热带病学术热点追踪报告

2014 年第 5 期（总第 10 期）　　5 月 20 日-6 月 30 日

目　录

一、国际热带病热点研究

1. 疟疾相关

（1）*Automated Hematology Analyzers in Diagnosis of Plasmodium vivax Malaria: an Adjunct to Conventional Microscopy.*

Malaria is one of the most pervasive parasitic diseases ever known to mankind affecting nearly 300 million people every year. The need for rapid diagnosis of malaria in tropical and subtropical malaria endemic areas is on the rise. In this study, we evaluated the usefulness of hematology autoanalyzers, Sysmex XE-2100 & XT-2000i in the presumptive diagnosis of malaria. Our study shows that abnormalities in WBC/BASO scattergram when combined with presence of thrombocytopenia had a high sensitivity and positive predictive value in the presumptive diagnosis of Plasmodium vivax (P.vivax) malaria [1].

（2）*Patient satisfaction and uptake of private-sector run malaria diagnosis clinics in a post-conflict district in Sri Lanka.*

In this prospective descriptive study, data was collected on the proportion of fever patients being referred by the health care provider (HCP) in hospitals for malaria screening, and the proportion thereof who underwent screening. An interviewer-administered questionnaire was also used to assess patient satisfaction among those attending MDL, which was graded on a scale of 0-4. [2]. *This study demonstrates the success of a public-private partnership in the malaria control programme in Sri Lanka. Malaria is considered low on the differential diagnosis in patients with fever even in previously malaria-endemic areas, due to the declining incidence of malaria and the increase in other febrile illnesses in these areas during the recent past. Private sector run malaria diagnostic services provided free of charge within government hospitals are viable and effective, and had good patient satisfaction ratings. In a country on the brink of eliminating malaria, there should be further emphasis on ensuring that HCPs refer patients for malaria diagnosis, in order to prevent a resurgence of the disease*[2].

（3）*Drugs use pattern for uncomplicated malaria in medicine retail outlets of Enugu urban, southeast Nigeria: implications for malaria treatment policy.*

This study analyzed the use pattern of anti-malarial drugs in medicine outlets to assess the current state of compliance to policy. A prospective cross-sectional survey of randomly selected medicine outlets in Enugu urban, southeast Nigeria, was conducted between May and August 2013, to determine the types, range, prices, and use pattern of anti-malarial drugs dispensed from pharmacies and patent medicine vendors (PMVs). Data were collected and analyzed for anti-malarial drugs dispensed for self-medication to patients, treatment by retail outlets and prescription from hospitals. Findings suggest vastly improved use of ACT in the retail outlets after eight years of policy change, with significant contributions from AMFm drugs. However the use of monotherapy, particularly through self-medication remain significant with increasing risk of undermining treatment policy, suggesting additional measures to directly target consumers and providers in the sector for improved use of anti-malarial drugs in Nigeria [3].

（4）*Evaluation of the immune response to RTS, S/AS01 and RTS, S/AS02 adjuvanted vaccines: Randomized, double-blind study in malaria-naïve adults.*

This phase II, randomized, double-blind study evaluated the immunogenicity of RTS, S vaccines containing Adjuvant System AS01 or AS02 as compared with non-adjuvanted RTS, S in healthy, malaria-naïve adults. Thirty-six subjects were randomized (1:1:1) to receive RTS, S/AS01, RTS,S/AS02, or RTS,S/saline at months 0, 1, and 2. Antibody responses to Plasmodium falciparum circumsporozoite (CS) and hepatitis B surface (HBs) antigens were assessed and cell-mediated immune responses evaluated by flow cytometry using intracellular cytokine staining on peripheral blood mononuclear cells. Anti-CS antibody avidity was also characterized. Safety and reactogenicity after each vaccine dose were monitored. In conclusion, in comparison with non-adjuvanted RTS,S, both RTS,S/AS vaccines exhibited better CS-specific immune responses. The anti-CS antibody response was significantly higher with RTS,S/AS01 than with RTS,S/AS02. The adjuvanted vaccines had acceptable safety profiles [4].

（5）*Malaria control in Nepal 1963-2012: challenges on the path towards elimination.*

The aim of this paper is to highlight the past and present malaria situation in this country and its challenges for long-term malaria elimination strategies. Malariometric indicator data of Nepal recorded through routine surveillance of health facilities for the years between 1963 and 2012 were compiled. Trends and differences in malaria indicator data were analysed. In conclusion, based on the achievements the country has made over the last decade, Nepal is preparing to move towards malaria elimination by 2026. However, considerable challenges lie ahead. These include especially, the need to improve access to diagnostic facilities to confirm clinically suspected cases and their treatment, the development of resistance in parasites and vectors, climate change, and increasing numbers of imported cases from a porous border with India. Therefore, caution is needed before the country embarks towards malaria elimination. [5].

2. 血吸虫病相关

（1）*Evaluation of schistosome promoter expression for transgenesis and genetic analysis.*

We recently reported the use of polyethyleneimine (PEI) as a simple and effective method for schistosome transfection and gene expression. Here, we use PEI-mediated schistosome plasmid transgenesis to define and compare gene expression profiles from endogenous and nonendogenous promoters in the schistosomula stage of schistosomes that are potentially useful to misexpress (underexpress or overexpress) gene product levels. In addition, we overexpress schistosome genes in vivo using a strong promoter and show plasmid-based misregulation of genes in schistosomes, producing a clear and distinct phenotype- death. These data focus on the schistosomula stage, but they foreshadow strong potential for genetic characterization of schistosome molecular pathways, and potential for use in overexpression screens and drug resistance studies in schistosomes using plasmid-based gene expression [6].

（2）*Cytokine responses to the anti-schistosome vaccine candidate antigen glutathione-S-transferase vary with host age and are boosted by praziquantel treatment.*

An anti-schistosome vaccine based on Schistosoma haematobium glutathione-S-transferase (GST) is currently in Phase III clinical trials, but little is known about the immune responses directed against this antigen in humans naturally exposed to schistosomes or how these responses change following PZQ treatment. Blood samples from inhabitants of a Schistosoma haematobium-endemic area were incubated for 48 hours with or without GST before (n=195) and six weeks after PZQ treatment (n=107). Concentrations of cytokines associated with innate inflammatory (TNFα, IL-6, IL-8), type 1 (Th1; IFNγ, IL-2, IL-12p70), type 2 (IL-4, IL-5, IL-13), type 17 (IL-17A, IL-21, IL-23p19) and regulatory (IL-10) responses were quantified in culture supernatants via enzyme-linked immunosorbent assay (ELISA). Factor analysis and multidimensional scaling were used to analyse multiple cytokines simultaneously. In areas where schistosomiasis is endemic host age, schistosomeinfection status and PZQ treatment affect the cellular cytokine response to GST. Thus the efficacy of a GST-based vaccine may also be shaped by the demographic and epidemiological characteristics of targeted populations[7].

（3）*Gonad RNA-specific qRT-PCR analyses identify genes with potential functions in schistosome reproduction such as SmFz1 and SmFGFRs.*

We describe tissue-specific qRT-PCR analyses comparing transcript levels of selected genes on the basis of RNA from gonads and whole worms. Gene expression in ovary and testes was in some cases found to be significantly influenced by pairing, which was not traceable in whole worms. Among the candidate genes identified as regulated by pairing in gonads were the frizzled homolog SmFz1 and the two fibroblast growth factor receptor homologs SmFGFR-A and SmFGFR-B. First functional characterizations were done, including comparative qRT-PCR analyses, in situ-localization experiments, heterologous expression in Xenopus oocytes (SmFGFR-A/B), and inhibitor studies using the Fz/Dvl-pathway inhibitor 3289-8625, or BIBF1120 blocking FGFR-signaling. In summary, these results emphasise the

usefulness of tissue-specific qRT-PCRs for selection of candidate genes with important roles in reproduction, allowing subsequent studies to determine their suitability as drug targets [8].

3. 其他寄生虫病相关

（1）*Spatial epidemiology and climatic predictors of paediatric dengue infections captured via sentinel site surveillance, Phnom Penh Cambodia 2011-2012.*

We report basic epidemiological characteristics in a series of 701 patients at the National Paediatric Hospital in Cambodia, recruited during a prospective clinical study (2011-2012). To more fully explore this cohort, we examined climatic factors using multivariate negative binomial models and spatial clustering of cases using spatial scan statistics to place the clinical study within a larger epidemiological framework. Our results identify clustering of infections at the neighbourhood scale, suggesting points for targeted interventions, and we find that the complex interactions of vectors and climatic conditions in this setting may be best captured by rising minimum temperature, and median (as opposed to mean) relative humidity, with complex and limited effects from rainfall. These results suggest that real-time cluster detection during epidemics should be considered in Cambodia, and that improvements in weather data reporting could benefit national control programs by allow greater prioritization of limited health resources to both vulnerable populations and time periods of greatest risk. Finally, these results add to the increasing body of knowledge suggesting complex interactions between climate and dengue cases that require further targeted research [9].

（2）*Variability in dengue titer estimates from plaque reduction neutralization tests poses a challenge to epidemiological studies and vaccine development.*

We used repeated assays on the same two pools of serum using five different viruses (2,319 assays) to characterize the variability in the technique under identical experimental conditions. We also assessed the performance of multiple statistical models to interpolate continuous values of neutralization titer from discrete measurements from serial dilutions. We

found that the variance in plaque reductions for individual dilutions was 0.016, equivalent to a 95% confidence interval of 0.45-0.95 for an observed plaque reduction of 0.7. We identified PRNT75 as the optimum evaluation point with a variance of 0.025, indicating a titer reading of 1：500 had 95% confidence intervals of 1:40-1:1000. Finally, we estimated that only 0.7% of assays would falsely detect a four-fold difference in titers between acute and convalescent sera where no true difference exists. Estimating and reporting assay uncertainty will aid the interpretation of individual titers. Laboratories should perform a small number of repeat assays to generate their own variability estimates. These could be used to calculate confidence intervals for all reported titers and allow benchmarking of assay performance [10].

（3）*Efficient Genome Engineering of Toxoplasma gondii Using CRISPR/Cas9.*

Toxoplasma gondii is a parasite of humans and animals, and a model for other apicomplexans including Plasmodium spp., the causative agents of malaria. Despite many advances, manipulating the T. gondii genome remains labor intensive, and is often restricted to lab-adapted strains or lines carrying mutations that enable selection. Here, we use the RNA-guided Cas9 nuclease to efficiently generate knockouts without selection, and to introduce point mutations and epitope tags into the T. gondii genome. These methods will streamline the functional analysis of parasite genes and enable high-throughput engineering of their genomes [11].

（4）*Toxoplasma gondii infection can induce retinal DNA damage: an experimental study.*

The aim is to detect whether Toxoplasma gondii (T. gondii) infection of mice can induce retinal DNA damage. The obtained results showed that T. gondii infection induced a statistically significant increase in the frequency of tailed nuclei, tail length, percentage of DNA in the tail, and tail moment in mice retinal cells compared to the control group (which showed some degree of DNA damage). In immunosuppressed infected group, retinal DNA damage was severing and there was significant increase in various comet assay parameters compared to both control and infected groups. After treatment with sulfadiazine and pyrimethamine, retinal DNA damage decreased and all comet assay parameters showed a statistical

significant decrease compared to infected groups. The conclusion is that T. gondii infection can induce DNA damage in mice retinal cells [12].

二、国内热带病热点研究

1. 疟疾相关

（1）2004-2013 年中国疟疾发病情况及趋势分析

分析 2004-2013 年 7 月全国疟疾发病趋势和规律，为消除疟疾工作的开展提供依据。利用中国疾病预防控制中心疾病监测信息报告管理系统(网络直报系统)以及全国疾病控制调查制度《疟疾防治工作调查表》(年报系统)，收集 2004-2013 年 7 月全国疟疾疫情数据资料，用 Excel2010 软件进行统计分析。结论为全国疟疾疫情已得到有效控制，但输入性疟疾尤其是输入性恶性疟所占比例呈大幅度上升趋势 [13]。

（2）红细胞和血小板参数对恶性疟疾的诊断价值分析

本研究选取红细胞和血小板参数，对 65 例恶性疟疾患者及同期 65 例健康体检者进行了比较。本研究发现，患者组红细胞、血红蛋白、红细胞比容、红细胞平均体积均显著低于正常组，提示恶性疟疾患者红细胞参数出现了明显改变，其机制可能为：作为一种抗原刺激，疟原虫使得机体巨噬细胞功能显著亢进，导致其寄居的红细胞被大量破坏，对红细胞和血红蛋白水平造成了较大影响，是引发贫血症状的主要原因[14]。

（3）疟疾病例血液参数变化及其诊断价值的研究

探讨疟疾病例血液参数变化及其诊断价值，为疟疾诊断提供科学依据。方法是采用全自动血球分析仪分别检测 20 例疟疾患者和 20 例健康体检者 WBC、EOS、RBC、HGB、PLT 等血液参数，应用 t 检验对参数进行统计分析。结果

为疟疾患者血液参数 RBC、HGB 和 PLT 低于健康组，二者差异有统计学意义（P <0.01），而 WBC、EOS 与健康组差异无统计学意义（P >0.05）。结论为血液参数 RBC、HGB 和 PLT 变化与疟疾病例有着密切联系，在发热患者的诊断中应引起重视，进而科学、准确诊断疟疾病例[15]。

2. 血吸虫病相关

（1）腹腔镜与开腹脾切除术治疗血吸虫性肝硬化致脾功能亢进的比较

探讨腹腔镜脾切除术治疗血吸虫性肝硬化引起的脾功能亢进的临床应用价值。方法是对 50 例血吸虫性肝硬化脾亢患者行脾切除术，其中腹腔镜组（A 组）31 例行完全腹腔镜手术，开腹组（B 组）19 例行传统开腹手术。比较两组患者的手术时间、术中出血量、术后住院时间、术后 1 d 切口疼痛评分、术后 3 d 超敏 C 反应蛋白（hs-CRP）及引流液淀粉酶（Amy）、术后 7 d 血小板计数（Plt）、白细胞计数（WBC）。结论为采用腹腔镜脾切除术治疗血吸虫性肝硬化患者脾功能亢进是安全有效的。相对传统开腹手术而言，具有创伤小、恢复快，住院时间缩短，并发症少，术后疼痛轻等优点[16]。

（2）日本血吸虫感染经吡喹酮治疗后血清中抗体及细胞因子水平的变化

目的是观察人感染日本血吸虫经吡喹酮治疗后血清中可溶性虫卵抗原(SEA)特异性抗体 IgG、IgM 及 IL-4、IFN-γ 水平的变化，并观察治疗后外周血中 SEA 特异性分泌 IFN-γ 的淋巴细胞数量的变化。通过 ELISA 的方法检测血清中 SEA 特异性 IgG、IgM 抗体及 IL-4、IFN-γ 的水平。取各组样本中 3 例进行 ELISPOT 实验，检测外周血中 SEA 特异性 IFN-γ 淋巴细胞数量。结论为血清中 IL-4、IFN-γ 水平及外周血中 IFN-γ 淋巴细胞数量的检测可以用于吡喹酮治疗血吸虫感染疗效的考核，而血清中 IgG、IgM 水平变化对于吡喹酮疗效的考核也具有一定的辅助作用[17]。

（3）血吸虫肝硬化患者合并肝癌的 CT 影像学表现及研究

血吸虫肝硬化主要原因为血吸虫卵沉积在肝组织中，导致肝脏的慢性病理变化。当晚期血吸虫肝硬化患者合并乙型肝炎病毒(HBV) 感染时，可进一步加重肝细胞的损害程度，有协同致肝癌作用。加强对血吸虫性肝硬化并发肝癌的诊断与治疗研究，具有临床实践意义。本研究发现，在血吸虫肝硬化的基础上合并肝癌的 CT 表现有一定的特征性，与通常的肝硬化合并肝癌有所不同[18]。

3. 其他寄生虫病相关

（1）抗弓形虫药物的研究进展

刚地弓形虫是一种能引起人畜共患的机会致病性孢子虫，可感染人及多种恒温动物，严重威胁着人类健康和畜牧业的发展，然而至今仍没有理想的治疗弓形虫病的药物。本文对具有抗弓形虫活性的西药、中药、新型生物制剂的治疗效果、毒副作用及复发率等方面进行综述，为开发新型毒副作用小、疗效显著的抗弓形虫药物提供理论参考[19]。

（2）云南省龙陵县 HIV 阳性者感染弓形虫的 SAG2 基因位点分析

目的为初步了解云南省龙陵县 HIV 阳性者感染弓形虫的基因型特征。方法是使用基因提取试剂盒提取龙陵县HIV 阳性者感染弓形虫的基因，运用巢式 PCR 技术分别对弓形虫 SAG2 基因（241bp、221bp）进行扩增，扩增产物用 1.5%琼脂糖凝胶电泳，紫外投射仪下观察结果。用 DNA 胶回收试剂盒切胶回收 PCR 产物并进行酶切，酶切产物置于 37℃恒温培养箱孵育 16 h，孵育后的酶切产物用 2.5%琼脂糖凝胶电泳，凝胶成像系统摄像观察结果并与弓形虫基因Ⅰ型标准株进行对比鉴定。结论是初步确定云南省龙陵县 HIV 阳性者感染弓形虫的基因型以Ⅰ型为主，Ⅲ型少见，未见Ⅱ型及其他基因型[20]。

（3）中国不同流行疫区利什曼原虫分离株的微卫星多态性分析

目的是了解中国荒漠、山丘和平原疫区利什曼原虫分离株的种群遗传学和流行病学特点。方法为选用 7 个微卫星标记，分别对中国不同疫区的 5 株杜氏利什曼原虫分离株与 WHO 杜氏利什曼原虫参照株进行 PCR 扩增和测序，分析序列的微卫星多态性，使用 MEGA5.0 软件构建系统发育树，推断杜氏利什曼原虫的种群结构。结论为中国不同疫区杜氏利什曼原虫分离株的微卫星序列存在丰富的多态性，种系发育分析显示利什曼原虫遗传多态性与地理来源之间存在相关性[21]。

【参考文献】

（如需参考文献中论文全文，请发送论文标题至 yaoyaoyu1987@163.com）

1. *Mubeen KH, Devadoss CW, Rangan RA et al. Automated Hematology Analyzers in Diagnosis of Plasmodium vivax Malaria: an Adjunct to Conventional Microscopy[J].Mediterr J Hematol Infect Dis,2014,6(1):e2014034*
2. *Fernando D, de Silva NL, Ackers I et al. Patient satisfaction and uptake of private-sector runmalaria diagnosis clinics in a post-conflict district in Sri Lanka[J].BMC Public Health,2014,14(1):641*
3. *Ezenduka CC, Ogbonna BO, Ekwunife OI et al. Drugs use pattern for uncomplicated malarial in medicine retail outlets of Enugu urban, southeast Nigeria: implications for malaria treatment policy[J].Malar J,2014,13(1):243*
4. *Leroux-Roels G, Leroux-Roels I, Clement F et al. Evaluation of the immune response to RTS,S/AS01 and RTS,S/AS02 adjuvanted vaccines: Randomized, double-blind study in malaria-naïve adults[J].Hum Vaccin Immunother,2014,10(8)*
5. *Dhimal M, Ahrens B, Kuch U et al .Malaria control in Nepal 1963-2012:challenges on the path towards elimination[J].Malar J,2014,13(1):241*
6. *Liang S, Varrecchia M, Ishida K et al. Evaluation of schistosome promoter expression for transgenesis and genetic analysis[J].PLoS One,2014,9(5):e98302*
7. *Bourke CD, Nausch N, Rujeni N et al. Cytokine responses to the anti-schistosome vaccine candidate antigen glutathione-S-transferase vary with host age and are boosted by praziquantel treatment[J].PLoS Negl Trop Dis,2014,8(5):e2846*

8. *Hahnel S, Quack T, Parker-Manuel SJ et al. Gonad RNA-specific qRT-PCR analyses identify genes with potential functions in schistosome reproduction such as SmFz1 and SmFGFRs[J].Front Genet,2014,5:170*
9. *Lover AA, Buchy P, Rachline A et al. Spatial epidemiology and climatic predictors of paediatric dengue infections captured via sentinel site surveillance, Phnom Penh Cambodia 2011-2012[J].BMC Public Health,2014,14(1):658*
10. *Salje H, Rodr ́guez-Barraquer I, Rainwater-Lovett K et al. Variability in dengue titer estimates from plaque reduction neutralization tests poses a challenge to epidemiological studies and vaccine development[J]. PLoS Negl Trop Dis,2014,8(6):e2952*
11. *Sidik SM, Hackett CG, Tran F et al. Efficient Genome Engineering of Toxoplasma gondii Using CRISPR/Cas9[J].PLoS One,2014,9(6):e100450*
12. *El-Sayed NM, Aly EM. Toxoplasma gondii infection can induce retinal DNA damage: an experimental study[J].Int J Ophthalmol,2014,7(3):431-436*
13. 丰俊,夏志贵.2004-2013 年中国疟疾发病情况及趋势分析[J].中国病原生物学杂志,2014,9(5):442-446
14. 马庆,吕宗军.红细胞和血小板参数对恶性疟疾的诊断价值分析[J].中国地方病防治杂志,2014,29(3):228
15. 朱同林.疟疾病例血液参数变化及其诊断价值的研究[J].中国医药指南,2014,12(15):41-42
16. 赵红欣,周鸿鲲,张浩等.腹腔镜与开腹脾切除术治疗血吸虫性肝硬化致脾功能亢进的比较[J].全科医学临床与教育,2014,12(3):253
17. 刘向芹,张影,张瑾等.日本血吸虫感染经吡喹酮治疗后血清中抗体及细胞因子水平的变化[J].药物分析杂志,2014,34(5):790-794
18. 吴世勇,郑银元.血吸虫肝硬化患者合并肝癌的 CT 影像学表现及研究[J].中国地方病防治杂志,2014,29(3):231
19. 王旗,杨雯,杨小迪等.抗弓形虫药物的研究进展[J].中国病原生物学杂志,2014,9(5):478-480
20. 贾玉玺,聂大平,陈凌娟等.云南省龙陵县 HIV 阳性者感染弓形虫的 SAG2 基因位点分析[J].中国病原生物学杂志,2014,9(5):438-446
21. 张春莹,宋兴勃,严可宁等.中国不同流行疫区利什曼原虫分离株的微卫星多态性分析[J].现代预防医学,2014,41(10):1852-1855

编辑：中国疾病预防控制中心寄生虫病预防控制所
报告制作：路瑶、周征奇
审核：卢延鑫、付青、郑彬、王汝波、李石柱
签发：周晓农
联系电话：021-64377008
传真：+86-021-64332670　　邮编：200025
地址：上海市卢湾区瑞金二路 207 号

寄生虫病预防控制所