural health products; (2) communication of adverse reaction reports, recalls, and other public warnings; and (3) conduction of joint workshops, technical exchanges and visits.

Source of News: Media-Newswire.com

『任重道遠』

主編先生：

當我收到新一期HKPJ時，真感到有點驚喜。因為我曾經以為這本期刊已無聲無息地消失了！多謝您及一班熱心的同業願意接棒肩負這項艱巨的任務。筆者是一個普通的藥劑師，並非學者無法提供與學術研究有關的文稿或報告供貴刊使用。為了表示對各位無私奉獻精神的支持，也胡亂地寫一些個人對藥劑界在過去半世紀的感想和對未來的期望。

1957年本人入讀臺灣的『國防醫學院』藥學系。數算起來已經是五十一年前的事。畢業後本人返港在QMH實習並考取了香港藥劑師執業資格，正式投入社區藥房服務，不經不覺也44年了！隨著時代浪潮的升降進退，感恩的是有神的帶領及愛護，至今仍在業界工作。

2008年可說得是一個極不平凡的一年。對中國人來說，更是向全世界展現了災難與歡樂融匯的一年。其中包括了雪災、地震、奧運及毒粉等幾項重大事

件。而全球性的經濟惡化也突顯了中國在發展中國家的行列中的領導地位。對筆者來說2008年也是一個值得驕傲的一年！因為在今年初舉行的PPA餐會中，會長邀請了香港藥房業德高望重的前輩江永安太平紳士頒授本人一個『榮譽大獎』，肯定了本人在1972年參與創立PPA的貢獻。這個大獎來得正是時候，因為今年適逢本人的母校『國防醫學院』藥學系成立一百週年。正當大家在籌備十一月底舉辦的西方藥學教育在華百年慶典，要求各校友交功課，以便刊印在紀念特刊中。這個合時大獎的來龍去脈讓本人可以大做文章向母校作了交待。

PPA 於1972年創立，為香港藥劑界開展了新的一頁。在同業不斷的努力下，以Michael Ling 為首的一小撮人於1983年出版了首期的『執業藥劑師藥刊』，英文名稱是 "The Journal of Practising Pharmacist"。到了1988年由 Grace Lau 開始接任總編輯時，她認為藥師的工作到了八十年代尾已於不同領域中參與，各類工作有不同的問題和意見，藥刊應

多開放給會員交流溝通。遂增開 "Letter to Editor" 及 "Pharmacy Practice" 兩個專欄。到了1992年Michael Ling 認為隨著藥學教育在港成熟建系，將不斷有藥學畢業生和藥學專家、教授的參與和供稿(註1)，為提升藥界在本港及國際上的專業及學術地位，遂建議將藥刊正名為『香港藥學期刊』英文名稱是 "Hong Kong Pharmaceutical Journal"。只可惜十五年過去了，從事藥學教育和研究的專家、教授卻極少去耕耘利用，以致這本學術期刊仍無法登上世界的學術舞臺。在此僅呼籲他們在爭取名利之餘，亦應負上社會責任，替本港整體藥界作出貢獻。筆者也希望會員能提交稿件，支持這份代表我們專業地位的學術期刊繼續發行，並且使她更加充實壯茁。

柯宇春 藥劑師 2008.12.10

(註1): 參閱PPA 20週年特刊訪問稿。Michael Ling and Grace Lau 的意見。

Role of Pharmacists in Patient-Centered Drug Education Programs

Chan, Timothy

PATIENT-CENTERED CARE

Day in, day out, pharmacists are facing rising challenges in ensuring that patients avoid adverse effects of medications as well as achieving the desired outcome of therapy. Patients inherently are not active in identifying and expressing their drug-related problems to doctors or pharmacists. A study in the U.S. shows that about 31% of adverse drug reactions experienced by patients are not reported to doctors in a community setting.⁽²⁾ Patients do not report the problems to doctors or pharmacists due to multiple reasons. For example, patients may feel embarrassed to disclose sensitive problems like sexual dysfunction or incontinence, or patients cannot judge if an adverse effect is medication-related, or they just do not want to discourage the doctor by raising bad news about the therapy, etc.^(1,2) Pharmacists have to use a more patient-centered approach in providing pharmaceutical care.

Patient-centered care is not a new term for the medical profession. In fact, the term “patient-centered approach” in medical care, has been advocated in extensive literature resources during the past 30 years. In contrast to the conventional “biomedical model” which treats the illness experience of patients as solely “signs and symptoms”, patient-centered approach emphasizes “empathy” and “patient’s involvement” in the whole treatment process.⁽³⁾ A more systematic description of patient-centered care is summarized as the following five points:⁽¹⁾

1. Practitioners should understand both biomedical and psychological factors related to the illness.
2. Practitioners should treat each patient as an unique individual and understand the personal meaning of the illness.
3. Practitioners should share the power and responsibility with patients in the decision-making process.

4. Practitioners should promote a “therapeutic alliance” with patients and set therapeutic goals for patients with their agreement.

5. Practitioners should be aware of their own attitude which may affect the perception of patients about their care.

As pharmacists who are experts in medications, we are in a very good position to educate our patients about drugs in different practice settings. The five points about patient-centered care can be selectively incorporated into our patient education activities in order to bring the greatest benefit to patients. There are myriads ways to carry out drug education to patients or the general public such as individual counseling, group counseling, public talks or even exhibition on drug use.

Drug education by healthcare professionals is more common in overseas countries, and there are various examples of better outcome when patients undergo interventions by healthcare professionals such as pharmacists. A study in the U.S. found that patients with low literacy level are 5 times more likely to receive a pneumococcal vaccine than the control group after education by physicians.⁽⁷⁾ The role of community pharmacists in foreign countries is more extensive. There is an example in Canada where a community pharmacist held weekly lunch to educate and reinforce patients who were undergoing smoking cessation, and the successful experience was being extended to other community pharmacy.⁽⁸⁾

As a pharmacy intern at Pfizer, I am very fortunate to have a chance to conduct drug educational talks in two different occasions, one in Queen Elizabeth Hospital (QEH) and one in a community center at Shek Kip Mei. In this article, I will illustrate all the necessary steps in preparing and conducting a drug education talk, as well as some special points that pharmacists should pay attention to

during their interactions with patients.

PROCESS OF CONDUCTING A DRUG EDUCATION PROGRAM

The target audience of the first talk was a group of patients suffering from heart failure. In the second talk, I talked to a group of middle-aged mothers and their children. In the ensuing paragraphs I will list out and explain the steps that I have gone through in light of my experience. I hope the insights gained may be useful to the readers.

Information assembly

The topic of the first program at QEH was “common cardiovascular drugs” and that of the second program at the community center was “pediatric nutrition and insomnia”. Both topics were given by the organizing committees about two months before the talks. Sufficient preparation time is the very first element of a successful talk because the process of information gathering, selection, presentation slide production and practice of presentation take a considerable amount of time. Usually, preparation time of 1-2 months is needed for an half-hour talk. If the topic is more sophisticated that requires more literature search, the preparation can take even a longer time.

After receiving a topic, we have to know the background of the audience. Take my talk at QEH as an example. The audience was a group of elderly patients with some of them having heart failure. Therefore, my presentation slide is expected to contain no professional terms or jargons. My information search should target at sources that give me knowledge for layman. The following table summarizes the common source of information that is written in layman language.

Sometimes, there is no available resource written in simple or layman language. We will have to resort to finding treatment guidelines that are intended for healthcare professionals. As professional pharmacists, we have

Organization	Content	Website Address
National Institute for Health and Clinical Excellence, UK	There is information for the public on common disease management	http://www.nice.org.uk/
American Academy of Family Physicians	There is information about OTC products, health food, common disease management and health tips for special groups of people	http://familydoctor.org/online/famdocen/home.html
Center for Disease Control and Prevention, US	There is information about health tips, disease prevalence and prevention.	http://www.cdc.gov/
Department of Health, HK	There is general health information for the public and local health statistics.	http://www.dh.gov.hk/english/useful/useful.html
Health InfoWorld, Hospital Authority, HK	There is Chinese information on local health campaigns initiated by the Government.	http://www3.ha.org.hk/healthinfoworld/index.aspx
Center for Health Protection, Department of Health, HK	There is information for the general public on health topics, infection control and health statistics	http://www.chp.gov.hk/submenu.asp?lang=en&id=466

Organization	Content	Website Address
National Institute for Health and Clinical Excellence, UK	There are treatment guidelines on various diseases for clinicians	http://www.nice.org.uk/
National Guideline Clearinghouse, US	There are treatment guidelines on various diseases and other interventions	http://www.guideline.gov/
Cochrane Library	Abstracts of reviews on vast amount of topics can be retrieved in this database on a free basis.	http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME

the knowledge to extract or simplify the information and turn it into something that can be understood by a layman. The following table summarizes some convenient and comprehensive information source which can be good choices when you want to find treatment guidelines in a short period of time.

The resources listed above do not provide guidelines for all types of diseases. For specific diseases, we ought to search for the corresponding academic organization. For example, we can obtain the treatment guideline of GERD in the website of American College of Gastroenterology.

Screening of raw information

Every drug education program has limitations of different kinds. The most prominent restriction is time. Even if you have obtained enough guideline or other pertinent information about disease that you are going to talk about, you cannot present everything to your audience. A community talk usually lasts for half an hour to one hour. According to my experience, a presenter can only present 20-25 slides at normal talking speed, so it is important to limit the amount of education material to avoid overloading the audience. As a professional, we really want the audience to take home a few important messages.

Besides, it is necessary to select the information of appropriate difficulty which will suit your audience by considering their educational

background, learning ability, age or sex. The elderly, as a group of common audience in a drug education program, generally have poorer eye-sight, hearing ability, learning ability and educational level. During the screening of raw information, we should select articles with more layman context. For example, when I searched for information on pediatric nutrition, I visited the website of "Central Health Education Unit" and "Central Food Safety Center" and extract useful information regarding general recommendation on children's diet and health. One of the advantages of these websites with layman context is that much of the material is written in Chinese, so we do not need to bother with the translation.

When we educate patients, we have to pay attention to their education level. We should avoid English terms when we talk to elderly patients unless we clearly know that they are capable of understanding the terms. Inappropriate use of English terms in patient counseling or educational talks will not only confuse the audience, but also create an unfriendly atmosphere because they just think that you do not want to communicate with them in the language they are most comfortable with.⁽⁹⁾ The effectiveness of patient education certainly drops as they do not trust you or do not understand what had been taught.

Last but not least, we have to judge the validity of the information. As the internet is congested with information

of varying quality, we can easily be misled by fraud information. It is essential to always look for information from reputable sources. Examples of reputable information sources include National Institute of Health, Food and Drug Administration, Department of Health, etc. Commercial websites are not the preferred information sources due to the possible bias. Information from textbook is also of high reference value, but we should examine whether the book is the most updated or not. Clinical paper is not always trustworthy. As a healthcare professional with the concept of evidence-based medicine, we should critically appraise a clinical paper on its level of evidence and methodology before using any of the conclusions for our purposes. For more information about evidence-based medicines and critical appraisal of clinical paper, please visit the website of Center of EBM. <http://www.cebm.net>

Compilation of slides or education material

A comprehensive and user-friendly presentation slide is an essential component of a successful patient education program. Many people think that making a slide is a simple task, which just involves directly transferring texts and pictures. In fact, from my own experience and the comments from various colleagues, we should be aware of the following key areas regarding making any patient education material:

- Keep the number of slides reasonable. For example, a 30-minute talk should carry approximately 30 pages of slides.
- Limit the number of words and points in each page. Do not exceed four bullet points per page. Put only key words in it. Avoid direct copying from source documents. It is of paramount importance that one first assimilates the information to internalize the material.
- Use suitable font type and size which is appropriate for the audience.^(4, 5) For example, the font size should be as large as 24-28 for a slide targeting at elderly patient. A white background with black font is considered boring and irritating to the eyes. A blue background with white or yellow font is more comfortable for most people.
- Avoid using plain text. Try to illustrate the ideas by graphics, simple charts and tables, etc.⁽⁹⁾ Slides containing large amount of text can easily send the audience to sleep or make them lose interest immediately.
- Introduce the objective and outline of the talk briefly in the very beginning. It is important to inform the audience of what you are going to talk about. Remind the audience of the expected duration of the talk and any other features such as the presence of quiz or Q & A section, if possible.
- Emphasize the main points by highlights, visual effectst, or pictures which help the audience understand and remember your points more quickly.
- Set wake-up quiz in between topics to grap the attention of the audience and to test their understanding on the previous topics. Re-capturing is important in any education program and should not be missed out.

Seeking input from other pharmacists or colleagues

The power of team spirit is something we all recognize in our daily work. The idea from one person is always limited and is subject to errors. The only way to minimize error and maximize benefit is to seek advice from other colleagues who are perhaps more experienced. For my experience, I always ask my tutor to proof-read my slides before any rehearsal of the presentation. Leaving

ample amount of time, say two weeks, before the real presentation for proof-reading, refining of the slides and rehearsal is crucial for a smooth and professional presentation.

Effective presentation and communication skills

With all the necessary materials and preparation, we are ready to do the most important part of an education program, the real patient contact. To get myself warmed up, I always arrive at the venue at least half an hour earlier. I could utilize the time to run through the slides once more and talk to the patients who arrive early. Through causal chatting, we can get familiar with the background of the audience and understand what they want to know. We can then adjust our presentation style according to patients' age, educational background, or even personal character. For example, if the audience tends to be passive and quiet, we can raise more questions and encourage someone to speak up in order to enhance the participation and stir up the overall atmosphere.

When the audience is ready for the talk, we can begin with a brief self-introduction about ourselves or any other helpers. An introduction about the background of speakers, purpose of the talk, expected duration and encouragement to participate is an example of an appropriate opening. It helps to bridge the gap between the speaker as well as the audience. For the actual presentation, there are a few more points that are noteworthy:

- Adjust the lighting to make the screen more visible, but not too dark which can drive the audience to sleep.
- If you use a laser pointer in order to correlate your speech to the slide content, do not sweep it around the screen because your audience will get lost and annoyed.
- Mind your tone and speed of speech carefully. Always be concise. Slow down a bit if your audience is mainly the elderly people. Suitable intonation can add flavour to a dry content.
- Ask questions in between slides to wake people up, test their

understanding and give yourself a chance to elaborate more on a particular point.

- Prepare simple treats to encourage participation during a wake-up quiz. It is interesting to discover that even candies serve a miraculous role in stirring up the atmosphere considerably.
- Avoid any English terms or jargons if you are talking to elderly patients or laymen with a low educational level.⁽⁹⁾ Do NOT go into abstract or complicated concepts; otherwise, the audience will be frustrated and their interest will be lost. Try to use analogy that everyone understands, if applicable.

Setting a Q&A section is a common practice in almost every presentation. A lot of people find it challenging because people can ask any unpredictable questions and an answer has to be given immediately without any time to dig up the reference. I find it difficult to handle this kind of scenario either. Nevertheless, I would like to share with you my limited experience in handling Q&A section.

First of all, we should try our best to get exposed to the potential questions that patients may ask you during the Q&A section. As I mentioned earlier, always look for reputable information sources to prepare the answers. Moreover, as said, teamwork is very important in a presentation. We should always invite a few colleagues to help you tackle the Q&A section. In case you do not know the answer, your colleagues may know and help you. In the Q&A process, patients always tend to ask about their own personal problem, such as "Is this drug suitable for me?", "Why do I experience this side effect?". Always try to give general recommendation instead of subjective answers, because it is impossible to know the complete medical history of the patients without a detailed counseling session. It is very unprofessional to give any advice without complete information and analysis. As an alternative, we may suggest patients to discuss their personal issues with us after the talk. This provides a platform for the patients to actively seek advice from us. Sometimes patients ask several questions at the same time, such as

“What is glucosamine? Is it good for the knee joint? Can I take this as a supplement?” Due to limited time and fairness, we have to identify the “questions” and answer them selectively. In the example mentioned, we can explain the nature of glucosamine in simple language and its efficacy based on evidence from literature. For question on individual suitability, we should advise the patient to seek personal counseling with us after the talk and give a chance for other patients to raise questions. Lastly, when we encounter questions that we cannot answer, simply apologize and promise to do a research on the topic and return to the patient as soon as possible.⁽¹⁰⁾ Generally, patients understand your situation and appreciate your effort. For some questions which should not be handled by a pharmacist, we should refer the patient to a doctor for proper treatment.

Patient counseling after a drug education program

I have a chance to participate in a patient counseling session after I have delivered the talk at QEH. There were about fifteen patients and four pharmacists. We decided to divide the patients into four groups with each group being led by a pharmacist. There are two ways of leading a patient counseling. A pharmacist can either invite each patient within the group to share his/her problem to all group members and the pharmacist can highlight the main points to all members, or he/she can individually counsel patients and let the other group members wait. Both methods bring out certain advantages and disadvantages. The former one certainly saves time, and enables patients to learn from other people’s experience. However,

privacy is a concern to some patients. Hence, we need to make sure all of them agree before going forward. The latter one enables the pharmacist to explore individual patient’s problem to greater details, but the other patients may lose patience while waiting for their counseling.

As experienced by a lot of pharmacists, patients usually ask about the side effects of drugs, the functions of each drug, information about health supplements, etc, when they see a pharmacist. To my surprise, patients that I met are confused on basic medication managements and their disease status. Many of them take out their “pill box”, which contain different colours and shapes of pills in a messy way. They claim that they can recognize different drugs in the pill box, but they show poor performance when I asked them to pick out the correct pills per dose. Poor medication management undoubtedly leads to more medication error and reduce patient compliance. Moreover, when I tried to test their understanding about putting drugs into refrigerator, many of them fail to answer the question correctly. Most of them think that pills should be refrigerated to keep them “fresh”, which actually worsens the stability of pills and decreases their shelf life. Pharmacist is in a very good position to educate them the correct way to store and manage medication in order to optimize the treatment.

Soliciting feedbacks from audience

One of the key elements of achieving continuous improvement is evaluation. Opinions from others are important to reflect the shortcomings of our performance. Therefore, it is an excellent idea to distribute an

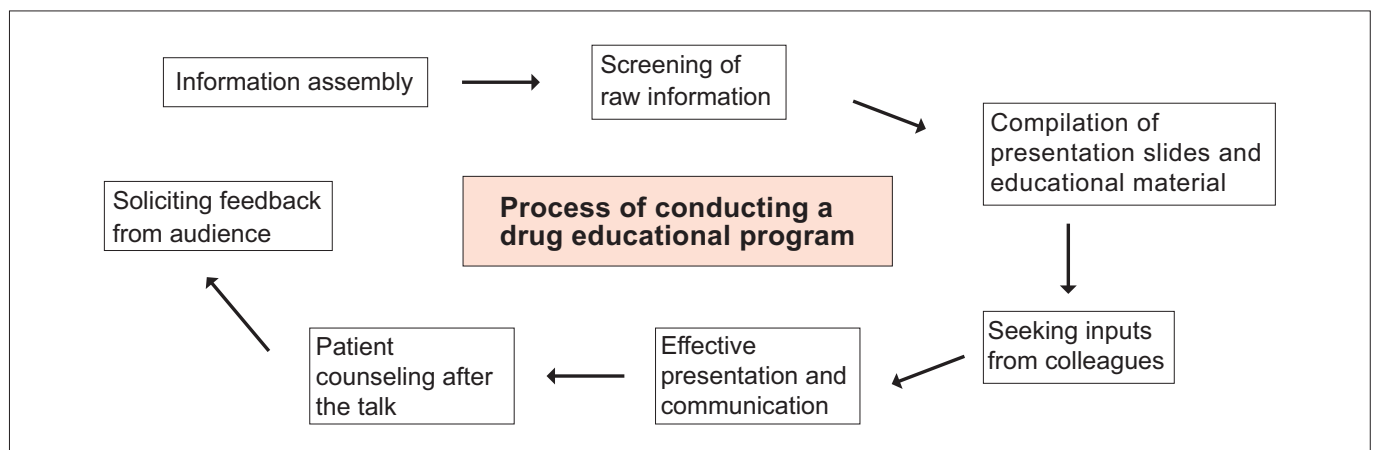
evaluation form to the audience after all the events to capture their feedback. Direct face-to-face contact may not be an effective way to capture sincere feedbacks because people may tend to hide their negative opinions when speaking to you. Writing provides an indirect way to express true comments, which are essential to get yourselves inspired and do better in the next time.

The experience I described above is only an example on conducting a patient education program for your reference. We have to be flexible depending on time, audience and resource allocation when we actually practice. In the following paragraphs, I would like to highlight some key points regarding patient counseling.

SALIENT POINTS ON SUCCESSFUL PATIENT COUNSELING

Patient counseling is central to pharmacy practice. The primary function of patient counseling is to establish patient-pharmacist relationship and to create a channel to exchange information on treatment plans, disease information, drug information and special concerns in regimens.⁽¹⁾ Patient counseling is an old topic that has been discussed by various pharmacy practice textbooks and articles, so I am not going to repeat the technical aspect of it. Instead, I would like to discuss the emotional aspect of interaction between the healthcare professionals and the patients.

Care for emotion of patients is a critical element in raising the quality of patient counseling. There are two core skills in caring emotion of patients, which are known as active listening and empathy.⁽¹⁾ As a healthcare professional, one always wants to provide information to patients



about the disease, the treatment plan and drugs. There is, however, another equally important component in the interaction with patients, which is active listening. Active listening is different from ordinary listening in terms of the process and level of attention. In an active listening process, we may utilize the following skills:

- Summarizing: restate the essential points of the concerns of patients. This is useful in checking the accuracy of our understanding about the problems of patients.
- Paraphrasing: reply patients with the essence of their statements together with some personal feelings. We can check our understanding and also provide some recognition of patients' feelings by applying this skill.
- Empathy: it is the reflection of understanding of patients' feeling in a verbal and explicit way. It is different from paraphrasing because empathy focuses on purely emotional aspect while paraphrasing more or less focuses on content.

Empathy brings out many benefits. First of all, empathetic pharmacists can be more likely to earn the trust and respect of patients because they think that you really care for them but not just solve a medical problem.^(1, 6) Besides, with pharmacist's support and care, patients can be empowered to explore their own feelings, and it is easier for people to figure out their own solution if they feel safe and being supported. In order to express empathy to patients, the following response which we sometimes make unintentionally and should be avoided:

- Judging response: as healthcare professionals, we always tend to judge or evaluate patients' feelings, which only make them more frustrated or isolated. Examples of this type of response include "I am sure the doctor has given the best treatment to you. Do not worry.", "The drug is very safe. You should not worry too much."
- Advising response: giving practical advice is the job of pharmacist. However, sometimes it is not appropriate to give actual advice to patients when they only have

emotional concerns rather than actual needs. Example includes "Try the medicines for several days. If you are still sick, go to another doctor."

- Falsely reassuring response: when patients are facing a real threat such as cancer, it is not appropriate to try to comfort them over-optimistically. For example, "You take the medicines and I am sure you will be fine soon."
- Quizzing response: it is not appropriate to ask patients' question during an empathetic interaction because this will distract the emotional context.
- Distracting response: do NOT shift the topic to other things that are not mostly concerned by the patient. Sometimes what we need to offer is just a listening ear and understanding heart.

Of course, practical scenario is different from theories. Pharmacists are always restricted by time and resources in their service provided. In applying the concepts above, we have to judge carefully the appropriateness of each situation and the characteristics of patients. Ordinary patient counseling process is still vital to conveying factual drug information. Empathetic approach can work only when it is combined with ordinary patient counseling. It shall be used depending on the situation we have to cope with to comfort the emotional side of patients.

SUMMARY

After conducting the two drug educational programs, I have gained practical knowledge on patient-centered care in interactions between pharmacists and patients. Besides the technical skills regarding presentation during a drug educational talk, what I have learnt from the programs is that every patient should be treated as an individual, rather than a collection of medical problems. The psychological side of patients can be well-comforted by pharmacists by their expertise in drug regimens and the use of empathy is of vital importance.

As mentioned by the government in the health care reform, the focus on health care system should be shifted from secondary care to primary care.

The role of pharmacist in primary care is expected to grow continuously. To cope with this change, all pharmacists should be well-equipped with the essential knowledge and internal quality required for patient-centered care. With increasing opportunity in providing primary health care, I hope local pharmacists can contribute more to raising quality of life of people in Hong Kong in the near future.

Author's background

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References

1. Robert S. Beardsley, "Communication Skills in Pharmacy Practice", LWW, 5th edition
2. Weingart et al., "Patient-Reported Medication Symptoms in Primary Care", *Arch Intern Med.*, 2005; **165**: 234-240
3. N Mead, P. Bower, "Patient-centredness: a conceptual framework and review of the empirical literature", *Social Science & Medicine*, 2000; **51**: 1087-1110
4. How to present with PowerPoint <http://www.skillsworkshop.net/a2.html> (Accessed on 16-Dec-2008)
5. Preparing presentation slides http://bcs.bedfordstmartins.com/techcomm/content/cat_030/preparingpresentationslides/index.html (Accessed on 15-Dec-2008)
6. Jamie C. Barner, "Implementing Service-Learning in the Pharmacy Curriculum", *College of Pharmacy*, The University of Texas at Austin, Austin TX 78712-1074
7. Terry A. Jacobson, MD et al., "Use of a Low-Literacy Patient Education Tool to Enhance Pneumococcal Vaccination Rates", *JAMA*. 1999; **282**: 646-650.
8. Alicia Spence, "Pharmacy ambassador empowers patients", *Pharmacy Practice*, Nov 2008; **24**(9): 35
9. Bruce Berger, Ph.D., "Effective Patient Counseling", *U.S. Pharmacist* http://www.uspharmacist.com/oldformat.asp?url=newlook/files/Phar/ACD59D.cfm&pub_id=8&article_id=157
10. Tips for Handling Q&A Sessions http://speaking_center.agnesscott.edu/documents/questionandanswertips.pdf

Osteoporosis and Its Pharmacological Managements

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INTRODUCTION

Osteoporosis is a progressive skeletal disorder leading to loss of bony tissue, resulting in brittle bones which are liable to fracture. The phenomenon of low bone mass and deterioration of bone tissue increase the incidence of fractures of areas such as wrist and vertebra. The clinical outcome could be life-threatening in particular elderly suffering from hip fracture. Since these fractures might cause a certain degree of disability in elderly, it poses a significant burden on health services nationwide.⁽¹⁾ World-wide incidence and prevalence of osteoporosis is difficult to determine because of the variation in definition and diagnosis. The WHO definition of osteoporosis is a bone mineral content (BMC) or bone mineral density (BMD), measured by technique such as dual-energy X-ray absorptiometry, that is more than 2.5 SD below the young adult mean for the population.⁽²⁾ While osteoporosis is a prevalent disease in which most of the time is clinically silent, long term patient compliance and persistence with medication is difficult.⁽³⁾ A thoughtful risk-factor assessment together with preventive measures and appropriate treatment if necessary is essential. This article outlines the bone physiology and the current treatments of osteoporosis. A pharmacological overview of various therapeutic agents will also be discussed.

BONE PHYSIOLOGY

Human skeleton provides a framework for the muscle system as well as being a barrier for the protection of the internal organs from physical stress and trauma. It also serves as the body's major haematopoietic organ. Although bone looks static in appearance, it is physiologically active. A bone re-modeling process continuously takes place, which includes resorption and formation phases, by which both the cortical and cancellous bones are maintained. This remodeling process involves bone cells such as osteoblasts and osteoclasts.

Osteoclasts, the large multinucleate cells responsible for resorbing the calcified bone; whereas osteoblasts are those responsible for bone formation. These two kinds of bone cells interact with each other, and the interaction is dependent on different hormones, such as cytokines and growth factor.⁽⁴⁾ The rates at which osteoclasts resorb bone and osteoblasts replace the lost bone with the new one are tightly coupled,⁽⁵⁾ creating a phase where resorption and formation are balanced. If the 'coupling' is disturbed, bone disease such as osteoporosis would occur.

Osteoblasts are found abundantly across the bone-forming surface. It is apparent that the rate of bone resorption is mediated by controlling the number of osteoclasts at the site of bone resorption;⁽⁶⁾ therefore altering the mechanism of osteoclasts differentiation, as well as inducing osteoclasts apoptosis would be the target method in regulating bone loss. It is acknowledged that the endocrine and paracrine systems are involved in the mechanism of osteoclasts formation.⁽⁷⁾ In particular, estrogen plays an important role in regulating the osteoclasts activities by decreasing the cell formation⁽⁸⁾ and increasing the apoptosis.⁽⁹⁾

Recent findings have identified the RANK (receptor activation of NF- κ B), a member of the tumor necrosis factor (TNF) receptor family on osteoclast precursors;⁽¹⁰⁾ and the RANK ligand (RANKL), a TNF-like protein, highly expressed in osteoblast precursor.⁽¹¹⁾ Studies show that the activities of RANKL to its receptor (RANK) are key factors in osteoclastogenesis.⁽¹²⁾ Activation of RANK by RANKL is antagonized by another member of the TNF receptor, called osteoprotegerin (OPG), a soluble decoy receptor expressed in mature osteoblasts. The OPG/RANKL/RANK system explains the signaling cascade in regulating bone remodeling. The RANKL/OPG ratio in bone marrow thus is a pivotal determinant of bone mass in normal and disease state.⁽¹³⁾

One of the major calcitropic hormones affecting serum calcium levels and bone resorption is the parathyroid hormone (PTH). PTH enhances renal and intestinal calcium reabsorption, leading to bone remodeling.⁽¹⁴⁾ Studies have concluded that PTH interferes with bone activities by affecting OPG and RANKL gene expression.⁽¹⁵⁾

PHARMACOLOGICAL INTERVENTION

Pharmacological therapies that effectively improve bone mass are widely used nowadays. Bisphosphonates and the selective estrogen receptor modulator (SERM) are currently the major treatments being used, aiming at lowering the bone loss by reducing bone resorption. Calcium is the fundamental building block of bone. Vitamin D, in conjunction with PTH & calcitonin, regulates calcium homeostasis, therefore synthetic calcitonin and synthetic PTH also play a role in the treatment of osteoporosis. Other drug of choice includes strontium.

Bisphosphonates

Bisphosphonates are widely prescribed antiresorptive agents in women with postmenopausal osteoporosis. They bind to the hydroxyapatite crystals in the bone and are taken up by the osteoclasts during bone resorption process, where they inhibit the activation of osteoclasts.⁽¹⁶⁾ In the osteoclasts, the nitrogen-containing bisphosphonates inhibit the key enzyme, farnesyl pyrophosphate synthase, resulting in the disruption of the mevalonate metabolic pathway. Due to the lack of the protein prenylation, osteoclasts become unable to resorb bone and hence die.⁽¹⁷⁾

Most of the nitrogen-containing bisphosphonates are administered daily or weekly, such as alendronate and risedronate. Ibandronic acid is the only bisphosphonate available as a monthly dosage form. Patient is recommended to take the bisphosphonates in the

morning 30 mins (in case of monthly ibandronic acid 60mins) before the first food or liquid, including mineral water. The tablet should be swallowed whole with a glass of tap water (200 ml) in an upright sitting and standing position. Patients should not lie down for 30 min (in case of monthly ibandronic acid 60mins) after taking the tablet. Bisphosphonates might cause skeletal pain and FDA recommends patients taking bisphosphonates should contact their physicians if they develop severe bone, joint, and/or muscle pain.⁽¹⁸⁾

Zoledronic acid, a third generation bisphosphonate and the monohydrate of 1-hydrox-2-((H-imidazole-1-yl)-ethylidene)-bisphosphonic acid, is available as a yearly dosage form. The regime contains a single 15 min IV infusion of 5mg zoledronic acid once a year, for the treatment of postmenopausal osteoporosis.

Selective estrogen receptor modulator

Studies have shown that estrogen prevents bone loss through effects on bone cells, by increasing osteoclasts destruction.⁽¹⁹⁾ Estrogen targets RANKL-induced osteoclast differentiation by repressing c-Jun activation.⁽²⁰⁾ Selective estrogen receptor modulator (SERM), such as raloxifene, exerts both estrogen-like effects on bone and lipid metabolism, and antagonizing estrogen effects on breast and breast tissue.⁽²¹⁾ Raloxifene has been indicated for the treatment and prevention of osteoporosis in post-menopausal women. However, it is contraindicated in patient who has a history of venous thromboembolism.⁽²²⁾

Calcitonin

Calcitonin is a polypeptide hormone secreted by parafollicular cells of the thyroid. It is associated with decreased resorptive activity and number of osteoclasts. It is indicated for early, and advanced postmenopausal osteoporosis where conventional combination therapy of estrogen/calcium is contraindicated.⁽²³⁾ It may also be considered in high risk population where bisphosphonate is unsuitable.⁽²⁴⁾ The available dosage form of calcitonin is synthetic salmon calcitonin. It is administered by either nasal absorption, SC or IM injection.

Parathyroid Hormone

Parathyroid hormone (PTH) is an amino-acid peptide responsible for

calcium homeostasis. It is the primary regulator of calcium and phosphate. PTH acts either directly on osteoblasts and osteoclasts, or indirectly via the synthesis of 1,25-dihydroxyvitamin D₃.⁽²⁵⁾ A synthetic parathyroid hormone (PTH; 1-34; teriparatide) has been adopted in the management of postmenopausal osteoporosis. The regime is 20mcg once daily administered by SC injection in thigh or abdomen. The maximum duration of treatment of teriparatide should not exceed 18 months.⁽²⁶⁾ Patient should receive supplemental calcium and vitamin D if dietary intake is insufficient. National Institute for Health and Clinical Excellence (NICE) guidance recommends the use of teriparatide for women over 65 years who are at high risk of fracture but cannot tolerate bisphosphonate.⁽²⁷⁾

Strontium Ranelate

Strontium ranelate consists two atoms of strontium bound to ranelic acid. In vitro studies, strontium enhances bone formation⁽²⁸⁾ and inhibits bone resorption.⁽²⁹⁾ It is available in powder form, and the patient is advised to mix the content of one sachet with plain water and take daily on an empty stomach between meals, preferable at bedtime at least 2 hr after food, milk products or calcium supplement.⁽³⁰⁾

CONCLUSION

Osteoporosis is currently one of the major concerns in health problem in post-menopausal women and elderly. Patients suffer from osteoporosis are prone to fractures, which lead to chronic pain, physical disability and mental depression. Despite the conventional preventive measure such as dietary supplement of calcium and vitamin D or the behavior adaptation to maintain bone health, pharmacotherapy plays an essential role in treating the osteoporosis population. Bisphosphonates, SERMS, calcitonin, PTH and strontium remain the major drug of choice in these aspects. Patient should be carefully classified to ensure rational treatment is prescribed. They should also be properly counseled on the proper administration method of individual drug product and the possible side effects they might encounter.

Author's background

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References

1. **Johell O.** The socioeconomic burden of fractures: today and in the 21st century. *American Journal of Medicine*, 1997, **103**(Suppl.2A):S20-S25
2. World Health Organisation. Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis. *WHO Technical Report Series 843*. Geneva: World Health Organisation, 1994.
3. **Osterberg L, Blaschke T.** Adherence to medications. *N Engl J Med* 2005; **353**:487-497.
4. **Takahashi E et al.** High Extracellular Calcium Affects Osteoclastogenesis in Mouse Bone Marrow Cell Culture. *J Med Dent Sci* 2002; **49**: 109-120
5. **Suda T et al.** Cell of Bone: Osteoblast generation. In: Bilzikian JP, Raisz LG, rodan GA, editors; Principles of Bone Biology. San Diego: Academic Press, 1996: 87-102
6. **Oursler MJ** Direct and indirect effects of estrogen on osteoclasts *J Musculoskel Neuron Interact* 2003; **3**(4):363-366
7. **Khosla S. Minireview** The OPG/RANKL/RANK system. *Endocrinology* 2001; **142**:5050-5055
8. **Pacifici R.** Estrogen, cytokines and pathogenesis of postmenopausal osteoporosis. *J Bone Miner Res*. 1996; **11**:1043-1051.
9. **Hughes DE, et al.** Estrogen promotes apoptosis of murine osteoclasts mediated by TGF-beta. *NatMed*. 1996; **2**:1132-1136.
10. **Hsu. H et al.** Tumor necrosis factor receptor RANK mediates osteoclast differentiation and activation induced by osteoprotegerin ligand. *Proc Nat Acad Sci* 1999; **96**: 3540-3545
11. **Pivonka P et al** Model structure and control of bone remodeling: a theoretical study *Bone* 2008 Aug; **43**(2): 249-63
12. **Yasuda H et al** osteoclast differentiation factor is a ligand for oesoprotegerin/osteoclastogenesis inhibitory factor and is identified to TRANCE/RANKL. *Proc Natl Acad Sci USA* 1998; **95**:3597-3602
13. **Boyce BF et al** The RANKL/RANK/OPG pathway *Curr Osteoporos Rep*.2007 Sep; **5**(3):98-104
14. **Mulder JE et al** Drug Insight: Existing and Emerging Therapies for Osteoporosis *Nat Clin Pract Endocrinol Metab*. 2006;**2**(12):670-680
15. **Huang JC et al** PTH Differentially regulates Expression of RANKL and OPG *J of Bone and Mineral Research* 2004; **19**(2)
16. **Fleisch H** Bisphosphonates in bone disease. From the laboratory to the patient, London: Academic Press; 2000
17. **Reid IR** Bisphosphonate: New Indications and Methods of Administration *Curr Opin Rheumatol* 2003 **15**(4):458-463
18. FDA Alert Jan 7 2008: **Information for Healthcare Professionals** Bisphosphonates (marketed as Actonel, Actonel+Ca, Aredia, Boniva, Didronel, Fosamax, Fosamax+D, Reclast, Skelid, and Zometa)
19. **Manolagas SC et al** Bone marrow, cytokines, and bone remodeling *N Engl J med* 1995;**332**:305-311
20. **Shevde NK et al** Estrogens suppress RANK ligand-induced osteoclast differentiation via a stromal cell independent mechanism involving c-Jun repression. *Proc Natl Acad Sci USA* 2000; **97**:7829-7834
21. **Sheryl L et al** Current approaches to the prevention and treatment of postmenopausal osteoporosis *AmJ Health-syst Pharm* 2003; **60**(9):883-901,
22. British National Formulary 56 edition p.397
23. Product Information of Miacalcic, Novartis, MIMS Annual 2007/2008 p.830-831
24. British National Formulary Edition 56 p.409
25. **Akesson K** *Bulletin of the World Health Organization* 2003;**81**(9)
26. Product Information of Forteo, Eli Lilly, MIMS Annual 2007/2008 p.504-505
27. National Institute of Clinical Excellence (NICE) Technical Appraisal Guidance 87 Jan 2005
28. **Canalis E et al** The divalent Strontium salt S12911 enhances bone cell replication and bone formation in vitro 1996. *Bone* **18**:517-523
29. **Baron R et al** In vitro effects of S12911-2 on osteoclast function and bone marrow macrophage differentiation 2002 *Eur J Pharmacol* **450**: 11-17
30. Product Information of Protos, Servier, MIMS Annual 2007/2008 p.1074-1075.

Peritoneal Dialysis: Principles and Related Practical Issues

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BACKGROUND

Renal disease is one of the leading causes of deaths in Hong Kong. Although it only ranked seventh in the list of diseases following the major three – malignant neoplasms, heart diseases, and pneumonia, it claimed 1,000 out of 30,000 lives in the year 2003.⁽¹⁾ End stage renal disease (ESRD), one form of renal disease manifestations, is becoming more and more prevalent in the world. From the data of United States Renal Data System (USRDS), the number of cases was nearly doubled over six years from 1991 to 1997.⁽²⁾ Dialysis and transplantation are the two treatments available for the management of patients with ESRD with peritoneal dialysis (PD) being one of the commonly adopted treatment modality. This article reviews the various issues concerning PD and aims to provide an update on the relevant information.

END STAGE RENAL DISEASE (ESRD)

ESRD is a part of chronic kidney disease which describes the continuum of kidney dysfunction from early to late-stage disease. A patient has ESRD is defined as the glomerular filtration rate of the kidneys of patient is less than 15 mL/min.^(3,4) In order to sustain life, patients need renal replacement therapy in the form of dialysis or transplantation. ESRD is associated with fluid and electrolyte abnormalities, anemia, cardiovascular disease, hyperparathyroidism, bone disease and malnutrition. These complications have to be managed. Therefore, Both drugs and dialysis are essential.

PRINCIPLE OF PERITONEAL DIALYSIS

PD is performed by introducing 1 to 3 liters of a dialysis fluid into the peritoneal cavity. The basic principle of PD is that the solute composition of the dialysis fluids infused into the peritoneal cavity tends to equilibrate with the plasma water solute composition during the

dialysis. The walls of the peritoneal cavity are lined with a membrane called the peritoneum. During PD, the dialysis solution which contains a mixture of dextrose, salt and other minerals dissolved in water is placed in a person's abdominal cavity through a catheter. By diffusion and by ultrafiltration, waste products and extra body fluid are passed through the peritoneal membrane from the blood into the dialysis solution.

The crucial components of the PD system are peritoneal blood flow, the highly vascular membrane, and the flow rate and volume of the PD fluids.⁵ Since neither peritoneal blood flow nor the vascularity of the membrane can be manipulated, the only factors that can be adjusted to achieve maximum solute and fluid removal are the flow rate and composition of the dialysis fluids. On the other hand, whether a patient can be placed on PD treatment depends on the membrane vascularity.

TYPES OF PERITONEAL DIALYSIS⁽⁵⁾ (Diagram 1)

PD is divided into two types; namely, Continuous Ambulatory Peritoneal Dialysis (CAPD) and Automated Peritoneal Dialysis (APD). APD refers to all forms of peritoneal dialysis that use a mechanical device to assist in the delivery and drainage of the dialysate from the peritoneal cavity.⁽⁶⁾ APD can be further divided into Continuous Cycler-assisted Peritoneal Dialysis (CCPD), Nocturnal (Night-time) Intermittent Peritoneal Dialysis (NIPD) and Tidal Peritoneal Dialysis (TPD). The details of different PD methods are explained below:

1. Continuous ambulatory peritoneal dialysis (CAPD)

Dialysate is always present in the abdomen. The dialysate is drained into the abdomen by gravity but not a machine. The dialysate is exchanged by draining and refilling 4 to 5 times per day. The abdomen is filled with dialysate overnight.

2. Continuous cycler-assisted peritoneal dialysis (CCPD)

Dialysis begins at bedtime when the patient gets connected to a cycler machine that will periodically replace the dialysate in the patient's abdomen with fresh dialysis solution while the patient sleeps. Usually the dialysate is changed 3 to 5 times during the night. In the morning the patient is disconnected from the cycler, leaving a fresh exchange of dialysis solution in the abdomen. This daytime exchange is drained at bedtime when the cycler machine is reconnected.

3. Nocturnal intermittent peritoneal dialysis (NIPD)

The patient is connected to the cycler only at bedtime as in the case for CCPD. The number of exchanges during the night is increased to 5 to 8 times or more. In the morning, before the patient is disconnected from the cycler, the abdomen is drained and is left dry during the day. NIPD is usually reserved for patients whose peritoneum is able to transport waste products very rapidly or for patients who still have substantial residual kidney function.

4. Tidal Peritoneal Dialysis (TPD)⁽⁷⁾

Tidal peritoneal dialysis is another variant of automated peritoneal dialysis which leaves a large portion of the dialysis fluid in contact with the peritoneum and exchanges a small portion of PD fluid; this eliminates the time between exchanges in which there is a minimal amount of fluid in the cavity. In some patients, pain or discomfort occurs with complete drain of the PD fluid or upon initiation of dialysis filling when the peritoneal cavity is empty. The use of tidal peritoneal dialysis can act as a modality to alleviate this pain.⁽⁸⁾

COMPOSITION OF PERITONEAL DIALYSIS FLUID

As mentioned previously, the solute composition of the peritoneal fluid is the main tool for removing excess water and waste products, supplying needed substances and restoring the balance of disturbed solutes in uremic patients. The composition of PD fluid usually is standardized within certain limits of electrolyte content as mentioned in Table 1.^(9,10)

Management of electrolyte balance is important for end stage renal disease patients since the kidney cannot carry out its normal function for electrolyte homeostasis. From Table 1, we can see that sodium and potassium have to be removed in order to maintain body homeostasis to try to achieve the normal plasma levels. Magnesium needs to be replenished and studies show that the small amount of magnesium present in the PD fluids (0.5 - 1.5 mEq/L) is clinically enough to elevate the magnesium level in patients.^(12,13) The plasma calcium level in patients is lower than normal. It is due to the decreased calcium uptake from the gastrointestinal tract. Hypocalcaemia is a common feature in the pre-dialysis phase if oral calcium and/or vitamin D are not supplemented. On the other hand, the pH of the PD fluid is much lower than the physiological pH for maintaining the stability of the components, although it is quite contradictory since renal patients are at risk of developing metabolic acidosis due to decreased

Table 1: Electrolyte Composition of Patient Plasma Level vs. PD Fluid

Solute	Normal Plasma Level (mEq/L) ⁽¹¹⁾	Patient Plasma level (mEq/L)	PD Fluid (mEq/L)
Sodium	134 - 149	135 - 142	132 - 134
Potassium	3.5 - 5.2	4 - 6	0 - 2
Calcium	4.4 - 5.2#	2.7 - 3.3	2.5 - 3.5
Magnesium	1.3 - 2.1#	1.1 - 1.4	0.5 - 1.5
Chloride	95 - 108	95 - 100	95 - 106
Lactate	-	-	35 - 40
pH	7.3 - 7.4	~7	5.5

Values are converted from mg/dL to mEq/L by equation listed in Drug Information Handbook

production of bicarbonate in the body. Consequently, lactate is normally added as a bicarbonate-generating compound to avoid the risk of precipitation during the preparation, sterilization and storage of the dialysis solutions if the latter are bicarbonate-containing.⁽¹⁰⁾ A biocompatibility issue also arises due to the low pH of PD fluids. The pH of the solution has to be kept low to prevent caramelization* of glucose during the heat sterilization process.⁽¹⁴⁾

Most PD fluids have similar electrolyte contents. However, several large pharmaceutical companies produce PD fluids sterilized in varying volumes with different concentrations of glucose as the osmotic agent. There are now more alternative substances such as glycerol, amino acids and glucose polymers being used as osmotic agents. The difference in osmotic agents will be

discussed later.

*Caramelization is defined as the thermal degradation of sugars leading to the formation of volatiles (caramel aroma) and brown-colored products (caramel colors). The process is acid or base catalyzed and generally requires temperatures > 120°C at pH<3 or >9.

DIFFERENT TYPES OF PERITONEAL DIALYSIS FLUIDS

The PD fluids used in Hong Kong public hospitals are mainly supplied by three companies - Baxter®, Fresenius® and Gambro®. There are various brands with different composition as listed below:

Different calcium concentrations, glucose concentrations and volume are used according to the needs of patients. If a patient is hypocalcemic, PD fluid

Table 2: Comparison of Different Brands of Peritoneal Dialysis Fluids available in Hong Kong

Companies	Brands	Osmotic agent	Concentration	Calcium Content (mEq/L)*	Osmolarity (mosmol/L)
	Spike	Glucose	1.5%	2.5/3.5	344-346
			2.5%	2.5/3.5	395-396
			4.25%	2.5/3.5	483-485
Baxter®	Ultra-bag	Glucose	1.5%	2.5/3.5	344-346
			2.5%	2.5/3.5	395-396
			4.25%	2.5/3.5	483-485
	Extraneal	Icodextrin	7.5%	3.5	282-286
Nutrineal	Amino acids	1.1%	2.5	367	
Fresenius®	Andy Disc	Glucose	1.5%	2/3.5	356-358
			2.3%	2/3.5	399-401
			4.25%	2/3.5	508-511
	Safe lock	Glucose	1.5%	2/3.5	356-358
			2.3%	2/3.5	399-401
			4.25%	2/3.5	508-511
Gambro®	Gambrosol trio	Glucose	Varies#	Varies^	Varies@

* The "/" separates two calcium contents, one is for low calcium content and the other is for standard calcium content

Change with different mixing methods (1.5, 2.5, 3.9%)

^ Change with different mixing methods (2.62, 2.7, 2.76 mEq/L)

@ Change with different mixing methods (356, 408, 482 mosmol/L)

There are three compartments – A, B & C. The two smaller compartments (A and B, B is of larger volume) each contains 50% glucose solution and sodium chloride and a larger third compartment (C) contains the electrolyte solution. After breaking the frangible pin between compartments A and C and thoroughly mixing the two fluids a PD fluid containing 1.5% glucose (2.76 mEq/L calcium, 356 mosmol/L) is produced. Similarly mixing the contents of compartments B and C produces a PD fluid containing 2.5% glucose (2.7 mEq/L calcium, 408 mosmol/L). Finally by breaking both frangible pins and mixing the contents of all three compartments produces a solution containing 3.9% glucose (2.62 mEq/L calcium, 482 mosmol/L). (Reference: Product information of Gambrosol trio)

forecasted to reach 5 billions in 2015. Although microfluidic systems are convenient platforms for biological assays, their use is still limited mainly due to the high-level fabrication expertise required for construction.⁽³⁾

TOP 9 - OPTICAL LOCK-IN DETECTION (LOID) - FRET⁽⁴⁾ FOR MEASURING DYNAMIC INTERACTIONS BETWEEN MOLECULES

FRET (Fluorescence Resonance Energy Transfer) technique is widely used for measuring dynamic interactions between two proteins in vivo.⁽⁵⁻⁷⁾ In this technique, two different fluorescent molecules (fluorophores) are genetically fused the two proteins of interest. Regular (non-FRET) fluorescence occurs when a fluorescent molecule (fluorophore) absorbs electromagnetic energy of one wavelength (the excitation frequency) and re-emits that energy at a different wavelength (the emission frequency). Conceptually, one can imagine each fluorophore to have a two-peaked spectrum in which the first peak is the excitation peak, and the second is the emission peak. For the combined FRET effect, the emission peak of the donor must overlap with the excitation peak of the acceptor. In FRET, light energy is added at the excitation frequency for the donor fluorophore, which transfers some of this energy to the acceptor, which then

re-emits the light at its own emission wavelength. The net result is that the donor emits less energy than it normally would (since some of the energy it would radiate as light gets transferred to the acceptor instead), while the acceptor emits more light energy at its excitation frequency because it is getting extra energy input from the donor fluorophore (Figure 3, Top diagram).

Sources of background noise, or cross-talk, occur because (1) the donor radiates slightly (but not optimally) at the acceptor's emission wavelength, and (2) the acceptor is excited somewhat by the donor's excitation wavelength. Both of these will cause a non-FRET signal at the emission wavelength of the acceptor that needs to be controlled for. There are two ways of doing this. One is to express each fluorophore individually in the same conditions in vivo in which FRET will be performed, and measuring this cross-talking. Thus, one would want to measure how much energy the donor radiates at the acceptor emission wavelength, as well as measuring how much the acceptor can be excited by the donor's excitation wavelength. A second, and easier, control to perform is to photobleach the acceptor fluorophore (by overwhelming it with light at its excitation frequency) to "knock out" its activity. This eliminates the energy transfer from donor to acceptor and

should cause an increase in the emission from the donor (due to the fact that it is not transferring energy to the acceptor). This increase of donor emission due to photobleaching of the acceptor is known as "dequenching" and allows one to determine how much the donor fluorophore is radiating at the acceptor emission frequency.

The benefit of FRET technology is that it has excellent resolution. The physics of the FRET energy transfer between donor and acceptor (which is non-radioactive) is such that the efficiency falls off with the sixth power of the distance between molecules. Thus, FRET only occurs when the two fluorophores are within 20-100Å (0.002-0.01 μm) of each other, which means that the fluorophores must be brought together via very close protein-protein interactions. Since biomolecules can be 50-200Å in diameter, the position of the fluorophores within the protein complex is critical. OLID-FRET, utilizing NitroBIPS, is a technique similar in concept to both photoactivation of the acceptor and photobleaching of the acceptor, which can detect FRET between labeled proteins by many magnitude and is used as an indicator of complex formation in cells.

TOP 8 - WHITE LASER CONFOCAL INSTRUMENT

A conventional confocal microscope focuses the illumination light to a single diffraction limited spot and moves that spot line by line over the specimen. The technical solution for diffraction limited high intensity illumination requires laser light, which is perfectly collimated. Consequently, current confocal laser scanning microscopes employ a series of lasers that emit only at distinct lines. Best cases are gas lasers, which emit a series (up to five) lines simultaneously. Nevertheless, to cope with the requirement for full spectral performance, a bulky setup of several combined lasers is necessary - still offering only the physically possible emission lines of lasers that restrict flexibility in tuning into the correct excitation wavelength for the many fluorescent probes.

For flexible selection of the excitation wavelength, white light laser was developed recently. It emits white light and allows selecting the excitation band similar to wide-field microscopy. In addition, new fiber technology, crystal photonic fibers also called supercontinuum fibers is applied. These fibers have a core that consists of an assembling of hollow tubes, usually arranged in a hexagonal pattern (crystal). If intense light pulses of a

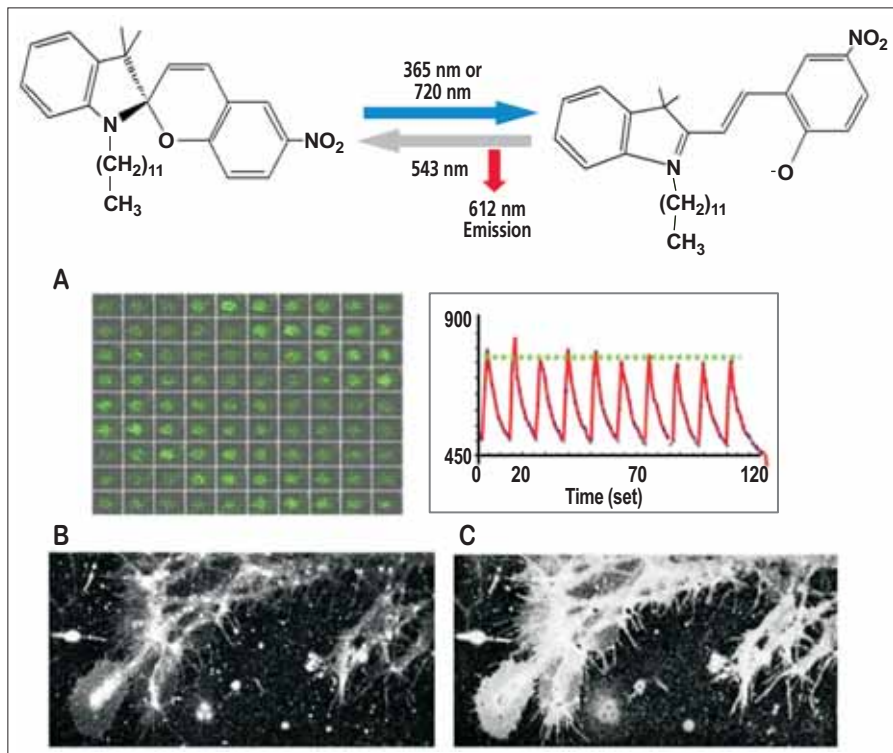


Figure 3. Top. Optically-driven, reversible transitions in nitro BIPS-like optical switches. (A). Left: Montage of MC-fluorescence in cells of a xenopus spinal cord explants and (Right), profile of the modulated MC-fluorescence intensity within a ROI for the cell shown in the montage. (B), MC-intensity image of C12-nitroNIPS (Top). A membrane specific optical switch in a xenopus spinal cord explants and (C), corresponding image of the ":AC" component or correlation coefficient of the optical switch probe.

containing higher calcium content will be used for replenishment of calcium ions. As glucose is an osmotic agent, a higher concentration of glucose can be used to remove more water from a patient. If a patient has a heavy water load, PD fluid of a higher glucose concentration should be used. The volumes of PD fluids to be used depend on the modes of PD. For example, 2 L is used for CAPD while larger volumes may be used for APD. It also depends on the time of administration. If the PD fluid will remain in the peritoneal cavity for a longer time, e.g. overnight, a larger volume should be used.

PD entails a closed system (Figure 1), in which fluid is initially instilled by gravity into the peritoneal cavity and then drained out after several hours. The basic PD system consists of a collapsible plastic bag containing 1 L to 6 L PD fluid, a transfer set, a Tenckhoff catheter or other catheter. Different brands contain different devices to serve various purposes. One of the major purposes is to reduce the risk of PD-associated peritonitis. The Spike of Baxter® is the most common form of device. It consists of a rigid pointed hollow plastic tube. The point of entry of the spike to the bag of dialysis fluid is protected by a barrier consisting of two small sponges soaked in povidone iodine. On the other hand, the Safe Lock system (Picture 1) of Fresenius® is a luer lock system with sprayed antiseptic preparation consisting of an alcoholic solution containing phenol. For Gambro, the luer lock system is a protective povidone iodine laden clam shell.⁽¹⁰⁾

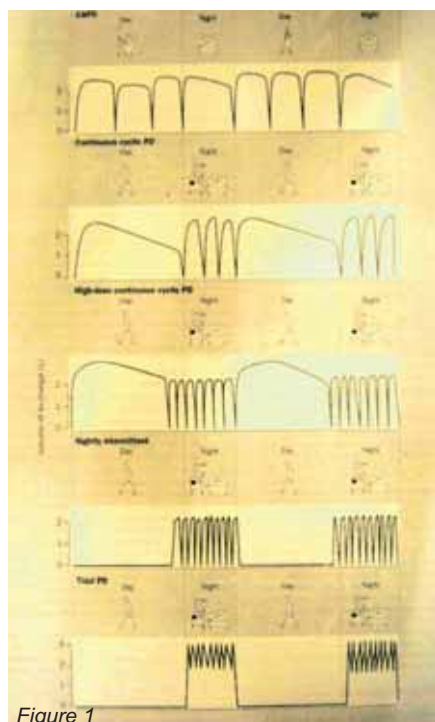
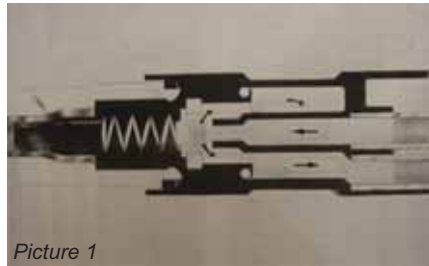


Figure 1



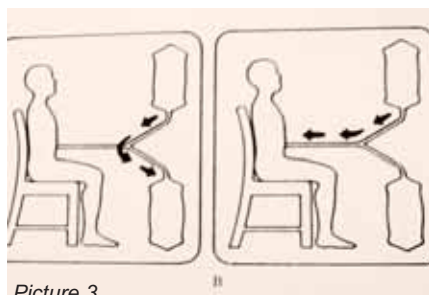
Picture 1

The more recent concept is the 'Y' system (Picture 2). This Y or disconnect systems free the patient from carrying the empty fluid bag during the long dwell period. This system was first described in Italy. The dialysis fluid transfer set may be formed into a 'Y' shape, to which a full bag and an empty bag are attached at either end of the upper limbs of the 'Y' while the lower limb of the 'Y' is connected to the patient via a connector. This concept (flush & fill, see Picture 3) is that the delivery of fluid into the patient is preceded by running out spent dialysate into a waiting empty bag, carrying with it any contaminating bacteria introduced by 'touch' contamination of the connection. The Baxter® Ultra bag and Fresenius® Andy Disc are variations of the 'Y' system. This system has resulted in reduction in the frequency of peritonitis compared to standard CAPD.⁽¹⁰⁾

Gambrosol trio is filled in a three-compartment bag. The two smaller compartments each contains



Picture 2



Picture 3

50% glucose solution and sodium chloride and a larger third compartment contains the electrolyte solution. By breaking the frangible pin between different compartments, glucose of different concentrations can be produced. The manufacture and storage of conventional PD fluids leads to the formation of cytotoxic glucose degradation products (GDPs) or advanced glycation end products (AGEs).^(15,16) The GDPs may damage the peritoneum and decrease its capacity to perform ultrafiltration. The Gambrosol trio 3-compartment bag separates the components and reduces the formation of GDPs and AGEs, thus improving the biocompatibility of the solution so that patients can remain on PD for longer. It is also convenient for prescribers since the concentration of the osmotic agent can be adjusted by the 3-compartment system.

From Table 2, we can see that there are three different osmotic agents - glucose, icodextrin and amino acids. Glucose is the most common of the three. Related problems include hyperglycemia, hyperinsulinemia⁽¹⁷⁾ and formation of GDPs. A hyperlipidemic effect was also demonstrated in several studies. These effects were attributed to the continuous peritoneal absorption of glucose. Given these backgrounds, icodextrin and amino acids have been suggested as alternatives to glucose as osmotic agents. Extraneal of Baxter® contains icodextrin 7.5%. Icodextrin is a glucose polymer which is a mixture of polysaccharides consisting of linked glucose residues of varying chain length obtained by the hydrolysis of corn starch. Some experts queried the use of icodextrin as some trials found accumulation of poorly metabolisable polymers in the body⁽¹⁸⁾ although some trials showed that a 8% glucose polymer solution was comparable to the 4.25% glucose solution in terms of ultrafiltration.⁽¹⁹⁾ One important concern with the use of icodextrin is the possibility of an allergic reaction. Up to 15% of patients on icodextrin may experience skin reactions, which may be serious in about one-third of cases.⁽²⁰⁾

The Nutrineal of Baxter® contains amino acids as the osmotic agent. It has several advantages over the conventional PD fluids that use glucose as the osmotic agent. The absence of glucose improves blood glucose control in diabetic patients and the pH is more physiological. Moreover, on nutritional side, the use of amino acid dialysate has

been shown to improve the nutritional status of malnourished CAPD patients.⁽²¹⁾ In terms of ultrafiltration, Amino acid 1.1% has similar osmolarity as 1.5% of glucose. In a trial, a 2% amino acid-based solution induced equivalent amounts of ultrafiltration and removal of urea, creatinine and potassium compared to a 4.25% glucose solution over a 6-hour dwell time.⁽²²⁾

ADVANTAGES AND DISADVANTAGES OF PERITONEAL DIALYSIS

The main advantage of PD is that it is relatively simple to teach, so patients can quickly be established on home dialytic therapy. Unlike hemodialysis, PD usually does not require specific and complex equipment, and the therapy results in continuous steady-state biochemical and fluid status, therefore it can avoid the fluctuation of intermittent haemodialysis.⁽²³⁾ The cost of PD is lower, for example, the cost of CAPD is at least 25% lower than that for in-hospital haemodialysis.⁽²⁴⁾ Moreover, patients have a better experience with PD. In a trial with 736 patients, patients receiving PD rated their care higher than those receiving haemodialysis.⁽²⁵⁾

The main disadvantage is related to infections, mechanical and metabolic complications inherent in the technique, and a higher rate of technique failure and the need to transfer to haemodialysis.⁽²⁶⁾

FUTURE OF PERITONEAL DIALYSIS

There has been a huge expansion in both the clinical and research areas of PD over the past 20 years. The technique is now used worldwide, mainly in the form of CAPD, but the use of APD is increasing. Dialysis, drug treatment and dietary considerations are the three main components of the management of patients with end stage renal disease. The implementation of clinical practice guidelines (CPGs) to guide rational treatment of patients is a relatively new concept.⁽²⁷⁾ In 1997, the National Kidney Foundation instituted the Dialysis Outcomes Quality Initiative (DOQI) and commenced the development of CPGs to guide the practice of dialysis therapy. Prevention of PD-associated peritonitis is also a major issue. It is hoped that the advance in technology will continue to improve the treatment outcomes and patients' quality of life and reduce the cost of treatment.

References

1. Number of Deaths by Leading Causes of Death by Sex by Age, 2003. Department of Health Homepage <http://www.info.gov.hk/dh/diseases/index.htm>.
2. Kidney Disease Facts and Statistics – Prevalent Statistics. American Society of Nephrology.
3. National Kidney foundation. NKF-K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. *Am J Kidney Dis* 2002;**39**:S1.
4. Joanna Q. Hudson, Curtis A. Johnson. Chronic Kidney Disease. *Applied Therapeutics: the Clinical Use of Drugs* (8th Edition) 2004;**32**:6.
5. Michael I. Sorkin and Jose A. Diaz-Buxo. Physiology of Peritoneal Dialysis. *Handbook of Dialysis* 1994;**13**.
6. Diaz-Buxo JA, Suki WN. Automated peritoneal dialysis. *Textbook of peritoneal dialysis* 1994:399-418.
7. Michael F. Flessner. Transport Kinetics During Peritoneal Dialysis. *The Artificial Kidney: Physiological Modeling and Tissue Engineering* 1999;**3**:31.
8. Juergensen PH; Murphy AL; Pherson KA; Chorney WS; Kliger AS; Finkelstein FO. Tidal peritoneal dialysis to achieve comfort in chronic peritoneal dialysis patients. *Adv Perit Dial* 1999;**15**:125-6.
9. Thomas J. Comstock. Renal Dialysis. *Applied Therapeutics: the Clinical Use of Drugs* (8th Edition) 2004;**33**:1-13.
10. Mariano Feriani et al. CAPD Systems and Solutions. *The Textbook of Peritoneal Dialysis* 1994, 233-270.
11. Charles F. Lacy, Lora L. Armstrong, etc. Laboratory Values - Reference Values for Adults. *Drug Information Handbook (11th Edition)*; p.1666.
12. Kohant EC, balfe JW, porter D, Alexandre S. Hypermagnesemia and mild hypocarbia in pediatric patients on CAPD. *Perit Dial Bull* 1983; **3**:41-2.
13. Rahman R, Heaton A, Goodship T. et al. Renal osteodystrophy in patients on CAPD: a five year study. *Pert Dial Bull* 1987; **7**:1-4.
14. Michael I. Sorkin. Apparatus for Peritoneal Dialysis. *Handbook of Dialysis* 1994;**14**:263.
15. Cappelli G et al. Low concentration of glucose degradation products in peritoneal dialysis fluids and their impact on biocompatibility parameters: prospective cross-over study with a new three-compartment bag. *Adv Periton Dialysis* 1999;**15**:238-42.
16. José Carolino Divino Filho, MD, PhD, Assoc. Medical Director, Clinical Affairs, Baxter Renal Division Europe. Peritoneal Dialysis solutions. *2nd International Conference of Nephrology in Internet*.
17. Armstrong VW, Creutzfeldt W, Ebert R, Fuchs C, Hilgers R, Scheler F. Effect of dialysis glucose load on plasma and glucoregulatory hormones in CAPD patients. *Nephron* 1985;**39**:141-5.
18. L Martis, T Shockle, L Henderson. CAPD with dialysis solution containing glucose polymer. *The Lancet*; Jul 17, 1993;**342**: 8864; Health Module p. 176.
19. Winchester JF, Stegink LD, Ahman S et al. A comparison of glucose polymer and dextrose as osmotic agents in CAPD. *Frontiers in Peritoneal Analysis* 1986; **23**:40.
20. David Goldsmith, Satish Jayawardene, Nikant Sabharwal, Katrina Cooney. Allergic reactions to the polymeric glucose-based peritoneal dialysis fluid icodextrin in patients with renal failure. *The Lancet*; Mar 11 2000; **355**:9207; Health Module p. 897.
21. Misra M, Ashworth J, Reaveley DA, Muller B, Brown EA. Nutritional effects of amino acid dialysate (Nutraeal) in CAPD patients. *Adv Perit Dial* 1996;**12**:311-4.
22. William PF, Marliss EB, Harvey Anderson G et al. Effective use of amino acid dialysate over four weeks in CAPD patients. *Perit Dial Bull* 1983; **3**:66-73.
23. Mallick NP, Gokal R. Haemodialysis. *The Lancet* 1999; **353**: 737-42.
24. Mallick NP, Gokal R. Peritoneal dialysis. *The Lancet* 1999; **353**: 823-28.
25. Haya R Rubin, Nancy E Fink, Laura Cplantinga, John H sadler, et al. *Jama* Chicago:Feb 11 2004. **291**: Iss. 6 p. 697-703.
26. Maioraca R, Vonesh EF, Cavalli P, et al. A multicentre selection adjusted comparison of patient and technique survival on CAPD and haemodialysis. *Perit Dial Int* 1991; **11**:118-27.
27. George R. Bailie, Pharm.D., Ph.D., FCCP. Dialysis Outcomes Quality Initiative to Kidney Disease Outcomes Quality Initiative: New Clinical Practice guidelines in Nephrology - What the Practicing Pharmacist Needs to Know. *Pharmacotherapy* 2004;**24**(5):551-557.T

Questions for Pharmacy Central Continuing Education Committee Program

(Please be informed that this article and answer sheet will be available on PCCC website concurrently. Members may go to PCCC website (www.pccchk.com) to fill in their answers there.)

1. Which of the following statements concerning end stage renal failure (ESRD) is false?

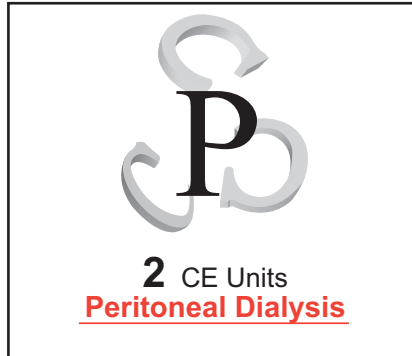
- The global prevalence of ESRD is on rising trend.
- Dialysis and transplantation are the two treatments available for the management of patients with ESRD.
- ESRD may be associated with hypertension or heart failure.
- It is a term used to cover the continuum of kidney dysfunction from early to late-stage disease.
- Both drugs and dialysis are essential to manage fluid and electrolyte abnormalities in ESRD patients.

2. Which component listed below is not a factor affecting the ultrafiltration of a peritoneal dialysis system?

- Peritoneal blood flow
- Flow rate of peritoneal dialysis fluid
- The system connecting the dialysis bag and the peritoneum
- Volume of peritoneal dialysis fluid
- Vascularity of peritoneal membrane

3. What is the major difference between Continuous Ambulatory Peritoneal Dialysis (CAPD) and Automated Peritoneal Dialysis (APD)?

- APD can be further divided into 3 types of dialysis.
- They use different peritoneal dialysis fluids.
- The abdomen is filled with dialysate overnight for CAPD which is not the case for APD
- They are used according to different degree of severity.
- APD employs a mechanical device to assist in the delivery and drainage of the dialysate while the dialysate is drained into the abdomen by gravity in CAPD.



4. Which electrolyte listed below has to be replenished in an ESRD patient?

- Sodium
- Magnesium
- Potassium
- Chloride
- Lactate

5. Why is the pH of the PD fluid much lower than the physiological pH?

- For management of electrolyte balance
- Due to the presence of lactate as a buffer
- For maintaining the stability of the components
- For correcting metabolic acidosis of the patient
- For increasing production of bicarbonate ions in patient's body

6. Which of the followings are the osmotic agents being used in the commercially available peritoneal dialysis fluids?

- Glucose
 - Amino Acids
 - Propylene glycol
 - Icodextrin
 - Povidone iodine
- i & ii
 - ii & iii
 - i, ii & iii
 - i, ii & iv
 - All of the above

7. Which of the following(s) is/are method(s) used by different brands of peritoneal dialysis fluids to reduce the risk of peritoneal dialysis-associated peritonitis?

- A 3-compartment system
- A protective povidone iodine laden clam shell
- A 'Y' system
- b & c
- None of the above

8. Which statement below is incorrect concerning the 3-compartment system in Gambrosol trio?

- To prevent caramelization of glucose during the heat sterilization process
- To reduce the production of cytotoxic glucose degradation products
- To improve the bioavailability of peritoneal solution
- To produce different concentrations of osmotic agent
- To produce different volumes of peritoneal solution

9. What of the followings is true about the Nutrineal of Baxter®?

- It contains icodextrin 7.5%.
- A 1.1% amino acid solution has a similar ultrafiltration capacity as a 4.25% glucose solution.
- It can be used to improve the nutritional status of malnourished CAPD patients.
- Glucose and amino acids are combined to produce the desired osmotic effects.
- The occurrence of allergic reaction is a major limitation associated with the use of Nutrineal.

10. Which is not an advantage of peritoneal dialysis?

- Peritoneal dialysis does not require specific and complex equipment.
- Patient can be established on home dialytic therapy.
- The cost of peritoneal dialysis is lower.
- Peritoneal dialysis can avoid the fluctuation of intermittent haemodialysis.
- None of the above

Answers will be released in the next issue of HKPJ.

Answers for the past issue (July-Sep 2008)

Suggested answers:

1. a 2. a 3. b 4. e 5. b 6. c 7. b 8. c 9. d 10. e

Top Ten Innovations of the Year 2008 for Life Science, Biomedical and Pharmacological Research

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ABSTRACT

The life sciences, biomedical and pharmacological research are moving fast. Across the world, new techniques and products are introduced from time to time to make the search for new knowledge and their applications feasible. At the end of year 2008, ten most outstanding new technologies or products have been picked by a panel of experts and lauded for their best innovative to biological and pharmaceutical research. These ten innovative items according to magnitude of their impact from the less to the biggest are: microfluidics; optical lock-in detection (OLID)-FRET, white laser confocal instrument, in-vivo multispectral imaging, PET/MRI combined imaging, in vivo cell cycle imaging, open source sequencing, zinc finger nuclease for gene editing platform, continuous focus microscopy and low cost sequencing. This article briefly reviews their principle and applications.

INTRODUCTION

According to one latest study disclosed by The Scientist⁽¹⁾, a panel of expert, comprising of David Piston, Simon Watkins, Klaus Hahn and Steven Wiley, was asked to identify and pick some technologies or products that most likely to have the biggest impact in year 2008. The criteria to become the chosen technologies or products must either make our work easier (and cheaper) or push us into new frontiers, letting us visualize and capture molecular processes that were heretofore invisible. Out of all items assessed, some are totally novel, while others improve on existing technology, an indication that the field is still growing and developing. The outcome of the evaluation reveals that microfluidics; optical lock-in detection (OLID)-FRET, white laser confocal instrument, in-vivo multispectral imaging, PET/MRI combined imaging, in vivo cell cycle imaging, open source sequencing, zinc finger nuclease for gene editing

platform, continuous focus microscopy and low cost sequencing are the winning technologies.

TOP 10 - MICROFLUIDICS DEVICES FOR ASSAY AND DETECTION

Microfluidics deals with miniaturizing fluids at sub-millimeter scale. Typically, **micro** means one of the following features: (1) small volumes (nl, pl, fl); (2) small size; (3) low energy consumption or (4) effects of the micro domain. It offers plenty of advantages for studying cells

and small organisms. Biologic-scale microfluidic devices can mimic many in vivo situations, such as laminar blood flow through a capillary or the three-dimensional structures that culture plates can't capture. Such systems can also help researchers to use scarce primary cells and expensive materials.

Microfluidics has emerged in the beginning of the 1980s and is used in the development of inkjet printheads, DNA chips, lab-on-a-chip technology, micro-propulsion, and micro-thermal technologies. It is a multidisciplinary field intersecting engineering, physics, chemistry, microtechnology and biotechnology, with practical applications to the design of systems in which such small volumes of fluids will be used. It is enabling technology with a tremendous potential in many applications fields and makes possible to integrate different protocols and compartments in one chip to automate analysis and reduce reaction time.⁽²⁾ Microfluidics' main expected growth is in the diagnostic market (Figure 2). Microfluidic components market in diagnostic is

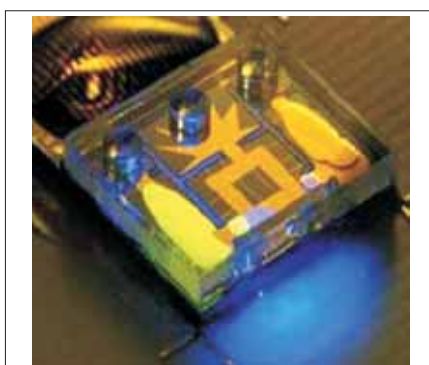


Figure 1. ©CEA LETI Digital microfluidic chip EWOD processor mixing droplets of 64 nrolufluidics device

Current applications	Microdispensers & microflow platforms	Academic & pharmaceutical research
	Proteomics, cell chips, electrophoresis analysis	
Emerging applications	Laboratories microbiology diagnostic analysis	Diagnostic
	Point-Of-Care analysis	
	Microbiology analysis in Water	
Long term applications	Food industrial process control (CQ – microbio. species)	Medicine
	Inhalers implantable pumps	
	Synthesis of chemical and pharmaceutical ingredients	Chemistry

Figure 2. Microfluidics applications in life sciences, biomedical and pharmacological fields.

conventional laser are delivered at the fiber-entrance, the originally narrow line is broadened to a wide emission band - a "white" emission. The efficiency in broadening depends on the fiber-pattern and on the mere length of the fiber. For imaging, the emission also needs to be bright enough to create a good and noise-free image in a reasonable time.



Figure 4. A setup of white laser confocal microscope. (adopted from <http://www.lehigh.edu/~inbios/facilities/confocal.htm>)

The white laser confocal microscope consists of three fiber-based parts. First, a seed laser, generating a pulsed emission at 80 MHz in the infrared; second is a strong pump source, and third, the supercontinuum fiber, that emits the visible light. This arrangement produces a continuous spectrum from 470 nm to 670 nm. The classical way to feed excitation light into the microscope would use a set of filters for the various spectral parts to select appropriate colors for the fluorochromes applied. A much better way is to employ an Acousto Optical Tunable Filter (AOTF) that is continuously tunable and offers intensity regulation at the same time. In addition, the excitation regime may be reprogrammed in a matter of microseconds. Consequently, laser in this kind of microscope is an integrated design of a white light emitting laser source with an appropriate acousto optical tunable filter. The control software offers sliders that can set to any wavelength in the emission range and have an additional handle to control the intensity of the line selected. Up to 8 lines may be active simultaneously.

White laser confocal microscope is different from the conventional confocal instruments which limit the researcher's choice of both fluorescent dyes and the experiments that can be performed with the system. The white laser confocal microscope integrates a white light laser that provides users with the full spectrum of wavelengths between 470 and 670 nm and this can allow researchers to tune in excitation and turn down laser power, to increase viability for longer live cell experiments. The white light system completes the system and makes it the most flexible. This, in turn, allows optimal adjustment of the excitation line to the sample, which reduces cross-excitation

and sample damage. In addition, it frees you from compromising and allows you to make the most of every sample you put on it.

TOP 7 - MULTISPECTRAL SIGNALING + X-RAY

Advanced multispectral fluorescence, luminescence, digital X-ray and radio-isotopic imaging for in vivo imaging were successfully assembled in a single system called Multispectral Imaging System FX for the first time. The system was designed by Kodak. It can be used for in vivo and in vitro molecular imaging of materials. It is also designed to precisely locate and monitor changes in molecular activity of specific cells or organs - long before morphological changes can be detected - expediting the development of effective therapeutics for disease treatment (Figure 6). In vivo optical molecular imaging allows non-invasive measurement of biological processes within a living organism.⁽⁹⁾



Figure 5. Molecular Imaging System (adopted from <http://www.marketlinkscientific.com/systemfx.php>)

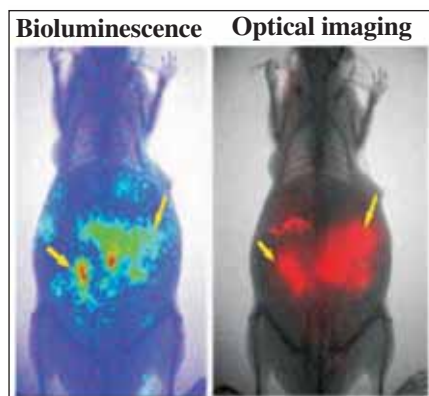


Figure 6. Optical Imaging of Peritoneal Tumor Metastases Using Quantum Dots. Mouse mammary tumor 4T1 cells stable transfected with a firefly luciferase gene were incubated with Tat peptide-labeled quantum dots (emission 650 nm) for 2 hours before injection into mouse peritoneal cavity. Eight days later, bioluminescence imaging was performed on the mouse with a Kodak in vivo FX imaging system, and tumor locations (arrows) were determined. Optical imaging of peritoneal cavity confirmed the tumor lesions (arrows).

The system's new multispectral tuning of excitation light provides enhanced sensitivity allowing for the identification and separation of multiple fluorochromes and the removal of auto-fluorescence background noise. Sophisticated software, native to the system, automatically generates and analyzes a series of images taken at different wavelengths with spatially co-registered x-ray and white light images for improved localization of biomarkers in vivo. Further, the system's multimodal capabilities include bioluminescence and radio-isotopic signal detection, giving researchers a wide range of options for precisely identifying biomarkers of interest in small animals. A key tenet of this technology is fluorescence, the process in which molecules absorb light, transition from a ground state to an "excited" state, and then emit light of a longer wavelength.

TOP 6 - PET/MRI COMBINED IMAGING

Scanners that combine the capability of positron emission tomography (PET) with magnetic resonance imaging (MRI) have recently been developed.⁽¹⁰⁾ PET tomography is a nuclear medicine medical imaging technique which produces a three-dimensional image or map of functional processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radioisotope, which is introduced into the body on a metabolically active molecule. PET tomography is primarily used to detect diseases of the brain and heart.

A combined PET/MRI scanner generally includes a magnet for producing a magnetic field suitable for magnetic resonance imaging, a radiofrequency (RF) coil disposed within the magnetic field produced by the magnet and a ring tomograph disposed within the magnetic field produced by the magnet. The ring tomograph includes a scintillator layer for outputting at least one photon in response to an annihilation event, a detection array coupled to the scintillator layer for

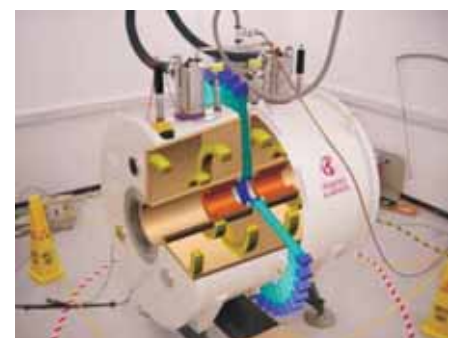


Figure 7. The MR magnet in the Cavendish with an overlay of the proposed PET

detecting the at least one photon outputted by the scintillator layer and for outputting a detection signal in response to the detected photon and a front-end electronic array coupled to the detection array for receiving the detection signal, wherein the front-end array has a preamplifier and a shaper network for conditioning the detection signal. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radio-isotope, which is introduced into the body on a metabolically active molecule. Positron emission tomography is primarily used to detect diseases of the brain and heart.^(11,12)

TOP 5 - IN VIVO CELL CYCLE IMAGING WITH FLUORESCENT PROBES

The fluorescent ubiquitination-based cell cycle indicator (Fucci) is a set of fluorescent probes that lets the investigator see the cell-cycle activity of their experiment. The Fucci construct can aid in experiments applying to cell proliferation and activity, such as regeneration, development, and carcinogenesis. Figure 8 demonstrates that HeLa cells stably expressing Fucci-G1 Orange and Fucci-S/G2/M Green. Fucci effectively labels individual nuclei in G1 phase orange and those in S/G2/M phases green (Figure 8).

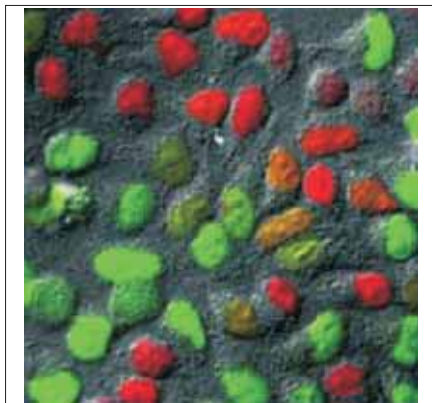


Figure 8. HeLa cells stably expressing Fucci-G1 orange and Fucci S/G2 Green. Fucci effectively labels individual nucleus in G1 phase (orange) and those in S/G2/M phases (green)⁽¹³⁾

TOP 4 - OPEN SOURCE SEQUENCING MACHINE FOR THE MASSES⁽¹⁴⁾

George Church, a genomics pioneer in the Center for Computational Genetics at Harvard Medical School, has been developing prototypes of DNA sequencing device - known as the Polonator - from off-the-shelf components. His team partnered with Danaher Motion, a precision-instrument maker that built movable microscope stages for earlier versions of the technology. Over the last 10 years, the Polony Sequencer was explored by Church'. Millions of beads coated with

small fragments of the DNA to be sequenced are spread on a glass slide. Next, a series of fluorescently labeled DNA bases bind to the fragments and finally, a standard fluorescence microscope reveals which base is at each position on a fragment. Today, the commercial version of Church' technology (Figure 9) can accommodate a billion beads and has a more sophisticated imaging instrument attached. The inexpensive device can sequence 10 billion base pair in a single 80-hour run; a capacity equal to or greater than that of currently available technologies.



Figure 9. The Polonator Sequencing Machine

TOP 3 - ZINC FINGER NUCLEASE TECHNOLOGY FOR TARGETED GENOMIC EDITING⁽¹⁵⁻¹⁹⁾

Zinc Finger Nucleases (ZFNs) are a class of engineered DNA-binding proteins that facilitate targeted editing of the genome by creating double-strand breaks in DNA at user-specified locations (Figure 10). Double-strand breaks are important for site-specific mutagenesis in that they stimulate the cell's natural DNA-repair processes, namely homologous recombination and Non-Homologous End Joining (NHEJ). By implementing established, field-proven methods, these processes can be harnessed to generate precisely targeted genomic edits, resulting in cell lines with precise and heritable gene deletions, integrations or modifications.

Benefits of ZFNs include (1) rapid disruption of, or integration into, any genomic loci; (2) mutations made are



Figure 10. Recognition and heterodimerizing of targeted site in dDNAs by ZFN pair

permanent and heritable; (3) Works in a variety of mammalian somatic cell types; (4) edits induced through a single transfection experiment; (5) knockout or knock-in cell lines in as little as two months; (6) single or biallelic edits occur in 1-20% of clone population and (7) no antibiotic selection required for screening.

This technique could be applied to the work of (1) functional genomics/target validation; (2) cell-based screening and (3) cell line optimization

TOP 2 - CONTINUOUS FOCUS MICROSCOPY⁽²⁰⁾

Focus drift of microscopy is one of the biggest obstacles to acquiring high resolution and "live cell". Prolonged periods of observation and stage movement as well as a host of other factors can result in focus drift. The continuous focus system substantially eliminates focus drift for high power microscopy. The system effectively monitors the distance between the objective lens of the microscope and the cover slip used to mount the sample under examination. Minute changes in the distance between the sample and the objective lens are sensed using an optical detector. This detector provides a feed back signal for the closed-loop positioning system that actively controls the focus of the microscope.

The new Perfect Focus System (PFS), developed by Nikon Co., automatically detects the surface of the coverslip optically and continually corrects focus to compensate for even the most infinitesimal changes (Figure 11). When PFS is turned on, the position of the coverslip surface is always detected during observation, and the data is continuously fed back to the focusing mechanism. The rapid change of



Figure 11. A continuous focus microscope (adopted from <http://www.lin.com.tw/menu/products>)

cells can be caught because PFS instantaneously corrects focus drift resulting from temperature drop when adding reagents. Focus is continuously corrected at any plane of interest throughout the specimen by the Optical Offset feature. Unlike other systems that have to initially focus on the coverslip interface and then shift the focal point to the plane of interest, PFS can continuously keep focusing on the focus plane. Consequently, you will never again miss rapid events in your specimen because of focus drift.

By combining the highly sensitive focus detection system and the extremely accurate Z-axis control system, focusing precision of less than 1/3 the focal depth of the objective is achieved. PFS uses an LED in the infrared range and an internal linear CCD detector to detect the focal point, so it does not intrude on wavelengths used for observation. As a result, observation and focus maintenance can be carried out at the same time, with no influence at all on captured images. Since the wavelength of the LED does not affect the image quality, high-contrast visualization of single fluorescent molecules is possible.

PFS strongly supports live cell applications and is compatible with various fluorescence imaging platforms, for example, Laser TIRF system-with

laser light source and ultrahigh S/N ratio, white-light TIRF Multi-fluorescence Imaging System, fluorescence system with high S/N capability

TOP 1 - LOW COST HIGH THROUGHPUT SEQUENCING SYSTEM

Analysis of gene expression patterns provides valuable insight into the role of differential expression in normal biological and disease processes. Classical gene expression assays are considered the "gold standard" when a defined number of genes are being studied due to the wide dynamic range. High density microarrays have been used to globally assay mRNA expression levels, however, microarrays are limited in their dynamic range and can be relatively ineffective at measuring low copy genes. Furthermore, traditional microarray approaches depend upon 3' based sample preparation and hypothesis driven probe design, limiting their ability to detect novel exons or differentiate between splice variants. Sequence tag-based expression techniques such as SAGE (Serial Analysis of Gene Expression), SuperSAGE, CAGE (Cap Analysis Gene Expression), and 5' SAGE, provide extremely sensitive, hypothesis-neutral sample preparation methods. To date, however, these assays have been limited by the throughput of traditional sequencing technologies.

The SOLiD™ System (Figure 12) is a highly accurate, massively parallel genomic analysis platform that supports a wide range of applications. It is very flexible. The two independent flow cells and multiplexing capability of the system allow researchers to conduct multiple sequencing experiments in a single run. With unparalleled throughput and greater than 99.94% base calling accuracy, the SOLiD System enables scientists to complete large-scale sequencing and tag experiments more cost effectively than previously possible. It overcomes the limitations of both microarray and SAGE technologies by providing a highly sensitive, hypothesis-neutral method for the detection of gene expression on a genome-wide scale.



Figure 12. The low cost SOLiD Sequencing System (Courtesy of Applied Systems)

References

- Roberts JP (2008). **Let it flow.** *The Scientist*, January 1 issue.
- Rhee M, Burns MA (2008). **Microfluidic assembly blocks.** *Lab Chip*, 8(8):1365-1373.
- Paguirigan AL, Beebe DJ (2008). **Microfluidics meet cell biology: bridging the gap by validation and application of microscale techniques for cell biological assays.** *Bioessays*, 30(9):811-821.
- Mao S, Benninger RKP¹, Yan YL, Petchprayoon L, Jackson D, Easley CJ, Piston DW, Marriott G (2008). **Optical lock-in detection of FRET using synthetic and genetically encoded optical switches.** *Biophys. J.*, 94, 4515-4524.
- Yan Y, Marriott G (2003). **Analysis of protein interactions using fluorescence technologies.** *Curr. Opin. Chem. Biol.*, 7:1-6.
- Jares-Erijman, E, Jovin T (2003). **FRET imaging.** *Nat. Biotechnol.*, 21:1387-1395.
- Koyama-Honda I, Ritchie K, Fujiwara T, Iino R, Murakoshi H, Kasai RS and Kusumi A (2005). **Fluorescence imaging for monitoring the colocalization of two single molecules in living cells.** *Biophys. J.* 88:2126-2136.
- Frank JH, Eldert AD, Swartling J, Venkitaraman AR, Jeyasekharan AD and Kaminski CF (2007). **A white light confocal microscope for spectrally resolved multidimensional imaging.** *J. Microscopy* 227(3):203-215.
- Wang X, Yang L, Chen Z and Shin DM (2008). **Applications of nanotechnology in cancer therapy and imaging.** *CA: A Cancer J. Clin.* 58:97-110.
- Wong TZ, Turkington TG, Hawk TC, Coleman RE (2004). **PET and brain tumor image fusion.** *Cancer J.* 10(4):234-242.
- Grosu AL, Weber WA, Franz M, St?rk S, Piert M, Thamm R, Gumprecht H, Schwaiger M, Molls M, Nieder C (2005). **Reirradiation of recurrent high-grade gliomas using amino acid PET (SPECT)/CT/MRI image fusion to determine gross tumor volume for stereotactic fractionated radiotherapy.** *Int J Radiat Oncol Biol Phys.* 63(2):511-519.
- Borgwardt L, Højgaard L, Carstensen H, Laursen H, Nowak M, Thomsen C, Schmiegelow K (2005). **Increased fluorine-18 2-fluoro-2-deoxy-D-glucose (FDG) uptake in childhood CNS tumors is correlated with malignancy grade: a study with FDG positron emission tomography/magnetic resonance imaging coregistration and image fusion.** *J Clin Oncol.* 23:3030-3037.
- Sakane-Sawan OA, Kurokawa H, Morimura T, Hanyu A, Hama H, Osawa H, Kashiwagi S, Fukami K, Miyata T, Miyoshi H, Imamura T, Ogawa M, Masai H, Miyawaki A (2008). **Visualizing spatiotemporal dynamics of multicellular cell-cycle progression.** *Cells* 132(3):487-488.
- Porreca GJ, Zhang K, Li JB, Xie B, Austin D, Vassallo SL, LeProust EM, Peck BJ, Emig CJ, Dahl F, Gao Y, Church GM, Shendure J (2007). **Multiplex amplification of large sets of human exons.** *Nat Methods* 4(11):931-936.
- Doyon Y, McCammon JM, Miller JC, Faraji F, Ngo C, Katibah GE, Amora R, Hocking TD, Zhang L, Rebar EJ, Gregory PD (2008). **Heritable targeted gene disruption in zebrafish using designed zinc-finger nucleases.** *Nat. Biotechnol.* 26(6):702-708.
- Lombardo A, Genovese P, Beausejour CM, Colleoni S, Lee YL, Kim KA, Ando D, Urnov FD, Galli C, Gregory PD, Holmes MC, Naldini L (2007). **Gene editing in human stem cells using zinc finger nucleases and integrase-defective lentiviral vector delivery.** *Nat. Biotechnol.* 25(11):1298-1306.
- Moehle EA, Rock JM, Lee YL, Jouvenot Y, DeKaveler RC, Gregory PD, Urnov FD, Holmes MC (2007). **Targeted gene addition into a specified location in the human genome using designed zinc finger nucleases.** *Proc. Natl. Acad. Sci. U.S.A.* 104(9):3055-3060.
- Santiago Y, Chan E, Liu PQ, Orlando S, Zhang L, Urnov FD, Holmes MC, Guschin D, Waite A, Miller JC, Rebar EJ, Gregory PD, Klug A, Collingwood TN (2008). **Targeted gene knockout in mammalian cells by using engineered zinc-finger nucleases.** *Proc. Natl. Acad. Sci. U.S.A.* 105(15):5809-5814.
- Urnov FD, Miller JC, Lee YL, Beausejour CM, Rock JM, Augustus S, Jamieson AC, Porteus MH, Gregory PD, Holmes MC (2005). **Highly efficient endogenous human gene correction using designed zinc-finger nucleases.** *Nature* 435:646-651.
- US Patent 6760154. - **Microscope system with continuous autofocus** (Issued on July 6, 2004).

Establishing Hong Kong as a Chinese Medicine International Center

Modernized Chinese Medicine International Association
(MCMIA, 現代化中醫藥國際協會)

ABSTRACT

This proposal points out that the modernization trajectory of Chinese medicine (CM) in the past decade in China, HK and the world has transformed CM into an emerging high-technology industry. HK is in a unique position to capitalize on this opportunity to establish itself as a Chinese medicine international center and to turn the Chinese medicine industry into a substantial contributor to HK's economy. Towards this end, MCMIA (Modernized Chinese Medicine International Association) calls on the government to study the recent development of CM in order to draw up a comprehensive plan to modernize and strengthen the CM industry in HK and make it a foundation to develop the international center. Specifically, MCMIA suggests that the government should marshal sufficient public and private resources to organize a Chinese Medicine Development Commission (CMD) 中醫藥發展專署 to study and implement the plan. MCMIA believes that, as a start, the Commission should be charge-d with the responsibility to achieve 7 objectives. They are:

1. To foster the modernization of the CM industry in HK;
2. To support and promote ICMCM (International Conference & Exhibition of the Modernization of Chinese Medicine) as a trading and information exchange platform.
3. To promote the harmonization of CM regulations within the Greater China Region
4. To facilitate the development of integrative medicine with concurrent development of medical tourism.

5. To develop CM Specialty Colleges for quality assurance and enhancement of CM.
6. To establish a CM Informatics Center to support trade, R&D and communication.
7. To establish a CM Research Council to fund and drive strategic developments in CM sciences, technology, medicine and product commercialization studies.

MCMIA believes that when these objectives are accomplished, HK will gain a new robust CM industry which would bring health and prosperity to the Hong Kong citizens. At the same time, a CM international center will naturally emerge as a result of these efforts.

INTRODUCTION

Since the former Chief Executive, .Tung Chee-wah, called for the development of Hong Kong into an international center for Chinese medicine in his first Policy Address in 1997, the environments for Chinese medicine inside and outside of Hong Kong have changed dramatically. These changes created numerous unprecedented opportunities in business, medicine, sciences and education which Hong Kong now has the capability to take advantage of.

The leading force precipitating these changes came from the Central Government's recent series of national policies to modernize, internationalize and re-innovate CM. Together, these policies will eventually transform CM practice and products so that they can meet both domestic and international clinical and market needs by improving on CM's quality, safety and

effectiveness.

HK's CM industry, after a decade of evolution, now has the scientific know-how, personnel, credential and international networks to deliver these services and goods if it can be better organized into a modern industry. Furthermore, a robust CM industry in HK can contribute positively to HK's own healthcare system and eventually to the *globalization of CM*.

Once a modernized CM industry is established, HK could first position itself as a "*Quality-assured CM Trading Center* 中藥質量保證貿易中心 [貿易中心 QACMTC for brief]", an idea which was first advanced in an international conference on Chinese Medicine held in HK in 2001. CM trading activities can help invigorate the other related and supportive CM sub-sectors (such as clinical, manufacturing, plantation, R&D and marketing) in HK and Mainland. The strengthening of this sector is not only good for HK's CM industry, it also meets the recent appeal from MOFCOM's (Ministry of Commerce) calling for HK to play a constructive role in the development of "*Economic Cooperation Zones outside China* 境外經濟合作區" to help Mainland CM companies and products enter the global markets.

In fact, a foundation for this *Trading Center* has already been laid jointly by MCMIA (Modernized Chinese Medicine International Association) [See Appendix I and II] and HKTDC (HK Trade Development Council) during the past 7 years and it is called ICMCM (International Conference & Exhibition of the Modernization of Chinese Medicine & Health Products). This unique international event is the only one in the world dedicated to CM trading, science and technology exchange and regulatory information dissemination. However, the *Conference and Exhibition*

cannot continue to flourish without a strong, modern CM industry in HK and the further development of a global CM market.

On the healthcare front, CM's distinct advantages in pre-emptive treatment (治未病), disease prevention, chronic disease care and rehabilitation should be made an essential part of primary and community healthcare with private-public partnership and multi-disciplinary participation. Future private and public hospitals should also be designed to include CM as part of the integrative health services to provide the citizen with options for effective therapy and health maintenance.

Unfortunately, to date, HK does not have a comprehensive policy to help the CM industry to develop in a concerted manner. This lack of coherence impedes HK's ability to capitalize on the new opportunities. HK government's continual adherence to the principle of "positive non-interference" also hinders the government's support for promising emerging industries, such as the modernized Chinese medicine (MCM), to develop, mature and become a stronger constructive force to the economy.

MCMIA believes that it is time for the government's and its various bureaus to review their approach to CM, to formulate a new, comprehensive CM policy and to design a program to support the development of the CM industry in HK. Specifically, MCMIA suggests that the government could create a *Chinese Medicine Development Commission (CMDC)* 中醫藥發展專署 and charges the Commission with a long-term renewable mandate to foster the formation of a modern, robust CM industry in HK with the ultimate goal of establishing HK as *an international center of CM*.

The following sections describe the changes that have taken place in CM during the past 10 years and the new opportunities that are appearing domestically and abroad. Specific proposals are also made as to how HK's CM industry can be organized to achieve its goals as a major contributor

to HK's own healthcare system and a conduit to bring CM to the world.

"... Hong Kong has the potential to develop over time into *an international centre* for the manufacture and trading of Chinese medicina, for research, information and training in the use of Chinese medicina, and for the promotion of this approach to medical care."

Tung Chee-wah, 1997

CHANGES IN CHINA

During the past dozen years, the Central Government's attitude and policies towards CM has gone through a series of dramatic and pro-active changes with the tempo being accelerated in the last 5 years. These policies will lead to a complete makeover of the landscape for CM in the coming decades.

In 1996, several Central Government ministries and committees issued a policy paper called "*An Action Plan for the Scientific and Industrial Modernization of Chinese Medicines* 中藥現代化科技產業行動計劃" to call attention to the need to modernize CM. In the following year, the State Council formally called for the "*Realization of the Modernization of Chinese Medicines* 實現中藥現代化" as part of its reform and development for healthcare. These documents together set the stage for intense discussions and coalescence of efforts among the academia, government and industry on the path to modernize CM.

The subsequent implementation of the "*Drug Administration Law of the People's Republic of China (Amendment)* 《中華人民共和國藥品管理法》(修訂)" in 2000 and the "*Regulations for Implementation of the Drug Administration Law of the PRC* 《藥品註冊管理法》" in 2002 provided additional impetus to modernize CM by putting CM on the same level of regulatory rigor as western drugs. This is further reinforced by the progressive introduction of *Good Pharmaceutical Practice Guidelines* (see table) for both CM and western drugs. This is a critical step to modernize CM that lends CM credibility to their quality -a prerequisite for the internationalization process.

Good Pharmaceutical Practices

GAP - Good Agricultural Practice

GEP - Good Extractio Practice

GMP - Good Manufacturing Practice

GLP - Good Laboratory Practice

GCP - Good Clinical Practice

GSP - Good Sales/Supply Practice

In Fall 2002, seven State Council ministries and committees released a formal announcement called the "*Guidance for the Development of the Modernization of Chinese Medicines (2002-10)* 《中藥現代化發展綱要(2002-10年)》" which put China on a committed course to engage in modernizing CM with the necessary infrastructural supports.

In 2006, at the launching of 'the 11th Five- Year-Plan, MOST (Ministry of Science and Technology) and SATCM (State Administration of Traditional Chinese Medicine) jointly reached out to the international medical and scientific communities to seek their collaborations to conduct research projects on numerous aspects of CM. This plan was delineated in "*Guideline for International Scientific Cooperation in Chinese Medicine (2006-20)* 《中醫藥國際科技合作規劃綱要(2006-20年)》". This document clearly demonstrated the Central Government's confidence in opening up CM for the world to participate and its serious intent to internationalize it.

This was followed suit by the "*Guideline for the Development of Chinese Medicine Innovations (2006-20)* 《中醫藥國際科技合作規劃綱要(2006-20年)》"[See Appendix III] in 2007, which laid out a comprehensive plan with specific goals to encourage innovative developments of CM both as pharmaceuticals and as a practice. This document is an important blueprint to transform CM from a traditional discipline to a modern, scientific discipline, providing, for the first time, a channel connecting it to the western medical sciences.

On July 7, 2007, 17 ministries and committees jointly launched a 3-year, 90-city "*TCM China Tour* 中醫中藥中國行" under the leadership of then Vice Premier Wu Yi 吳儀 to demonstrate the State Council's resolve to support CM

and to propagate CM knowledge across the whole country. This was followed by the formal incorporation of the CM maxim and practice of "pre-disease treatment 治未病" into the national healthcare system in a summit forum organized by SATCM on January 25, 2008.

On July 16, 2007, SATCM and HKTDC co-organized a symposium in HK to discuss how the Mainland and HK could jointly establish and develop the CM service industry in China. On September 9, 2007, at the 11th International Investment & Trade meeting in Xi anen [See Appendix IV], the vice minister for trade, Yi Jian Guo 魏建國 noted that HK is the stepping stone for the globalization of Chinese corporations.

These symposiums pointed out a direction how a modern HK CM industry could help in the global business development of China's CM companies in terms of quality assurance, international product registration and marketing. In addition, with HK's experience and standards in hospital management, we are in a unique position to act as a referral centre to CM experts in China with due attention to quality and risk management through accreditation and medical insurance. Furthermore, HK's scientists could also contribute their talents in CM formulation, product R&D and, designs, certifications and clinical trials.

In June 2008, Vice Minister of Health, Wang Guo Qiang 王國強 signed an MOU with US's Department of Health and Social Services, outlining extensive cooperation between the two countries in the development of CM.

Many western countries are also getting on board for this fast-pace development. The Canadian Ministry of Commerce signed an MOU with China's MOST 2 years ago to collaborate in a number of life science fields including CM. Similar arrangements have also been successfully made with UK, Italy and Germany. These governmental agreements will lead to many collaboration opportunities for both HK and Mainland scientists.

The above declarations, policy statements and activities were backed by the Central Government with hundreds of millions of RMB and they were organized by top government

agencies. The impact of these policies was reflected in the recent strong leap in domestic CM sales in China as shown in the table on the following page.

CM sales now constitute about 41.5% of China's total domestic pharmaceutical sales, a considerable increase from 1980's 32.5%. These figures provide a clear indication for the trend and vitality of the CM market in China.

SALES OF TCM PRODUCTS IN CHINA (RMB)

	Raw Herbs 藥材	Cut herbs 飲片	Proprietary CM 中成藥
1978	1.257 Bn	0.92 Bn	0.788 Bn
2007	20.3 Bn	28.80 Bn	137.1 Bn

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Provinces and cities in the Mainland have also expressed openly their intentions to collaborate with HK to open international markets. These include Hainan, Shenyang, Chengdu, Changchun and Sichuan ---all of which have signed memorandums of understanding with MCMIA to collaborate on the internationalization of TCM. Other institutions, universities and commercial entities from Shanghai, Hangzhou, Guangzhou, Yunan etc. are also seeking HK's assistance in opening their channels to the international markets. Guangdong province went one step further and established a *Guangdong -Hong Kong Technology Cooperation Funding Scheme (TCFS 粵港科技合作資助計劃)* with *HKs Innovation Technology Commission*. Part of fund is earmarked to support CM modernization projects.

In mid 2008, plans are being finalized for the establishment of 10 Chinese Medicine Research Centres in China with central funding. Hong Kong is welcomed to form a unique CM research centre that could co-operate with all of them in a 10+ 1 model.

Another significant development in recently year is the establishment of CFCMS (World Federation of Chinese Medicine Societies 世界中醫藥學會聯合會), which boasts 150 international CM associations in 50 countries as its

members. This organization helps to set standards by organizing training and examinations in major languages in all continents. With their encouragement, the University of Science and Technology of Macau, recently founded the 『兩岸四地中醫藥科技合作中心』 in January 2008. A new hospital for integrative medicine has also been built in Macau with a view to capitalize on 'medical tourism'.

In Taiwan, great strides have been taken in the past decade with government funding for research through four sectors -health, education, technology and economics. Taiwan's Department of Health commissions strategic research with scientifically robust annual publications and high quality monographs. It also monitors and ensures quality CM products are made available to the public.

The Taiwan government supports Chinese and western medicine equally by providing reimbursement for treatment under either practice. In 80% of Taiwan's major western hospitals (with >2000 beds), there is a CM department with in-patient beds used for integrative medicine with cross referral and consultation. The China Medical University and the Chang Gang University support this integrative approach by awarding double degrees in CM and western medicine.

All these changes are likely to improve dramatically CM practice and products in the next few years such that CM will be moving into the global market at an accelerating pace on an unprecedented scale. In short, this could be the first steps of the *CM globalization*.

The question is: "Is Hong Kong' ready to capitalize on the approaching *CM globalization*?" Unfortunately, from all indications, only a small segment of the HK CM industry appreciates the significance of these events and even fewer are preparing themselves to take advantage of the benefits *CM globalization* could bring. Even the HK government is apparently completely oblivious to these events. As a result, HK could very well be caught off-guard when *CM globalization* begins to take off.

CHANGES IN THE WORLD

While fundamental changes are happening in China's healthcare system and the pharmaceutical sector, corresponding changes are also taking place in many parts of the world as herbal medicine is gaining prominence. WHO statistics showed that 80% or 4 billion of the world population still depend on traditional medicine for their primary healthcare. In reaching for the goal of "Health for All", WHO has set directives to support the development of traditional medicine through the harmonization of international standards. This resulted in the publication of a number of monographs on herbs, acupuncture points, terminology and preparations for the introduction of traditional medicine in the next edition of *International Classification of Diseases*. In the process, WHO has also commissioned the development of *Clinical Practice Guidelines* and standardization of the disease patterns for Chinese Medicine.

A 2008 *Nutraceuticals World* article quoted the German consulting firm, Analyze & Aequalize Ag's estimate of about US\$83 billion global market for herbal remedies across all segments with annual growths ranging between 3-12% depending on the segments. Herbal dietary supplements (\$11 billion) and herbal functional foods (\$14 billion) make up over a third of the market. The global herbal pharmaceutical industry (including drugs from herbal precursors and registered herbal medicine) contributes \$44 billion and herbal beauty products make up the remaining \$14 billion of the market. In the global cosmetics market, herbal ingredients are estimated to have a 6% share of the market and are exhibiting the strongest growth between 8% and 12%.

Today, the Asian herbal market (excluding Japan) is estimated to be worth about \$6.4 billion. This increase is expected to continue. In Japan alone, the market is worth well over \$2.6 billion today.

The growing international herbal markets generate demands for modernized and effective CMs to cater to the needs of both underdeveloped and advanced countries alike to help lower their overall healthcare and health maintenance costs. Hence, it is not

surprising that underdeveloped countries have long welcomed CM while the wealthier western nations in the world are opening their doors to Chinese medicine as well.

Countries, such as USA, Canada, UK, Thailand, S Africa, Singapore, Australia (the Victoria Province) etc., are embracing CM to various degrees, hoping that it will help mitigate their heavy healthcare burden and treat chronic diseases that plague most of the aging western societies. Thus far, none of these potentially vast markets' potentials have been fully recognized, let alone exploited. HK could stand a good chance to capture these markets if prompt actions are taken.

ON REGULATIONS -A number of western countries are becoming more cognizant about CM. Australia's Victoria Province recently has all but completely embrace CM by recognizing both the TCM practice and the herbal remedies. Canada's new *Natural Health Product* regulations allow a wide spectrum of claims for herbal preparations depending on the level of supporting clinical evidence and/or historical traditions. This new law has opened up a huge market in N America for CM to enter not only as healthfoods or dietary supplements but also as products in OTC markets. Japan also recently increased the TCM preparations included in the cXNational Insurance List to 210. These formulations are recognized to be safe and effective and their sales in Japan do not require additional clinical verification.

United States remains a relatively easy market to enter because it designates most over-the-counter CMs as dietary supplements, a category which has been rather loosely regulated since 1994. Even so, most CMs are still confined to China Towns because of their lack of distinguishing features, brand name recognitions and mainstream market acceptability. This may change soon when more CM companies participate in the *USP-MCMIA DSVP Certification Scheme* (see next section) for modernized CM.

Although some regions such as EU are tightening up their regulations towards CM, however, as more and more modernized and evidence-based

CMs enter the market these regulations could be used as a badge of confidence for the qualified CMs.

ON THE SCIENTIFIC FRONT

-International scientific collaborations of CM are expected to flourish following MOST's announcement of the "*Guideline for International Scientific Cooperation in Chinese Medicine (2006-20)*". A case at hand is Harvard University's *Division of Complementary and Integrative Medical Therapies of the Osher Institute*, which sought to form a research network with the CM researchers in the Greater China region to screen and develop anti-cancer CM. Yale University has also formed a company, Phytoceutica, to handle products of CM research, from laboratory to bedside. UK's Cambridge University formed an institute for CM research on campus with the support from a Mainland CM company.

In response to demand, the NCCAM (National Committee on Complementary and Alternative Medicine) under NIH (National Institute of Health) of USA has been increasing their research funding on CM. Australia has also formed a NICM (National Institute of Complementary Medicine Management) with federal funding supporting R&D leading to commercializable products/technologies.

HK's scientists and CM organizations, such as MCMIA, can play an important role in the organization of an international CM technology network for these entities and help them reap the benefits of being partners in this global CM scientific web. On the business side, with HKTDC as a partner and using ICMCM (see below) as a vehicle, MCMIA has already created an effective network connecting CM businesses, practitioners, scientists, academician and government officials from all over the world with HK as a platform.

At the dawn of a global CM scientific/business network and market, HK should try to engage itself early on with this new and potentially immense community. If HK does not get its foot in the door now, in a few years, it might find itself to have much fewer leverage to be a significant participant in this community.

When the wave of new, modernized

CMs from China begins to sweep the global market in the coming years, will HK be at the forefront to help usher them to the world? This will depend on whether HK begins now to prepare for this eventuality by starting to build a strong CM industry in HK.

CHANGES IN HONG KONG

During the last decade, the landscape of HK CM has also changed drastically. CM has, transformed itself from a practice that was benignly neglected or even looked down upon during the British rule to a more respected profession that often commands fees at par or higher than its western counterpart. Some high-end CM products are also selling at prices undreamed of in the past. Unlike prior to 1997, when the quality of CM practice and products are largely "unknown" to most people, now all CM activities operate within the purview of the *Chinese Medicine Ordinance* enacted in 1999. The CM industry and products have been regulated since 2000 by the *Chinese Medicine Board*. These legislative processes have brought higher confidence and credibility to the whole industry.

HK's CM education has now broken out of its former private, unlicensed tutoring mode and developed into 3 respected TCM medical schools located in 3 prestigious universities of HK. Today, 6 HK universities have their own CM research programs led by dozens of senior researchers, many of whom have cross-border and international collaborations. HKPU (HK Polytechnic University) even operates a CM research facility with a *State Key Laboratory* standing in Shenzhen.

In 2003, CGCM (Consortium for Globalization of Chinese Medicine 中藥全球化聯盟), led by Prof. Tommy Cheng of Yale University, was founded and headquartered in the Hong Kong University. It is a coalition of about 100 international institutions and universities that cooperate with one another to engage in various CM R&D projects. They range from basic research to new CM product developments funded by HSRF (Health Services Research Fund), ITF (Innovative Technology Fund), UGC (University Grants Committee), HKJC (Hong Kong Jockey

Club) and other local and international agencies. Its 'new drug discovery' resulted in several patent applications. CGCM exemplifies the overwhelming advantages HK has over other locations as a global CM scientific centre.

In 2006, MCMIA and 4 HK universities founded CMQA (Chinese Medicine Quality Advancement Group), an organization that is devoted to address the important issues of CM quality. The group has since been awarded its first grant from ITF to conduct research on a model CM formulation in order to determine the parameters that are relevant in CM quality control. The group is likely to secure additional funding in the near future so that other important CM problems can also be investigated. The results obtained could then be used to develop new CM quality assurance and regulation guidelines as well as novel products.

HK traditionally enjoys good international reputation and credibility in conducting clinical trials. By the end of FY 08-09, Hospital Authority (HA), would have established a network of 14 tri-partite CM centers in service, training and research. Working together with NGOs (Non Government Organizations) and universities, the network has identified, through systematic review of modern and classical literature, major disease burdens with clinical advantage of CM as topics for future research.

With supports from HA's expertise in clinical research methodology and ethics, the network is well positioned to engage in clinical studies for CM products. It also opened a toxicology laboratory with a strategy to address adverse drug reactions and drug-herb interactions. This will be valuable in helping CMs gain international recognition for their claimed safety and efficacy with data accumulated in HK. Furthermore, the CM centers offer reliable choices to local citizens and provide postgraduate training and career opportunities for CM graduates.

The potential important contribution of HK to the overall development of CM nationally is recognized in November 2007 with the signing of an MOU between SATCM and HK's Food and Health Bureau [See Appendix V]. In this MOU, both sides agreed to collaborate

in a wide range of areas and activities in CM. This is the first time the Hong Kong government commits itself to support CM in a document. The Bureau should now take concrete steps to implement the MOU in order to live up to its commitments.

One of the most prominent achievements in HK CM during the past ten years was the organization of the annual ICMCM (International Conference & Exhibition of the Modernization of Chinese Medicine & Health Products) by MCMIA and HKTDC. ICMCM is a collection of activities catering to all the sub-sectors within the local and international CM communities. It consists of an exhibition, a conference for the CM professionals, a series of business matching and promotional activities for the exhibitors and buyers at the fair, a free CM Health Forum for the general public, a CM Educational Display designed by the TCM Schools' students and a Postgraduate Student CM Symposium where university researchers' CM achievements can be showcased to international visitors. In addition, there are other activities sponsored or organized by foreign consulates, buyer groups and exhibitors.

In short, ICMCM, which was first launched in 2002, is now a unique leading international platform for TCM practitioners, company executives, government officials, scientists and academics to congregate to exhibit new products, equipment and technologies, to learn about the latest development in international regulations, exchange scientific information and to establish business connections.

Every year, about 90,000 visitors patronized ICMCM to view the exhibits displayed by about 200 exhibitors coming from about a dozen countries. In the last 2 years, the number of outside HK buyers and buyer groups jumped by about 50% per year, indicating clearly that ICMCM had been gaining international recognition and prominence. For example, in 2007, the Canadian delegation doubled in size to about 50 delegates while the Japanese delegation expanded 3 fold to 30 people. ICMCM has gained so much attention and respect that some Central government agencies have been monitoring it as an important

international platform for CM from China.

Last year (2007), ICMCM began to catch the attention of international press. Both the Asia Wall Street Journal and Reuter reported the event and the recent development of modernized Chinese medicines [See Appendix VI]. Other articles on similar subjects also appeared in Toronto Sun and the Canadian Asia Network Magazine.

As CM products improve in quality and the international regulatory environment becomes more cognizant and accommodating, services offered by HK firms to register, market and distribute HK and Mainland modernized CM products internationally will be more and more in demand. This is the kind of role HK plays best as an international portal and a professional distributor for high quality products to the global markets.

When HK's reputation for high quality is coupled with CEPA (Closer Economic Partnership Arrangement), the result is a scheme that entices both Mainland and international CM manufacturers (such as Tong Ren Tang and Eu Van Sang) to set up production facilities and headquarters in HK. The products are then sold to the Mainland market as tariff-free premium products and to the world market as quality and reliable preparations. This scheme is well served by HK's new CM Ordinance's GMP certification. In this case, HK government's continual support of CEPA serves as an example of what the government can do to re-energize the once declining CM manufacturing sector in HK.

The importance of HK as a two-way international conduit between China and the rest of the world was not lost among foreign government agencies either. A good example is the contractual engagement between USP (US Pharmacopoeia) and MCMIA to co-develop a DSVP (Dietary Supplement Verification Program) scheme for the Greater China Region to help exporting GM products verified by USP for their quality and safety. The companies of these products can then leverage on USP's authoritative certification to help create brand name recognitions for their products and their companies internationally. This scheme is likely to accelerate the internationalization of quality CM

product in the world market.

The development of CM in the past 10 years has been so overwhelmingly positive and promising that the HK government bureaus should study this evolving CM industry and markets. It should create and maintain the necessary conditions for the industry to thrive and excel. Specifically, the government should step in and help in the modernization of the industry so that it can capture the surging opportunities in the coming decades and to secure for HK a unique position as an international center for CM.

CAPTURING THE OPPORTUNITIES

As described in the previous sections, a global CM industry and its accompanying markets are emerging. Given the fast pace of economic growth in China, we expect this industry in the Mainland will move toward maturation very quickly.

However, many of the essential elements to help internationalize CM are still lacking in the Mainland. This gives HK a rare window of opportunity to step in and serve as a viable platform and a conduit in the globalization process of CM. In short, HK has the wherewithal to assume the position as a *Chinese Medicine international centre (CMIC)*.

There are many sub-sectors within the global CM industry (see table) and HK has the ability to serve and support most of these sub-sectors effectively at various capacities. Hence HK's role can be viewed as a HK mediated international exchange and service platform where domestic or international members of these sectors can gather to find their collaborators and to obtain useful information, products and services to further the advancement of their own concerns.

Sub-Sectors of CM Industry

1. Herbal plantation
2. R&D
3. Manufacturing
4. Trading/marketing
5. Informatics
6. Education
7. Insurance
8. Wellness & Treatment
9. Rehabilitation & Palliation

The success of a *Chinese Medicine international center* depends on a robust local modernized CM industry. The modernized HK CM industry will bring many benefits to the city that will go way beyond what the, traditional CM industry has hitherto delivered.

BENEFITS TO HONG KONG

Unlike the low-tech raw herb-based CM industry in the 20th century, the new, modernized Chinese medicine industry in the 21st century will be driven by science and technology. It will be an advanced, sophisticated, knowledge-based and globally-oriented industry that can take advantage of not only the markets in the Greater China Region but the global markets as well.

HK is an international business city that possesses excellent domestic and international business intelligence and know-how. Hence it can conduct businesses directly with both Mainland and the world. In addition, HK's CM scientific standing and reputation are so highly regarded in the world that domestic and international commercialization of CM by HK firms are more easily achievable.

Because of these characters, a modernized CM industry will bring many benefits to HK. Some of these benefits are:

1. Creating new, high-paying employment opportunities
2. Increasing HK's tax revenues
3. Lowering HK's overall healthcare expenses
4. Providing an alternative yet culturally attuned medical choice to the citizens
5. Widening of HK's economic base in support of HK's Economic Restructuring
6. Strengthening HK's position as a centre for the globalization of CM in commerce, medicine, science, technology, education and informatics.

If properly established, the modernized CM industry could add one more "dynamo" to HK's economy. This will not only contribute directly to HK's financial growth but will also reduce

HK's risk of relying on too few "old" industries. Furthermore, the modernized CM industry can also bring other intangible benefits such as the promotion of the citizens' health and well-being if it is properly integrated into the current healthcare system.

MODERNIZING THE HONG KONG INDUSTRY

For HK to participate in the approaching *CM globalization*, building up a modernized CM industry is the key. In the past, one viewed CM industry rather narrowly to include only manufacturing, trade/marketing and practice. A modern view of CM industry should include all the sub-sectors shown in the previous section. To modernize the HK CM industry, one must consider and plan for all the sectors in a comprehensive manner.

However, it would not be prudent to develop and promote all the sub-sectors all at once. A preferred approach would be to designate *trading* and *Chinese medical sciences* as the leading sub-sectors and allow them to pull all the other sub-sectors along based on business, product and service needs. While *trading* will utilize current available merchandise to generation revenue, CM sciences will help sort out the fundamentals of the traditional *CM disciplines* and develop the next generation of novel products. The financial returns this process generates will then be routed back to support the other sub-sectors and the subsequent rounds of development.

The advancement of the CM industry requires expert knowledge from many CM disciplines. The government bureaus can engage directly in these developmental activities or it can appoint a civilian body equipped with the necessary expertise to handle this task. In comparison, a dedicated civilian body has the advantage of being more agile, more professional and unencumbered by bureaucracy.

We propose that, after the government has studied the CM development issues thoroughly and finds it a practical project to proceed, it should then appoint a civilian body, name it the Chinese Medicine Development Commission (CMDC) 中醫

藥發展專署 and make it the sole agency to be responsible for the planning and the development of CM in HK. The Commission could consist of a board of directors, a secretariat and a number of advisory/expert committees. Since its activities span over a number of bureaus, it'd be better for it to report directly to the Chief Executive or Chief Secretary for Administration.

In the following paragraphs, in order to keep the discussion focused, we assume a CMDC is to be established to foster the development of the CMIC. If CMDC were not to be formed, the following ideas can still be applied separately to the relevant government bureaus and agencies.

CMDC's MISSIONS, OBJECTIVES AND OPERATIONS

With the benefits listed in the previous section as a guide, the mission of *CMDC* can be set accordingly "to foster the establishment of a robust, modern, knowledge- and technology-based CM industry in HK and to secure and maintain HK as a *CM international center*."

After consultation with the CM and other stakeholders, CMDC can set up a number of near-term and long-term objectives for itself. Some of the objectives that it can consider are listed in the following table:

Although *CMDC* is an independent agency, however, it should operate in concert and in consultation with other bureaus and agencies, such as the Department of Health, Chinese Medicine Council of HK, JCICM (Jockey Club Institute of Chinese Medicine), Fisheries and Conservation Department, Food and Environmental Hygiene Department, Trade and Industry Department, Customs and Excise Department, HK Productivity Council and HKTDC etc. While all the agencies, institutions and organizations above are expected to contribute one way or another to support CM in general and to maintain HK as an international center of CM in particular, *CMDC* is the umbrella organization that is specifically charged with the responsibilities to develop the CM industry and to foster and coordinate CM-related activities in HK.

More on the Objectives

For clarity purpose, additional information on the *CMDC* objectives is shown below:

1. **MODERNIZATION OF THE CM INDUSTRY:** To meet the *CM globalization* challenge, HK's CM industry must be transformed expeditiously from a traditional industry to a modern one while striving to retain tried-and-true traditional knowledge and practices. A new generation of CM executives

Suggested Objectives for *CMDC*

1. To foster the *modernization of the CM industry* in HK through professional training, business intelligence dissemination, scientific supports, forward-looking and coherent policy, realistic regulations and financial supports
2. To support and promote *ICMCM* as an international trading/exchange platform for CM.
3. To promote the *harmonization* of CM regulations and policies within the Greater China Region
4. To facilitate the development of evidence-based healthcare programs for *integrative medicine* with the CM and western medical practitioners collaborating in the community as well as in hospitals.
5. To develop *CM Specialty Colleges* to enhance modernized CM postgraduate training with knowledge, attitude and skills consistent with Mainland experts' practice
6. To establish an *Informatics Center* consisting of an international multi-dimensional and multi-professional network to generate, disseminate and exchange CM knowledge
7. To establish a *CM Research Council* to commission strategic projects leading to the advancement of CM science, technology, products, education and practice

and workers should be trained to master the modern management skills and CM-related technologies. A centre for CM quality control/verification/accreditation should be set up to support the *Quality-assured CM Trading Centre*. This transition and transformation will require strong supports from the scientific community and a set of reasonable regulations matching the industry's capability to conform as it grows.

2. ICMCM: 7 years after it was launched by MCMIA, ICMCM has now become the only serial international CM mega event that attracts top botanical scientists, government officials and company executives to congregate in Hong Kong to bring themselves up to date with the latest information on the scientific, regulatory and commercial development in CM. Strong reinforcement of this valuable platform from the HK government is needed to ensure HK's hitherto undisputed leadership in the internationalization of CM using this platform.
3. HARMONIZATION: Currently, the Cross Strait Four Regions 兩岸四地 has 4 independent regulatory jurisdictions on CM, each enforcing a different set of rules. This lack of regulatory uniformity has been impeding cross-border and cross-strait CM trades. Hong Kong is the ideal party to initiate an effort to harmonize the regulations of the 4 regions through a number of reciprocation steps. Success in harmonization will not only spur market activities. It will also expose issues of common concerns which can then be addressed by the 4 parties collectively without duplications of efforts.
4. INTEGRATIVE MEDICINE: Minister Chen Zhu 陳竺 of MOH once declared that the healthcare in the 21st century would be a combination of CM with western medicine. The resulting medicine would be better than either one modality on its own. HK is in a unique position to identify the strengths of CM so as to supplement and strengthen the weakness of conventional medicine, particularly in the prevention,

treatment and rehabilitation of major disease burdens. With our expertise in healthcare management and research, we could develop and evaluate evidence-based CM programs for their cost-effectiveness so as to determine their possible impacts on the total healthcare costs, health maintenance of our population and the quality of life of the community. The establishment of CM departments and beds in public and private hospitals would provide choices and accesses to accredited experts in China through "service trading" (服務貿易). In this context, HK can serve as the stepping stone to local and international clients in search of superior CM services.

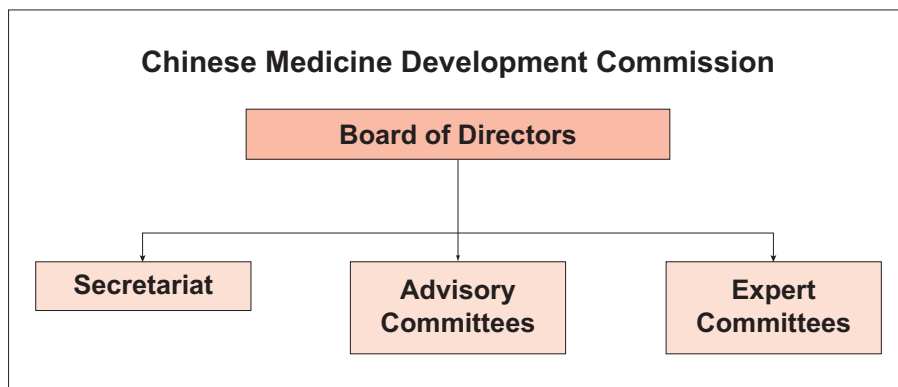
5. INFORMATICS CENTER: During the past decade, a number of CM databanks covering a wide range of subjects such as herbal resources, chemical markers, pharmacognosy, toxicology, CM diagnosis, treatments, herbal formulas, component standards, classical literature and business intelligence have been undergoing development in Hong Kong, Shanghai, Guangzhou, Beijing, Sichuan, Hangzhou and Taiwan etc. However, no effective attempt has been made to weave all these information nodes into a network with shared ontology to facilitate data mining, international search and knowledge generation. Hong Kong, being a leader in information technology and medical sciences in this region, is well positioned to coordinate an effort to create this virtual network. International business intelligence collection by this center will also be essential to enhance the industry's competitiveness.
6. CHINESE MEDICINE SPECIALTY COLLEGES: As a world-renowned center for western medicine, HK has established a robust system for the training, examination and continued professional development for major specialties and sub-specialties through a series of specialty colleges. The MOH in China has deemed it an appropriate model for the Mainland to emulate. The establishment of corresponding Specialty Colleges in CM will similarly help enhance the definition,

standards, mentorship and postgraduate education, leading to a comprehensive advancement of the various fields in CM. We propose that plans should be made to identify CM experts to develop their specialties with a view to form Colleges which could be managed under one roof comparable to the Academy for western medicine.

7. CHINESE MEDICINE RESEARCH COUNCIL: Since 1997, HK and neighboring governments have made more funding available towards CM scientific and clinical researches. However, to date, apparently, no consensual strategic plan for the direction and priority of CM R&D has been developed. As a result, there are duplications and unnecessary competitions among the researchers, resulting in an overall slow progress in CM R&D. Meanwhile, many new fields (such as proteomics, genomics, and metabolomics) and novel research methodologies have been added into the CM R&D arena, giving the researchers more research tools to work with. Therefore, it is time to review HK's CM R&D programs and to design a comprehensive scheme to co-ordinate, commission and fund CM projects. We propose that CMDC should help organize a central expert body, such as, a *Chinese Medicine Research Council*, to prioritize, maximize and optimize HK's investment in CM R&D.

STRUCTURE AND FINANCING OF CMDC

A simple organizational structure for CMDC is proposed on the right. The Board of Director (BoD) shall have the responsibilities to operate and direct all the actions and activities of the Commission. Directives from the BoD to achieve the 7 objectives shall be executed by the Secretariat which will be composed of an Executive Director and a number of staff members. The BoD shall also be supported by a number of advisory or expert committees which provide the BoD with expert consultation for specific tasks or disciplines.



The BoD shall consist of members representing the various sub-sectors constituting the CM community as well as experts in the relevant fields. The Chairmen of the committees could also be eligible as Board members to provide continuity and to enhance communication.

Financial support of **CMDC** could come, at least, from the following 3 sources:

1. Direct government funding
2. Philanthropic and charity donations
3. Proceeds resulting from **CMDC** sponsored/organized activities and the use of **CMDC** services and facilities

It is difficult to estimate the annual budget for CMDC without agreeing on its operational mode and activity scope. However, for a project of this magnitude and significance, the Government should commit substantial capital and recurrent funding commensurate with the anticipated overall long term return on investment.

ACTION ITEMS

The creation of CMDC should be done in a stepwise and consultative manner with the helps of stakeholders, government agencies, legislators and other relevant individuals inside and outside of HK. Therefore, a consultation procedure should be carried out before proceeding with CMDC.

With that in mind, we suggest the following action items to take place and to be completed in about a year:

1. The government appoints a Chinese Medicine Enquiry Group (*CMEG*) to conduct an in-depth study through a series of consultation sessions on the

subject with the help of experts, interested parties and stakeholders.

2. At the end of the study and consultation, the CMMG shall report to the Chief Executive (CE) its findings. The report should include:

1. A detail study result on the national and international conditions relating to the development of a modern CM industry in HK and the promotion of HK as an international centre for CM
2. A set of recommendations regarding the *CMDC*'s organization, funding sources, operations, goals/objectives and mandates
3. A proposed budget for the Commission.

3. Once the plan is completed, C.E. proceeds to seek allocation of the resources and appoint the start-up personnel for *CMDC*.

MONITORING AND ASSESSING THE CMDC PERFORMANCE

The progress of the **CMDC** should be monitored continually and periodically report back to C.E. to ensure it stays on course and to guarantee its effective use of the allocated resources. The following could be used as benchmarks to measure *CMDC*'s performance:

1. International recognition of HK as a CM center with measurable increase in international CM business and scientific traffic through HK
2. Overall confirmation of CM quality and safety improvements by unbiased authorities
3. Establishment of one or more integrative medicine service models in HK with exchange in service and

training with centres of excellence in China.

4. Establishment of a CM informatics centre as an international hub for cooperation in the construction, collation, analysis, dissemination and exchange of CM information.
5. Establishment of Chinese Medicine Specialty Colleges with the development of standards and training programs in CM specialties
6. Establishment of a CM Research Council with measurable increases in the development of novel CM products and advancement of CM culture, philosophy, science and technology.

CONCLUSION

This proposal points out that the recent Central Government's CM policy changes and the improving international receptiveness toward CM are creating an international CM industry and a global CM market. Fortunately, the development of HK's CM in recent years has made it possible for HK to take advantage of the emerging opportunities. However, HK government needs to be a strong supporter to the local CM industry by formulating a comprehensive and consistent policy to modernize the CM industry, to establish the CM infrastructure and to declare HK's firm determination to be an international centre for CM.

Towards these ends, MCMIA proposes that the government should establish and fund an agency, **CMDC**, to implement a plan to build up a modern CM industry and to establish the **CMDC** in Hong Kong.

The modernized CM industry could play a constructive role in the economic restructuring of HK and strengthen its base to face the tumultuous economic challenges of the 21st century. Being a sophisticated knowledge- and technology-based industry, it is expected to create many new high-paying jobs and high returns for Hong Kong, Mainland and other parts of the world. If nurtured properly, the modern CM industry could also become a stout social and economic pillar that brings health and prosperity to the HK citizens in the decades to come.

Date proposed: November 2008

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Recapture of Some Important Events of the Hong Kong Pharmacy Conference 2008

Lee, Chui Ping

Chairlady of the Hong Kong Pharmacy Conference 2008

The 21st Hong Kong Pharmacy Conference was successfully held in the AsiaWorld Expo, Hong Kong on 1st and 2nd of November 2008. The conference theme this year was “One Profession One Dream, Connect to Advance Health Care”, portraying the common will of pharmacists - to collaborate and contribute to a brighter future for health care. With a record high number of 557 registrants from local and overseas, the conference served as a platform to broaden pharmacists’ horizon and to promote collaboration among various health care providers.

This year, the conference organizing committee was honored to have invited many eminent speakers from local and overseas to share on a wide variety of topics. Topics encompassing medication risk management, clinical pediatrics and geriatrics, generics, pharmacogenomics, evidence based medicine, integrative medicine and practice model sharing was covered. One of the theme speakers, Prof Barry Carter from the University of Iowa, USA, gave the audience his remarkable insights on successful implementation of physician-pharmacist collaboration. His speech highlighted the need for stronger data to support collaborative practice that will be acknowledged by other healthcare professionals, and potentially recognized by government authorities when planning for resources allocation in the future.

To increase the content diversity for day 1 program, this year the conference introduced two concurrent theme sessions. Many practicing pharmacists attended the practice-oriented sessions delivered by Prof Ian Wong and Dr Annie Lam. Their

feedback reveals that the speeches were stimulating and relevant. Meanwhile, Prof Vincent Lee’s speech on education reform and Prof Kevin Chan’s speech on Worldwide Development of Chinese Medicine in Pharmaceutical Care provided unique perspectives and ideas to further expand the pharmacy arena.

Both the conference opening ceremony and dinner reception were sparkled off with a spectacular performance many dedicated pharmacists, interns and students. The team leaders, Mr Yip Ho Wah, Chris Lee and Ms Moon Tsang have been extremely dedicated in incorporating innovative ideas that blend in with the conference theme. Behind the stage, the dinner performers attended intensive training sessions on mime during the previous 2 months before conference. Their superb performance fully demonstrated their talents and stunned the audience.

The day 2 conference continued its tradition in delivering more versatile lectures to satisfy the learning needs of attendees. Besides a variety of lecture, many new implementations including the lunch symposiums, issuing of the “CU next year” coupon”, provision of instant translation service and transportation rebates, etc were incorporated this year. All of these could be attributed to the spirit of continuous improvement from every single dedicated members of the conference organizing committee. Of course, our attendees’ feedback over the past years served as the best guidance and stimulation for us to improve.

It is absolutely my honor to have the opportunity to chair the Hong Kong Pharmacy Conference 2008. Sometimes I think conference is quite representative of our profession; characterized by a small group that strives to make things to happen with limited manpower and resources. We do not have any overt recognition for our efforts; and therefore often times we feel frustrated and overwhelmed. Fortunately after months (and years) of hard work, the members in the organizing team have built up a culture of support, friendship and teamwork. To me, what I gained and learnt from conference is definitely much more than what I contributed. I truly hope our spirit had influenced the conference attendees and paved way to more collaborative work in the future. Eventually, “One Profession, One Dream – Connect to advance Health care” will come true.

It was a relief after delivering such a “big” conference this year; meanwhile we also recognize there are still lots of room for improvement. Most of our team members have agreed to stay on with the organizing family this upcoming year, but we also are actively looking for new helps, new ideas and potentially, new friends. Please feel free to contact me at cplee@cuhk.edu.hk if you are interested to join us. We are encouraged by what we have jointly achieved this year, and we promise to make it better next year with our experience earned. The same will hold for our profession. The show must stay on, until the day we are recognized and appreciated.



Chairlady & PPAGC welcoming Dr York Chow



Organizing Committee & guests at conference dinner



Heads of 6 organization at opening ceremony



Dr Chui Ping Lee & VIPs at opening ceremony



dinner performance given by pharmacists



Doctors, Nurses & Pharmacists at dinner performance



Ceremony of connecting to advance healthcare



A full room of participants at lecture

NEW PRODUCTS

Abilify® (Otsuka)

Active ingredient:
Aripiprazole

Presentation:
Abilify tablets are available in 5-mg, 10-mg and 15-mg strengths.

Pharmacological Properties:
Aripiprazole exhibits high affinity for dopamine D₂ and D₃, serotonin 5-HT_{1A} and 5-HT_{2A} receptors. The mechanism of action of aripiprazole, as with other drugs having efficacy in schizophrenia and bipolar disorder, is unknown. However, it has been proposed that the efficacy of aripiprazole is mediated through a combination of partial agonist activity at D₂ and 5-HT_{1A} receptors and antagonist at 5-HT_{2A} receptors.

Indications:
Abilify is indicated for the treatment of schizophrenia, acute manic and mixed episodes associated with Bipolar Disorder.

Dosage and Administration:
Schizophrenia:
The recommended starting and target dose is 10 or 15mg per day administered on a once-a-day schedule without regard to meals.

Bipolar Disorder:
The starting dose of 30mg per day was found to be effective when administered as the tablet formulation.

Contraindication:
Abilify is contraindicated in patients with a known hypersensitivity to the product.

Precautions:
Aripiprazole may be associated with orthostatic hypotension. Seizures occurred in 0.1% of aripiprazole-treated patients with schizophrenia in short-term, placebo-controlled trials. Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents.

Drug Interaction:
Co-administration of ketoconazole (200mg/day for 14 days) with a 15-mg single dose of aripiprazole increased the AUC of aripiprazole and its active metabolite by 63% and 77% respectively.

Co-administration of a 10-mg single dose of aripiprazole with quinidine (166mg/day for 13 days), a potent inhibitor of CYP2D6, increased the AUC of aripiprazole by 112% but decreased the AUC of its active metabolite, dehydro-aripiprazole, by

35%. Aripiprazole dose should be reduced to one-half of its normal dose when concomitant administration of quinidine with aripiprazole occurs.

Co-administration of carbamazepine (200mg BID), a potent CYP3A4 inducer, with aripiprazole (30mg QD) resulted in an approximate 70% decrease in C_{max} and AUC values of both aripiprazole and its active metabolite, dehydro-aripiprazole.

Side Effects:
Commonly observed adverse events include: headache, asthenia, peripheral edema, hypertension etc.
Dose-Related Adverse Events:
Extrapyramidal Symptoms, weight gain in schizophrenia.

Forensic Classification:
P1S1S3

Sebivo® (Novartis)

Active ingredient:
Telbivudine

Presentation:
600mg film-coated tablets

Pharmacological Properties:
Telbivudine is a synthetic thymidine nucleoside analogue with activity against HBV DNA polymerase.

Indications:
Treatment of chronic hepatitis B in patients with evidence of viral replication and active liver inflammation.

Dosage and Administration:
Adults
The recommended dose for the treatment of chronic hepatitis B is 600mg once daily. Sebivo may be taken with or without food.

Renal impairment / insufficiency
Sebivo may be used for the treatment of chronic hepatitis B in patients with impaired renal function. No adjustment of the recommended dose is necessary in patients whose creatinine clearance is ≥ 50 ml/minute.

ESRD patients
Sebivo should be administered after haemodialysis.

Contraindication:
Hypersensitivity to the active substance or any of the excipients

Precautions:
Severe acute exacerbations of hepatitis B have been reported in patients who have discontinued anti-hepatitis B therapy. Hepatic

function must be monitored closely with both clinical and laboratory follow-up for at least 1 year in patients who discontinue anti-hepatitis B therapy.

Drug Interaction:
Since telbivudine is eliminated primarily by renal excretion, co-administration of Sebivo with substances that impair renal function may affect plasma concentrations of telbivudine and/or the co-administered substance.

Side Effects:
Most adverse effects were classified as mild or moderate in severity. Common adverse effects, whether or not associated with telbivudine, were infections of the upper respiratory tract, nasopharyngitis, fatigue and headache.

Forensic Classification:
P1S1S3

Tygacil® (Wyeth)

Active ingredient:
Tigecycline

Presentation:
Each TYGACIL vial contains 50 mg tigecycline lyophilized powder for intravenous infusion.

Pharmacological Properties:
TYGACIL (tigecycline) is a glycylicycline antibacterial

Indications:
TYGACIL is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the conditions listed below for patients 18 years of age and older:
Complicated skin and skin structure infections caused by *Escherichia coli*, *Enterococcus faecalis* (vancomycin-susceptible isolates only), *Staphylococcus aureus* (methicillin-susceptible and -resistant isolates), *Streptococcus agalactiae*, *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Streptococcus pyogenes* and *Bacteroides fragilis*.

Complicated intra-abdominal infections caused by *Citrobacter freundii*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, *Enterococcus faecalis* (vancomycin-susceptible isolates only), *Staphylococcus aureus* (methicillin-susceptible isolates only), *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*), *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides vulgatus*, *Clostridium perfringens*,

and *Peptostreptococcus micros*.

Dosage and Administration:
The recommended dosage regimen for TYGACIL is an initial dose of 100 mg, followed by 50 mg every 12 hours. Intravenous (IV) infusions of TYGACIL should be administered over approximately 30 to 60 minutes every 12 hours.

The recommended duration of treatment with TYGACIL for complicated skin and skin structure infections or for complicated intra-abdominal infections is 5 to 14 days. The duration of therapy should be guided by the severity and site of the infection and the patient's clinical and bacteriological progress.

No dosage adjustment is warranted in patients with mild to moderate hepatic impairment

No dosage adjustment of TYGACIL is necessary in patients with renal impairment or in patients undergoing hemodialysis.

Contraindication:
TYGACIL is contraindicated for use in patients who have known hypersensitivity to tigecycline.

Precautions:
Caution should be exercised when considering TYGACIL monotherapy in patients with complicated intra-abdominal infections (cIAI) secondary to clinically apparent intestinal perforation.

As with other antibacterial drugs, use of TYGACIL may result in overgrowth of non-susceptible organisms, including fungi.

Drug Interaction:
TYGACIL (100 mg followed by 50 mg every 12 hours) and digoxin (0.5 mg followed by 0.25 mg, orally, every 24 hours) were coadministered to healthy subjects in a drug interaction study. Tigecycline slightly decreased the C_{max} of digoxin by 13%, but did not affect the AUC or clearance of digoxin. This small change in C_{max} did not affect the steady-state pharmacodynamic effects of digoxin as measured by changes in ECG intervals.

Concomitant administration of TYGACIL (100 mg followed by 50 mg every 12 hours) and warfarin (25 mg single-dose) to healthy subjects resulted in a decrease in clearance of R-warfarin and S-warfarin by 40% and 23%, an increase in C_{max} by 38% and 43% and an increase in AUC by 68% and 29%, respectively.

Side Effects:
Adominal pain, abscess, fever, headache, hypertension, diarrhea, nausea, vomiting.

Forensic Classification:
P1S1S3

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- ↑ 30% bone volume in 1 year after switching from bisphosphonates ⁵

Additional Benefits

- Relief from back pain ⁶
- Good tolerability profile ⁷
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1. Reginster JY, et al. Osteoporos Int. 2008;19(Suppl 1):S131-S132 (Abstract P311) 2. Reginster JY, et al. Osteoporos Int 2006;17:S11-12. 3. Roux C, Isaia G., Cannata Andia J.B., et al. Ann Rheum Dis. 2007;66(Suppl.11):681 (LB0005) 4. Roux C, et al. J Bone Miner Res 2006;21(4):536-542 5. Busse B, et al. J Bone Miner Res 2007; 22(suppl1):S1-S582 6. Marquis P, et al. Osteoporos Int. 2005;16(suppl3):S54:P223 7. Bruyère O, et al. Ann Rheum Dis 2006; 67:335-339

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- Tolerability comparable to placebo⁸



ARB: Angiotensin receptor blocker
ACEI: Angiotensin converting enzyme inhibitor
CV: Cardiovascular
BNP: Brain natriuretic peptide
*Heart failure (HF) therapy includes beta blocker plus ARB or ACEI

References: 1. Oh BH, Mitchell J, Herron JR, et al. Aliskiren, an oral renin inhibitor, provides dose-dependent efficacy and sustained 24-hour blood pressure control in patients with hypertension. *J Am Coll Cardiol*. 2007;49:1157-1163. 2. Uresan Y, Taylor AA, Kilo C, et al. Efficacy and safety of the direct renin inhibitor aliskiren and ramipril alone or in combination in patients with diabetes and hypertension. *J Renin Angiotensin Aldosterone Syst*. 2007 Dec;8(4):190-8. 3. Villami A, Chrysant SG, Calloun D, et al. Renin inhibition with aliskiren provides additive antihypertensive efficacy when used in combination with hydrochlorothiazide. *J Hypertens*. 2007;25:217-226. 4. Operti S, Yarows SA, Patel S, et al. Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomized, double-blind trial. *Lancet*. 2007;370:221-229. 5. Chrysant SG, Murray AV, Hoppe UC, et al. Long-term safety, tolerability and efficacy of aliskiren in combination with valsartan in patients with hypertension: a 6-month interim analysis. *Curr Med Res Opin*. 2008 Apr;24(4):1039-47. 6. Parving HH, Persson F, Lewis JB, et al. Aliskiren Combined with Losartan in Type 2 Diabetes and Nephropathy. *N Engl J Med*. 2008;358:2433-46. 7. McMurray JJV, Pitt B, Latini R, et al. Effects of the Oral Direct Renin Inhibitor Aliskiren in Patients With Symptomatic Heart Failure. *Circ Heart Fail*. 2008;1:17-24. 8. Gradman AH, Schneider RE, Livi RL, et al. Aliskiren, a novel orally effective renin inhibitor, provides dose-dependent antihypertensive efficacy and placebo-like tolerability in hypertensive patients. *Circulation*. 2005;111:1012-1018.

RASILEZ® Film-coated tablet:
Presentation: Film-coated tablets containing 150 mg and 300 mg of aliskiren. Indications: Treatment of hypertension. Dosage: 150 mg to 300 mg once daily, alone or in combination with other antihypertensive agents. Contraindications: Hypersensitivity to aliskiren or to any of the excipients. Precautions/Warnings: Not recommended with ciclosporin. Not recommended during pregnancy or when planning to become pregnant, to be discontinued if pregnancy occurs. Rare cases of hypotension after initiation of treatment. Close medical supervision in patients with an activated renin-angiotensin system (e.g. volume- and/or salt-depleted patients). Caution in patients with severe renal dysfunction, renal artery stenosis, a history of dialysis, nephrotic syndrome, or renovascular hypertension. Interactions: Monitoring when used concomitantly with furosemide. Interactions with ketoconazole, ciclosporin. Concomitant treatment with drugs that may increase serum potassium levels. Adverse Drug Reactions: Common: Diarrhea. Uncommon/Rare: Angioedema. Laboratory values: decrease in haemoglobin and haematocrit, increase in serum potassium. Note: Before prescribing, please read full prescribing information.

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Aims and Scope of the Journal

The Hong Kong Pharmaceutical Journal (HKPJ) was founded in 1992 and is co-owned by the Pharmaceutical Society of Hong Kong, the Practising Pharmacists Association of Hong Kong and the Society of Hospital Pharmacists of Hong Kong. It is published to facilitate the dissemination and procurement of advanced knowledge in the professional field relevant to all sorts of pharmacy practices. It is published quarterly and four issues per annum. *HKPJ* will consider for publication articles on all aspects of the practices of pharmacy. The Journal is currently divided into several sections as indicated below, but papers or articles which cut across these sections or which are on any other aspect of pharmacy practices will also be considered.

Editorial Comment will be statements on pharmacy related topics of regional or global interest and are covered in a particular issue. This section is written only by managing editors, board members or other invited professionals.

News & Short Communications will cover the latest developments or announcement in pharmacy practices. Comments on any aspects of the profession are also welcome as Letters to the Editor.

Pharmacy Practice will consider articles relevant to the area of regulatory issues, practicing experiences and work experiences.

Over-the-Counter & Health will contain reports on the safety and efficacy aspect and problems arise of medicinal substances sought over the counter.

Drug & Therapeutics will contain reports on the biochemical, pharmacological, molecular mechanistic activities or clinical studies of drug.

Herbal Medicines & Nutraceuticals section will publish papers or articles on the usefulness evaluation of Chinese medicines, functional food or nutraceuticals. Reports of work that employ contemporary scientific methods will be particularly welcome.

Pharmaceutical Technology will focus on any technology relevant to the quality control, manufacturing and delivery of therapeutics. Issues on Good Manufacturing Practices of drug manufacturing are also welcome.

New Products. This section contains brief description of therapeutics recently obtained registration code from the Department of Health in Hong Kong.

BRIEF INSTRUCTIONS FOR CONTRIBUTION:

The editorial board of *HKPJ* welcomes contributions from readers. There is no restriction on the length of the articles to be submitted. They can be written in English or Chinese. The editorial board, however, may make editorial changes to the articles but major amendments will be communicated with the contributing authors prior to publishing. All contributions should be written in a format adopted by the Journal. It is preferable to have the original articles submitted as an electronic file, in Microsoft Word with version indicated and typed in Arial 9 pt. **Authors should refer to "Instruction for Authors" for details in the first issue of each volume before preparing their manuscripts.**

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Great News

Continuing Education Units (CEUs) for Authors of Articles in the *HKPJ*. At the most recent meeting of the Pharmacy Central Continuing-education Committee (PCCC), it was decided that CEU would be awarded to authors of articles published in the *HKPJ*. For each issue, the Editorial Committee, led by the Managing Editor, will choose an article from all the published articles in that issue, for PCCC to use for CE purposes. The author(s) is(are) responsible for setting questions for the approved CE article. Primary authors are entitled to receive 6 CEUs and other co-authors of the same CE article are entitled for 4 CEUs granted by PCCC. For details on how to get CEU, please refer to the article named "PCCC Continuing Education Units (CEU) Accrediting System" [*HKPJ* 2002;11(2):79-80] or visit the PCCC Website at www.pccc.hk.com

Great news to boost the professional standard and recognition of the contributions to the *HKPJ*!



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* Results of a randomized, multicenter, double-blind study of 256 patients with candidemia and/or other forms of invasive candidiasis. Patients received either Eraxis (200-mg loading dose, 100-mg maintenance dose) or IV fluconazole (800-mg loading dose, 400-mg maintenance dose); either agent could be followed by oral fluconazole after ≥ 10 days of IV therapy. Global success required clinical cure or improvement and documented or presumed microbiologic eradication.²

¹ Centre effect considered in statistical analysis

ERAXIS ABBREVIATED PACKAGE INSERT: 1. **TRADE NAME:** ERAXIS for injection 100mg. 2. **PRESENTATION:** Each vial contains 100mg anidulafungin. Powder: White to off-white lyophilized solid; Diluent: Clear colourless solution. 3. **INDICATIONS:** Treatment of invasive candidiasis in adult non-neutropenic patients. It has been studied primarily in patients with candidemia and only in a limited number of patients with deep tissue Candida infections or with abscess-forming disease. 4. **DOSAGE:** A single 200mg loading dose on Day 1, followed by 100mg daily thereafter. Duration of treatment should be based on patient's clinical response. In general, antifungal therapy should continue for at least 14 days after the last positive culture. It is recommended that ERAXIS be administered at a rate of infusion that does not exceed 1.1mg/minute (equivalent to 3.0ml/minute). Infusion-associated reactions are infrequent when the rate of anidulafungin infusion does not exceed 1.1mg/minute. ERAXIS should not be administered as a bolus injection. 5. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, to any of the excipients and/or to other medicinal products of the echinocandin class. 6. **WARNINGS & PRECAUTIONS:** **Efficacy:** (1) not established: in neutropenic patients with candidemia and in patients with deep tissue Candida infections or intra-abdominal abscess and peritonitis. (2) not studied: in patients with candida endocarditis, osteomyelitis or meningitis and known *C. krusei* infection. (3) evaluated primarily: in non-neutropenic patients with *C. albicans* infections and in a smaller number of patients infected with non-*albicans*, mainly *C. glabrata*, *C. parapsilosis* and *C. tropicalis*. Hepatic: increased levels of hepatic enzymes have been seen in healthy subjects and patients treated with anidulafungin. In some patients with serious underlying medical conditions who were receiving multiple concomitant medicines along with anidulafungin, clinical significant hepatic abnormalities have occurred. Isolated cases of significant hepatic dysfunction, hepatitis, or worsening hepatic failure have been reported. Patients with increased hepatic enzymes during anidulafungin therapy should be monitored. Infusion-related: Care should be taken when co-administering anidulafungin and anesthetic agents due to the possibility of exacerbation of infusion-related reactions. Alcohol content: Ethanol could be harmful for those suffering from alcoholism, pregnant or breast-feeding women, children, and those with liver disease or epilepsy. May alter effects of other medicines and impair the ability to drive or use machines. Fructose content: Patients with rare hereditary problems of fructose intolerance should not take this medicine. 7. **INTERACTIONS:** Not a clinically relevant substrate, inducer, or inhibitor of cytochrome P450 (1A2, 2B6, 2C8, 2C9, 2D6, 3A). No dosage adjustment of either medicinal product is recommended when anidulafungin is co-administered with cyclosporin, voriconazole or tacrolimus, and no dosage adjustment for anidulafungin is recommended when co-administered with amphotericin B or rifampin. 8. **PREGNANCY AND LACTATION:** ERAXIS is not recommended in pregnancy as there are no data in pregnant women. It is not known whether anidulafungin is excreted in human breast milk. A decision on whether to continue/discontinue breastfeeding or therapy with anidulafungin should be made taking into account the benefit of breast-feeding to the child and the benefit of anidulafungin to the mother. 9. **SIDE EFFECTS:** Adverse reactions were typically mild to moderate and seldom led to discontinuation. Infusion-related adverse reactions have been reported, such as flushing/hot flash, pruritus, rash and urticaria. The common ($\geq 1/100$ to $< 1/10$) drug-related adverse reactions include conjunctivopathy, convulsion, headaches, diarrhoea, vomiting, nausea, blood creatinine increased, rash, pruritus, hypokalaemia, flushing, stannic aminotransferase increased, blood alkaline phosphatase increased, aspartate aminotransferase increased, blood bilirubin increased & gamma-glutamyltransferase increased.

References: 1. Reboli AC, Rotstein C, Pappas PG, et al, for the Anidulafungin Study Group. Anidulafungin versus fluconazole for invasive candidiasis. *N Engl J Med.* 2007; 356:2472-2482. 2. Eraxis [package insert]. Hong Kong: Pfizer Corp. HK Ltd.; 2008. 3. Vazquez JA. Anidulafungin: a new echinocandin with a novel profile. *Clin Ther.* 2005;27:657-673.

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