香港中文大學－新界東醫院聯網臨床研究統籌處通訊
Joint CUHK-NTEC CRMO Newsletter
Issue 10 Dec 2017

守護兒童健康無疆界
Protecting Children's Health Without Border

卓越研究團隊掠影－香港中文大學兒科學系
Research Unit Highlight - Department of Paediatrics (CUHK)

做好今天預防工作　為兒童未來打好基礎
Do Prevention Well Today, Eye On Children's Future

香港中文大學醫學院兒科學系一直重視兒童的健康成長，對兒童的身體成長、智能發展、精神及情緒健康、營養飲食以及疾病的預防等的兒童社區醫學都是他們的一些重點關注範疇。本著「預防勝於治療」理念，為兒童的未來健康著想，中大兒科學系近年進行了許多與疫苗相關的大型臨床研究，其中包括人類乳頭瘤病毒疫苗（簡稱HPV 疫苗，又稱子宮頸癌疫苗）、輪狀病毒疫苗、流感疫苗等。

Department of Paediatrics (the "Department") of the Chinese University of Hong Kong (CUHK) has been concerned with child health in the community. Growth, intellectual development, psychological and mental health, nutrition, disease prevention are some of the focus areas of community medicine within paediatrics. Based on the principle "Prevention is better than cure" and the benefit of the children's health in the future, the Department has conducted a number of large scale vaccine clinical trials in recent years. The vaccine trials include human papilloma virus (HPV) vaccine, rotavirus vaccine and influenza vaccine.

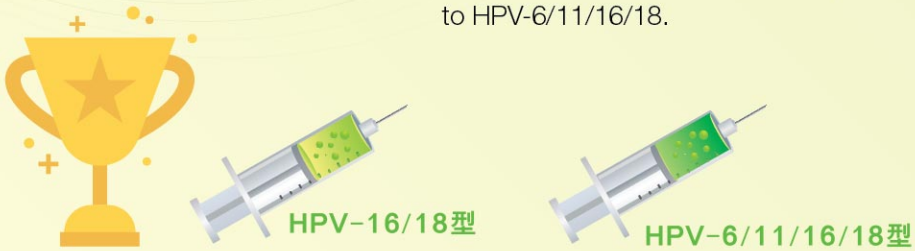
腸胃炎是兒童成長期的常見疾病，在香港被視為普通病痛；然而，因感染輪狀病毒而致兒童死亡的人數每年高達215,000人，大部份死亡個案發生在發展中國家。有見及此，中大兒科學系與新加坡及台灣的研究團隊合作，自2002年展開一項評估輪狀病毒疫苗的安全及成效的大型多中心臨床研究，為期3年的研究共招募超過一萬名幼兒參與。研究結果顯示，疫苗在亞洲地區能有效預防由輪狀病毒引致的嚴重腸胃炎(Rotavirus gastroenteritis, RVGE) 高達96.1%。在2014/15輪狀病毒流行季節期間，中大兒科學系亦在本地進行首個輪狀病毒疫苗的實際成效研究，結果同樣顯示，疫苗能預防5歲以下兒童因感染病毒而住院達90%。

Gastroenteritis is very common in children during their childhood and is regarded as a mild disease in Hong Kong. However, rotavirus gastroenteritis causes 215,000 deaths of which most are in developing countries annually. From 2002, the Department collaborated with Singapore and Taiwan to conduct a 3-year large-scale multicenter clinical trial to assess the safety and efficacy of the rotavirus vaccine. This study recruited more than 10 thousand of infants. The results showed that the vaccine could provide high level of protection against severe rotavirus gastroenteritis (RVGE) (96.1% efficacy) in Asia. The Department also conducted the territory's first study on real-world effectiveness of rotavirus vaccine during the peak season of rotavirus in 2014/2015 in Hong Kong. The results showed that rotavirus vaccine can prevent about 90% of hospitalizations of children below 5 years of age.

輪狀病毒疫苗在亞洲能有效預防嚴重腸胃炎達96.1%
Rotavirus vaccine can protect against RVGE in Asia (96.1 % efficacy)

根據美國國家癌症研究所資料，約7成的子宮頸癌是因持續感染人類乳頭瘤病毒（ HPV ）16及18型而引致。在2011－2015期間，中大兒科學系聯同全球21個臨床研究中心，就市面HPV-16/18型及HPV-6/11/16/18型兩款 HPV 疫苗，邀請1075位受試者進行一項疫苗安全性及引起免疫的能力比較的隨機對照研究；結果顯示HPV-16/18型疫苗在誘發抗體反應比HPV-6/11/16/18型疫苗較優勝。

According to the information from National Cancer Institute, HPV type 16 and 18 are responsible for about 70% of all cases of cervical cancer. In 2011-2015, the Department conducted a randomized trial with 21 sites to compare the immunogenicity and safety of HPV-16/18 vaccine and HPV-6/11/16/18 vaccine. After analyzing the results from 1075 participants, it concluded that the HPV- 16/18 vaccine could elicit superior antibody response to HPV-6/11/16/18.



HPV-16/18型疫苗在誘發抗體反應比HPV-6/11/16/18型疫苗較優勝
HPV- 16/18 vaccine could elicit superior antibody response to HPV-6/11/16/18

除進行本地的研究外，中大兒科團隊亦心繫世界各地兒童的健康。他們夥拍世界衛生組織研究團隊，對5歲以下兒童患百日咳的預測方法再重新檢視，為各國在籌劃應對兒童患百日咳的政策上，提供一個更準確的預測，結果已刊登於 *The Lancet Infectious Diseases*〈刺針傳染病醫學期刊〉。

In addition to conducting local studies, the Department also cares the children's health around the world. In collaboration with a research team at World Health Organization (WHO), they revised the model to provide a more accurate estimation of pertussis in children younger than 5 years, and hence improve country-level decision making in pertussis control. This study has been published in *The Lancet Infectious Diseases.*

問到有什麼動力推動中大兒科從事兒童的疫苗研究時，學系系主任梁廷勳教授說：「疫苗對孩童健康有著長遠的影響。以乙型肝炎疫苗為例，自1988年開始，香港政府為所有嬰兒提供免費乙型肝炎疫苗注射；據香港衞生防護中心最新統計，在2015年只有2位年齡介乎15-24歲的人士確診乙型肝炎，人數比20年前少了22倍。」梁教授繼續說：「雖然大眾未能即時受惠於臨床研究，但研究結果能提供制定日後政策的基礎，對社會有著深遠的影響。同樣，子宮頸癌疫苗的研究顯示，它能有效預防子宮頸癌發生。若該疫苗能納入香港兒童免疫接種計劃內，不單接種人士獲益，長遠上亦能減輕政府在治療子宮頸癌上的醫療負擔。」

梁廷勳教授希望政府在保障兒童健康的議題上有長遠計劃
Professor Leung Ting Fan hopes that HK government has long-term planning in protecting children's health

從事輪狀病毒研究多年的臨床專業顧問倪以信教授亦抱著同一信念，倪教授說：「在高收入地區如香港、新加坡等地因輪狀病毒導致兒童死亡的個案雖不多，但感染病毒而住院的病童及其照顧者所受的肉體和精神苦況，也不容忽視。我們正積極透過不同途徑，從研究實證和經濟效益等角度，游說香港及各國政府將輪狀病毒疫苗納入兒童免疫接種計劃內。」

倪以信教授致力游說各國政府將輪狀病毒疫苗納入兒童免疫接種計劃
Professor Tony Nelson has been persuading governments to incorporate the rotavirus vaccine into their regular CIP

So, what is the motivation that drives the Department to study vaccines in children?

Professor Leung Ting Fan, the Chairman of the Department of Paediatrics said, "Vaccine has long-term impact on children's health. Take Hepatitis B vaccine as an example, the Hong Kong government has provided free Hepatitis B vaccination for all newborns in Hong Kong since 1988. According to the latest statistical report from Centre of Health Protection of Hong Kong, only 2 people aged between 15- 24 were diagnosed with Hepatitis B in 2015. This figure is less 22 times as compared with 20 years ago". He continued, "The public may not benefit from the clinical trial immediately, but the results can provide evidence for drawing up the policy, and hence has far-reaching influence on the society. The results of HPV vaccine study showed that HPV vaccine can protect against cervical cancer effectively. If HPV vaccine can be incorporated into the Hong Kong Childhood Immunisation Programme (HKCIP), it is not only beneficial to those that get vaccination, but also alleviates government's burden in the medical expense of cervical cancer treatment".

Professor Tony Nelson, Clinical Professional Consultant of the Department of Paediatrics, also shares the same vision. Prof. Nelson said, "The mortality of rotavirus illness is very low in high-income countries such as Hong Kong and Singapore. But the physical and psychological burden of hospitalization caused by rotavirus infection influences both children and their parents/ carers. We have been working hard to persuade the Hong Kong government as well as those in other countries to incorporate rotavirus vaccine into their regular immunisation programmes using study evidence and economic evaluations".

迎難而上 締造有利科研環境
Take On The Challenges, Create Better Research Environment

中大兒科在從事大型研究上面對不少挑戰。梁教授說：「其中一個困難是向孩子父母解釋為何要做臨床研究，因兒科臨床研究顧及的層面包括孩童及其整個家庭。曾有一例子，縱然父母同意孩子參加臨床研究，最終因祖父母反對而退出。」另一挑戰就是人手問題，大型的臨床研究需要大量的人手協助。倪教授說：「幼童經常因輕度疾病而入院。在從事輪狀病毒疫苗研究期間，研究人員每天都要在HA CMS 系統尋找參與研究的1200個小孩有否入院的記錄，並每2星期致電父母跟進小孩曾否入住私家醫院，一旦證實曾經住院，便要在獲悉後24小時內向CREC提交嚴重不良事件(SAE)報告，工作量之大可想而知。」

The Department has many challenges ahead when they are conducting large-scale clinical trials. Prof. Leung said, “Explaining the reason for conducting clinical trial to parents is one of the challenges. Children as well as their whole family are needed to take into considerations in paediatric research. There was a case, a child withdrew from our previous study because of the opposition from its grandpa, even if both parents agreed their child to participate the study”. Great manpower demand is another issue in conducting large scale studies. Prof. Nelson said, “Young children are admitted into hospital often because of mild diseases. During the study period, we needed to check the hospitalization records of our 1200 subjects via the HA CMS system everyday. We also phoned the parents twice a month to confirm if their children had been admitted to a private hospital. In case of any hospitalization, we are required to send the Serious Adverse Event (SAE) report to Clinical Research Ethics Committee (CREC) within 24 hours of being alerted of the event. The workload was really heavy.”

中大兒科建立了一支有10多位富經驗的兒科護士及研究員的研究團隊
The Department has established a clinical trial team with experienced paediatric research nurses and research assistants

中大兒科在週末向醫管局借用空置的兒科候診大堂作研究覆診用
The Department borrowed a vacant HA paediatric clinic for a trial visit on Saturday

問到為何兒科臨床研究前線工作多是由護士負責時，梁教授解釋道：「父母對臨床上實踐的問題有很多的關注，例如怎樣在嬰孩的小手臂上抽血？要抽多少血？抽血會否影響嬰孩等等？再者，父母比較信賴醫護人員，所以我們的前線人員多是研究護士。」為此，兒科建立了一支10多位富經驗的兒科護士和研究員組成的團隊。梁教授說：「以之前參與評估配方奶粉的研究為例，單一次的覆診，我們就要處理超過100個受試者家庭。由於參與人數眾多，我們需要在星期六借用醫管局(HA)的兒科候診大堂，作會見受試者家庭之用。我們能順利完成該研究，實有賴研究團隊的護士和醫管局的幫助。

Research nurses are mostly found on the frontline in paediatric trial. Why?

Prof. Leung explained, “Parents have lots of concern regarding the clinical practice. For example: How can we phlebotomize from the baby’s small arm? How much blood would be drawn? Does the phlebotomy affect the baby? In addition, parents generally trust the healthcare professionals; therefore, our research nurses are on the frontline of the clinical trials”. The Department has established a team with more than 10 experienced pediatric nurses and research assistants. Prof. Leung said, “Take the example of last formula milk study, we handled more than 100 families in a single visit. Because of the high participation number, we borrowed the vacant Hospital Authority (HA) pediatric clinic to meet the families on Saturday. We can successfully complete the study because of the participation of our enthusiastic nurses and the help from HA”.

中大兒科亦為臨床研究建立中央協調小組，為進行臨床研究的醫生、護士提供行政和統籌等支援。除此之外，兒科學系亦透過不同方法，積極鼓勵及幫助醫管局醫生參與臨床研究。梁教授說：「主要研究者(PI)要承擔研究上的所有責任及風險，大學做研究的旗幟清楚鮮明；相比醫管局來說，外界比較接受大學研究人員進行研究。有見及此，中大同事都會擔起主要研究者角式，並邀請醫管局同事擔任合作研究者(Co-I)。」

The Department has also established a core team to provide administrative support and coordination for the investigators and the nurses. In addition, the Department actively encourages HA clinicians to join the research by different means. Prof. Leung added, "Principal Investigator (PI) is ultimately accountable for all trial-related responsibilities and risk. The direction of the University in conducting research is definite. The public generally accepts the university staff to conduct research than that of the HA. In view of this, our university staff often takes the PI's role and invites HA staff to be the Co-Investigator (Co-I)".

對於研究資助和經費來源，梁教授說：「我們是最基層的一層；基於一些歷史、安全和倫理因素，不論是政府資助或是廠商贊助，在兒童開展藥物的研究也不多。話雖如此，我們也不會為做而做。參與藥廠/奶粉廠的研究是完全取決其臨床前的研究，是否可信及有意義。至於一些罕見遺傳病如戈謝病Gaucher's disease，由於藥廠在這方面的投入不多，我希望政府能給予多些資源去支持這類研究。」

For the sources of research grant and funding, Prof. Leung said, "Due to the historic, safety and ethical issues, the research money for conducting drug trial in pediatrics are insufficient from both government and pharmaceutical companies. Nevertheless, we solely consider the significance and the credibility of the preclinical research data before engaging in any research sponsored by pharmaceutical company or milk powder manufacturer. As there is not much support from pharmaceutical company to study orphan diseases, e.g., Gaucher's disease, we hope government could provide more resources to support the research of these orphan diseases".

香港政府科研政策較關注本地的研究，並傾向投放在可預計的研究項目上。然而，倪教授仍堅決致力改善全球兒童的健康問題；他對普世兒童的關注緣自在津巴布韋、馬拉維、南非等窮困地區及新西蘭等地工作。倪醫生說：「要在香港取得經費探討環球性的問題殊不容易。幸運地，很多的輪狀病毒研究取得Bill & Melinda Gates Foundation 的資助。事實上，世界衞生組織 (WHO)、美國疾控及預防中心(USCDC)都有為環球性的健康議題提供研究經費。這類基金會或組織會採用另一角度；就如Bill & Melinda Gates Foundation會向『有趣』但有風險的研究提案提供研究經費。很多這類研究項目未必有利於獲取研究經費，卻可能對兒童有益。」

The research policy of Hong Kong Government tends to focus on local issues for prospective research projects. This is not a good news to the investigator like Prof. Tony Nelson who has a strong commitment to address the global health problems of children. His global commitment comes from his working experience in New Zealand and the poor countries like Zimbabwe, Malawi, and South Africa. Prof. Tony Nelson said, "It is difficult to get the money for global issues from Hong Kong. However, it is lucky that much rotavirus vaccine research gets sponsorship from Bill & Melinda Gates Foundation and there are many opportunities and money around the world for global issues, such as World Health Organization (WHO) and the Centre for Disease Control and Prevention of United States (USCDC). Those foundations and organizations choose different approaches. For example, Bill & Melinda Gates Foundation may fund projects that are risky but interesting. Some research studies may not be good for obtaining grants, but they may be good for children".

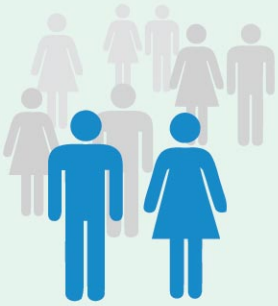
縱然面對很多的挑戰，憑著守護孩童健康的信念，梁教授、倪教授以及其他中大兒科學系人員，會繼續堅持改善香港以至全球兒童的健康。

Although Prof. Leung, Prof. Nelson and other colleagues are facing many challenges, their belief inspires them to improve the children's health endlessly without border.

登記臨床研究於公共領域事宜 (一)
Clinical Trial Registration in Public Domain (Part1)

CRMO自今年8月29日透過電郵發出有關於公共領域登記臨床研究的提示後，我們收到不少查詢此登記的目的及程序。今期，我們先解答一部份收到的疑問。

On 29 Aug 2017, an email reminder was sent from CRMO regarding the clinical trial registration requirements. We have received numerous enquiries regarding the purposes and procedures for clinical trial registration. In this issue, let's answer some of the questions we received.



1.登記臨床研究於公共領域的最主要目的是什麼?
What are the primary purposes of registering our clinical studies in a public registry?

- 為臨床研究提昇透明度，並為患者、家屬、患者群體和其他人士提供臨床研究信息
- 負面或沒有結果的研究往往不被公佈，此要求的目的正是為解決“通報上的偏見”這類問題
- To provide increased transparency and access to clinical trial information for patients, families, patient groups and others;
- To address the problem to “reporting bias” where negative or null results were less likely to be published.

2.於公共領域登記臨床研究是何時成為強制性的要求?
When did this requirement become mandatory?

- 這項要求於1997年首次制定為美國聯邦法例
- 國際醫學期刊編輯委員會 (ICMJE) 自2005開始要求為臨床研究進行登記
- 於2006年，世界衛生組織 (WHO) 申明應為所有臨床研究進行登記
- 自2008年起，“赫爾辛基宣言”（世界醫學協會）也加入為臨床研究進行登記的要求
- The requirement was first made into a US federal law in 1997
- International Committee of Medical Journal Editors (ICMJE) began requiring trials to be registered since 2005
- In 2006, the World Health Organization (WHO) stated that all clinical trials should be registered
- The trial registration requirement was also included in the Declaration of Helsinki (World Medical Association) since 2008

ICMJE
INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

3.如我的研究沒有登記在公共領域上會有什麼後果?
What are the possible consequences if my study were not registered?

- ICMJE 自2005年7 月1 日開始要求為臨床研究進行登記。如未曾為你的研究進行登記，那些遵循 ICMJE 建議的醫學期刊未必接受你的研究手稿
- The ICMJE began requiring trials to be registered since 1 Jul 2005. If your study was not registered, manuscripts might not be accepted by medical journals following the ICMJE Recommendations.

通告 Announcement

最新消息: 藥物臨床試驗質量管理規範 (GCP)線上測驗

由2018年1月2日起，GCP線上測驗將會全年開放。如通過測驗，你將會即時收到合格証書。

請注意測驗的連結將保留不變，詳情如下:

- 連結: http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/Quiz.aspx（須事先進行登記）
- 舉辦日期: 全年開放
- 合格分數: 80%
- 測驗限時1小時

Update of GCP online test

The online GCP test will be available all year round starting from 2 Jan 2018. If you pass the test, you will receive the certificate immediately.
Please note the test link is the same as before with details below:

- Link: http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/Quiz.aspx (Pre-registration is required)
- Date: All year round
- Passing score: 80%
- Time limit: 1 hour

線上參考資料

GCP 已於2016年11月作出更新! GCP 最新修訂版本(E6)、國家食品藥品監督管理總局（CFDA）GCP、威爾斯親王醫院復甦手冊及其他參考資料均可在CRMO 網頁下載http://intranet.crmo.med.cuhk.edu.hk/DownloadLinks/StudyRefMaterials.aspx。

如你對我們之前所舉辦的工作坊感興趣，你可瀏覽http://intranet.crmo.med.cuhk.edu.hk/DownloadLinks/WorkshopSlides.aspx 下載投影片。如需協助下載工作坊投影片，歡迎聯絡我們。

Online Reference Resources

Good Clinical Practice (GCP) has been updated in Nov 2016! You can visit our website at http://intranet.crmo.med.cuhk.edu.hk/DownloadLinks/StudyRefMaterials.aspx to download the latest version of GCP, i.e. (E6) and other reference materials such as GCP guidelines from CFDA and PWH resuscitation manual.
If you interest in our previous workshops, you can download the slides at http://intranet.crmo.med.cuhk.edu.hk/DownloadLinks/WorkshopSlides.aspx . You are welcomed to contact us if you need assistance in accessing our workshop slides.

新標準操作程序 (SOP) 及服務– 臨床研究統籌處臨床研究監查

CRMO-SOP 新增了3份與臨床研究監查服務相關的SOP，分別是（1）臨床研究啟動訪視，（2）臨床研究進行中的監查及（3）臨床研究結束訪視，並於2017年10月23 日生效。

請注意，這套SOP只供CRMO內部使用，CRMO 以外的同事無須就這3份SOP進行培訓。

是次CRMO推出的臨床研究監查服務為收費項目，如想進一步獲得更多資訊，歡迎致電3505 4284 與我們聯絡。

New CRMO SOPs and Service: CRMO Clinical Trial Monitoring

CRMO has launched 3 new Standard Operating Procedures (SOPs) with effect from 23 Oct 2017. They are related to CRMO monitoring service on (1) Site Initiation, (2) Clinical Trial Monitoring, and (3) Site Close-Out.

Please note that these SOPs are applicable to CRMO internal only. Colleagues outside CRMO do not need to train on these SOPs.

CRMO is rolling out a new paid service on Clinical Trial Monitoring. Please feel free to contact us at 3505 4284 for more details.

工作坊 Workshops

報讀臨床研究入職培訓班的分享

我們很高興能透過入職培訓班向不同範疇的同事，如基礎科學、護理、管理和其他專職部門分享我們的臨床研究經驗。我們不妨看看他們的分享。

Sharings for Clinical Research Induction Program

Through the program, we are pleased to share our experience of clinical research with our colleagues from different background such as basic science, nursing, management and other professionals. Let's see our participants' sharings.

我從這個培訓班認識了很多有關GCP的知識。富經驗的講者能對我的疑問能給予適時的回答。教學的投影片和材料十份實用。我強烈推薦這個課程給有興趣進行臨床研究的每一位。

I learned a lot about what good clinical practice (GCP) is from this program. The speakers were knowledgeable and responsive to my questions in a timely manner. The PowerPoint and program material were well made and useful. I would strongly recommend this program to any other who is interested in conducting clinical research.

整個臨床研究是一個充滿挑戰的旅程。我們期盼能透過這個課程，讓同事對臨床研究有全面的認識。此培訓班定於每月第一個星期五（特殊情況除外）舉行。第7次臨床研究入職培訓班將於2018年1月5日再次舉行。如有任何關於課程的查詢，歡迎聯絡我們；您也可在以下連結直接登記參加 http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/InductionProgram.aspx。

Clinical research is a challenging journey. We hope our colleagues have an comprehensive overview of this journey through our program. This program is often held on the first Friday of every month (except for some special circumstances). The 7th induction program will be run on 5 Jan 2018. Please feel free to contact us for more information or do the registration directly at http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/InductionProgram.aspx

午餐研討會：藥物開發－由實驗室研究到臨床應用

從實驗室分離到臨床應用，每個新的化合物都必需經過一系列嚴謹的測試和研究才能成為藥物並推出市場應用。

我們很高興能邀請生物醫學學院關耀華教授，藥劑學院院長左中教授及內科及藥物治療學系陳重娥教授就藥物開發過程中的臨床前測試、配方設計及臨床研究等範疇給同事一個概覽。工作坊將於2017年12月12日舉行。你可到CRMO網頁http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/DrugDevelopment.aspx 獲取詳情並登記參加。

Luncheon Seminar: Med Talk: Drug Development from Bench to Bedside

From isolation to clinical application, each new chemical entity has to go through a series of rigorous tests and studies before being marketed as a drug.

On 12 Dec 2017, we are delighted to have our honorable speakers Prof. KWAN Yiu Wa (School of Biomedical Sciences), Prof. ZUO Zhong (School of Pharmacy) and Prof. Juliana CHAN (Department of Medicine & Therapeutics) to give our colleagues an overview of drug development process focusing on laboratory tests, formulation strategies and clinical trials. You can get more details and register the workshop at CRMO website http://intranet.crmo.med.cuhk.edu.hk/CRMCApps/DrugDevelopment.aspx

聯絡方法 Contact us

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