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香港醫務化驗學會 Hong Kong Institute of Medical Laboratory Sciences

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On behalf of the Council, I wish all our members a happy and prosperous year of the Tiger!

In this issue, we have a number of articles that are both informative and educating. While most of us in Hong Kong are deeply concerned (or worried) with the approaching of the swine flu, Dr Kent Tsang's timely article on the subject should pacify the people at large. There is a detailed historic review of the novel influenza A (H1N1), symptoms, mode of infection, strategies of self protection, including vaccination, and a very up to date account of the current situation worldwide in facing this pandemic, though it does not help us decide on the vital issue: "To Jab or Not to Jab". Ms Hermia Lam continues with her systematic approach to purchasing new laboratory equipment. In fact, there are points in the many salient points she has mentioned. They should be useful not only to the novice managers, but also a valuable reminder to experienced professionals to areas they might have overlooked. The journal review article on P. knowlesi by Ms Nancy Wong is very interesting and stimulating. The great morphological similarities with P. malariae, and P. falciparum to a certain extent, make the diagnosis of P. knowlesi by microscopy almost impossible. The importance of differentiating between these species is because P. knowlesi can easily reach dangerously high and lethal densities. Laboratory workers and clinicians alike should be aware of this emerging fifth human malaria parasite.

In recent years, HKIMLS is quite active in conducting conferences, particular among the Chinese on both shores of the Strait. The article on the practice of the medical laboratory science profession in Taiwan, including details of its formal university course and professional training, is very informative. It is written by a very senior council member of our Institute. 2010 is the Election Year for HKIMLS. Written by another senior council member, the infrastructure of the Council is clearly displayed. The need for "exchanged transfusion" in the Council is well emphasized. Do come and join the Council.

T T Cheung,
Editor

選舉年

不經不覺，自本學會的前身“香港醫事技術學會”於 1966 年成立至今，已經踏入第 45 個年頭了。以歲數來計算，雖然正值盛年，但好一些孕育他的老前輩，早已離開我們，另一些於近十數年間陪伴他成長的委員們，亦都行將退休了。

日漸年老的學會就算不需打羊胎素，也需要換換血，好讓新血令他更加充滿活力與幹勁。

適逢今年是兩年一度的選舉年，改選委員會即將成立，並會寄交提名表格給擁有選舉及被選權的會員們〔高級會士、會士和普通會員〕。屆時懇請各位有志於貢獻更多力量的會員踴躍提名和參選，一起推廣及發展醫務化驗技術，促進相關教育及訓練的發展，鼓勵同業互相合作，以提高專業水準。

經會員們選出的理事將會互選成為正副會長及下述各個委員會的正副主任。

秘書及管理委員會：負責擬訂及統籌處理本會文件；保管本會文卷；記錄各項會議議案；保管本會公印。

財務委員會：負責本會一切款項收支及保管一切單據及賬目；每月向理事會匯報財政狀況；編制年結，送交會計師稽核，並呈報會員大會、公司註冊處和稅務局。

學術委員會：定期舉辦學術活動；統籌有關學術事宜。

福利委員會：負責籌辦會員之一切康樂及聯誼活動；統籌會員之福利事宜。

會籍委員會：辦理會員入會及退會手續，並審查申請者之資歷；保管會員名冊及負責會員資料之保密；統籌會籍之推廣事宜；維繫各個化驗室的聯絡代表。

出版及通訊委員會：統籌、編輯、印製和分發本會的期刊和通訊。

學會極為需要一些新血的加入，群策群力，共同創造醫務化驗專業更美好的明天。

筆者再次懇請各位會員踴躍提名和參選，亦歡迎有興趣參加各委員會的會員們發送電郵到 info@hkimls.org 與我們聯絡。

Novel Influenza A (H1N1) Pandemic: are you prepared ?

KS Tsang

Hong Kong Institute of Medical Laboratory Sciences Quality Assurance Programme

Influenza pandemics recur periodically yet unpredictably. They spread to all parts of the world very quickly, usually in less than a year and tend to recur in second and sometimes third waves, and may cause more severe diseases in subsequent waves leading to high morbidity and mortality and great social and economic disruption. In human history, there were four influenza pandemics namely, Spanish flu in years 1918-1919, Asian flu in years 1957-1958 and Hong Kong flu in years 1968-1969. It is estimated that Spanish flu has killed 20-40 million people worldwide, a greater toll than that of World War I. In the last pandemic of Hong Kong flu in years 1968-1969, there were approximately 15% of Hong Kong population affected.

On 18th March 2009 onwards, the Federal District of Mexico began picking up cases of influenza-like illness. The number of cases rose steadily. On 23rd April 2009 there were more than 854 cases of pneumonia from the Mexico capital and approximately 7% (59/854) died. In San Luis Potosi of central Mexico, 13% (3/24) deaths of influenza-like illness were reported. On 24th April 2009 the US Government announced seven confirmed human cases of swine-origin influenza A/H1N1 (five in California and two in Texas) and nine suspect cases. Eighteen cases in Canada were laboratory confirmed as the Mexican type and 12 of them were genetically identical to the swine-origin influenza A/H1N1 viruses from California, USA. The swine-origin influenza A (H1N1) viruses, which spread geographically to multiple communities through rapid and frequent international travel, were not previously detected in pigs or humans. On 25th April 2009, Dr Margaret Chan, the Director-General of the World Health Organization (WHO) commented the event a public health emergency of international concern under the rules of the international health regulations.[1] On 11th June 2009, the WHO declared that the influenza pandemic was caused by the novel swine-origin influenza A (H1N1) virus (S-OIV A).

Symptoms of the novel influenza A (H1N1) are usually similar to those of human seasonal influenza and include fever, cough, sore throat, runny nose, muscle pain and headache. The only differentiating characteristics are nausea, vomiting and diarrhoea in some infected patients, which are rarely encountered in patients contacting seasonal influenza. The transmission of the novel influenza A (H1N1) virus among people is mainly through coughing or sneezing. It is advisable to wash hands thoroughly with soap and water on a regular basis, and seek medical attention, should any symptom of influenza-like illness develop. There is no risk of the novel influenza A (H1N1) from consumption of well-cooked pork and pork products.

Schools in 15 countries were closed for the summer of 2009. Strategic measures were implemented to close again if the pandemic of the novel influenza A (H1N1) worsens. Hong Kong has issued the most specific policy. School classes have to be suspended for seven days if 10% of students become sick with novel influenza A (H1N1), if one percent of students are admitted to hospital, or if two or more students are admitted to intensive care or die.

The four influenza pandemics were characterized by a shift in the virus subtype.[2] The recent influenza pandemic was caused by a swine-origin influenza virus A/H1N1 (S-OIV) which contains a novel constellation of gene segments of viruses found in swine and probably arose through re-assortment of two viruses of swine origin.[3,4] It is understandable that mutants of the novel influenza A (H1N1) virus will soon develop.

As of 3rd January 2009, worldwide more than 208 countries/territories/communities have reported laboratory confirmed cases of novel influenza A (H1N1), claiming at least 12,799 lives.[5] Figure 1 shows the affected countries and deaths. The actual number of fatal cases may be under represented as many deaths are never tested or recognized as novel influenza A (H1N1)-related. A report from the US President's Council of Advisors on Science and Technology pointed out that the novel human influenza A (H1N1) virus could infect nearly half the US population over the winter flu season resulting in 1.8 million hospitalisations and 90,000 deaths.[6]

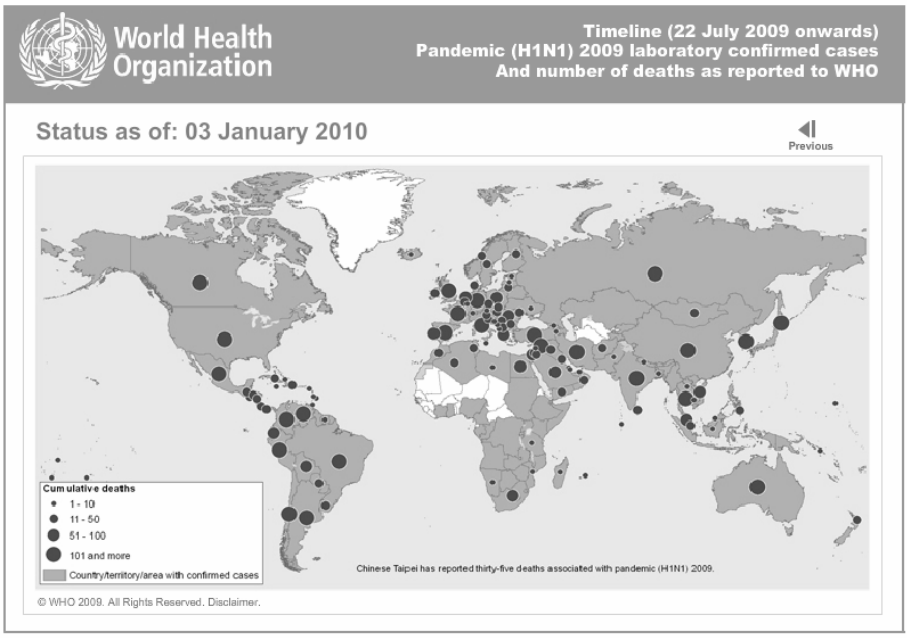

Figure 1. Affected countries and death of Pandemic H1N1 as of 3rd January 2010 (http://gamapserver.who.int/h1n1/cases-deaths/h1n1_casesdeaths.html)

Vaccination is the only way to dampen the influenza pandemic and protect people from contracting illness during pandemics. On 9th June 2009, The Executive Council of Hong Kong Government Special Administrative Region endorsed a vaccination programme for novel influenza A (H1N1). The programme involved procuring vaccines for health workers, children aged from six months to six years, seniors aged 65 and above, and people at higher risk of death and complications from novel influenza A (H1N1) due to pre-existing medical conditions. The total cost is estimated to be approximately 700 million Hong Kong dollars and one hundred million doses had to be delivered right before Christmas opening the way for the ones to get protected. However, the Hong Kong Government cancelled the tender for the novel influenza A (H1N1) vaccines on 20th August 2009 because none of the offers met the specifications which included delivery by the end of the year, an agreement to buy back unused shots, and a minimum order of three million doses up to a maximum of six million doses.

All vaccines for the novel influenza A (H1N1) virus are based on the viral strain called A/California/7/2009 (H1N1)v. They differ in the conditions of viral propagation using vero cells or chicken eggs, adjuvant, antigen preparation and antigen content. There are two types of vaccines containing inactivated (killed) and live (attenuated) viruses. Inactivated vaccines are administered by injection. They commonly cause local reactions such as soreness, swelling and redness at the injection site but less often bring about fever, muscle-/joint-aches or headache. These symptoms are generally mild, last for one to two days and do not need medical attention. Rarely, there are allergic reactions such as hives, asthma due to hypersensitivity to certain vaccine components. Live vaccines are given via nasal spray. The common side-effects and adverse reactions are runny nose, nasal congestion and cough. They can less frequently cause sore throat, low grade fever, irritability and head- and muscle-aches. Wheezing and vomiting episodes have been described in children.

In 23rd December 2009, nearly 5 million doses of novel influenza A (H1N1) vaccine in nasal sprays were recalled.

The vaccine, which was strong when it was distributed in last October and November, lost some potency over time. The recall was a non-safety-related issue and the decrease in potency is not likely to be clinically significant. Individuals who received doses from the recalled lots do not need to be revaccinated. The recall is the second episode of its kind in last December prompted by a decline in potency. The manufacturer Sanofi Pasteur recalled nearly 800,000 children's doses of injectable influenza A (H1N1) vaccine because tests showed that they had lost some protective effect, though not enough to require re-vaccination.

Most nations are planning to vaccinate at-risk groups of people and healthcare staff when the vaccines are available. Notwithstanding some countries are yet to decide whether to include children. The German Health Ministry is awaiting clinical trial data. Other countries like Croatia, will stick to the guidance of the WHO and France is waiting for the advice of European Medicines Agency. As governments gear up to launch regional and national vaccination programmes against novel influenza virus A (H1N1), questions are beginning to emerge about how many people will be prepared to take up the offer of the vaccine. A recent survey showed that 52% of the healthcare workers in Hong Kong are not willing to get vaccination against novel influenza A (H1N1) because of fears of side effects and doubts about the effectiveness of the vaccine.[7] A Canadian survey also indicated that parents and healthcare workers may refuse to be vaccinated or to vaccinate their children considering that the risks outweigh the benefits.[8] A survey by the Ministry of Health, Israel similarly found that at least 25% of the population is reluctant to be vaccinated against novel influenza A (H1N1). A poll of English nurses found that a third would reject the offer. Those who opposed to the novel influenza A (H1N1) vaccine worried about a lack of evidence about the safety and efficacy of the vaccine.

Large clinical trials of novel influenza A (H1N1) vaccines in Australia, USA, Hungary and China lately confirmed the immunogenicity.[9-12] A single dose of pandemic novel influenza A (H1N1) vaccine is sufficient for sero-conversion in healthy adults. However, the optimum use of a novel influenza A (H1N1) vaccine remains an unanswered question. People who are allergic to egg should not get vaccinated with the current influenza vaccines, unless they have been desensitized under the care of an allergist.

According to the US vaccine adverse event reporting system, there was no substantial difference between the novel influenza A (H1N1) and seasonal influenza vaccines in the proportion or types of serious adverse events reported per million vaccines distributed (82 vs. 47). Hong Kong started the novel influenza A (H1N1) vaccination programme on 21st December 2009. Despite Mr Donald Tsang, the Chief Executive and Dr York Chow, the Secretary for Food and Health of Hong Kong Government together with more than 10 representatives of the medical sector encouraged the public at large to get vaccinated against the novel influenza A (H1N1) virus by having the vaccination four days ahead of the official launching, the initial response was not encouraging. The cumulative total of jabs in the past three weeks accounts to 119,615.[13] A 58-year man presented serious adverse reactions four days after vaccination and was hospitalized.[14] He developed bilateral calf pain and increasing lower limb weakness. The clinical features were compatible with Guillain-Barre Syndrome –acute inflammatory demyelinating polyneuropathy affecting the peripheral nervous system and leading to paralysis.[15] On 9th January 2010, a total of 77,155 Macau citizens have vaccinated. There were 37 reports of adverse events accounting to 4.8 episodes per million. A 79-year man died two days after being vaccinated against novel influenza A (H1N1) virus according to information released by the Health Bureau, Macau.

There are different laboratory diagnostic tests for detecting the presence of influenza viruses in respiratory specimens namely, direct antigen detection

tests, virus isolation in cell culture and real-time reverse transcriptase-polymerase chain reaction (RT-PCR).[16-19] These tests differ in their sensitivity and specificity in detecting influenza viruses and the turn-around-time. Rapid influenza diagnostic tests detect influenza viral nucleoprotein antigen and can provide results within 30 minutes. Compared to RT-PCR, the sensitivity of rapid influenza detection tests for detecting novel influenza A (H1N1) virus infections ranged from 10-70%.[17,18] A negative result derived from rapid influenza detection test should be interpreted with caution.

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購買新化驗儀器（二）

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在這之前談及過購買新儀器時在價錢方面的考慮，現在我們談談安放儀器的地方及位置。香港寸金尺土，儀器及其附件的大小再加上散熱空間，都需要預先籌劃，而儀器的重量也不可忽略，特別是大型的儀器，座檯的要考慮檯的承托力，座地的也要考慮地板的承托力；重型的儀器可能要安放在橫樑之上，否則開動時下層的天花震盪，就很難處理。另外，儀器如果需要供水或排水，也會影響擺放的位置；用電量也要考慮，因有些儀器可能需要三相電；再者，儀器的敏感度、操作時的需要的溫度及濕度、是否需要遠離離心機或發熱儀器的干擾等等，都會影響擺放的位置。

另一方面要考慮的是其售後服務，保用期過後，續保的價錢，所包括的零件，零件的價格及可使用期限，因為都是成本的一部份，要清楚知道；而供應商維修部的結構，員工的人数及能力，都影響日後儀器的使用；供應商更要為使用者提供指導及訓練，同樣要為員工提供足夠的訓練以支援使用者。

還有一點，現時行業內大都已經電腦化，儀器能否簡易地與化驗室資訊系統溝通接駁，對日後工作程序的影響關係極大。

最後，還要補充一點選擇儀器時要注意的事，其一是儀器採用的化驗方法是否與現時所用的相同，如果方法轉變，須要了解清楚得到的結果與現時的是否相容，如果不相容，又是否更好更普及，顧客是否容易接受，如何安排過渡，都要考慮周全。另外，還要考慮品質控制，供應商是否有提供品質控制物料，物料的價格及可使用期限，是否有提供品質控制資料分析服務及組織所有用家比較品質控制的結果；亦可參考獨立的品質控制計劃，計劃中目標儀器參與的数目能夠反映它的普及性，而如果儀器是行內普遍使用的，就可以有更多參考及支援，有利於日後的工作。

以上都是我粗略的一己之見，希望能拋磚引玉引起大家討論交流，分享心得，以期能得到一個更好的做法。

台灣醫療化驗的點滴

台灣 MT

近年學會積極參與國際的學術研討會活動，台灣是其中交流較頻繁的一個地區，相信大家都有興趣了解多一些關於台灣醫療化驗的發展和近況。加上香港醫療化驗界中有不少同事是在台灣接受教育後回香港工作的，到目前為止已累積有一百多人，他們分別服務於大學、醫院管理局、私家醫院、私營化驗所、醫療和生物科技公司等機構。

為了方便讀者閱讀以下的文章，首先向大家介紹兩個英文的專業名詞在香港和台灣不同的中文翻譯：Medical Laboratory Sciences 香港翻譯為醫療化驗科學，台灣則為醫學檢驗科學；Medical Technologist 香港翻譯為醫務化驗師，台灣簡稱為醫檢師。

台灣院校式的醫檢教育啟動和香港類同。在 1954 年美國 Duke University 醫學院院長 Dr. Davison 到台大醫學院訪問，建議成立醫事技術學系訓練技術員，提升醫學檢驗的水平。在 1956 年台灣大學招收第一屆的學生十人，是醫學院的第三個建立的學系，同時為亞洲地區第一所提供醫事技術學位課程的大學。香港的 Higher Certificate in Medical Technology course 也是由來自英國 University of Napier 學者 Dr. Dunning 推動而成立的。其後台灣在 1964 年至 1972 年之間先後有數家五專院校成立五年制醫事技術專科訓練課程，五專是專門招收初中畢業學生的專科學院，學歷相等於香港完成中三課程的學生。1975 年到 1994 年間，再有七所大學成立新的醫事技術學系。從 2002 年起，為了專業的持續發展，各大學的醫事技術學系陸續更名為醫學檢驗暨生物技術學系，部份大學成立研究所，開辦碩士和博士班，完成醫檢的高級教育系統。為了解決五專學生醫檢教育的斷層，部份大學開設二年制醫檢學科在職進修，簡稱為二技課程。

關於課程的規劃，大學第一年大多為通識課程，第二年則進入醫學基礎課程，如生理學、解剖學和寄生蟲等等，第三年開始修習專業醫學課程，例如生物化學，微生物學、免疫學，血液學及病理學等，此外也有一些臨床專業課程，第四年之後著重在臨床知識與實習經驗的獲得，其中病理組織學（Histopatholgy）所佔的比重較香港輕。五專的課程，首次年是延續高中的科目和基礎科學，其後三年的課程和香港的 Medical Laboratory Sciences 證書課程（OTC, SPACE）和文憑課程（Diploma, HK Polytechnic）相近，但在醫院實習的時間較多。而二技課程主要是加強臨床專業學科和生物科技的應用，如分子生物學和細胞培養技術等等。

台灣目前有十四所院校提供醫學檢驗學位課程，包括九間醫學院，四間科技大學和一所五專，每年有近 1500 的畢業生。畢業生必須通過由政府舉辦的專業考試，近年的合格率只有三十至四十左右，登記取得執業執照後，才可以加入醫檢的工作，每四年提出完成繼續教育（CPD）證明文件，才可更新執業執照。目前登記的約 7800 人，新入職人員薪資約港幣八至九千元。

從上述數據，台灣的醫檢教育和就業需求失衡，只有約 30% 畢業生從事醫檢工作，大部份繼續進修和其他行業。香港早年亦經歷過類似的情況。

相關資料來源：

1. 各大學網頁
2. 2009 亞太醫學檢驗科學國際研討—台灣高雄市
3. 台灣行政院衛生署

The Fifth Human Malaria Parasite

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Plasmodium knowlesi is a malaria parasite of Old World monkeys (simian malaria), and occurs in nature in long-tailed and pig-tailed macaques commonly found in forested areas of Southeast Asia. Knowles and Das Gupta succeeded in transmitting this monkey malaria to humans in 1932. Since then, P. knowlesi was used as a pyretic agent through blood passage between humans for treatment of general paralysis of the insane (neurosyphilis). Naturally acquired infection of P. knowlesi in humans was rare. Its zoonotic potential, that is, power of transmitting the infectious disease from non-human animals, both wild and domestic, to humans was quite limited. However, it soon turned out that malaria therapy using P. knowlesi was unsafe, as several fatal cases developed as a result of uncontrollable infection. P. knowlesi was replaced by the less virulent species P. vivax.

The first case of a naturally occurring P. knowlesi malaria infection was reported in 1965 in an American who had returned from visiting Peninsular Malaysia. However, sporadic incidence of P. knowlesi infections among humans in the Southeast Asia region, namely Thailand, Malaysia, China, Singapore have been reported since 2004.

Studies of the Kuching Group

The following is condensed from studies of Cox-Singh et al in ***Plasmodium Knowlesi Malaria is Widely Distributed and Potentially Life Threatening*** published in Clin Infect Dis 2008, Jan 15, 46(2): 165-71.

The method employed was sensitive and specific nested polymerase chain reaction (PCR) to identify all Plasmodium species present in (1) blood samples obtained from 960 patients with malaria diagnosed by microscopy who were hospitalized in Sarawak Malaysian Borneo during 2001 to 2006; (2) 54 cases of P. malariae archival blood films from 15 districts in Sabah, Malaysian Borneo during 2003 to 2005, and 4 districts in Pahang, Peninsular Malaysia during 2004 to 2005; and (3) four patients whose suspected cause of death was P. knowlesi malaria.

According to microscopy, the malaria species identified from 960 Sarawak samples collected between years 2001 to 2006 from 12 hospitals were: 45% P. vivax; 33% P. malariae and, 23% P. falciparum.

But according to polymerase chain reaction (PCR) methods, 28% (266/960) were P. knowlesi and 85% (266/312) were misdiagnosed as P. malariae. There were only 4 cases of true P. malariae but they were all imported cases.

PCR findings of 54 P. malariae archival blood films were: 84% (41/49) from Sabah were P. knowlesi; 100% (5/5) from Pahang were P. knowlesi; 100% (4/4) fatal cases from Sarawak were P. knowlesi. All four fatal patients were presented with hyperparasitemia, fevers, chills, and abdominal pains.

Cox-Singh studies concluded that human infections with P. knowlesi, commonly misidentified as the more benign P. malariae, are widely distributed across Malaysia Borneo and extend to Peninsular Malaysia. The importance of differentiating P. knowlesi from P. malariae is that P. malariae seldom reaches dangerously high densities in the blood as it multiplies every 3 days (quartan) whereas P. knowlesi has a daily cycle and can, within a very short period of time, reach potentially lethal densities.

The Laboratory Diagnosis

(1) Microscopy

Early trophozoites of P. knowlesi appeared as ring

forms and were indistinguishable from early trophozoites of P. falciparum. Occasionally, more than one ring form and double chromatin dots could be seen inside an erythrocyte, resembling those found in P. falciparum infection.

Late trophozoites occupied not more than two-thirds of the erythrocytes and the cytoplasm was compact and not amoeboid. In some infections, late trophozoites "band forms", typical of P. malaria, were also seen.

Schizonts had 8 to 16 merozoites arranged in a rosette pattern with a clump of pigment in the center. The mature schizonts did not fill the whole erythrocytes. Late trophozoites and schizonts were densely pigmented with dark brown/black malaria pigment. Gametocytes were round, filled most of the erythrocyte, and malaria pigment was scattered. There were no enlargement and stippling seen in the late trophozoite and schizont-infected erythrocytes.

The above morphological characteristics of P. knowlesi were also typical of those found in P malariae-infected erythrocytes (Figure 1 and Figure 2). Thus, P. knowlesi parasites in human erythrocytes were difficult to distinguish from P. malariae by microscopy.

(2) Confirmation by Molecular Assay (DNA)

Morphological similarities between P. knowlesi and P. malariae necessitate the use of molecular methods for correct identification.

Currently, PCR assay and molecular characterization are the most reliable methods for detecting and diagnosing P. knowlesi infection.

PCR identifies the parasite protein of the Plasmodium species as well as the protein specific for each malaria species. Subsequent DNA sequencing of the small subunit ribosomal RNA (SSU rRNA) and circumsporozoite protein (csp) genes of the malaria parasites with the PCR product confirms that it is phylogenetically indistinguishable from those of P. knowlesi, a malaria parasite of long-tailed macaque monkeys.

Clinical Tactics

In Hong Kong, in the past 5 years, there were around 150 cases of malaria infection reported, and nearly all were imported cases.

Being located in the vicinity of Southeast Asia, and with many travelers visiting us everyday, it is important for laboratory workers and clinicians to recognize P. knowlesi as the fifth human malaria.

Taking advice from Cox-Singh studies, in order to prevent a fatal outcome, for patient with a travel history to Southeast Asia, a diagnosis of "P. malariae" by microscopy and with hyperparasitemia should be regarded as the potentially lethal P. knowlesi malaria, and should be managed carefully as appropriate for severe P. falciparum malaria.

Take home message:

For confirmation of malaria diagnosis, you can contact Central Malaria Reference Laboratory, Public Health Laboratory Centre, Department of Health at tel no.: 2319 8350.

References:

Cox-Singh J, Davis TM, Lee KS, Shamsul SS, Matusop A, Ratnam S, Rahman HA, Conway DJ, Singh B. Plasmodium knowlesi malaria in humans is widely distributed and potentially life threatening. Clin Infect Dis 2008; 46(2): 165-171.

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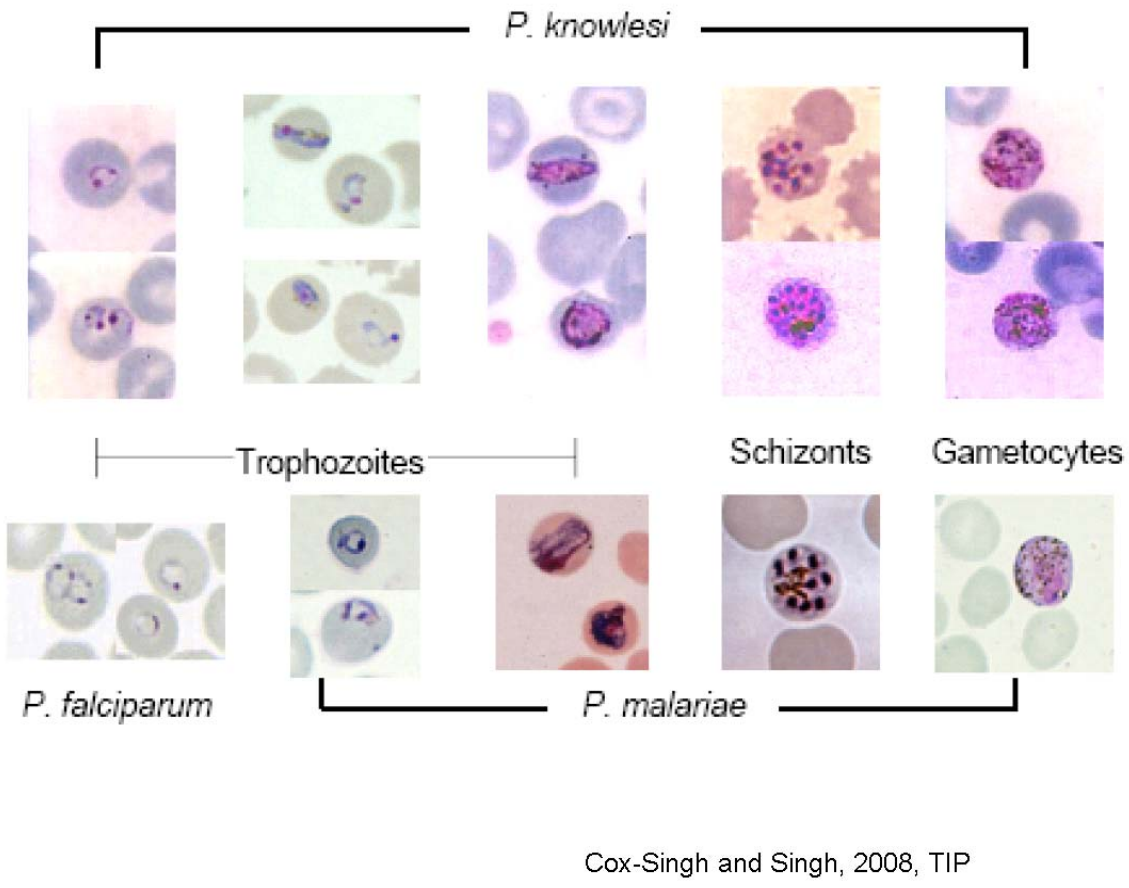

Figure 1 (courtesy of Cox-Singh and Singh)

P. Knowlesi vs P. malariae

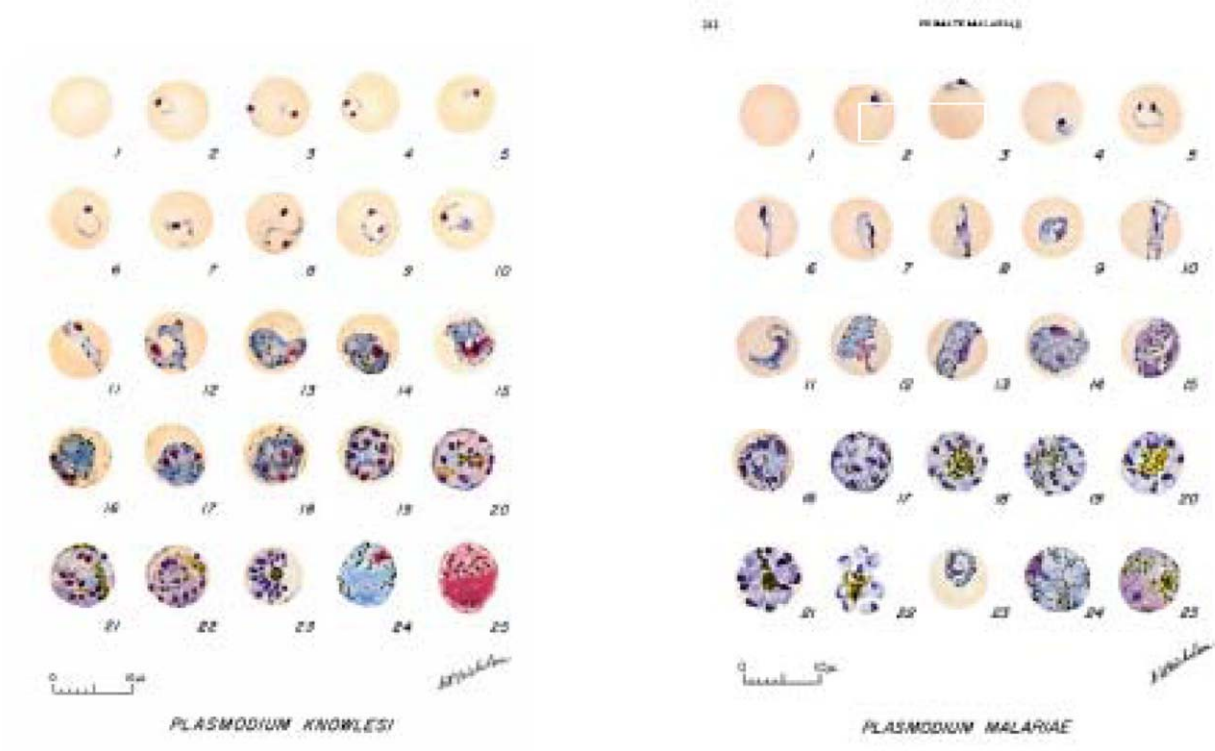

Figure 2 (courtesy of CDC)

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