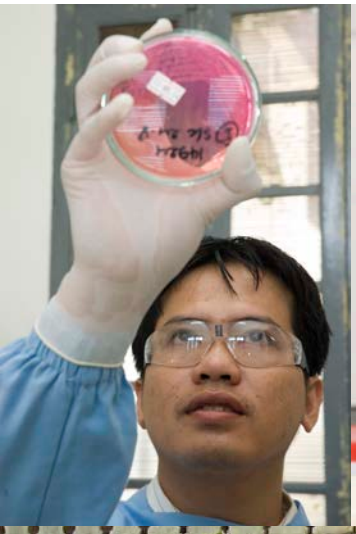
Lao - Oxford - Mahosot Hospital - Wellcome Trust Research Unit

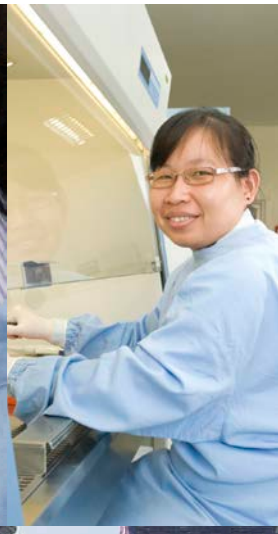
SCIENTIFIC ANNUAL REPORT FOR 2013

LAO-OXFORD-MAHOSOT HOSPITAL-WELLCOME TRUST RESEARCH UNIT
MICROBIOLOGY LABORATORY
MAHOSOT HOSPITAL
VIENTIANE, LAO PDR

TO

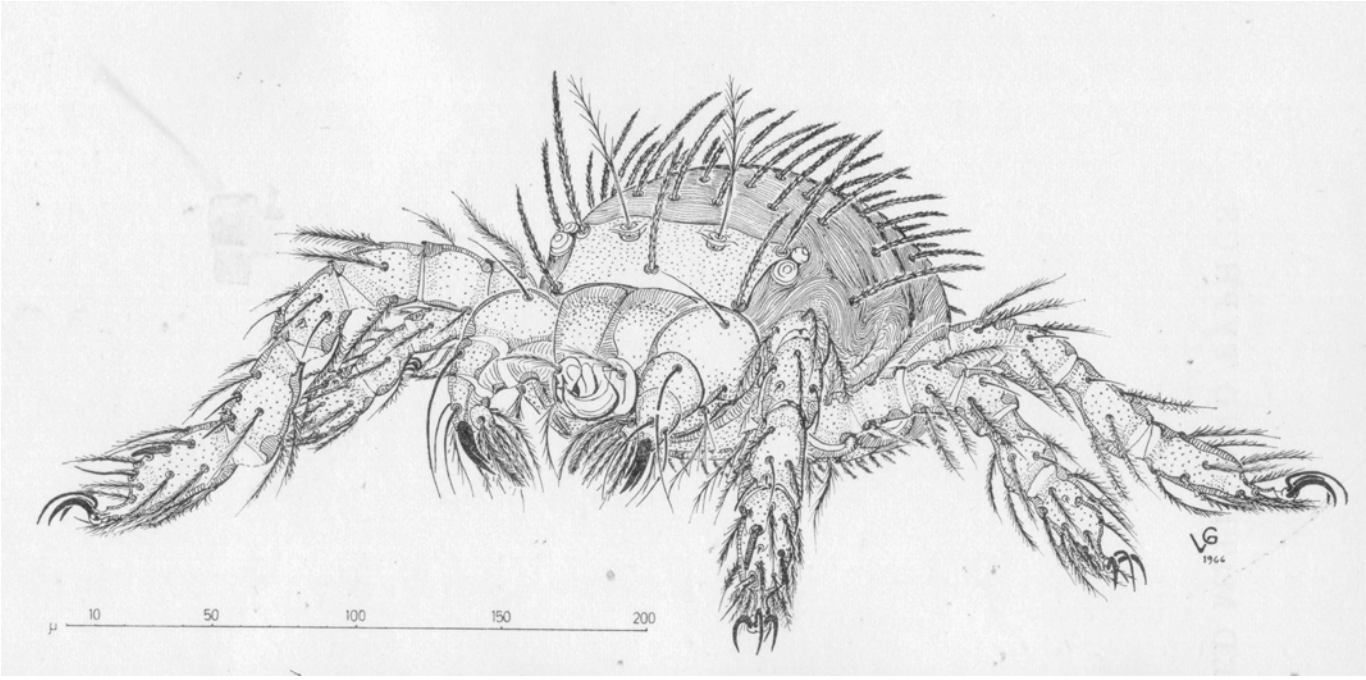
MINISTRY OF HEALTH
GOVERNMENT OF THE LAO PDR






CONTENTS

A chigger mite, vector of scrub typhus, from J Ralph Audy (1968)



ບົດສັງລວມຫຍໍ້

ກ. ໂຄງການຄົ້ນຄວ້າພະຍາດເຂດຮ້ອນລະຫວ່າງໂຮງໝໍມະໂຫສົດ-ແອວຄຳຫຼ້ສ-ມະຫາວິທະຍາໄລອ໋ອກຝອດ ຫລື The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) ເປັນໜ່ວຍງານຄົ້ນຄວ້າທາງຄລີນິກ ເຊິ່ງ ນອນຢູ່ໃນພະແນກວິເຄາະຈຸລິນຊີ, ໂຮງໝໍມະໂຫສົດ. ໂຄງການນີ້ໄດ້ຮັບທຶນຊ່ວຍເຫລືອຫລັກ ຈາກທາງແອວຄຳຫຼ້ສ ປະເທດ ອັງກິດ ແລະ ທຶນອີກສ່ວນໜຶ່ງແມ່ນໄດ້ຈາກ CDC ສະຫະລັດອາເມລິກາ, ມູນນິທິ FIND, ອົງການອະນາໄມໂລກ, ແລະ ສະຖາບັນຄົ້ນຄວ້າ IRASEC. ນອກນີ້ ທາງໂຄງການຍັງໄດ້ຮັບການຊ່ວຍເຫລືອເປັນເຄື່ອງອຸປະກອນ ຈາກສະຖາບັນຄົ້ນຄວ້າ ເພື່ອການພັດທະນາ/ມະຫາວິທະຍາໄລແອ໋ກຊ-ມາກໄຊ ປະເທດຝລັ່ງ ແລະ ໂຄງການຄົ້ນຄວ້າພະຍາດຣິກເກັດເຊຍ ຂອງສູນ ຄົ້ນຄວ້າທາງການແພດກອງທັບເຮືອ ສະຫະລັດອາເມລິກາ.

ຂ. LOMWRU ມີພະນັກງານທັງໝົດ 43 ຄົນ, ໃນນີ້ 93% ແມ່ນຄົນລາວ ແລະ 58% ເປັນເພດຍິງ. ສ່ວນ ພະແນກວິເຄາະ ຈຸລິນຊີ ມີພະນັກງານ (ພາກລັດ) ທັງໝົດ 23 ຄົນ. ພວກເຮົາມີຫ້ອງວິເຄາະທາງຄລີນິກຕ່າງໆເຊັ່ນ: ຫ້ອງວິເຄາະຈຸລະຊີວະ ວິທະຍາ, ຫ້ອງວິເຄາະທາງພັນທຸກຳສາດ, ຫ້ອງວິເຄາະເຊໂຣໂລຊີ, ແລະ ຫ້ອງວິເຄາະລະດັບ 3 (BSL3). ການປະຕິບັດງານ ໃນຫ້ອງວິເຄາະດັ່ງກ່າວ ແມ່ນເປັນໄປຕາມແນວທາງ ແລະ ລະບຽບການຄວາມປອດໄພ ຂອງມະຫາວິທະຍາໄລອ໋ອກຝອດ.

ຄ. LOMWRU ຊ່ວຍບໍລິການບົ່ງມະຕິພະຍາດຊຶມເຊື້ອພາຍໃນໂຮງມະໂຫສົດ ແລະ ໂຮງໝໍຕ່າງແຂວງ ເຊັ່ນ ໂຮງໝໍແຂວງ ຫລວງນ້ຳທາ ແລະ ສາລະວັນ, ເຮັດການຄົ້ນຄວ້າທາງຄລີນິກ, ແລະ ສ້າງຄວາມເຂັ້ມແຂງໃຫ້ແກ່ພະນັກງານພາກລັດ ທາງ ດ້ານການບົ່ງມະຕິພະຍາດ ແລະ ການເຮັດຄົ້ນຄວ້າ ໂດຍຜ່ານການຝຶກອົບຮົມ ແລະ ການປະຕິບັດງານຕົວຈິງ.

ງ. ຈຸດສຸມສຳລັບວຽກຄົ້ນຄວ້າຂອງພວກເຮົາໄດ້ແກ່ ສາເຫດ ແລະ ລະບາດວິທະຍາຂອງໄຂ້ ລວມທັງການບົ່ງມະຕິ ແລະ ປິ່ວປົວຢ່າງສົມເຫດສົມຜົນ ໃນ ສປປ ລາວ, ລະບາດວິທະຍາ ແລະ ການປ້ອງກັນພາວະຂາດວິຕະມິນເບ1 ໃນເດັກລຸ່ມ 1ປີ, ແລະ ການສຶກສາຄົ້ນຄວ້າກ່ຽວກັບຄຸນນະພາບຂອງຢາ ໃນລະດັບສາກົນ.

ຈ. ນັບແຕ່ປີ 2000 ເປັນຕົ້ນມາ ພວກເຮົາໄດ້ຕີພິມເຜີຍແຜ່ຜົນຂອງການຄົ້ນຄວ້າລົງໃນວາລະສານການແພດສາກົນ ຈຳນວນ 165 ບົດ ແລະ ລົງໃນປຶ້ມຕຳລາທາງການແພດຈຳນວນ 12 ພາກ. ສະເພາະ ປີ 2013 ພວກເຮົາໄດ້ຕີພິມເຜີຍແຜ່ຜົນຂອງ ການຄົ້ນຄວ້າລົງໃນລາລະສານການແພດສາກົນຈຳນວນ 22 ບົດ ແລະ ອີກ 3 ບົດ ຖືກຮັບຮອງ ແລະ ກຳລັງຈະຖືກຕີພິມ ເຜີຍແຜ່.

ສ. ຜົນການຄົ້ນຄວ້າທີ່ຜ່ານມາຂອງ LOMWRU ໄດ້ຖືກນຳໄປຜັນຂະຫຍາຍເປັນແນວທາງນະໂຍບາຍດ້ານສາທາລະນະສຸກ ພາຍໃນປະເທດ ເຊັ່ນ: ໃນປີ 2013 ໄດ້ມີການຈັດຕັ້ງປະຕິບັດການສັກຢາກັນພະຍາດທີ່ເກີດຈາກເຊື້ອ Pneumococcus ແລະ ການສັກຢາກັນພະຍາດອັກເສບສະໝອງຍີ່ປຸ່ນ. ຜົນຈາກວຽກຄົ້ນຄວ້າຂອງ LOMWRU ຍັງນຳໄປສູ່ການປ່ຽນແປງແນວທາງ ການປິ່ນປົວພະຍາດໄຂ້ຍູງ ແລະ ພະຍາດໄຂ້ທໍລະພິດ (Typhoid). ນອກນີ້ ພວກເຮົາຍັງໄດ້ຄົ້ນພົບພະຍາດທີ່ສຳຄັນ ບາງ ຢ່າງເປັນຄັ້ງທຳອິດໃນປະເທດລາວ, ໄດ້ຊີ້ໃຫ້ເຫັນຄວາມສຳຄັນຂອງພະຍາດໄຂ້ແມງແດງ, ໄຂ້ຢ່ຽວໜູ, ເມລີອອຍໂດສຊິສ, ອັກ ເສບສະໝອງຍີ່ປຸ່ນ ເຊິ່ງເຮັດໃຫ້ພວກເຮົາເຂົ້າໃຈຢ່າງເລິກເຊິ່ງຕື່ມກ່ຽວກັບລັກສະນະດ້ານລະບາດວິທະຍາ ແລະ ແນວທາງການ ປ້ອງກັນພະຍາດດັ່ງກ່າວ.

ຊ. ສະຫລຸບຜົນຂອງການຄົ້ນຄວ້າທີ່ສຳຄັນ ເຊິ່ງໄດ້ຕີພິມເຜີຍແຜ່ ຫລື ກຳລັງຈະຖືກຕີພິມເຜີຍແຜ່ ໃນປີ 2013 ມີດັ່ງຕໍ່ໄປນີ້:

- ໄຂ້ຍຸງລາຍ, ໄຂ້ແມງແດງ, ໄຂ້ຢ່ຽວໜູ ແລະ ອັກເສບສະໝອງຍີ່ປຸ່ນ ເປັນສາເຫດຕົ້ນຕໍຂອງໄຂ້ ໃນກຸ່ມຄົນເຈັບອາຍຸ 5-49 ປີ ຢູ່ເຂດຊົນນະບົດຂອງລາວ
- ລັກສະນະທາງດ້ານລະບາດວິທະຍາຂອງພະຍາດຊຶມເຊື້ອ ແມ່ນມີຄວາມແຕກຕ່າງກັນ ລະຫວ່າງພາກເໜືອ ແລະ ພາກໃຕ້ຂອງລາວ
- ໃນກຸ່ມຄົນເຈັບທີ່ເຂົ້າມາຍ້ອນໄຂ້ (ມີຜົນກວດໄຂ້ຍູງລົບ ດ້ວຍແຜ່ນຈຸ່ມ), ຖ້າເຮົາໃຊ້ຢາ Doxycycline ໃນກຸ່ມຄົນ ເຈັບດັ່ງກ່າວ ຈະໄດ້ຜົນປະມານ 12%
- ເຮົາສາມາດບົ່ງມະຕິພະຍາດໄຂ້ທໍລະພິດ ຢ່າງໄວວາ, ແມ່ນຢຳ ແລະ ມີລາຄາຖືກ ໂດຍນຳໃຊ້ຊຸດການກວດວິເຄາະ ແບບໄວວາເພື່ອຊອກຫາແອນຕິເຈນຂອງເຊື້ອໄຂ້ທໍລະພິດໃນແກ້ວປູກເລືອດ. ເຕັກນິກນີ້ ອາດຊ່ວຍໃຫ້ຫ້ອງວິເຄາະ ຂອງໂຮງໝໍແຂວງ ສາມາດບົ່ງມະຕິພະຍາດດັ່ງກ່າວໄດ້ ໃນອະນາຄົດ.
- ພວກເຮົາພົບວ່າ ພະຍາດໄຂ້ແມງແດງ, ມູຣິນໄທຟັສ, ແລະ ໄຂ້ຢ່ຽວໜູ ເປັນສາເຫດທີ່ສຳຄັນຂອງການຊຶມເຊື້ອລະບົບ ປະສາດສູນກາງ ໃນວຽງຈັນ ແລະ ອາດພົບໃນແຫ່ງອື່ນໆຂອງຂົງເຂດອາຊີເຊັ່ນກັນ.

- ຜົນການຄົ້ນຄວ້າພວກເຮົາພົບວ່າ ເຊື້ອ ***Staphylococcus aureus*** ເປັນເຊື້ອສາເຫດຕົ້ນຕໍຂອງການຊຶມເຊື້ອເລືອດ ໃນເດັກລຸ່ມ 1 ປີ ຂອງລາວ ເຊິ່ງສາເຫດອາດເປັນຍ້ອນການນອນໄຟຂອງແມ່ຫລັງເກີດລູກ. ສະນັ້ນ ເຮົາຄວນພິຈາ ລະນານຳໃຊ້ຢາ Cloxacillin ເພື່ອປິ່ນປົວຊຶມເຊື້ອເລືອດໃນເດັກເກີດໃໝ່ 3 ອາທິດແລກ ແລະ ເດັກລຸ່ມ 1 ປີ ໃນ ຂະນະທີ່ລໍຖ້າຜົນປູກເລືອດ.
- ພວກເຮົາຍັງພົບວ່າ ໄຂ້ຍູງລາຍ ແລະ ໄຂ້ແມງແດງ ເປັນສາເຫດຂອງໄຂ້ທີ່ພົບເລື້ອຍ ໃນກຸ່ມແມ່ຍິງຖືພາ ໃນວຽງຈັນ ແລະ ອາດເປັນສາເຫດການຕາຍທີ່ສຳຄັນຂອງແມ່ ໃນປະເທດລາວ ແລະ ໃນແຫ່ງອື່ນໆ.
- ພວກເຮົາສາມາດກວດຫາດີເອັນເອຂອງເຊື້ອຈຸລິນຊີ ໃນນ້ຳໄຂສັນຫລັງ (ຂອງຄົນເຈັບທີ່ເປັນເຍື່ອຫຸ້ມສະໝອງອັກເສບ) ທີ່ເກັບຮັກສາໃນເຈ້ຍຊັບ ເຊິ່ງເຕັກນິກນີ້ອາດນຳໄປໃຊ້ເພື່ອບົ່ງມະຕິເຊື້ອສາເຫດຂອງອັກເສບເຍື່ອຫຸ້ມສະໝອງຈາກເຊື້ອ ຈຸລິນຊີ ໃນລະດັບໂຮງໝໍແຂວງ.
- ເຊື້ອຈຸລິນຊີ Enterobacteriaceae ທີ່ດື້ຕໍ່ຢາຕ້ານເຊື້ອກຸ່ມເບຕາລັກຕາມິນ ແມ່ນພົບເຫັນຫລາຍໃນອາຈົມຂອງເດັກ ໂຮງຮຽນອະນຸບານທີ່ມີສຸຂະພາບແຂງແຮງ ໃນນະຄອນຫລວງວຽງຈັນ ແລະ ແຂວງວຽງຈັນ – ການຄົ້ນພົບນີ້ ເຮັດໃຫ້ ເຮົາກັງວົນໃນເລື່ອງການແຜ່ກະຈາຍຂອງເຊື້ອທີ່ດື້ຕໍ່ຢາຕ້ານເຊື້ອ ໃນລາວ.
- ພວກເຮົາພົບຄົນເຈັບທີ່ເປັນອັກເສບຫົວໃຈຊັ້ນໃນ ຈາກເຊື້ອ ***Bartonella henselae*** ເປັນຄັ້ງທຳອິດໃນລາວ ສະນັ້ນ ແພດໝໍເຮົາຄວນຄິດຫາເຊື້ອດັ່ງກ່າວ ໃນເວລາບົ່ງມະຕິຈຳແນກພະຍາດ.
- ການລະບາດຂອງໄຂ້ຍູງລາຍ ສາມາດເກີດຂຶ້ນໃນເຂດຊົນນະບົດຫ່າງໄກສອກຫລີກຂອງລາວ ໃນຊ່ວງລະດູໜາວ – ສະນັ້ນ ເຮົາຕ້ອງເຂົ້າໃຈຢ່າງເລິກເຊິ່ງຕື່ມອີກກ່ຽວກັບການເກີດຂຶ້ນຂອງໄຂ້ຍູງລາຍໃນຊ່ວງລະດູໜາວ.
- ພະຍາດ ມື-ຕີນ-ປາກ ຖືກຄົ້ນພົບໃນລາວ ແລະ ເຊື້ອທີ່ເປັນສາເຫດໄດ້ແກ່ EV71 ແລະ CVA16. ມີຄວາມຈຳ ເປັນ ຕ້ອງວາງແຜນຮັບມືກັບການລະບາດຂອງພະຍາດທີ່ເປັນຮຸນແຮງ ພາຍໃນປະເທດ.
- ພວກເຮົາຄົ້ນພົບວ່າ ການແປຜົນສຳລັບເຕັກນິກ Immunofluorescence assays ສຳລັບກວດຫາທາດກາຍຕ້ານ ຕໍ່ພະຍາດໄຂ້ແມງແດງ ແລະ ມູຣິນໄທຟັສ ແມ່ນມີ Inter- and intra-observer agreement ຂອນຂ້າງຕ່ຳ ຫລາຍ. ສະນັ້ນ ຈະຕ້ອງມີເຕັກນິກການກວດເຊໂຣໂລຊີທີ່ສາມາດແປຜົນໄດ້ຢ່າງຊັດເຈນກວ່ານີ້ ເຊັ່ນ ເຕັກນິກ ELISA ເປັນຕົ້ນ ເພື່ອຊ່ວຍໃນການບົ່ງມະຕິພະຍາດດັ່ງກ່າວ.
- ພວກເຮົາພົບວ່າ ເຊື້ອ ***Rickettsia typhi*** ໃນເລືອດຄົນເຈັບທີ່ເປັນພະຍາດມູຣິນໄທຟັສ ແມ່ນມີປະລິມານຕ່ຳກວ່າ ເຊື້ອ ***Orientia tsutsugamushi*** ທີ່ພົບໃນຄົນເຈັບທີ່ເປັນໄຂ້ແມງແດງ. ເຕັກນິກ LAMP assay ທີ່ພວກເຮົາ ພັດທະນາຂຶ້ນມາ ສຳລັບບົ່ງມະຕິພະຍາດມູຣິນໄທຟັສ ແມ່ນມີຄວາມແມ່ນຢຳໜ້ອຍ ຍ້ອນປະລິມານເຊື້ອທີ່ມີໃນເລືອດ ຄົນເຈັບມີໜ້ອຍ. ສະນັ້ນ ແນວທາງການບົ່ງມະຕິທີ່ດີສຳລັບພະຍາດດ່ງກ່າວ ຄວນຈະເປັນການສົມທົບກັນ ລະຫວ່າງ ເຕັກນິກເຊໂຣໂລຊີ ແລະ ເຕັກນິກທາງພັນທຸກຳ.
- ພວກເຮົາຄົ້ນພົບວ່າ ເຊື້ອໄຂ້ຍູງຟານຊີປາຣອມ ດື້ຕໍ່ຢາກຸ່ມ artemisinin ທີ່ແຂວງອັດຕະປື ເຊິ່ງສະແດງອອກດ້ວຍ ການທີ່ຄົນເຈັບຫາຍຈາກອາການໄຂ້ຊ້າກວ່າປົກກະຕິ – ເຖິງວ່າ ຍັງພົບໃນຈຳນວນຄົນເຈັບໜ້ອຍໜຶ່ງກໍ່ຕາມ (6%). ສະນັ້ນ ເຮົາຈຳເປັນຕ້ອງມີການຕິດຕາມຢ່າງລະມັດລະວັງ ແລະ ຕ້ອງເພີ່ມທະວີການປ້ອງກັນການແຜ່ກະຈາຍຂອງມັນ ດ້ວຍການບົ່ງມະຕິພະຍາດ ແລະ ປິ່ນປົວໃຫ້ທັນການ.
- ພວກເຮົາພົບວ່າ ຄຸນນະພາບຂອງຢາປິ່ນປົວ ຍັງເປັນບັນຫາທີ່ໜັກໜ່ວງ. ພວກເຮົາຄົ້ນພົບວ່າ FDA CD3 device ເປັນເຄື່ອງມືກວດຢາປອມທີ່ດີ. ນອກນີ້ ພວກເຮົາຍັງພົບວ່າ ການຫັກແບ່ງຢາເມັດ (ທີ່ເຮົາມັກເຮັດເປັນປະຈຳ) ເປັນ ບັນຫາທີ່ເຮົາຍັງມອງຂ້າມ ເຊິ່ງອາດມີຜົນຕໍ່ການປິ່ນປົວຄົນເຈັບ ແລະ ຍັງພົບອີກວ່າ ເຮົາຈະຕ້ອງໄດ້ເອົາໃຈໃສ່ບັນຫາ ເລື່ອງຂໍ້ຄວາມພາສາ ແລະ ຄວາມຊັດເຈນຂອງພາສາ ໃນພາຊະນະຫໍ່ຫຸ້ມຢາ.

SEA Encephalitis Meeting opening ceremony, November 2013, attended by His Excellency Professor Dr Bounkong Syhavong, Vice-Minister of Health, and His Excellency, the Ambassador of France, Mr Yves Carmona

SUMMARY

Amphayavanh Seupsavith (left) and Souliyasak Thongpaseuth processing specimens

A. The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) is a clinical research unit embedded within the Microbiology Laboratory of Mahosot Hospital. It is funded predominantly by the Wellcome Trust of Great Britain, with significant additional support from the US Centres for Disease Control (CDC), the Foundation for Innovative New Diagnostics (FIND), the World Health Organisation (WHO) and the Institut de Recherche sur l'Asie du Sud-Est Contemporaine (IRASEC). Considerable assistance in kind is given by the Institut de Recherches pour le Développement/Université d'Aix-Marseille and the Rickettsial Diseases Research Program, Naval Medical Research Center, USA.

B. LOMWRU is composed of 24 Lao Government staff and 39 project-funded staff; 93% of the staff are Lao and 58% are female. The Microbiology Laboratory has clinical microbiology, molecular, serology and BSL3 laboratories. It follows University of Oxford biosafety policies and guidelines.

C. LOMWRU supports the infectious disease diagnostic service of Mahosot Hospital, assists provincial hospitals in Luang Nam Tha and Salavan, performs clinical research and builds diagnostic and research human capacity through training and active participation.

D. The main focus of the research work is on the causes of fever and their epidemiology, their optimal diagnosis and optimum treatment in Laos, the diagnosis, epidemiology and prevention of infantile beriberi, and the quality of medicines globally.

E. Since 2000 we have published 165 peer-reviewed papers and 12 book chapters. LOMWRU authors are the most cited in the Lao public health literature since 2000. In 2013 we published 22 peer-reviewed papers and have 4 in press.

F. Previous LOMWRU research was translated into policy in Laos in 2013 with the implementation of vaccination against pneumococcus and the Japanese encephalitis virus (JEV). LOMWRU research led to change in national antimalarial and typhoid treatment policy. It also demonstrated the presence of numerous important pathogens for the first time in Laos, and highlighted the importance of scrub typhus, leptospirosis, melioidosis and JEV, providing evidence on their epidemiology and prompting interventions.

G. The main findings, in brief, from work published or in press in 2013 or continuing (please see caveats in text!), are:

- Dengue, scrub typhus, leptospirosis and the Japanese encephalitis virus are the most common causes of

non-malarial acute fever in patients aged 5-49 years in rural Laos

- There are important differences in infectious disease epidemiology between northern and southern Laos
- Doxycyline is estimated to have significant efficacy for 12% of patients presenting with a malaria-like syndrome who are malaria rapid diagnostic (RDT) test negative
- Typhoid bacteria can be accurately, quickly and relatively inexpensively identified in blood culture fluid using typhoid antigen detecting RDTs. This technique may enable provincial hospital laboratories to diagnose this important pathogen
- Scrub typhus, murine typhus and leptospirosis are important causes of central nervous system infections in Vientiane and probably elsewhere in Asia
- *Staphylococcus aureus* is the leading cause of bacteraemia in Lao infants, probably because of maternal hot bed use, suggesting that cloxacillin use should be especially considered as empirical treatment for late onset sepsis in infants in their first three weeks of life
- Dengue and scrub typhus are frequent causes of fever in pregnant women in Vientiane and may be important contributors to high maternal mortality in Laos and elsewhere
- Bacteria can be detected by polymerase chain reaction (PCR) of DNA extracted from cerebrospinal fluid blotted onto filter paper from patients with meningitis. This may be a technique for remote support of aetiological diagnosis of bacterial meningitis at provincial hospitals
- Extended spectrum beta-lactamase producing Enterobacteriaceae are common in stools of healthy kindergarten children in Vientiane City and Province. This is of great concern for the spread of drug resistance in Laos
- *Bartonella henselae* endocarditis occurs in Laos and should be considered in the differential diagnosis
- Dengue outbreaks can occur in rural Laos in the winter: A better understanding of dengue 'overwintering' is needed
- Hand, foot and mouth disease (HFMD) occurs in Laos and both EV71 and CVA16 are present. Planning is needed for intervention for when an outbreak of severe disease occurs in Laos
- The immunofluorescence assays for detecting antibodies against scrub typhus and murine typhus have poor inter- and intra-observer agreement. There is a great need for serological assays that can be read more objectively, such as ELISA, to assist in the diagnosis of these diseases
- The *Rickettsia typhi* bacterial load in blood is low in patients with murine typhus, usually less than the loads of *Orientia tsutsugamushi* in scrub typhus. The loop-mediated isothermal amplification (LAMP) assay for murine typhus that LOMWRU developed had low sensitivity because of these low bacterial loads. It is likely that the optimum diagnosis of these typhus diseases involves combined serological and molecular detection
- *Plasmodium falciparum* artemisinin resistance, in the form of prolonged parasite clearance, occurs in Attapeu, southern Laos, albeit in a minority of patients (~6%). This needs to be monitored carefully and prevention, diagnosis and treatment of malaria enhanced
- There remain severe, at least focal, problems with the quality of diverse medicines. The FDA CD3 device is a promising tool for detection of falsified packaging. Tablet splitting is a common practice that may have a neglected deleterious impact on patient outcomes and more attention needs to be paid to packaging language and readability.

Mahosot Hospital

The Plain of Jars, looking north

INTRODUCTION

The Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU) is a clinical research unit embedded within the Microbiology Laboratory of Mahosot Hospital, a Lao Government primary-tertiary hospital in Vientiane. The majority of the funding is from the Wellcome Trust of the United Kingdom (UK), a charity, through the University of Oxford. LOMWRU was founded in 2000 and is guided by a Memorandum of Understanding between Mahosot Hospital, the Wellcome Trust and the University of Oxford (2012-2022). It is housed in two buildings: The old Microbiology Laboratory (from the 1920s), which houses the clinical microbiology laboratory, offices, administration and the medicine quality project, and the upper floor Infectious Disease Centre (funded by the Wellcome Trust and opened in 2008), which contains the Molecular, Serology and BSL3 Laboratories and offices.

Oxford University headquarters are at the Centre for Tropical Medicine, in the Nuffield Department of Medicine on the Churchill Hospital site. We are greatly assisted by the supplies, logistic and accounting staff of Mahidol Oxford Research Unit (MORU) in the Faculty of Tropical Medicine, Mahidol University, Bangkok, and have many scientific liaisons. MORU, the Shoklo Malaria Research Unit (SMRU), in Mae Sot, Thailand, the Cambodia-Oxford Medical Research Unit (COMRU) and LOMWRU are integrated into the Thailand/Lao Major Overseas Programme of the Wellcome Trust and Oxford University. We are also linked to the Oxford University Clinical Research Unit (OUCRU), based in Ho Chi Minh City, Vietnam, and have important collaborations with them.

LOMWRU is composed of 24 Lao Government staff and 39 project funded staff; 93% of the staff are Lao and 58% are female. In addition, we have four goats, resident in the Laboratory garden, who assist with the preparation of blood agar. LOMWRU has received significant recent support, in addition to that from the Wellcome Trust, from the US Centres for Disease Control (CDC), the Foundation for Innovative New Diagnostics (FIND), the World Health Organisation (WHO) and the Institut de Recherche sur l'Asie du Sud-Est Contemporaine (IRASEC). Considerable assistance in kind is given by the Institut de Recherche pour le Développement (IRD)/Université d'Aix-Marseille.

LOMWRU supports the infectious disease diagnostic service of Mahosot Hospital and assists provincial hospitals in the far northwest (Luang Nam Tha), the far south (Salavan) and other hospitals and institutions on request, performs clinical research and builds diagnostic and research human capacity. Of routine diagnostic specimens, in 2013 the Laboratory processed blood cultures from 6,315 patients, cerebrospinal fluid from 275, urine from 1,158, stool from 575, pus from 759, genital swabs from 2,799 and throat swabs from 1,182 patients. Dengue IgG, IgM and NS1 ELISAs were performed for 2,623 patients and scrub typhus and murine typhus rapid diagnostic tests for 639 patients.

Dr Rattanaphone Phetsouvanh reading IFAs

Since 2000 we have published or have in press 168 peer-reviewed papers and 12 book chapters. LOMWRU authors are the most cited in the Lao public health literature since 2000 and are the most cited authors on medicine quality and public health. In 2013 we published 22 peer-reviewed papers and have four papers and five book chapters in press. Here we describe this work and briefly summarize diverse activities for the past year.

Previous research has recently been translated into practice in Laos in 2013 with the implementation of vaccination against pneumococcus and the Japanese encephalitis virus. Our work on typhus and leptospirosis has highlighted these pathogens in the Lao health care system with, anecdotally, an increase in doxycycline use.

Infectious Disease Centre at Mahosot Hospital

RESEARCH RESULTS AND THEIR PUBLIC HEALTH IMPLICATIONS

Phonpasith Panyanouvong (right) reading a Gram stain

Infectious Disease Epidemiology and Treatment

A. Non-malarial fever in rural Laos. The data published in Mayxay *et al.* (2013) in Lancet Global Health demonstrated the importance of a wide spectrum of neglected infectious diseases, especially dengue, scrub typhus, leptospirosis and the Japanese encephalitis virus, as the causes of non-malarial acute fever in patients in rural Laos. We recruited 1,938 in- and out-patients at Luang Nam Tha (northern Laos) and Salavan Hospitals (southern Laos) aged 5-49 years with fever of ≤8 days, eligible for malaria testing. With conservative definitions of cause, we assigned 41% patients a diagnosis. Influenza testing was only performed at Luang Nam Tha where influenza B was important but only 53% of those with influenza fulfilled ILI criteria. The two sites are ~600km apart but disease frequency differed significantly between them with Japanese encephalitis virus infection, typhoid and leptospirosis more common at Luang Nam Tha and dengue and malaria more common at Salavan. We estimated that azithromycin, doxycycline, ceftriaxone, and ofloxacin would have had significant efficacy for 13%, 12%, 8% and 2% of patients, respectively.

These data suggest that empirical treatment with doxycycline for patients with undifferentiated fever and negative rapid diagnostic tests for malaria and dengue could be an appropriate strategy for rural health workers in Laos. However, even though it is a small country, one algorithm may not be optimum for the whole of Laos. Community-acquired septicaemia was relatively uncommon, suggesting that accessible diagnostic and treatment strategies for pathogens such as dengue, scrub typhus and leptospirosis may be of more immediate cost-effective public health impact than expensive facilities for blood culture. Further programmatic and cost-effectiveness analysis of different options is being conducted.

This work has involved collaborations in eight countries. We plan to expand this large collaborative study and include another provincial hospital in 2014 and to expand the work that we do with Luang Nam Tha and Salavan Hospitals.

B. Mixed concurrent infections, especially of common pathogens, are to be expected. However, there has been much confusion in the literature about the evidence needed to confirm mixed infections. We described a patient with PCR confirmed concurrent infection with murine typhus and scrub typhus in southern Laos (Phommasone *et al.* 2013). We used this example to suggest that reports of mixed infections should include an explicit discussion of the likely specificity and sensitivity of the diagnostic assays used and the likelihood that the observations represent true concurrent mixed infections (or co-infections), or sequential infections due to persistence of antibody or false positives due to assay cross-reactions ('dual positivity'). We proposed the first grading system of evidence for mixed infections.

C. Causes of fever at Mahosot. We are working on amalgamating all the data on the causes of sepsis (conventional bacteraemia, rickettsia, leptospira, dengue and JEV) over four recent years so that we can estimate the frequency of hospital admission of diverse aetiologies for a large series of patients and describe their comparative clinical features. For the conventional bacteria we are also analysing how antimicrobial resistance patterns have changed since 2000.

D. Central nervous system infections. We are also analyzing the data from the first ~1,000 patients to have a lumbar puncture at Mahosot Hospital since 2003 to describe the aetiologies for a large series of patients with meningitis/encephalitis and describe their comparative clinical features and impact. As described below, both 'conventional' bacterial and viral infections are important but rickettsial and leptospiral infections are also key – with evidence that these pathogens are more frequent causes of CNS infections than 'conventional' bacteria. This is also a large collaborative project with multiple partners, especially with Institut de Recherche pour le Développement (IRD)/ Université d'Aix-Marseille and Khon Kaen University. In 2014 this work will be expanded in collaboration with the Institut Pasteur, Paris, Vietnam and Cambodia. We work with the Centre d'Infectiologie Christophe Mérieux du Laos on detection of molecular markers of *M. tuberculosis* drug resistance from patients with TB meningitis.

E. Aetiology and impact of fever in pregnancy. Dr Vilada Chansamouth has started a large cohort study of the causes and impact of fevers in pregnancy in Pak Gnum District, Vientiane. Maternal mortality is reported as the highest in SE Asia and data from Mahosot Hospital (in prep.) suggests that common infectious diseases, such as dengue and scrub typhus may be important contributors. This study is linked to the National Centre of Laboratory and Epidemiology for surveillance of respiratory infections in pregnant women, supported by US CDC in Laos.

Plus, we are looking in the blood samples of patients without a diagnosis for diverse other pathogens such as *Bartonella*, *Neorickettsia sennetsu*, *Anaplasm*a and *Erhlichia* species. We are investigating the aetiology of endocarditis in collaboration with Paris Descartes University and l'Université d'Aix-Marseille and have recently discovered the first patients with *Bartonella henselae* endocarditis. We are a centre for the Cryptodex clinical trial of dexamethasone *versus* placebo in HIV-positive patients receiving amphotericin B for cryptococcal meningitis. This trial is coordinated by OUCRU. We are also working with the London School of Hygiene & Tropical Medicine (LSHTM), the WorldWide Antimalarial Resistance Netowrk (WWARN) and FIND on the mapping of the aetiology of fevers globally, building on Acestor *et al.* (2012; *PLoS One 7,* e44269).

Clinical Microbiology

A. Accelerated, inexpensive detection of typhoid in blood cultures. Typhoid (*Salmonella enterica* serovar Typhi) remains an important pathogen in Laos but there are very few health facilities with accessible blood culture and antimicrobial susceptibility testing facilities. We therefore explored whether initial blood culture bacterial amplification followed by testing of blood culture fluid for *S.* Typhi antigen using rapid diagnostic tests (RDT) could be an accurate and inexpensive tool for the accelerated diagnosis of patients with acute typhoid in Laos (Castonguay-Vanier *et al.* 2013). These tests were originally developed for detecting *S.* Typhi antigen in stools. After 1-2 days of incubation in blood culture bottles, the test was very accurate, in comparison to reference assays, both on a series of relevant reference organisms and in a prospective study. The test needs much less human capacity and consumables and accelerates aetiological diagnosis by one day, in comparison to reference tests. We are exploring the use of the tests in more detail and determining whether we can detect molecular markers of *S.* Typhi fluoroquinolone resistance from the RDTs, in collaboration with OUCRU. Tests have been given to the National Centre for Laboratory & Epidemiology for their use in investigating outbreaks and colleagues in Cambodia are evaluating them in Siem Reap.

We are also exploring the use of simple systems to identify diverse other common causes of community-acquired septicaemia that could be appropriate at provincial hospital level in Laos and in other countries globally that do not have microbiology facilities in peripheral centres.

B. Bacteraemia in Lao infants. We reviewed the aetiology and antibiotic susceptibilities of bacteremia in young infants admitted at Mahosot Hospital (Anderson *et al.* 2013). As *Staphylococcus aureus* is the leading cause of bacteremia in Lao infants, we also examined risk factors for this infection, in particular the local practice of warming mothers during the first weeks postpartum with hot coals under their beds (hot beds). The most common isolates were *S. aureus, Escherichia coli* and *Klebsiella pneumoniae*. Whereas no methicillin-resistant *S. aureus* was found, only 18% of *E. coli* isolates were susceptible to ampicillin. A history of sleeping on a hot bed with mother was significantly associated with *S. aureus* bacteraemia. The study therefore supports evidence that *S. aureus* is a surprisingly common pathogen for young infants and that hot beds are a major risk factor for infant hospital admission with *S. aureus* sepsis.

We are planning further studies to investigate this, to measure the temperatures infants are exposed to on hot beds, and to perform prospective investigations to test this relationship and to increase our understanding of the knowledge, attitude and practice of maternal and infant hot bed use.

Phonlavanh Phouminh processing blood cultures

C. Diagnosis of bacterial meningitis from cerebrospinal fluid on filter paper. There are very few facilities in Laos for diagnosis of central nervous system infections. We investigated whether dried cerebrospinal fluid (CSF) conserved on filter paper can be used as a substrate for accurate PCR diagnosis of important causes of bacterial meningitis. Using mock CSF, the Elute Micro Card was the most sensitive, consistent and practical variety of filter paper. Following optimization, the lower limit of detection for *Streptococcus pneumoniae* from dried mock CSF spots was 14 genomic equivalents (GE)/µL. A prospective clinical evaluation for *S. pneumoniae, S. suis* and *Neisseria meningitidis* was performed for PCR of CSF on paper versus PCR and culture of liquid CSF, estimating sensitivity at 90% (Elliott *et al.* 2013). Dried CSF filter paper spots could potentially help us to better understand the epidemiology of bacterial meningitis in resource-poor settings and guide empirical treatments and vaccination policies.

Prompted by the potential value of filter papers as easily transportable substrates for specimen collection, we reviewed in collaboration with the London School of Hygiene and Tropical Medicine (LSHTM) the literature on the subject, including for diverse types of body fluid and for veterinary medicine, especially for neglected tropical diseases (Smit *et al.* in press). This suggests that, at least for some pathogens, filter papers are appropriate substrates, but there remains much confusion over terminology, analysis and reporting that needs to be improved.

D. *Burkholderia pseudomallei*. Defining the global pattern of *B. pseudomallei* distribution underpins efforts to prevent infection, and is dependent upon robust environmental sampling methodology. Limmathurotsakul *et al.* (2013) reviewed the literature on the detection of environmental *B. pseudomallei*, updated the risk map for melioidosis, and proposed international consensus guidelines for soil sampling. We developed consensus guidelines with the goals of reducing the probability of false negative results, and the provision of affordable and 'low-tech' methodology that is applicable in both developed and developing countries. The proposed consensus guidelines provide the basis for the development of an accurate and comprehensive global map of environmental *B. pseudomallei.* We are analysing further data that suggest that the methods recommended in these guidelines may not work equally well with all soils and are working to develop and apply methods that have greater sensitivity, including PCR following enrichment culture. There is a need for new culture techniques to allow for efficient detection of *B. pseudomallei* in fecal and other contaminated specimens. We found that the addition of norfloxacin, ampicillin, and polymyxin B to Ashdown's medium (NAP-A) resulted in increased specificity without affecting the growth of 25 *B. pseudomallei* strains (Goodyear *et al.* 2013). Furthermore, recovery of *B. pseudomallei* from human clinical specimens was not affected by the three additional antibiotics, suggesting that NAP-A medium provides a new tool for more sensitive isolation of *B. pseudomallei* from heavily contaminated sites.

Plus, we are completing two field studies with the Institut de Recherche pour le Développement (IRD) to examine the distribution of *B. pseudomallei* in soil and water in Laos in relation to physicochemical variables. Much of the melioidosis work is performed in collaboration with the Microbiology Department at MORU. We are analyzing the data from the first ~700 patients with culture positive melioidosis diagnosed at Mahosot Hospital since 1999 and evaluating a new RDT for *B. pseudomallei* antigen detection in blood culture fluid. We have started to establish a artificial soil system which can hopefully be extended as an *in vitro* system to study *B. pseudomallei* ecology in the BSL-3 laboratory.

We are working with OUCRU and the Wellcome Trust Sanger Institute on the comparative genomics of *Salmonella* species in Asia, both typhoid and non-typhoidal. We have completed a pilot study with Institut de la Francophonie pour la Médecine Tropicale (IFMT) on childhood faecal carriage of Extended spectrum beta-lactamase producing Enterobacteriaceae (ESBLE) in Vientiane kindergartens, finding that 23% were colonised with ESBLE, mainly *Escherichia coli* carrying bla_{CTX-M} and *Klebsiella pneumoniae* carrying bla_{SHV} or bla_{CTX-M}, which were frequently resistant to multiple unrelated antibiotics. Faecal carriage of ESBLE was more common in Vientiane Capital (30%) than the more rural Vientiane Province (16%). Residence in Vientiane Capital and antibiotic use in the last three months were found to be independent risk factors for ESBLE carriage on multivariable analysis. This finding plus the recent, not unexpected, discovery of *Clostridium difficile* in the stools of patients at Mahosot Hospital suggests that strategies to reduce inappropriate antibiotic consumption both within health services and in the community are urgently needed.

Virology

The virology work of LOMWRU is also supported by Institut de Recherche pour le Développement (IRD)/ Université d'Aix-Marseille.

A. Japanese encephalitis virus. We reported the first complete genome of the Japanese encephalitis virus (JEV) from a Lao patient, a JEV genotype I strain (Aubry *et al.* 2013). JEV vaccination started in NW Laos in 2013.

B. Dengue. We described a dengue-1 virus outbreak in a rural northwestern Lao forest village during the cool season of 2008 (Dubot-Pérès *et al.* 2013). The isolated genotype 1 strain was genotypically 'endemic' and not 'sylvatic'. Phylogenetic analyses of 37 other dengue-1 sequences from diverse areas of Laos between 2007 and 2010 showed that the geographic distribution of some strains remained focal over time while others were dispersed throughout the country and across national borders. Whether the outbreak arose from dengue importation from an urban centre into a dengue-naïve community or crossed into the village from a forest cycle is unknown. More epidemiological and entomological investigations are required to understand dengue epidemiology and the importance of rural and forest dengue dynamics in Laos. Further discussion is needed to clarify terminology that confuses the term sylvatic as a genotype and as a habitat.

C. Hand, Foot and Mouth disease. We support enteroviral PCR for surveillance of Hand, Foot and Mouth disease (HFMD) as it is likely that there will be a large outbreak in Laos, as has happened in adjoining countries in the last decade. So far we have only found EV71 in children in uncomplicated disease. The genomes of the isolated viruses are being investigated and discussions held on how to respond to an outbreak.

Plus, we are analyzing the distribution of dengue serotype across Laos for the last five years, evaluating the diagnostic accuracy and long term 'field' stability of dengue rapid diagnostic tests (RDT), testing whether dengue RNA can be extracted from dengue RDTs to allow serotyping and mapping the epidemiology of dengue in Salavan using dengue RDTs.

Rickettsiology

A. The immunofluorescence antibody (IFA) test has been the mainstay of the serological diagnosis of all rickettsial pathogens since the 1960s. Extraordinarily, however, there has never been an evaluation of inter- and intra-observer variation or investigation as to how long slides can be kept without altering diagnostic accuracy. Phetsouvanh *et al.* (2013) examined these among six microscopists who read 50 scrub typhus (ST) and murine typhus (MT) indirect immunofluorescence assay (IFA) immunoglobulin M (IgM) slides. Inter-observer agreement was only moderate to fair, but was significantly correlated with experience. Storage at 4°C for 2 days showed a change from positive to negative in 20–32% of slides and therefore we recommended that slides should be read as soon as possible after processing. In view of the subjectivity of IFA we are attempting to move diagnosis to an ELISA system.

B. Scrub typhus genotypes. Working with the US Navy, the 47-kD HtrA protein diversity among diverse human isolates of *Orientia tsutsugamushi*, the agent of scrub typhus, was characterized (Jiang *et al.* 2013). The percentage similarity of translated amino acid sequences between 16 new isolates and 9 reference strains of *O. tsutsugamushi* ranged from 96.4% to 100%. It will be necessary that future scrub typhus vaccines takes this diversity into account.

C. Murine typhus diagnosis using LAMP assays. Although treatment of murine typhus (*Rickettsia typhi*)

with tetracycline antibiotics is effective, treatment is often misguided or delayed due to diagnostic difficulties. As the gold standard immunofluorescence assay is imperfect, we developed and evaluated a loop-mediated isothermal amplification assay (LAMP). In the prospective evaluation amongst 266 consecutive patients with suspected scrub typhus or murine typhus, the clinical sensitivity was disappointing at 33% (95% CI: 9.2 - 56.8) (specificity: 98.5% (95% CI: 97.0% - 100%)) (Dittrich *et al.* in press). This low diagnostic accuracy was attributed to low patient *R. typhi* bacterial loads and suggests that LAMP assays for *R. typhi* are unlikely to be diagnostically useful.

Plus, We have many collaborative rickettsiology projects with MORU and we are also working with the US Navy to determine whether different *Orientia tsutsugamushi* genotypes are associated with disease severity and with Mahidol University to determine the genetic diversity of the pathogen in Laos using a multilocus sequence typing (MLST) scheme. It has become apparent that scrub typhus, murine typhus and leptospirosis are important causes of central nervous system infections in Laos and we are investigating their frequency and clinical features and examining blood-brain barrier function. We are working on disease severity scores for scrub typhus, and analyzing the scrub typhus and murine typhus clinical trials of doxycycline and azithromycin and the first PK-PD work on typhus and doxycycline and azithromycin therapy with the Pharmacology Department of MORU. We are working with Institut Pasteur-Laos on a large survey of bacterial pathogens in Lao ticks.

We continue to work on *Neorickettsia sennetsu*, screening patients (four positive patients in Laos so far) and with the University of North Dakota a variety of invertebrate and vertebrate taxa to try to elucidate the natural history of this intriguing pathogen. We have also found *Rickettsia felis* in Lao patients for the first time, interestingly only so far in those with compromised immune systems.

Malaria

A. Artemisinin resistance. We participated, with the Lao Government Centre for Malariology, Parasitology and Entomology and MORU, in the multicentre TRAC study 2011/12 that provided the first evidence that artemisinin resistance *Plasmodium falciparum* parasites are present in Laos, as has been documented on the Cambodia/Thailand, Thailand/Burma borders and southern Vietnam. Of 120 patients with uncomplicated *P. falciparum* malaria recruited in Phouvong District, Attapeu, 6% had parasitaemia on day three and the slope of the parasite clearance curves were reduced. These data suggest that the situation should be closely monitored in Attapeu and elsewhere in southern Laos.

The recent description of a molecular marker of artemisinin resistance ('K-13 propeller') will hopefully make mapping the extent of these parasites simpler and easier. We are working with collaborators to look for this mutation in Lao parasites and repeating the TRAC study in 2013/14 in Attapeu to monitor the frequency of slow clearing parasites.

B. Insecticide in bed nets. Dr Mike Green of the USA's CDC invented a rapid and inexpensive colorimetric field test for cyanopyrethroid insecticide used in bed nets (Cyanopyrethroid Field Test or CFT). We used this to measure surface levels of deltamethrin on insecticide-coated polyester nets in Phalanxay District over a two-year period, compared to whole net levels assayed by high-performance liquid chromatography HPLC. At 12 months, ~15-40%, and at 24 months <10% of deltamethrin was retained on the nets. The CFT is a useful and accurate indicator of net efficacy and may be substituted for mosquito bioassays (Green *et al.* 2013).

C. Severe malaria. Newton *et al.* (2013) performed a retrospective analysis of the clinical and laboratory data of 988 adult patients, hospitalized with *P. falciparum* malaria and in western Thailand between 1986 and 2002, to assess the factors associated with a fatal outcome and to compare diverse models. Models using parameter sets based on WHO 1990, 2000 and Adapted AQ criteria plus blood smear parasite-stage assessment gave the best mortality prediction. A malaria prognostic index (MPI), derived from the dataset using five clinical or laboratory variables gave similar prognostic accuracy. The mortality of severe malaria in adults has fallen and the switch from quinine to artesunate has probably been an important contributor. Prognostic indices based on WHO 2000 definitions, and other simpler indices based on fewer variables, provide clinically useful predictions of outcome in Asian adults with severe malaria.

Plus, we have been working with the Foundation for Innovative New Diagnostics (FIND) to evaluate the positive control wells (PCWs) in the use of malaria rapid diagnostic tests (RDTs). The clinical trial of the efficacy of chloroquine in *P. vivax* malaria is continuing. In a large clinical trial, we found that thiamin supplementation did not reduce the frequency of symptoms during recovery from falciparum malaria in southern Laos. We have looked for *Plasmodium knowlesi* in filter paper blood spots from malaria patients but have not found evidence for this pathogen in Laos. We are working with the Spatial Ecology & Epidemiology Group in Oxford University to investigate the potential geographical range of this pathogen. We have been collecting filter paper blood spots from malaria patients all over Laos, with the Centre for Malariology, Parasitology & Entomology, to examine how the frequency of molecular markers of anti-malarial resistance have changed over the last 10 years, and reduction in chloroquine use in collaboration with the Southwest Foundation for Biomedical Research in Texas.

Dr Mayfong Mayxay testing patients for malaria

Community perceptions and engagement

Dengue. With the vast 2013 epidemic of dengue in Laos, more information on public knowledge and perceptions of this disease are vital. Mayxay *et al.* (2013a) interviewed people in eastern Vientiane City finding that 33% did not know that dengue and malaria are different diseases and that < 10% recognized that indoor water containers could be *Aedes* mosquito breeding sites. This work suggests that much more public engagement about dengue and its control are needed.

Respiratory infections. There is very little information on healthcare-seeking behavior in Laos and how it varies by syndrome, geography and ethnicity. Mayxay *et al.* (2013b) compared healthcare seeking behaviour for respiratory illnesses in a random survey of urban and rural communities, finding important variation probably due to differences in environmental and hygienic conditions, health service availability and socio-economic status.

Plus, now that there are more data on infectious disease epidemiology in Laos we are planning both public engagement research and implementation.

Medicine quality

WWARN. The WWARN Antimalarial Quality Scientific Group continues to tabulate and map reports of the quality of antimalarials (see http://www.wwarn.org/resistance/surveyors/antimalarial-quality) and we hope to be able to extend this to other classes of essential medicines and to display the results in both French and English. This is supported by the Bill & Melinda Gates Foundation and the Institut de Recherche sur l'Asie du Sud-Est Contemporaine (IRASEC) at the French Embassy, Bangkok.

A report on the repeat random survey of the quality of antimalarials in southern Laos, funded by IRASEC, is nearly complete.

Medicine quality problems. We are working on a report of analysis of samples of falsified artemether-lumefantrine and mebendazole seized in Angola, samples seized in the INTERPOL Operation Storm and falsified 'morning after pills' from Peru plus working with the Joint Inter-Agency Task Force (JIATF) of The Global Fund's Office of Inspector General, USAID's Office of the Inspector General, and UNDPs Office of Audit and Investigations. We work closely with with the USA's CDC and the Georgia Institute of Technology and the LSHTM in the UK.

Forensics. We have been working on innovative techniques to look for DNA in falsified medicines and using stable isotope ratios to try to determine the geographical origin of such 'medicines' in comparison to the genuine products.

Guidelines. We are revising the MEDQUARD guidelines

(Newton *et al.* 2009; *PLoS Medicine* 6, e1000052) on conducting and reporting surveys for the quality of medicines for the WHO, with the intention that this will become a WHO report and recommendation.

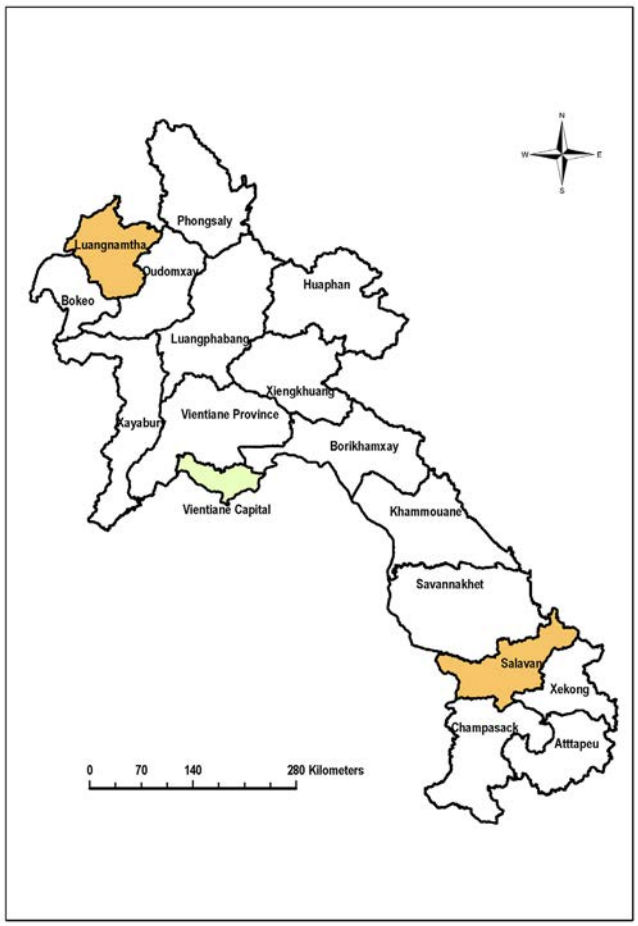
Tablet splitting is commonly practiced globally but there has been relatively little discussion on their clinical consequences for essential medicines in low- and middle-income countries. We therefore examined the accuracy of splitting and found severe problems, especially with coated and unscored tablets. Wider ranges of dosage units, particularly for narrow therapeutic index and critical dosage medicines, are needed so that splitting is not required.

Packaging. Working with the Institut de la Francophonie pour la Médecine Tropicale (IFMT), we have been surveying the information and language of antimalarial packaging – much of which is the wrong language or too small a font to read!

Medicine Stability. Similarly, another 'can of worms' is the stability of medicines in the tropics. There are very few 'field' data as to what actually happens to medicines in the tropics if they are not stored according to the manufacturer's recommendations. We are therefore performing long-term stability studies on antimalarials both in hot rural Laos and in the laboratory to examine the consequences of heat and time and determine the degradation products in collaboration with the CDC and the Georgia Institute of Technology in the USA.

CD3. We have been working with the U.S. Food and Drug Administration (FDA), the CDC and the Fogarty International Center of NIH in the USA and the Bureau of Food and Drug Inspection (BFDI), Food and Drug Quality Control Centre (FDQCC), Government of the Lao PDR, to evaluate the new CD3 device. This innovative, portable and relatively inexpensive instrument facilitates the examination of packaging to detect falsified medicines. When tested on our collection of genuine and falsified oral artesunate it demonstrated very high specificity and sensitivity against analysis by formal chemistry and packaging techniques.

Culzoni *et al.* (2013) reviewed high throughput and high resolution ambient mass spectrometry techniques for the investigation of the quality of pharmaceuticals with minimal or no sample preparation.



Map of Lao PDR showing Vientiane and the location of Luang Nam Tha and Salavan Provinces - LOMWRU supports infectious disease diagnosis for these provincial hospitals

KEY COLLABORATIONS

Dr Manivanh Vongsouvath with His Excellency Professor Dr Eksavang Vongvichit, Minister of Health, and His Excellency Mr Philipe Malone, the Ambassador of the United Kingdom to the Lao PDR

Within Lao PDR

Centre for Malariology, Parasitology & Entomology
National Centre for Laboratory & Epidemiology
Food and Drug Department, Ministry of Health
University of Health Sciences
Provincial Hospitals of Luang Nam Tha and Salavan
Mittabap, Sethathirat, Mother & Child, Police and Army Hospitals, Vientiane

World Health Organisation Lao Country Office, Vientiane
Institut de la Francophonie pour la Médecine Tropicale
Institut de Recherche pour le Développement
Centre d'Infectiologie Christophe Mérieux du Laos
Institut Pasteur – Laos
Health Frontiers, Vientiane
US CDC, US Embassy

International (in addition to collaborations with MORU, SMRU, COMRU and OUCRU),

in alphabetical order of institution

Dr Robert Gibbons, Department of Virology, Armed Forces Research Institute of Medical Sciences (AFRIMS), Bangkok, Thailand

Dr Mike Green, CDC, Atlanta, Georgia, USA

Professor Manfred Kayser, Department of Forensic Molecular Biology, Erasmus University Rotterdam, the Netherlands

Nicola Ranieri, Forensic Chemistry Center, Food & Drug Administration, Cincinnati, Ohio, USA

Professor Facundo Fernandez, Georgia Institute of Technology, Atlanta, Georgia, USA

Dr Dallas Mildenhall, GNS Science, New Zealand

Dr Mariana Mirabel, Paris Cardiovascular Research Centre, Inserm U970, European Georges Pompidou Hospital, Paris Descartes University, Cardiology Department, European Georges Pompidou Hospital, Paris, France

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Drs Philippe Buchy and Didier Menard, Institut Pasteur, Phnom Penh, Cambodia

Professor Marc Lecuit and colleagues, Institut Pasteur, Paris, France

Ms Aline Plançon, INTERPOL, Geneva, Switzerland

Dr Lesley Chesson and Jim Ehleringer, IsoForensics Inc., and Thure Cerling, University of Utah, USA

Dr Lee Smythe, Leptospiral Reference Laboratory, Coopers Plains, Australia

Drs David Schellenberg, Shunmay Yeung and Harparkash Kaur, ACT Consortium, London School of Hygiene and Tropical Medicine, London, UK

Mr Martin Cinnamond, Joint Inter-Agency Task Force, Geneva, Switzerland

Professors Pewpan Intapan & Wanchai Maleewong, Khon Kaen University, Thailand

Ms Lorna Cox, Nutritional Biomarker Analysis Laboratory, MRC Nutrition, Cambridge, UK

Dr David Litt, Respiratory and Vaccine Preventable Bacteria Reference Unit, Public Health England, London, UK

Dr SJ Gray, Meningococcal Reference Unit, Health Protection Agency, Manchester, UK

Dr Al Richards, Rickettsial Diseases Research Program, Naval Medical Research Center, USA

Professor Tim Anderson, Southwest Foundation for Biomedical Research, San Antonio, Texas, USA

Professor David Relman and Dr Stephen Popper, Department of Microbiology and Immunology, Stanford University, California, USA

Dr Souly Phanouvong and Dr Patrick Lukulay, United States Pharmacopeia, Rockville, Virginia, USA

Professor Xavier Nicolas de Lamballerie and Dr Audrey Dubot-Pérès, UMR190_Emergence des Pathologies Virales (l'Université d'Aix-Marseille, Institut de Recherche pour le Développement, EHESP French School of Public Health), Marseille, France.

Professor Didier Raoult and Professor Pierre-Edouard Fournier, Rickettsial Reference Laboratory, University of Marseille, France

Dr Fiona Russell and Prof Kim Mullholland, Murdoch Childrens Research Institute (MCRI), University of Melbourne, Victoria, Australia

Dr Andrew Steer and Dr Pierre Smeesters, Murdoch Childrens Research Institute (MCRI), University of Melbourne, Victoria, Australia

Professor Amir Attaran, Faculties of Law and Medicine, University of Ottawa, Ontario, Canada

Dr Nicole Stoesser and Prof Derrick Crook, Nuffield Department of Medicine, University of Oxford, UK

Dr Philippe Guerin and WWARN, WWARN, Centre for Tropical Medicine, University of Oxford, UK

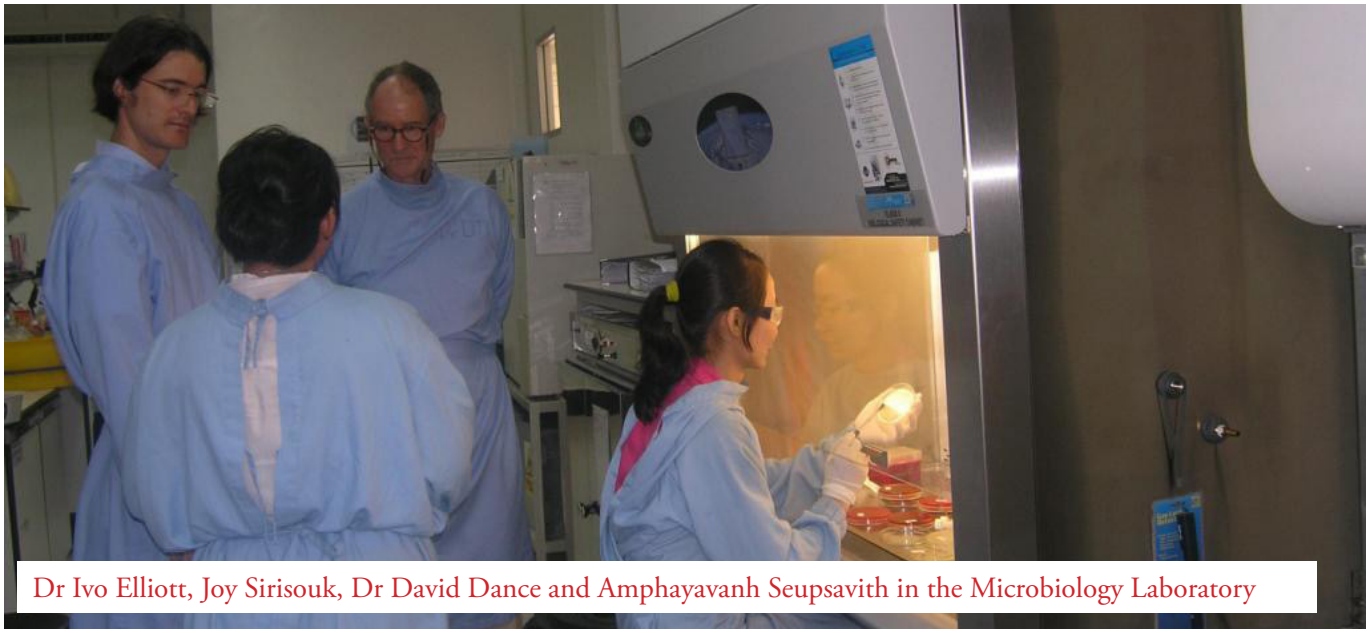
Dr David AuCoin, University of Nevada School of Medicine, Reno, Nevada, USA

Ms Aleisha Brock and Prof Adrian Esterman, University of South Australia, Adelaide, Australia

Dr Lesley Chesson & Prof Jim Ehleringer, IsoForensics Inc. and Thure Cerling, University of Utah, USA

Dr George Watt, US CDC, Bangkok, Thailand

STAFF AND HUMAN CAPACITY BUILDING



Dr Ivo Elliott, Joy Sirisouk, Dr David Dance and Amphayavanh Seupsavith in the Microbiology Laboratory

Thirty-two students in diverse health disciplines studied in the Microbiology Laboratory in 2013 and four residents wrote their theses related to the work of the Laboratory. The Laboratory staff assisted with the post-graduate internal medicine and paediatric training programme teaching and Dr Ko Chang, the first Lao physician to take an infectious disease postgraduate training programme, spent four months in the Laboratory.

Dr Rattanaphone Phetsouvanh is completing her PhD from Mahidol University, Bangkok, on scrub typhus, and Dr Manivanh Vongvousath is reading for her MSc in Clinical Tropical Medicine also at Mahidol University. Dr Vilada Chansamouth returned from successfully completing the MSc in Epidemiology at the London School of Hygiene and Tropical Medicine (the first Lao student to graduate from LSHTM), and Mr Sith Panyanouvong graduated from the Diploma in Medical Microbiology, Kuala Lumpur, Malaysia. Ms Kristin Mullins is doing her Uniformed Services University, USA, PhD with us on scrub typhus disease severity and *O. tsutsugamushi* genotypes.

Ms Bountoy Sibounheuang spent three months in the laboratory of Professor Xavier Nicolas de Lamballerie at Marseille working with Dr Audrey Dubot-Pérès, funded by the Institut de Recherche pour le Développement. She will spend two months a year there for the next three years, working on Lao projects and working to replicate the procedures used in Marseille in Vientiane. Dr Audrey Dubot-Pérès, who leads the LOMWRU virology, is based in Marseille but returned for three months of intensive virology work in LOMWRU in 2013.

In November 2013 we hosted, with Institut Pasteur - Paris, the SEA Encephalitis meeting In Vientiane. This meeting of a consortium of partners from SEA Asia and France discussed plans to investigate the causes and impact of encephalitis in the region. It was opened by His Excellency Professor Dr Bounkong Syhavong, Vice-Minister of Health, in presence of His Excellency, the Ambassador of France, Mr Yves Carmona.

We are fortunate to have strong links with Public Health England (PHE) who support a microbiology/infectious disease registrar to spend a year of training with us. Dr Caoimhe Nic Fhogartaigh has conducted much laboratory, clinical and research work during 2013 and Dr Kate Woods will start in 2014. This has been a very useful synergistic programme.

In addition, Dr Michael Knappik from Germany and Dr Elaine Cheong from Australia spent one year and three months, respectively, in LOMWRU contributing much to the clinical and research work.

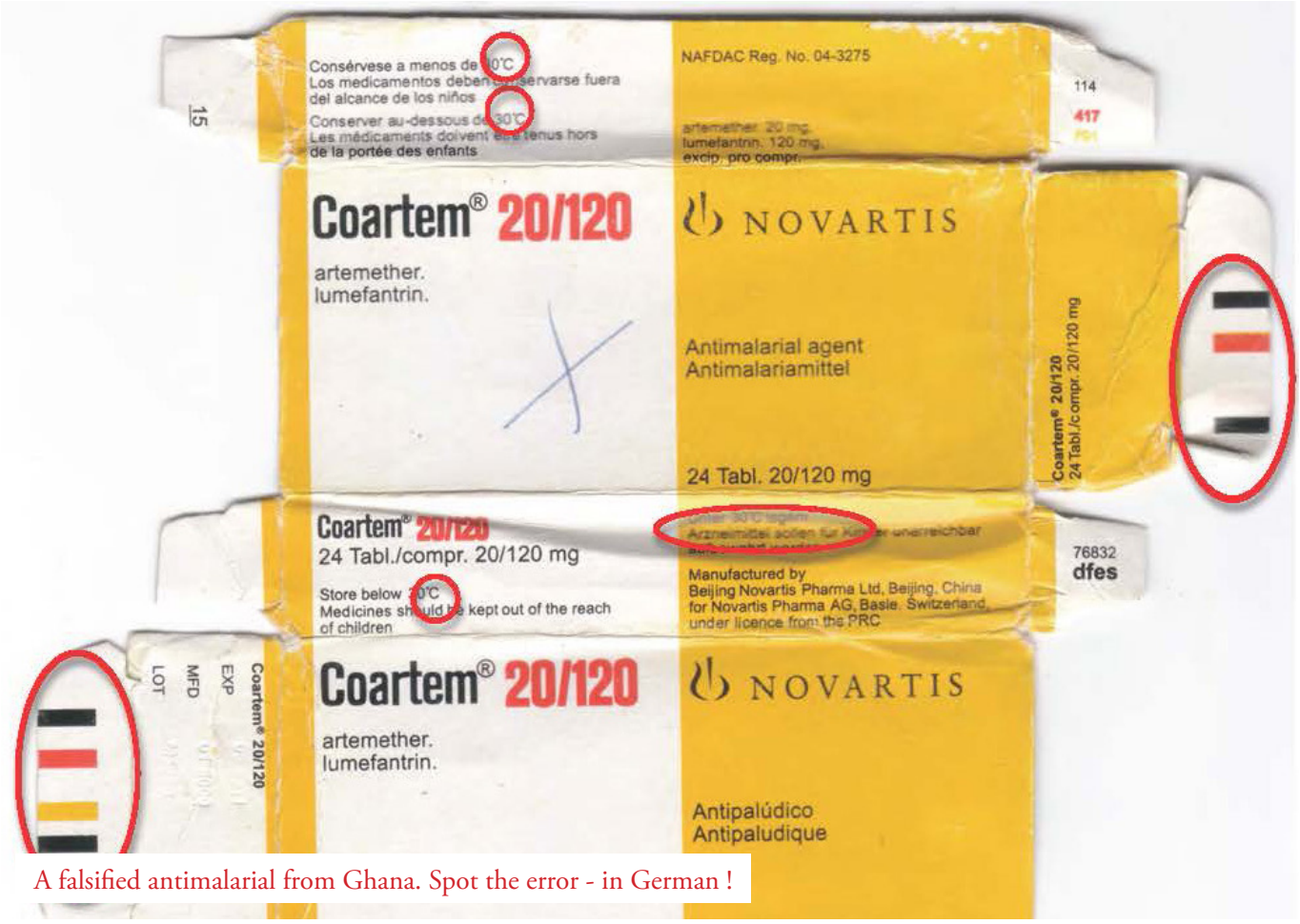
Professor Mike Parker ran the first course in medical bioethics in Laos. Regular classes have been held in basic mathematics for laboratory work and in English.

In 2013, we supported 16 staff and colleagues from other institutions in Laos to attend eight conferences and meetings outside of Laos.

We have continued to build capacity within the Unit with hands-on training in microbiology, ELISA, molecular diagnostic and BSL3 Laboratory work. We now have a Lao Deputy Safety Officer, a Lao Head of Field Research, a Lao deputy head of Virology, a Lao deputy WWARN Antimalarial Quality Coordinator, a Lao Laboratory Manager and a Lao BSL3 Manager.

LOMWRU staff teach at the University of Health Sciences and Institut de la Francophonie pour la Médecine Tropicale, Vientiane, the DTM&H of the London School of Hygiene and Tropical Medicine, and the MSc in Public Health of the École des hautes études en santé publique (EHESP), France.

OTHER ACTIVITIES



A falsified antimalarial from Ghana. Spot the error - in German !

A. Dengue outbreak. With the enormous dengue outbreak in Vientiane in 2013 we assisted with the diagnosis of patients admitted at Mahosot Hospital, using both ELISAs and RDTs and worked closely with the National Centre for Laboratory and Epidemiology (NCLE) and Institut Pasteur-Laos to help with this important public health problem.

B. External quality assurance. We participate in the UK National External Quality Assessement Service (NEQAS) scheme for general bacteriology and antimicrobial susceptibility testing and mycobacterial culture and the WPRO scheme for JEV/dengue IgM ELISA QA.

C. E-Library. We have been working with the University of Health Sciences (UHS) to build a page on their website as an e-library – as a repository of published and grey literature information about Lao public health. This will be completed in early 2014.

D. Mahosot Microbiology Review. We published the seventh Mahosot Microbiology Review in January 2013 and it is now translated into Lao language – it is attached and can be downloaded at http://www.tropmedres.ac/departments-units/laos/links-and-publications-laos.

E. Lao Medical Journal. We assist with the publication of the Lao Medical Journal (LMJ), the first Lao language medical journal. Assoc. Professor Mayfong Mayxay is an editor. We hope that the LMJ will be fully bilingual soon. It will be freely downloadable on the e-library at UHS.

F. LOMWRU website. We are starting to build a LOMWRU website linked to the www.tropmedres.ac site in MORU.

G. MOPSOP and Safety liaison. We have multiple links for liaison across the Major Overseas Programme for building consensus on Standard Operating Procedures for laboratory assays and for laboratory safety.

H. Talks etc. The Laboratory runs monthly lunchtime journal clubs, monthly scientific seminars and has frequent talks by academic visitors.

I. His Excellency Professor Dr Eksavang Vongvichit, Minister of Health, and His Excellency Mr Philipe Malone, the Ambassador of the United Kingdom to the Lao PDR, visited Mahosot Hospital and LOMWRU, Microbiology Laboratory in May 2013.

TITLES AND ABSTRACTS OF PAPERS PUBLISHED OR IN PRESS 2013

1. Mayxay M, Castonguay-Vanier J, Chansamouth V, Dubot-Pérès A, Paris DH, Phetsouvanh R, Tangkhabuanbutra J, Douangdala P, Inthalath S, Souvannasing P, Slesak G, Tongyoo N, Chanthongthip A, Panyanouvong P, Sibounheuang B, Phommasone K, Dohnt M, Phonekeo D, Hongvanthong B, Xayadeth S, Ketmayoon P, Blacksell SD, Moore CE, Craig SB, Burns M-A, von Sonnenburg F, Corwin A, de Lamballerie X, González IJ, Christophel EM, Cawthorne A, Bell D, Newton PN (2013) The causes of non-malarial fever in Laos – evidence to inform empirical treatment of fever. *Lancet Global Health* 1, e46-e54.

Abstract. Background. Because of reductions in the incidence of *Plasmodium falciparum* malaria in Laos, identification of the causes of fever in people without malaria, and discussion of the best empirical treatment options, are urgently needed. We aimed to identify the causes of non-malarial acute fever in patients in rural Laos. Methods For this prospective study, we recruited 1938 febrile patients, between May 2008, and December 2010, at Luang Namtha provincial hospital in northwest Laos (n=1390), and between September, 2008, and December, 2010, at Salavan provincial hospital in southern Laos (n=548). Eligible participants were aged 5–49 years with fever (≥38°C) lasting 8 days or less and were eligible for malaria testing by national guidelines. Findings. With conservative definitions of cause, we assigned 799 (41%) patients a diagnosis. With exclusion of influenza, the top five diagnoses when only one aetiological agent per patient was identified were dengue (156 [8%] of 1927 patients), scrub typhus (122 [7%] of 1871), Japanese encephalitis virus (112 [6%] of 1924), leptospirosis (109 [6%] of 1934), and bacteraemia (43 [2%] of 1938). 115 (32%) of 358 patients at Luang Namtha hospital tested influenza PCR-positive between June and December, 2010, of which influenza B was the most frequently detected strain (n=121 [87%]). Disease frequency differed significantly between the two sites: Japanese encephalitis virus infection (p=0.04), typhoid (p=0.006), and leptospirosis (p=0.001) were more common at Luang Namtha, whereas dengue and malaria were more common at Salavan (all p<0.0001). With use of evidence from southeast Asia when possible, we estimated that azithromycin, doxycycline, ceftriaxone, and ofloxacin would have had significant efficacy for 258 (13%), 240 (12%), 154 (8%), and 41 (2%) of patients, respectively. Interpretation. Our findings suggest that a wide range of treatable or preventable pathogens are implicated in nonmalarial febrile illness in Laos. Empirical treatment with doxycycline for patients with undifferentiated fever and negative rapid diagnostic tests for malaria and dengue could be an appropriate strategy for rural health workers in Laos.

2. Castonguay-Vanier J, Davong V, Bouthasavong L, Sengdetkha D, Simmalavong M, Seupsavith A, Dance D, Baker S, Phuong Tu Le Thi, Vongsouvath M, Newton PN (2013) Evaluation of a simple blood culture amplification and antigen detection method for the diagnosis of *Salmonella enterica* serovar Typhi bacteremia. *J Clinical Microbiology* 51, 142–148.

Abstract. In most typhoid endemic areas laboratory diagnosis is not possible due to the lack of appropriate facilities. We investigated whether the combination of blood culture amplification of *Salmonella enterica* serovar Typhi with an *S.*Typhi antigen rapid diagnostic test (RDT) could be an accurate and inexpensive tool for the accelerated diagnosis of patients with acute typhoid in Laos. For a panel of 23 Gram-negative reference pathogens the Standard Diagnostics (Cat No. 15FK20, Kyonggi-do, Korea) RDT gave positive results for *S.* Typhi NCTC 8385, *S.* Typhi NCTC 786 (Vi negative), *S.* Enteritidis (ATCC 13076) and *S.* Ndolo NCTC 8700 (all Group D). In a prospective study of 6,456 blood culture bottles from 3,028 patients over 15 months, 392 blood culture bottles (6.1%) from 221 (7.3%) patients had Gram negative Rods (GNR) seen in the blood culture fluid. The sensitivity, negative predictive value, specificity and positive predictive value were 96.7%, 99.5%, 97.9% and 87.9%, respectively, for patients with proven *S.* Typhi bacteremia and 91.2%, 98.4%, 98.9% and 93.9% for patients with Group D *Salmonella.* The median (range) number of days between diagnosis by RDT and reference assays, was one (minus 1 to +2) day for those with confirmed *S.* Typhi. The use of antigen-based pathogen detection in blood culture fluid may be a useful, relatively rapid, inexpensive and accurate technique for the identification of important causes of bacteremia in the tropics.

3. Phetsouvanh R, Taojaikong T, Phouminh P, Sibounheung B, Phommasone K, Chansamouth V, Lee S, Newton PN, Blacksell SD (2013) Inter- and intra-operator variability in the reading of indirect immunofluorescence assays for the serological diagnosis of scrub typhus and murine typhus. *Am J Trop Med Hyg* 88, 932–936.

Abstract. Inter- and intra-observer variation was examined among six microscopists who read 50 scrub typhus (ST) and murine typhus (MT) indirect immunofluorescence assay (IFA) immunoglobulin M (IgM) slides. Inter-observer agreement was moderate (k = 0.45) for MT and fair (k = 0.32) for ST, and was significantly correlated with experience (P = 0.03 and P = 0.004, respectively); k-scores for intra-observer agreement between morning and afternoon readings (range = 0.35– 0.86) were not correlated between years of experience for ST and MT IFAs (Spearman's r = 0.31, P = 0.54 and P = 0.14, respectively; P =0.78). Storage at 4°C for 2 days showed a change from positive to negative in 20–32% of slides. Although the titers did not dramatically change after 14 days of storage, the final interpretation (positive to negative) did change in 36–50% of samples, and it, therefore, recommended that slides should be read as soon as possible after processing.

4. Jiang J, Paris DH, Blacksell SD, Aukkanit N, Newton PN, Phetsouvanh R, Izzard L, Stenos J, Graves SR, Day NPJ, Richards AL (2013) Diversity of the 47 kDa HtrA nucleic acid and translated amino acid sequences from 17 recent human isolates of Orientia. *Vector-Borne and Zoonotic Diseases* 13, 367-375.

Abstract. *Orientia tsutsugamushi*, the etiologic agent of potentially fatal scrub typhus, is characterized by a high antigenic diversity, which complicates the development of a broadly protective vaccine. Efficacy studies in murine and nonhuman primate models demonstrated the DNA vaccine candidate pKarp47, based upon the *O. tsutsugamushi* Karp 47-kD HtrA protein gene, to be a successful immunoprophylactic against scrub typhus. To characterize 47-kD HtrA protein diversity among human isolates of *Orientia*, we sequenced the full open reading frame (ORF) of the 47-kD HtrA gene and analyzed the translated amino acid sequences of 17 patient isolates from Thailand (n = 13), Laos (n = 2), Australia (n = 1), and the United Arab Emirates (UAE) (n = 1) and 9 reference strains: Karp (New Guinea), Kato (Japan), Ikeda (Japan), Gilliam (Burma), Boryong (Korea), TA763, TH1811 and TH1817 (Thailand), and MAK243 (China). The percentage identity (similarity) of translated amino acid sequences between 16 new isolates and 9 reference strains of *O. tsutsugamushi* ranged from 96.4% to 100% (97.4% to 100%). However, inclusion of the recently identified *Orientia chuto* sp. nov. reduced identity (similarity) values to 82.2% to 83.3% (90.4% to 91.4%). These results demonstrate the diversity of *Orientia* 47-kD HtrA among isolates encountered by humans and therefore provide support for the necessity of developing a broadly protective scrub typhus vaccine that takes this diversity into account.

5. Green MD, Mayxay M, Beach R, Pongvongsa T, Phompida S, Hongvanthong B, Vanisaveth V, Newton PN, Vizcaino L, Swamidoss I (2013) Evaluation of a Rapid Colorimetric Field Test to Assess the Effective Life of Long-lasting Insecticide-treated Mosquito Nets in the Lao PDR. *Mal J* 12, 57.

Abstract. Background: Malaria morbidity and mortality have been significantly reduced through the proper use of insecticide-treated mosquito nets, but the extra protection afforded by the insecticide diminishes over time. The insecticide depletion rates vary according to location where wash frequency and wear are influenced by cultural habits as well as the availability of water. Monitoring of available insecticides on the net surface is essential for determining the effective life of the net. Therefore, a rapid and inexpensive colorimetric field test for cyanopyrethroids (Cyanopyrethroid Field Test or CFT) was used to measure surface levels of deltamethrin on insecticide-coated polyester nets (PowerNets™) in rural Lao PDR over a two-year period. Methods: Net surface levels of deltamethrin were measured by wiping the net with filter paper and measuring the adsorbed deltamethrin using the CFT. A relationship between surface levels of deltamethrin and whole net levels was established by comparing results of the CFT with whole levels assayed by high-performance liquid chromatography (HPLC). An effective deltamethrin surface concentration (EC80) was determined by comparing mosquito mortality (WHO Cone Test) with CFT and HPLC results. Five positions (roof to bottom) on each of 23 matched nets were assayed for deltamethrin surface levels at 6, 12, and 24 months. Mosquito mortality assays (WHO Cone Tests) were performed on a subset of eleven 24-month old nets and compared with the proportion of failed nets as predicted by the CFT. Results: At six months, the nets retained about 80% of the baseline (new net) levels of deltamethrin with no

significant differences between net positions. At 12 months, ~15-40%, and at 24 months <10% of deltamethrin was retained on the nets, with significant differences appearing between positions. Results from the CFT show that 93% of the nets failed (deltamethrin surface levels </= EC80) at 24 months. This value is in agreement with 91% failure as determined by the WHO Cone Test on a subset of 11 nets. The CFT results show that 50% of the nets from Laos failed at 12 months of normal use. Conclusion: The CFT is a useful and accurate indicator of net efficacy and may be substituted for mosquito bioassays.

6. Phommasone K, Paris DH, Anantatat T, Castonguay-Vanier J, Keomany S, Souvannasing P, Blacksell SD, Mayxay M, Newton PN (2013) Concurrent infection with murine typhus and scrub typhus in southern Laos - the mixed and the unmixed. *PLOS Negl Trop Dis* 7, e2163.

[A patient with PCR confirmed concurrent infection with murine typhus and scrub typhus in southern Laos is described. It is suggested that reports of mixed infections include an explicit discussion of the likely specificity and sensitivity of the diagnostic assays used and the likelihood that the observations represent true concurrent mixed infections (or coinfections), or sequential infections due to persistence of antibody or false positives due to assay cross-reactions ('dual positivity'). A grading system of evidence for mixed infections is proposed].

7. Elliott I, Dittrich S, Paris D, Sengduanphachanh A Phoumin P, Newton PN (2013) The use of dried cerebrospinal fluid filter paper spots as substrate for PCR diagnosis of the aetiology of bacterial meningitis in the Lao PDR. *Clinical Microbiology and Infection* May 2nd 2013.

Abstract. We investigated whether dried cerebrospinal fluid (CSF) conserved on filter paper can be used as a substrate for accurate PCR diagnosis of important causes of bacterial meningitis in the Lao PDR. Using mock CSF, we investigated and optimized filter paper varieties, paper punch sizes, elution volumes and quantities of DNA template to achieve sensitive and reliable detection of bacterial DNA from filter paper specimens. FTA Elute Micro Card™ (Whatman, Maidstone, UK) was the most sensitive, consistent and practical variety of filter paper. Following optimization, the lower limit of detection for *Streptococcus pneumoniae* from dried mock CSF spots was 14 genomic equivalents (GE)/**l**L (interquartile range 5.5 GE/**l**L) or 230 (IQR 65) colony forming units/mL. A prospective clinical evaluation for *S. pneumoniae, S. suis* and *Neisseria meningitidis* was performed. Culture and PCR performed on fresh liquid CSF from patients admitted with a clinical diagnosis of meningitis (n = 73) were compared with results derived from dried CSF spots. Four of five fresh PCR-positive CSF samples also tested PCR positive from dried CSF spots, with one patient under the limit of detection. In a retrospective study of *S. pneumoniae* samples (n = 20), the median (IQR; range) CSF *S. pneumoniae* bacterial load was 1.1 9 104 GE/**l**L (1.2 9 105; 1 to 6.1 9 106 DNA GE/**l**L). Utilizing the optimized methodology, we estimate an extrapolated sensitivity of 90%, based on the range of CSF genome counts found in Laos. Dried CSF filter paper spots could potentially help us to better understand the epidemiology of bacterial meningitis in resource-poor settings and guide empirical treatments and vaccination policies.

8. Aubry P, Vongsouvath M, Nougair A, Phetsouvanh R, Sibounheuang B, Charrel R, Rattanavong S, Phommasone K, Sengvilaipraserth O, Lamballerie X, Newton PN, Audrey Dubot-Pérès (2013) Complete genome of a Genotype I Japanese encephalitis Virus isolated from a patient with encephalitis in Vientiane, Lao PDR. *Genome Announcements* e00157-12.

Abstract. Japanese encephalitis virus (JEV) (Flaviviridae, Flavivirus) is an arthropod-borne flavivirus transmitted by *Culex* species mosquitoes. We report here the complete genome of the JEV genotype I strain JEV_CNS769_Laos_2009 isolated from an infected patient in Vientiane, Lao People's Democratic Republic (PDR) (Laos).

9. Limmathurotsakul D, Dance DAB, Wuthiekanun V, Kaestli M, Mayo M, Warner J, Wagner DM, Tuanyok A, Wertheim H, Cheng TY, Mukhopadhyay C, Puthucheary S, Day NPJ, Steinmetz I, Currie BJ, Peacock SJ (2013) Systematic review and consensus guidelines for environmental sampling of *Burkholderia pseudomallei*. *PLoS Negl Trop Dis* 7(3): e2105.

Abstract. Background: *Burkholderia pseudomallei*, a Tier 1 Select Agent and the cause of melioidosis, is a Gram-negative bacillus present in the environment in many tropical countries. Defining the global pattern of *B. pseudomallei* distribution underpins efforts to prevent infection, and is dependent upon robust environmental sampling methodology. Our objective was to review the literature on the detection of environmental *B. pseudomallei*, update the risk map for melioidosis, and propose international consensus guidelines for soil sampling. Methods/Principal Findings: An international working party (Detection of Environmental *Burkholderia pseudomallei* Working Party (DEBWorP)) was formed during the VIth World Melioidosis Congress in 2010. PubMed (January 1912 to December 2011) was searched using the following MeSH terms: pseudomallei or melioidosis. Bibliographies were hand searched for secondary references. The reported geographical distribution of B. pseudomallei in the environment was mapped and categorized as definite, probable, or possible. The methodology used for detecting environmental *B. pseudomallei* was extracted and collated. We found that global coverage was patchy, with a lack of

studies in many areas where melioidosis is suspected to occur. The sampling strategies and bacterial identification methods used were highly variable, and not all were robust. We developed consensus guidelines with the goals of reducing the probability of false negative results, and the provision of affordable and 'low-tech' methodology that is applicable in both developed and developing countries. Conclusions /Significance: The proposed consensus guidelines provide the basis for the development of an accurate and comprehensive global map of environmental *B. pseudomallei.*

10. Dubot-Pérès A, Vongphrachanh P, Denny J, Phetsouvanh R, Linthavong S, Sengkeopraseuth B, Khasing A, Xaythideth V, Moore CE, Vongsouvath M, Castonguay-Vanier J, Sibounheuang B, Taojaikong T, Chanthongthip A, de Lamballerie X, Newton PN (2013) An epidemic of dengue-1 in a remote village in rural Laos. *PLoS NTD* 7, e2360.

Abstract. In the Lao PDR (Laos), urban dengue is an increasingly recognised public health problem. We describe a dengue-1 virus outbreak in a rural northwestern Lao forest village during the cool season of 2008. The isolated strain was genotypically 'endemic' and not ''sylvatic', belonging to the genotype 1, Asia 3 clade. Phylogenetic analyses of 37 other dengue-1 sequences from diverse areas of Laos between 2007 and 2010 showed that the geographic distribution of some strains remained focal overtime while others were dispersed throughout the country. Evidence that dengue viruses have broad circulation in the region, crossing country borders, was also obtained. Whether the outbreak arose from dengue importation from an urban centre into a dengue-naive community or crossed into the village from a forest cycle is unknown. More epidemiological and entomological investigations are required to understand dengue epidemiology and the importance of rural and forest dengue dynamics in Laos.

11. Anderson M, Luangxay K, Sisouk K, Vorlasan L, Soumphonphakdy B, Sengmouang V, Chansamouth V, Phommasone K, Van Dyke R, Chong E, Dance DAB, Phetsouvanh R, Newton PN (2014) Epidemiology of bacteremia in young hospitalized infants in Vientiane, Laos 2000-2011. *J Trop Pediatrics* 60, 10-16

Abstract. As data about the causes of neonatal sepsis in low-income countries are inadequate, we reviewed the etiology and antibiotic susceptibilities of bacteremia in young infants in Laos. As *Staphylococcus aureus* is the leading cause of bacteremia in Lao infants, we also examined risk factors for this infection, in particular the local practice of warming mothers during the first weeks postpartum with hot coals under their beds (hot beds). Clinical and laboratory data regarding infants aged 0–60 days evaluated for sepsis within 72 h of admission to Mahosot Hospital

in Vientiane, Laos, were reviewed, and 85 of 1438 (5.9%) infants' blood cultures grew a clinically significant organism. Most common were *S. aureus, Escherichia coli* and *Klebsiella pneumoniae*. Whereas no methicillin-resistant *S. aureus* was found, only 18% of *E. coli* isolates were susceptible to ampicillin. A history of sleeping on a hot bed with mother was associated with *S. aureus* bacteremia (odds ratio 4.8; 95% confidence interval 1.2–19.0).

12. Culzoni MJ, Dwivedi P, Green MD, Newton PN, Fernández FM (2013) Ambient mass spectrometry technologies for the detection of falsified drugs. *Med Chem Commun* DOI: 10.1039/c3md00235g

Abstract. Increased globalization of the pharmaceutical market has facilitated the unobstructed and fast spread of poor-quality medicines. Poor-quality medicines include spurious/falsely-labeled/falsified/counterfeit drugs (those that are deliberately and fraudulently mislabeled with respect to content and/or origin), substandard drugs (legitimate drugs that do not meet their quality specifications), and degraded medicines (good quality pharmaceuticals that suffered from deterioration caused by improper storage or distribution). Consumption of poor-quality pharmaceuticals is likely to increase morbidity and mortality. Moreover, poor-quality drugs can also contribute to the development of resistance to anti-infective medicines and decrease the quality of health care received by patients. To assess the true prevalence of poor quality drugs, tiered technology approaches enabling the testing of drug samples

collected at points of sale are required, thus ensuring public health standards. High throughput and high resolution ambient mass spectrometry techniques allow investigation of pharmaceuticals with minimal or no sample preparation, thus possessing capabilities to survey a large number of drug samples for their authenticity.

13. Newton PN, Stepniewska K, Dondorp A, Silamut K, Chierakul W, Krishna S, Davis TME, Suputtamongkol Y, Angus B, Pukrittayakamee S, Ruangveerayuth R, Hanson J, Day NPJ, White NJ (2013) Prognostic indicators in adults hospitalized with falciparum malaria in Western Thailand. *Malaria Journal* 12: 229.

Abstract. Background: Severe malaria remains a major cause of death and morbidity amongst adults in the Asiatic tropics. Methods: A retrospective analysis of the clinical and laboratory data of 988 adult patients, hospitalized with *Plasmodium falciparum* malaria and prospectively recruited to malaria studies in western Thailand between 1986 and 2002, was performed to assess the factors associated with a fatal outcome. Different severity scores and classifications for defining severe malaria were compared and, using multiple logistic regression, simple models for predicting mortality developed. Results: The proportion of patients fulfilling the WHO 2000 definition of severe malaria was 78.1%, and their mortality was 10%. Mortality in patients given parenteral artesunate or artemether (16/317, 5%) was lower than in those given parenteral quinine (59/442, 13%) ($P < 0.001$). Models using parameter sets based on WHO 1990, 2000 and Adapted AQ criteria plus blood smear parasite-stage assessment gave the best mortality prediction. A malaria prognostic index (MPI), derived from the dataset using five clinical or laboratory variables gave similar prognostic accuracy. Conclusions: The mortality of severe malaria in adults has fallen and the switch from quinine to artesunate has probably been an important contributor. Prognostic indices based on WHO 2000 definitions, and other simpler indices based on fewer variables, provide clinically useful predictions of outcome in Asian adults with severe malaria.

14. Goodyear A, Strange L, Rholl DA, Silisouk J, Dance DA, Schweizer HP, Dow S (2013) An improved selective culture medium enhances the isolation of *Burkholderia pseudomallei* from contaminated specimens. Am J Trop Med Hyg. 89: 973-82.

Abstract. *Burkholderia pseudomallei* is a Gram-negative environmental bacterium found in tropical climates that causes melioidosis. Culture remains the diagnostic gold standard, but isolation of B. pseudomallei from heavily contaminated sites, such as fecal specimens, can be difficult. We recently reported that *B. pseudomallei* is capable of infecting the gastrointestinal tract of mice and suggested that the same may be true in humans. Thus, there is a strong need for new culture techniques to allow for efficient detection of B. pseudomallei in fecal and other specimens. We found that the addition of norfloxacin, ampicillin, and polymyxin B to Ashdown's medium (NAP-A) resulted in increased specificity without affecting the growth of 25 *B. pseudomallei* strains. Furthermore, recovery of *B. pseudomallei* from human clinical specimens was not affected by the three additional antibiotics. Therefore, we conclude that NAP-A medium provides a new tool for more sensitive isolation of *B. pseudomallei* from heavily contaminated sites.

15. Wang H, Yuan Z, Barnes E, Yuan M, Li C, Fu Y, Xia X, Li G, Newton PN, Vongsouvath M, Klenerman P, Pybus OG, Murphy D, Abe K, Lu L (2013) Eight novel hepatitis C virus genomes reveal the changing taxonomic structure of genotype 6. *J Gen Virol.* 94: 76-80.

Analysis of partial hepatitis C virus sequences has revealed many novel genotype 6 variants that cannot be unambiguously classified, which obscure the distinctiveness of pre-existing subtypes.

To explore this uncertainty, we obtained genomes of 98.0–98.8% full-length for eight such variants (KM35, QC273, TV257, TV476, TV533, L349, QC271 and DH027) and characterized them using phylogenetic analyses and per cent nucleotide similarities. The former four are closely related phylogenetically to subtype 6k, TV533 and L349 to subtype 6l, QC271 to subtypes 6i and 6j, and DH027 to subtypes 6m and 6n. The former six defined a high-level grouping that comprised subtypes 6k and 6l, plus related strains. The threshold between intra- and intersubtype diversity in this group was indistinct. We propose that similar results would be seen elsewhere if more intermediate variants like QC271 and DH027 were sampled.

16. Tarantola A, Goutard F, Newton PN, de Lamballerie X, Lortholary O, Cappelle J, Buchy (in press) Estimating the burden of Japanese encephalitis virus and other encephalitides in countries of the Mekong Region. *PLoS NTD*

Abstract. Diverse aetiologies of viral and bacterial encephalitis are widely recognized as significant yet neglected public health issues in the Mekong region. A robust analysis of the corresponding health burden is lacking. We retrieved 75 articles on encephalitis in the region published in English or in French from 1965 through 2011. Review of available data demonstrated that they are sparse and often derived from hospital-based studies with significant recruitment bias. Almost half (35 of 75) of articles were on Japanese encephalitis virus (JEV) alone or associated with dengue. In the Western Pacific region the WHO reported 30,000–50,000 annual JEV cases (15,000 deaths) between 1966 and 1996 and 4,633 cases (200 deaths) in 2008, a decline likely related to the introduction of JEV vaccination in China, Vietnam, and Thailand since the 1980s. Data on dengue, scrub typhus, and rabies encephalitis, among other aetiologies, are also reviewed and discussed. Countries of the Mekong region are undergoing profound demographic, economic, and ecological change. As the epidemiological aspects of Japanese encephalitis (JE) are transformed by vaccination in some countries, highly integrated expert collaborative research and objective data are needed to identify and prioritize the human health, animal health, and economic burden due to JE and other pathogens associated with encephalitides.

17. Dittrich S, Castonguay-Vanier J, Moore CE, Thongyoo N, Newton PN, Paris DH (in press) Loop-mediated isothermal amplification for *Rickettsia typhi* (murine typhus) - problems with diagnosis at the limit of detection. *J Clin Micro*

Abstract. Murine typhus is a flea-borne disease of worldwide distribution caused by *Rickettsia typhi.* Although treatment with tetracycline antibiotics is effective, treatment is often misguided or delayed due to diagnostic difficulties. As the gold standard immunofluorescence assay is imperfect, we aimed to develop and evaluate a loop-mediated isothermal amplification assay (LAMP). LAMP assays have the potential to fulfill the WHO 'ASSURED' criteria for diagnostic methodologies, as they can detect pathogen-derived nucleic acid with low technical expenditure. The LAMP assay was developed using samples of bacterial isolates (n=41), buffy coat from *R. typhi* PCR-positive Lao patients (n=42), and diverse negative controls (n=47). The method was then evaluated prospectively using consecutive patients with suspected scrub typhus or murine typhus (n=266). The limit of detection was ~40 DNA copies/ LAMP reaction, with an analytical sensitivity <10 DNA copies/reaction based on isolate dilutions. Despite these low cut-offs, the clinical sensitivity was disappointing with 48% (95%CI 32.5 - 62.7) (specificity 100 % (95%CI 100 - 100)) in the developmental phase and 33% (95% CI: 9.2 - 56.8) (specificity: 98.5% (95% CI: 97.0% - 100%)) in the prospective study. This low diagnostic accuracy was attributed to low patient *R. typhi* bacterial loads (median: 210 DNA copies/ mL blood, IQR: 130 – 500). PCR positive but LAMP-negative samples demonstrated significantly lower bacterial loads compared to LAMP-positive samples. Our findings highlight the diagnostic challenges for diseases with low pathogen burdens and emphasize the need to integrate pathogen biology with improved template production for assay development strategies.

18. The WorldWide Antimalarial Resistance Network (WWARN) DP Study Group (2013) The Effect of Dosing Regimens on the Antimalarial Efficacy of Dihydroartemisinin-Piperaquine: A Pooled Analysis of Individual Patient Data. *PLoS Med* 10: e1001564.

Abstract. Background: Dihydroartemisinin-piperaquine (DP) is increasingly recommended for antimalarial treatment in many endemic countries; however, concerns have been raised over its potential under dosing in young children. We investigated the influence of different dosing schedules on DP's clinical efficacy. Methods and Findings: A systematic search of the literature was conducted to identify all studies published between 1960 and February 2013, in which patients were enrolled and treated with DP. Principal investigators were approached and invited to share individual patient data with the WorldWide Antimalarial Resistance Network (WWARN). Data were pooled using a standardised methodology. Univariable and multivariable risk factors for parasite recrudescence were identified using a Cox's regression model with shared frailty across the study sites. Twenty-four published and two unpublished studies (n = 7,072 patients) were included in the analysis. After correcting for reinfection by parasite genotyping, Kaplan–Meier survival estimates were 97.7% (95% CI 97.3%–98.1%) at day 42 and 97.2% (95% CI 96.7%–97.7%) at day 63. Overall 28.6% (979/3,429) of children aged 1 to 5 years received a total dose of piperaquine below 48 mg/kg (the lower limit recommended by WHO); this risk was 2.3–2.9-fold greater compared to that in the other age groups and was associated with reduced efficacy at day 63 (94.4% [95% CI 92.6%–96.2%], p,0.001). After adjusting for confounding factors, the mg/kg dose of piperaquine was found to be a significant predictor for recrudescence, the risk increasing by 13% (95% CI 5.0%–21%) for every 5 mg/kg decrease in dose; p = 0.002. In a multivariable model increasing the target minimum total dose of piperaquine in children aged 1 to 5 years old from 48 mg/kg to 59 mg/kg would halve the risk of treatment failure and cure at least 95% of patients; such an increment was not associated with gastrointestinal toxicity in the ten studies in which this could be assessed. Conclusions: DP demonstrates excellent efficacy in a wide range of transmission settings; however, treatment failure is associated with a lower dose of piperaquine, particularly in young children, suggesting potential for further dose optimisation.

19. Smit PW, Elliott I, Peeling RW, Mabey D, Newton PN (in press) An overview of the clinical use of filter paper in the diagnosis of tropical diseases. *Am J Trop Med Hyg*

Abstract. Tropical infectious diseases diagnosis and surveillance are often hampered by difficulties of sample collection and transportation. Filter paper potentially provides a useful medium to help overcome such problems. We reviewed the literature on the use of filter paper, focusing on the evaluation of nucleic acid and serological assays for diagnosis of infectious diseases using dried blood spots (DBSs) compared with recognized gold standards. We reviewed 296 eligible studies: 101 studies evaluating DBSs and 192 studies on other aspects of filter paper use. We also discuss the use of filter paper with other body fluids and for tropical veterinary medicine. In general, DBSs perform with sensitivities and specificities similar or only slightly inferior to gold standard sample types. However, important problems were revealed with the uncritical use of DBS, inappropriate statistical analysis, and lack of standardized methodology. DBSs have great potential to empower healthcare workers by making laboratory-based diagnostic tests more readily accessible, but additional and more rigorous research is needed.

20. Nic Fhogartaigh C, Dance DAB (2013) Bacterial gastroenteritis. *Medicine* 41, 693-699.

Abstract. Infectious diarrhoea is a major public health concern worldwide. Bacteria, the focus of this review, are responsible for 20-40% of diarrhoeal episodes, contributing to high rates of childhood mortality in developing regions, and substantial morbidity and economic losses in developed regions. The epidemiology is changing with salmonellosis decreasing in industrialized countries and diarrhoeagenic *Escherichia coli* contributing to an increasing burden of disease worldwide. Molecular diagnostics have improved our understanding of the epidemiology, aetiology and pathogenesis of bacterial gastroenteritis, and have revealed new pathogenic agents, although widespread introduction of such diagnostics into clinical practice will require careful cost-benefit analyses. The development of antimicrobial resistance in gastrointestinal pathogens has implications for treatment options. We review the epidemiology of infectious diarrhoea, the principal aetiological agents and their clinical features, and the diagnosis, treatment and prevention of bacterial gastroenteritis; we also propose an investigation and management algorithm.

21. Mayxay M, Cui W, Thammavong S, Khensakhou K, Vongxay V, Inthasoum L, Sychareun V, Armstrong G (2013a) Dengue in peri-urban Pak-Ngum district, Vientiane capital of Laos: a community survey on knowledge, attitudes and practices. *BMC Public Health* 13:434.

Abstract. Background: Dengue remains an important cause of morbidity in Laos. Good knowledge, attitudes and practices (KAP) among the public regarding dengue prevention are required for the success of disease control. Very little is known about dengue KAP among the Lao general population. Methods: This was a KAP household survey on dengue conducted in a peri-urban Pak-Ngum district of Vientiane capital, Laos. A two-stage cluster sampling method was used to select a sample of participants to represent the general community. Participants from 231 households were surveyed using an interviewer-administered questionnaire. Results: Although 97% of the participants heard of dengue, there was a lack of depth of knowledge on dengue: 33% of them did not know that malaria and dengue were different diseases, 32% incorrectly believed that Aedes mosquito transmits malaria, 36% could not correctly report that Aedes mosquitoes bite most frequently at sunrise and sunset; and < 10% of them recognized that indoor water containers could be Aedes mosquito breeding sites. Attitude levels were moderately good with a high proportion (96%) of participants recognizing that dengue was a severe yet preventable disease. Self reported prevention methods were quite high yet observation of the participants' yards showed use of prevention methods to be only moderate. The majority (93%) of the interviewees did not believe that they had enough information on dengue. There was an association between good knowledge and better practices, but good knowledge was associated with worse attitudes. Conclusions: There is a lack of depth of knowledge regarding dengue in Pak-Ngum community and observation methods revealed that more needs to be done by community members themselves to prevent the spread of Aedes mosquitoes.

22. Mayxay M, Hansana V, Sengphilom B, Oulay L, Thammavongsa V, Somphet V, Taykeophithoune C, Nathavong S, Phanthady J, Chareunvong K, Chanthavilay P, Sychareun V (2013b) Respiratory illness healthcare-seeking behavior assessment in the Lao People's Democratic Republic (Laos). *BMC Public Health* 13:444

The Microbiology Laboratory at Mahosot Hospital

Abstract. Background: Respiratory illness (RI) remains a public health problem in Laos, but little is known about the overall burden and people's healthcare-seeking behavior for RI. Understanding the burden of RI and community patterns of healthcare-seeking behavior would provide better guidance for Lao public health program and policy planners to improve RI public health practice, surveillance systems, and prevention strategies. Methods: A quantitative and qualitative survey was conducted in 14 randomly selected villages of two purposively selected peri-urban and two rural provinces in Laos. A pre-designed and pre-tested questionnaire was used to collect information on RI in household members (defined as new fever with cough and/or sore-throat in the absence of other diagnoses during the preceding 30 days) from all heads of household in each village. Sixteen focus group discussions were conducted to obtain more information to support the quantitative survey. Results: Among 1,751 households (9,114 people) studied, 3.5% (317/9,114) had experienced RI (fever, cough, and/or sore-throat) in the 30 days before the survey [6.2% in rural and 2.4% in peri-urban areas (p<0.001)]. The percentage of RI among persons aged ≥15 years was 2.7%, 3.7% for those aged 5 – 14 years, and 8.2% for children < 5 years (p<0.001). Of all sick persons, 71% sought treatment [94% in peri-urban and 48% in rural areas (p<0.001)] and 31.5% of them self-medicated [55.5% in peri-urban and 29% in rural areas (p<0.001)]. Sick people in peri-urban areas preferred to chose private clinics and pharmacies as their first treatment option while in rural areas they frequently consulted with village health volunteers and visited health centres as their first choice. The qualitative study suggests that distance, costs of care, and service availability are the most important determinants of seeking healthcare. Conclusions: The RI burden and healthcare-seeking behavior are different between rural and peri-urban areas of Laos and this is probably due to the differences in environmental and hygienic conditions, health service availability and socio-economic status between the two areas. Therefore strategies for healthcare service improvement may also need to differ between the two areas.

23. Katangwe T, Purcell J, Bar-Zeev N, Denis B, Montgomery J, Alaerts M, Heyderman RS, Dance DA, Kennedy N, Feasey N, Moxon CA (2013) Human melioidosis, Malawi, 2011. Emerg Infect Dis. 19: 981-4

[A case of human melioidosis caused by a novel sequence type of *Burkholderia pseudomallei* occurred in a child in Malawi, southern Africa. A literature review showed that human cases reported from the continent have been increasing.]

The goat blood donors like baguettes

24. Wootton CI, Elliott IAM, Sengdetkha D, Vongsouvath M, Phongmany S, Dance D (2013) Melioidosis: an unusual cause of recurrent buttock abscesses. Clin Exp Dermatol 38, 427-8.

[An 18-year-old woman from Salavan who presented to Mahosot Hospital, Vientiane, with a 3-year history of widespread buttock abscess formation due to *Burkholderia pseudomallei,* is described.]

25. Cheng AC, Currie BJ, Dance DA, Funnell SG, Limmathurotsakul D, Simpson AJ, Peacock SJ (2013) Clinical definitions of melioidosis. Am J Trop Med Hyg. 88: 411-3.

Abstract. Clinical definitions of melioidosis and inhalation-acquired melioidosis (*Burkholderia pseudomallei* infection) are described together with the evidence used to develop these definitions. Such definitions support accurate public health reporting, preparedness planning for deliberate B. pseudomallei release, design of experimental models, and categorization of naturally acquired melioidosis.

26. Mayxay M, Soukaloun D, Newton PN (in press) A two-month-old Lao girl with dysnoea, irritability, poor breastfeeding and grunting. In: *Clinical Cases in Tropical Medicine*, Ed. Camilla Rothe, Elsevier-Saunders.

[A clinical description of a patient with infantile beriberi and discussion of epidemiology and treatment]

27. Slesak G, Inthalad S, Newton PN (in press) Extensive skin lesions on the lower leg in a 72-year-old farmer from Laos. In: *Clinical Cases in Tropical Medicine*, Ed. Camilla Rothe, Elsevier-Saunders.

[A clinical description of a patient with chromoblastomycosis and discussion of diagnosis and management]

LOMWRU Group Photo 2012

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38. Vilaphonh Manivanh (Tony)

28. Rattanavong S, Douangnoulak V, Norindr B, Newton PN, Nic Fhogartaigh C (in press) A 3-year-old boy with Right Suppurative Parotitis. In: *Clinical Cases in Tropical Medicine*, Ed. Camilla Rothe, Elsevier-Saunders.

[A clinical description of a patient with *Burkholderia pseudomallei* parotitis and discussion of management]

29. Rattanavong R, Keoluangkhot V, Sisouphonh S, Latthaphasavang V, Dance DAB, Nic Fhogartaigh C (in press) A 44-year-old farmer with diabetes and a back abscess. In: *Clinical Cases in Tropical Medicine*, Ed. Camilla Rothe, Elsevier-Saunders.

[A clinical description of a diabetic patient with *Burkholderia pseudomallei* septicaemia and abscess and discussion of management]

30. Newton PN, Keoluangkhot V, Mayxay M, Michael D Green, Facundo M Fernández (in press) A 30-year-old male Chinese trader with fever. In: *Clinical Cases in Tropical Medicine*, Ed. Camilla Rothe, Elsevier-Saunders.

[A clinical description of a patient with a recent history of falciparum malaria but failure of 'cure' with discussion of poor medicine quality]

ໂຄງການຮ່ວມມືຄົ້ນຄ້ວາດ້ານພະຍາດເຂດຮ້ອນ ລະຫວ່າງ ໂຮງໝໍມະໂຫສົດ - ແອວຄຳຕູ້ສ - ມະຫາວິທະຍາໄລອ໋ອກຊ໌ຟອດ

ວາລະສານຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາ, ໂຮງໝໍມະໂຫສົດ

ສະບັບທີ 7

ເດືອນມັງກອນ, 2013

ຫົວຂໍ້ໃນສະບັບນີ້:

ພາກສ່ວນຕໍ່ເຕີມຂອງພະແນກຈຸລິນຊີວິທະຍາ, ໂຮງໝໍມະໂຫສົດ; ຢູ່ທາງດ້ານ ຕາເວັນອອກສ່ຽງໃຕ້ ຂອງໂຮງໝໍມະໂຫສົດ

ພວກເຮົາຂໍສະແດງຄວາມຂອບໃຈມາຍັງ ທ່ານລັດຖະມົນຕີກະຊວງສາທາລະນະສຸກ, ພະນະ ທ່ານ ສຈ. ດຣ. ເອກສະຫວ່າງ ວົງວິຈິດ, ຫົວໜ້າກົມປິ່ນປົວ ຣຈ. ດຣ. ຈັນພົມມາ ວົງສຳພັນ ແລະ ຜູ້ອຳນວຍການໂຮງໝໍມະໂຫສົດ ຣຈ. ດຣ. ບຸນທະປານີ ບຸນຊ່ວຍ ທີ່ໃຫ້ການສະໜັບ ສະໜຸນ ແລະ ຊ່ວຍເຫລືອໂຄງການຂອງພວກເຮົາ. ຂໍສະແດງຄວາມຂອບໃຈມາຍັງພະນັກງານ ແພດໝໍທຸກຄົນໃນໂຮງໝໍມະໂຫສົດ, ຂໍຂອບໃຈບັນດາທ່ານທີ່ກວດແກ້ ວາລະສານສະບັບນີ້, CMPE, NCLE, UHS, IFMT, IRD, MORU, Foundation Merieux, Institut Pasteur, WPRO, WHO-Vientiane, Health Frontiers, ໂຮງໝໍແຂວງຫລວງນ້ຳທາ, ໂຮງໝໍແຂວງສາລະວັນ, ໂຮງໝໍໂພນສະຫວັນ, SFE, HPA-UK, Natural History Museum-London, LSHTM, MRC Human Nutrition, Royal Brompton Hospital-London ແລະ ມະຫາວິທະຍາໄລ Oxford, Aix-Marseille ແລະ Paris Ouest.

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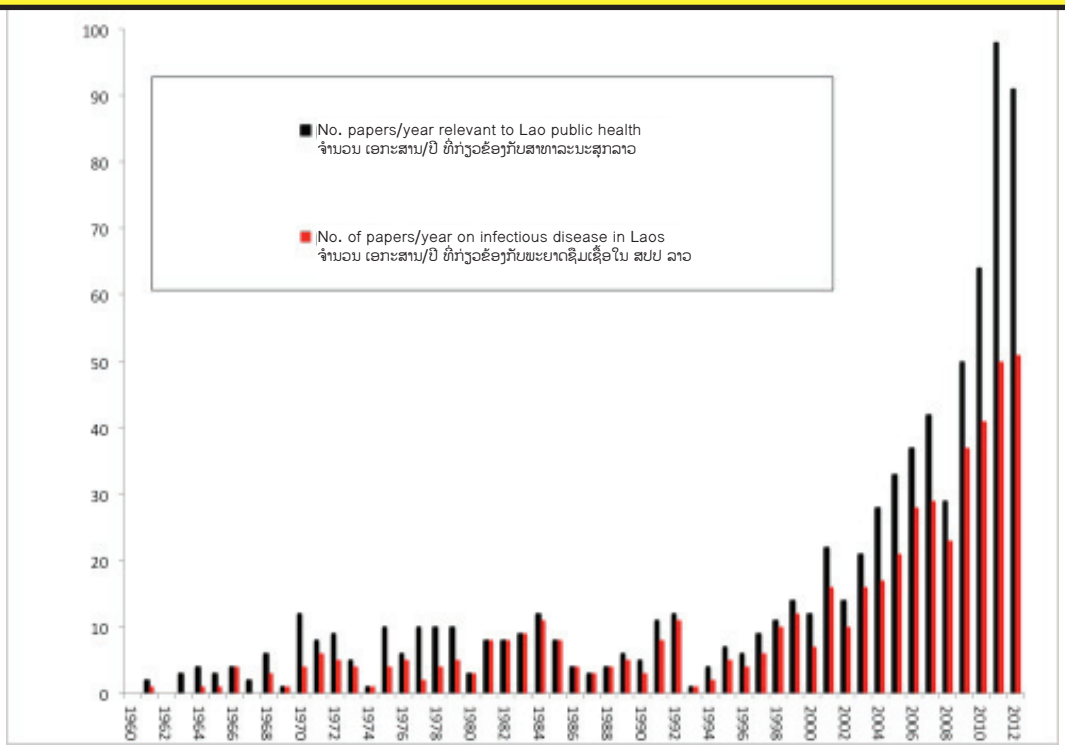
ໃນວາລະສານສະບັບນີ້ ພວກເຮົາໄດ້ສັງລວມຜົນການຄົ້ນຄວ້າ ທາງດ້ານຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາ ແລະ ພະຍາດຊຶມເຊື້ອ ທີ່ທາງໂຄງການຮ່ວມມືຄົ້ນຄ້ວາພະຍາດເຂດ ຮ້ອນ ລະຫວ່າງ ໂຮງໝໍມະໂຫສົດ - ແອວຄຳຕູ້ສ - ມະຫາວິທະຍາໄລອ໋ອກຊ໌ຟອດ ໄດ້ຈັດຕັ້ງປະຕິບັດຜ່ານມາ. ວາລະສານສະບັບພາສາລາວ ແມ່ນສາມາດເຂົ້າເບິ່ງໄດ້ ທາງ website ຂ້າງລຸ່ມນີ້. ກະລຸນາສົ່ງຄຳຄິດເຫັນ ແລະ ຄຳຕຳນິ-ຕິຊົມໃຫ້ແກ່ພວກເຮົາ ເພື່ອຈະໄດ້ ປັບປຸງວາລະສານສະບັບນີ້ໃຫ້ດີຂຶ້ນເລື້ອຍໆ.

ທ່ານສາມາດຂໍສຳເນົາທີ່ເປັນ PDF file ນຳພວກເຮົາໄດ້ໂດຍການ ຕິດຕໍ່ ໄປທາງທີ່ຢູ່ email ຂ້າງເທິງນີ້. ເນື່ອງຈາກມີຄວາມຫລ້າຊ້າໃນການຕີພິມ ວາລະສານສະບັບນີ້, ທ່ານສາມາດຕິດຕາມບັນດາບົດຕີພິມທາງການແພດທີ່ກ່ຽວຂ້ອງກັບປະເທດລາວໄດ້ທີ່ໜ້າ 16-28. ພວກເຮົາຄາດວ່າຈະໄດ້ຕີພິມວາລະສານ MMR-8 ໃນເດືອນກຸມພາ 2014. ທ່ານສາມາດເຂົ້າເບິ່ງວາລະສານ ສະບັບນີ້ໄດ້ທີ່: http://www.tropmedres.ac/study-sites/asia/laos/links-and-publications.html

Wellcome Trust ເປັນອົງກອນການກຸສົນ ທີ່ອຸທິດໃຫ້ແກ່ການຄົ້ນຄວ້າທາງດ້ານການແພດ ຂອງປະເທດອັງກິດ. ອົງກອນນີ້ສ້າງຕັ້ງຂຶ້ນຈາກເງິນຂອງທ່ານ Henry Wellcome ພາຍຫລັງການເສຍຊີວິດໃນປີ 1936. ອົງກອນນີ້ເປັນໜ່ວຍງານເອກະລາດ ແລະ ບໍ່ຂຶ້ນກັບບໍລິສັດການຢາໃດໆທັງນັ້ນ. ເຖິງວ່າວາລະສານສະບັບນີ້ ຈະສະ ຫງວນລິຂະສິດ, ແຕ່ທ່ານສາມາດນຳໃຊ້ເນື້ອຫາຕ່າງໆຂອງວາລະສານນີ້ພາຍໃຕ້ເງື່ອນໄຂຂອງ Creative Commons attribution licence v.2.0 ຂອງປະ ເທດອັງກິດ ແລະ ຂໍໃຫ້ທ່ານຂຽນອ້າງອີງຕາມຂໍ້ຄວາມຕໍ່ໄປນີ້: ວາລະສານຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາ, ໂຮງໝໍມະໂຫສົດ ສະບັບທີ 7, ປີ 2013.

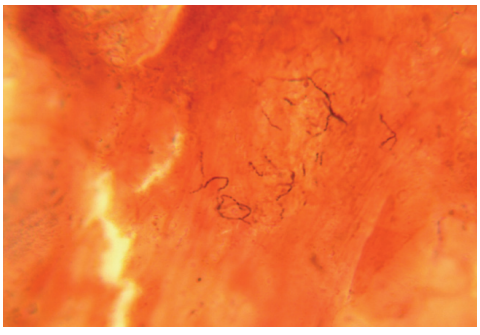
ບົດຕີພິມທາງການແພດທີ່ກ່ຽວຂ້ອງກັບປະເທດລາວ



ບັນດາບົດວິຊາການດ້ານສາທາລະນະສຸກໃນລາວຍັງສືບຕໍ່ຕີພິມເຜີຍແຜ່ອອກມາຢ່າງຫຼວງຫລາຍ

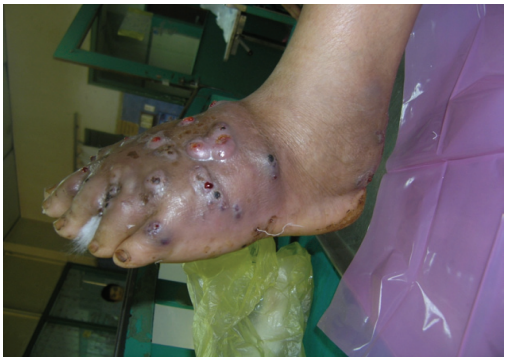
Actinomycosis

Mycetomas ຫຼື ຮູ້ຈັກກັນທົ່ວໄປໃນຊື່ Madura foot ແມ່ນ ພະຍາດຊຶມເຊື້ອຂອງຜິວໜັງ ແລະ ຊັ້ນກ້ອງຜິວໜັງແບບຊໍ້າເຮື້ອ, ເປັນກັບທີ່ ແລະ ມີການຂະຫຍາຍຕົວແບບຊ້ຳ. ເຊື້ອສາເຫດແມ່ນອາດມາຈາກເຊື້ອເຫັດ (ເອີ້ນຊື່ພະຍາດວ່າ: Eumycetoma) ຫຼື ຈາກຈຸລິນຊີທີ່ຕ້ອງການອາກາດໃນກຸ່ມ actinomycetes (Actinomycetoma). ເຊື້ອອາດຕິດຕໍ່ມາສູ່ຄົນຈາກບາດແຜຜິວໜັງທີ່ມາຈາກການກະທົບ,ໂດຍສະເພາະ ໃນກຸ່ມຄົນທີ່ມີອາ ຊີບເປັນຊາວກະສິກອນໃນເຂດຊົນນະບົດເຊິ່ງອາໃສໃນເຂດອາກາດຮ້ອນ. ເຖິງແມ່ນວ່າ ພະຍາດດັ່ງກ່າວເປັນທີ່ຮູ້ຈັກດີໃນອາຊີ ແຕ່ບໍ່ເຄີຍຖືກລາຍງານໃນປະເທດລາວມາກ່ອນ (Rattanavong *et al.* 2012). ຄົນເຈັບເພດຍິງອາຍຸ 30 ປີ ອາຊີບຄູ ແລະ ຊາວນາ ຈາກແຂວງຊຽງຂວາງ, ເຂົ້າໂຮງໝໍມະໂຫສົດດ້ວຍອາການຕີນເບື້ອງຊ້າຍຂະຫຍາຍໃຫຍ່ຜິດປົກກະຕິໂດຍບໍ່ມີປະຫວັດຖືກກະທົບມາກ່ອນ. ອາການດັ່ງກ່າວມີການຂະຫຍາຍຕົວຢ່າງຊ້າໆ, ບໍ່ເຈັບ ແລະ ມີຫຼາຍຮູຊຶມຕະຫຼອດໄລຍະເວລາ 5 ປີ. 10 ວັນກ່ອນເຂົ້າໂຮງໝໍ, ຕີນຄົນເຈັບມີຂະໜາດໃຫ່ຍຂຶ້ນຈົນບໍ່ສາມາດຍ່າງໄດ້. ໄດ້ມີການເຈາະເອົາຊິ້ນສ່ວນຂອງເນື້ອເຍື່ອໄປຍ້ອມສີ Gram ແລະ ເອົາໄປປູກເຊື້ອທາງດ້ານຈຸລິນຊີວິທະຍາ ເຊິ່ງພົບເຊື້ອຈຸລິນຊີ Gram-Positive ທີ່ມີຮູບຮ່າງເປັນ ສາຍຍາວ; ຫຼັງຈາກນັ້ນ ໄດ້ຖືກບົ່ງມະຕິວ່າເປັນ *Actinomadura madurae* ດ້ວຍວິທີການ 16S-rRNA sequencing. ຮູບຖ່າຍລັງສີ ສະແດງໃຫ້ເຫັນ ມີການທຳລາຍກະດູກຝ່າຕີນເບື້ອງຊ້າຍຢ່າງກວ້າງຂວາງ. ຄົນເຈັບຖືກປິ່ນປົວດ້ວຍຢາ Co-trimoxazole 20 ອາທິດ ສົມທົບກັບ Amikacin ໃນຫຼາຍຮອບວຽນ, ຮອບວຽນລະ 3 ອາທິດ, ແຕ່ລະຮອບວຽນຫ່າງກັນ 2 ອາທິດ ເຫັນວ່າມີການຕອບສະໜອງຕໍ່ການປິ່ນປົວທີ່ດີ. ເນື່ອງຈາກວ່າປະຊາຊົນລາວປະມານ 78% ປະກອບອາຊີບເປັນຊາວກະສິກອນ ແລະ ຍ້ອນປະເທດລາວຍັງຂາດເຂີນຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາເຊັ່ນດຽວກັນກັບບັນດາປະເທດເຂດຮ້ອນອື່ນໆ ສະນັ້ນອາດເປັນໄປໄດ້ທີ່ວ່າພະຍາດນີ້ຍັງບໍ່ຖືກບົ່ງມະຕິໄດ້ຕາມຄວາມເປັນຈິງ.



ຮູບເບື້ອງຊ້າຍ: ການຍ້ອມສີ Gram ຂອງຊິ້ນສ່ວນເນື້ອເຍື່ອຕີນ ເບື້ອງຊ້າຍ ພົບເຊື້ອຈຸລິນຊີ Gram positive ທີ່ມີລັກສະນະເປັນເສັ້ນ-ເປັນກ້ຽງ.

ຮູບເບື້ອງຂວາ: ຕີນເບື້ອງຊ້າຍຂອງຄົນເຈັບກ່ອນການປິ່ນປົວ.



ພາວະຂາດວິຕະມິນບີ 1 ໃນເດັກລຸ່ມ 1 ປີ

ພາວະ ຫຼື ອາການຂາດວິຕະມິນບີ 1 ໃນເດັກລຸ່ມ 1 ປີ ເປັນພະຍາດທີ່ຖືກຫລົງລືມໃນເຂດອາຊີ. ພາວະຂາດວິຕະມິນບີ 1 ເປັນບັນຫາສາທາລະນະສຸກທີ່ສຳຄັນໃນທ້າຍສະຕະວັດທີ 19 ເມື່ອມີການປະດິດເຄື່ອງສີເຂົ້າແບບກົນຈັກ-ເຊິ່ງການສີເຂົ້າແບບນີ້ ຈະເຮັດໃຫ້ເປືອກຂອງເມັດເຂົ້າທີ່ບັນຈຸວິຕະມິນບີ 1 ເສຍອອກໄປ ເຊິ່ງນຳໄປສູ່ການເສຍຊີວິດຂອງຄົນຈຳນວນຫຼວງຫຼາຍ. ເດັກອາຍຸລະຫວ່າງ 2-3 ເດືອນ ທີ່ສະແດງອາການແບບຫົວໃຈຊຸດໂຊມ ໂດຍທົ່ວໄປຈະຫາຍດີຢ່າງໄວ ຖ້າເມື່ອໄດ້ຮັບການສັກວິຕະມິນບີ 1 ໃຫ້. ພາວະຂາດວິຕະມິນບີ 1 ຍັງພົບໄດ້ຫລາຍສົມຄວນໃນວຽງຈັນ ໂດຍຈະມີເດັກລຸ່ມ 1 ປີ ທີ່ເປັນພະຍາດດັ່ງກ່າວ (ບິ່ງມະຕິອີງໃສ່ອາການສາດ) ເຂົ້ານອນປິ່ນປົວປະມານ 50-90 ຄົນຕໍ່ປີທີ່ໂຮງໝໍມະໂຫສົດ ເຊິ່ງອາດມີສາຍເຫດຈາກພຶດຕິກຳຄະລຳອາຫານແກ່ຍາວຂອງຜູ້ເປັນແມ່ໃນຊ່ວງໄລຍະຖືພາ ແລະ ຫລັງເກີດລູກ. ຈາກການສຶກສາຄົ້ນຄວ້າແບບ case control ໂດຍການສົມທຽບແມ່ທີ່ມີລູກຂາດວິຕາມິນບີ 1 ກັບແມ່ທີ່ມີລູກບໍ່ຂາດວິຕາມິນບີ 1 ຊີ້ໃຫ້ເຫັນວ່າ ເດັກທີ່ມີພາວະຂາດ ວິຕະມິນບີ 1 ນັ້ນ ແມ່ຂອງເຂົາເຈົ້າບໍ່ກິນອາຫານຫຼາກຫຼາຍໝູ່, ໄລຍະເວລາໃນການໝ່າເຂົ້າໝຽວດົນ, ເວລາຕົ້ມເຂົ້າມັກຖອກນ້ຳເຂົ້າທີ່ເກີນອອກ, ມີລະດັບການສຶກສາຕ່ຳ, ມີລາຍຮັບຕ່ຳ, ອອກແຮງງານໜັກ ແລະ ມີອາຊີບເປັນຊາວໄຮ່ນາ ຫລາຍກວ່າແມ່ທີ່ມີລູກບໍ່ມີພາວະຂາດວິຕະມິນບີ 1 (Soukaloun *et al.* 2003).

ການສຶກສາຄົ້ນຄວ້າຫາເຕັກນິກທີ່ດີທີ່ສຸດເພື່ອໃຊ້ບິ່ງມະຕິຢັ້ງຢືນພາວະຂາດວິຕະມິນບີ 1 ຍັງມີໜ້ອຍທີ່ສຸດ. ການສຶກສາຄົ້ນຄວ້າແບບ case control ໃນເດັກ ລຸ່ມ 1 ປີ ທີ່ນະຄອນຫຼວງວຽງຈັນ ໂດຍສົມທຽບເດັກທີ່ມີພາວະຂາດວິຕະມິນບີ 1 ຈຳນວນ 47 ຄົນ (ກຸ່ມສຶກສາ) ແບບຈັບກຸ່ມອາຍຸກັບເດັກທີ່ບໍ່ມີພາວະຂາດວິຕະມິນບີ 1 (ກຸ່ມປຽບທຽບ) ເຊິ່ງກຸ່ມນີ້ມີ 2 ກຸ່ມ ກຸ່ມໜຶ່ງມີໄຂ້ ແລະ ອີກກຸ່ມບໍ່ມີໄຂ້ ຈຸດປະສົງແມ່ນເພື່ອຊອກຫາເຕັກນິກການບິ່ງມະຕິທີ່ດີທີ່ສຸດ (Soukaloun *et al.* 2011). ໃນການສຶກສານີ້ ເຮົາພົບວ່າ basal erythrocyte transketolase activity (ETK) ເປັນຕົວຊີ້ວັດທີ່ບິ່ງບອກວ່າເດັກເປັນພາວະຂາດວິຕະມິນບີ 1 ໄດ້ດີກວ່າ activation coefficient ເຊິ່ງຜົນການສຶກສາແມ່ນກົງກັນຂ້າມກັບພາວະຂາດວິຕະມິນບີ 1 ໃນຜູ້ໃຫ່ຍ. ຄ່າ Plasma troponin T ອາດເປັນຕົວຊີ້ວັດທີ່ດີສຳລັບການບິ່ງມະຕິພາວະຂາດວິຕະມິນບີ 1 ໃນກຸ່ມເດັກນ້ອຍທີ່ມີຄວາມສ່ຽງ. ການກວດຫາປະລິມານຂອງສານດັ່ງກ່າວນີ້ອາດມີຜົນປະໂຫຍດຫຼາຍໃນການບິ່ງມະຕິ ເພາະໃນປະຈຸບັນແມ່ນໄດ້ມີຊຸດການ ກວດຫາຄ່າ Troponin ແບບໄວອາຢູ່ແລ້ວ.

ພາວະຂາດວິຕະມິນບີ 1 ທີ່ສະແດງອອກທາງດ້ານອາການສາດ ອາດເປັນສ່ວນນ້ອຍໜຶ່ງເທົ່ານັ້ນ ແຕ່ວ່າພາວະການຂາດວິຕະມິນບີ 1 ທີ່ບໍ່ມີອາການສະແດງອອກຢ່າງຊັດເຈນກໍ່ສາມາດເຮັດໃຫ້ເກີດການເຈັບປ່ວຍໄດ້ເຊັ່ນກັນ. ເພື່ອສຶກສາບັນຫາດັ່ງກ່າວນີ້ ເດັກນ້ອຍລຸ່ມ 1 ປີ ຈຳນວນ 778 ຄົນ ທີ່ເຂົ້າມານອນປິ່ນປົວທີ່ໂຮງໝໍມະໂຫສົດ ໄດ້ຖືກເອົາເຂົ້າມາໃນການສຶກສາ ເຊິ່ງເດັກເຫຼົ່ານີ້ແມ່ນບໍ່ມີອາການທີ່ສະແດງພາວະຂາດວິຕະມິນບີ 1, ໄລຍະທຳການຄົ້ນຄວ້າ 1 ປີ, ໂດຍໄດ້ເຈາະເລືອດໄປກວດຫາຄ່າ ETK. ຜົນການຄົ້ນຄວ້າພົບວ່າ 13.9% ຂອງເດັກເຫລົ່ານີ້ມີລະດັບ Basal ETK ຕ່ຳ ເຊິ່ງຊີ້ບອກວ່າມີພາວະຂາດວິຕະມິນບີ 1 (Khounnorath *et al.* 2011). ເປີເຊັນການຕາຍໃນກຸ່ມເດັກທີ່ທຳການສຶກ ສາທັງໝົດແມ່ນ 5.5% ແຕ່ອັດຕາການ ຕາຍໃນເດັກອາຍຸ > 2 ເດືອນ (ທີ່ມີລະດັບ basal ETK ຕ່ຳ) ແມ່ນສູງກວ່າ ຄື (3/48, 6.3%) ເມື່ອທຽບກັບເດັກອາຍຸດຽວກັນ ແລະ ມີລະດັບ basal ETK ທີ່ປົກກະຕິ (P=0.048, relative risk=9.06 (95%CI 0.97 - 85.1)). ແຕ່ວ່າ ເຮົາຄວນລະວັງໃນຕົວເລກນີ້ ເພາະອັດຕາການຕາຍໃນທີ່ນີ້ ແມ່ນອີງໃສ່ຕົວເລກການຕາຍພຽງ 4 ກໍລະນີເທົ່ານັ້ນ ຈາກຈຳນວນເດັກ 197 ຄົນ ທີ່ມີອາຍຸ > 2 ເດືອນ ເຊິ່ງການອ່ານຜົນດັ່ງກ່າວນີ້ແມ່ນພຽງອີງໃສ່ຄ່າ relative risk ທີ່ມີຄວາມສຳຄັນທາງດ້ານສະຖິຕິ. ພາວະຂາດວິຕະມິນບີ 1 ທີ່ບໍ່ສະແດງອາການອອກອາດເປັນສາເຫດການເສຍຊີວິດໃນເດັກ ແລະ ອາດມີຄວາມຈຳເປັນທີ່ຈະໃຫ້ວິຕະມິນບີ 1 ໃນເດັກບໍ່ສະບາຍຍ້ອນພະຍາດອື່ນທີ່ບໍ່ໄດ້ສະແດງອາການຂາດວິຕະມິນບີ 1. ມີແຕ່ການເຮັດຄົ້ນຄວ້າທົດລອງເທົ່ານັ້ນຈຶ່ງຈະສາມາດໃຫ້ຄຳຕອບວ່າເດັກລຸ່ມ 1 ປີ ກຸ່ມໃດຄວນຈະໄດ້ຮັບວິຕະມິນບີ 1 ເສີມ. ເດັກລຸ່ມ 1 ປີ ທີ່ເປັນພະຍາດອື່ນ ຄວນໄດ້ຮັບວິຕະມິນບີ 1 ທາງສັກ ເພື່ອເພີ່ມລະດັບຢາໃນຈິອະໃຫ້ສູງຂຶ້ນໃນທັນທີ. ມີຫຼັກຖານພົບວ່າການດູດຊຶມວິຕະມິນບີ 1 ທາງກະເພາະ-ລຳໄສ້ຈະອິ່ມຕົວ ໃນປະລິມານທີ່ເກີນ 5 ມິລິກຣາມ ເຊິ່ງສະແດງໃຫ້ເຫັນວ່າການໃຫ້ຢາໃນປະລິມານທີ່ສູງກວ່ານີ້ທາງປາກຜົນໄດ້ຮັບແມ່ນມີຂອບເຂດຈຳກັດ.

ຮູບ: ຫົວຫລ້ານຈາກປາກເຊ - ຫົວຫລ້ານທີ່ຢູ່ໃນຫໍ່ນີ້ ຖືກໃຊ້ຕົ້ມເປັນນ້ຳຢາ ໃຫ້ແມ່ລູກອ່ອນດື່ມເພື່ອແກ້ອາການຜິດກຳ.

ເຊື້ອ *Burkholderia pseudomallei* ໃນນ້ຳ ແລະ ດິນ

Melioidosis (ເຊື້ອສາເຫດ *Burkholderia pseudomallei*) ແມ່ນສາເຫດສຳຄັນຂອງພາວະຊຶມເຊື້ອໃນກະແສເລືອດ ໃນຂົງເຂດອາຊີຕາເວັນອອກສຽງໃຕ້ ແລະ ພາກເໜືອອິດສະຕາລີ ໂດຍສະເພາະໃນລາວ ແລະ ໄທ. ໃນປະຈຸບັນ, ພວກເຮົາຍັງບໍ່ທັນເຂົ້າໃຈການກະຈາຍຂອງເຊື້ອໃນສະພາບແວດລ້ອມດິນ ແລະ ນ້ຳ ແລະ ການສຶກສາຄົ້ນຄ້ວາເພື່ອທີ່ຈະເຂົ້າໃຈບັນຫານີ້ກໍ່ມີໜ້ອຍຫຼາຍ ແລະ ປັດໃຈທາງເຄມີ, ຟີຊິກ ແລະ ຊີວະໃດແດ່ ທີ່ຈຳເປັນຕໍ່ການກະຈາຍຕົວຂອງເຊື້ອໃນສະພາບ ແວດລ້ອມ. ໃນລາວເອງ, ເຊື້ອ *B. pseudomallei* ແມ່ນສາເຫດສຳຄັນຂອງພາວະຊຶມເຊື້ອໃນກະແສເລືອດໃນຂອບເຂດນະຄອນຫຼວງວຽງຈັນ ແລະ ສາມາດພົບໃນດິນໃນບັນດາຕົວເມືອງທີ່ຢູ່ຕາມລຳແມ່ນ້ຳຂອງ ແຕ່ມີຄົນເຈັບຈຳນວນໜ້ອຍໜຶ່ງເທົ່ານັ້ນ ທີ່ພວກເຮົາໝັ້ນໃຈວ່າເຂົາເຈົ້າດຳລົງຊີວິດ ໃນເຂດດິນສູງຕະຫຼອດເວລາ. ໃນໄລຍະຜ່ານມາມີ 2 ການສຶກສາ ທີ່ພະຍາຍາມອະທິບາຍເຖິງການກະຈາຍຂອງ *B. pseudomallei* ໃນສະພາບແວດລ້ອມໃນປະເທດເຮົາ.

ການສຶກສາທີ 1: ພວກເຮົາຕ້ອງການຢາກຮູ້ວ່າເຊື້ອ *B. pseudomallei* ສາມາດພົບໄດ້ໃນດິນທີ່ຫ່າງອອກຈາກແມ່ນ້ຳຂອງບໍ່, ໂດຍການຂີດ 3 ເສັ້ນສະແດງຜ່ານທິດຕາເວັນຕົກສຽງເໜືອ, ທິດຕາເວັນອອກສຽງເໜືອ ແລະ ທິດໃຕ້ ເຊິ່ງປະ ກອບມີ 9 ເຂດໃນ 6 ແຂວງ (Rattanavong *et al.* 2011). ທັ່ງນາໃນແຕ່ລະເຂດໄດ້ຖືກຊຸ່ມເລືອກ ແລະ ກຳນົດເປັນຕາໜ່າງທີ່ມີໄລຍະຫ່າງ 5 ແມັດ ຈຳນວນ 100 ຈຸດ. ດິນຖືກຂຸດໃນລະດັບຄວາມເລິກ 30 ຊັງຕີແມັດ ແລະ ນຳໄປປູກເພື່ອຊອກຫາເຊື້ອ *B. pseudomallei*. ຈາກທັງໝົດ 9 ເຂດທີ່ທຳການສຳຫຼວດ, ມີ 4 ເຂດ (44%) ແມ່ນພົບເຊື້ອ, ໂດຍໃນນັ້ນ ເຂດທີ່ພົບຫຼາຍທີ່ສຸດແມ່ນທິດຕາເວັນອອກຂອງແຂວງ ສາລະວັນ ເຊິ່ງ 94% ຂອງຈຳນວນຕົວຢ່າງແມ່ນໃຫ້ຜົນປູກພົບເຊື້ອ ແລະ ສະເລ່ຍຄວາມໜາແໜ້ນຂອງເຊື້ອໃນດິນແມ່ນ ~464 (25-10,850) cfu/g ເຊິ່ງສະແດງວ່າເຊື້ອ ດັ່ງກ່າວມີຄວາມເຂັ້ມຂຸ້ນສູງຫຼາຍ. ທີ່ຫຼວງນ້ຳທາ ມີພຽງ 1 ຕົວຢ່າງທີ່ໃຫ້ຜົນປູກພົບເຊື້ອ. ດັ່ງນັ້ນ, ເຊື້ອ *B. pseudomallei* ແມ່ນພົບໄດ້ໃນດິນ ທີ່ຫ່າງອອກຈາກແມ່ນ້ຳຂອງຢູ່ທາງພາກໃຕ້ຂອງລາວ. ສະນັ້ນ, ພະນັກງານແພດໝໍທີ່ເຮັດວຽກຢູ່ເຂດຕາເວັນອອກສ່ຽງເໜືອ ແລະ ຕາເວັນຕົກສ່ຽງເໜືອຂອງລາວແມ່ນໃຫ້ຄິດຫາພະຍາດ melioidosis ໜ້ອຍກວ່າເຂດພາກໃຕ້ຂອງລາວເວລາບົ່ງມະຕິຈຳແນກກັບພະຍາດອື່ນ.

ການສຶກສາທີ 2: ພວກເຮົານຳໃຊ້ Moore's swabs ທີ່ເຮັດມາຈາກຜ້າບັ້ງ (Vongphayloth e*t al.* 2012) ເພື່ອເກັບຕົວຢ່າງນ້ຳໃນທົ່ງນາ, ໜອງນ້ຳ, ແມ່ນ້ຳ, ນ້ຳສ້າງ ແລະ ຖັງເກັບນ້ຳ. 36 % ແລະ 6% ຂອງຕົວຢ່າງນ້ຳ ທີ່ມາຈາກພາກຕາເວັນອອກ ແລະ ຕາເວັນຕົກຂອງແຂວງສາລະວັນຕາມລຳດັບ ແມ່ນໃຫ້ຜົນປູກພົບເຊື້ອ. pH ຕ່ຳ ແລະ ຄວາມຊຸ່ມຂອງນ້ຳທີ່ສູງ ແມ່ນມີການພົວພັນຢ່າງອີດສະຫຼະຕໍ່ຜົນປູກເຊື້ອບວກ. ຕົວຢ່າງນ້ຳທີ່ໃຫ້ຜົນປູກເຊື້ອບວກ ສ່ວນໃຫຍ່ແມ່ນມາຈາກນ້ຳເຊໂດນ ແລະ ຕາມຫ້ວຍທີ່ຢູ່ເຂດຕາເວັນອອກຂອງແຂວງສາລະວັນ.

ການສຶກສານີ້ແມ່ນພົບພໍ້ຄວາມຫຍຸ້ງຍາກ ເນື່ອງຈາກບໍ່ໝັ້ນໃຈວ່າເຊື້ອ *B. pseudomallei* ອາດຈະມີຊີວິດຢູ່ໃນດິນ/ນ້ຳ ແຕ່ບໍ່ສາມາດປູກໃຫ້ເກີດໄດ້ດ້ວຍເຕັກນິກໃນປະຈຸບັນນີ້. ສະນັ້ນ,ການປຽບທຽບລະຫວ່າງ ການກວດທາງດ້ານພັນທຸກຳ ແລະ ການປູກເຊື້ອຈຶ່ງມີຄວາມຈຳເປັນ. ນອກນັ້ນ, ການປູກເຊື້ອເຮັດໃຫ້ສິ້ນເປືອງແຮງງານເປັນຈຳນວນຫຼວງຫຼາຍ ແລະ ບັນຫາລະເບີດບໍ່ທັນແຕກຢູ່ທາງພາກຕາເວັນອອກຂອງລາວ ເປັນອຸປະສັກທີ່ສຳຄັນສຳລັບການຂຸດດິນໄປກວດ ເພາະເຮົາຕ້ອງໄດ້ກວດເບິ່ງວ່າມີລະເບີດຕົກຄ້າງບໍ່.

ຮູບທາງເທິງ: ການກະຈາຍຂອງເຊື້ອ *B. pseudomallei* ຈາກການເກັບຕົວຢ່າງ 9 ເຂດໃນປະເທດລາວ, ປີ 2009. ຮູບດາວໝາຍ ເຖິງ ເຂດທີ່ຜົນປູກພົບເຊື້ອ ແລະ ຮູບວົງມົນ ໝາຍເຖິງເຂດທີ່ບໍ່ພົບເຊື້ອ. ເສັ້ນສີຟ້າແມ່ນແມ່ນ້ຳຂອງ.

ຮູບທາງລຸ່ມ: ຮູບຂອງ Moore's gauze swab ທີ່ຖືກນຳໃຊ້ໃນການເກັບຕົວຢ່າງໃນນ້ຳສ້າງຂະໜາດນ້ອຍ ເພື່ອຊອກຫາ *B. pseudomallei* ທີ່ແຂວງ ສາລະວັນ.

ເຊື້ອ Pneumococci ແລະ ນະໂຍບາຍການສັກຢາປ້ອງກັນພະຍາດທີ່ເກີດຈາກເຊື້ອດັ່ງກ່າວ

ການຕິດເຊື້ອນິວໂມຄອກຄັດແບບຮຸນແຮງ ຫຼື Invasive pneumococcal disease (IPD) ເປັນສາເຫດຫຼັກຂອງການເຈັບເປັນ ແລະ ການຕາຍໃນທົ່ວໂລກ ເຊິ່ງຄາດຄະເນວ່າມີປະມານ 1.6 ລ້ານຄົນ ເສຍຊີວິດຍ້ອນການຕິດເຊື້ອນິວໂມຄອກຄັດໃນແຕ່ລະປີ. ໃນນັ້ນ 0.7-1 ລ້ານຄົນ ແມ່ນເປັນເດັກນ້ອຍທີ່ມີອາຍຸຕ່ຳກ່ວາ 5 ປີ ແລະ ອາໃສຢູ່ໃນປະເທດກຳລັງພັດທະນາ. ທີ່ຜ່ານມາເຄີຍພົບກໍລະນີຕິດເຊື້ອນິວໂມຄອກຄັດແບບຮຸນແຮງໃນນະຄອນຫຼວງວຽງຈັນ ແຕ່ເຮົາຍັງບໍ່ມີຂໍ້ມູນກ່ຽວກັບສາຍພັນຂອງເຊື້ອນີ້ ເຊິ່ງຖືເປັນຂໍ້ມູນທີ່ສຳຄັນສຳລັບການວາງແຜນນະໂຍບາຍສັກຢາວັກແຊງປ້ອງກັນພະຍາດດັ່ງກ່າວ. ໄດ້ມີການດຳເນີນການສຶກສາໄປຂ້າງໜ້າ ທີ່ເຮັດຢູ່ໂຮງໝໍເພື່ອສຶກສາເບິ່ງສາຍພັນທີ່ມີຢູ່ໃນລາວ (ເບິ່ງ Moore *et al.* 2009). ນິຍາມຂອງ IPD ແມ່ນການກວດພົບເຊື້ອ *S. pneumoniae* ຢູ່ໃນຕົວຢ່າງເລືອດ ຫຼື ນ້ຳໄຂສັນຫຼັງຂອງຄົນເຈັບໂດຍການປູກເຊື້ອ, ແລະ/ຫຼື ການກວດພົບເຊື້ອ *S. pneumoniae* ໃນນ້ຳໄຂສັນຫຼັງດ້ວຍ real-time PCR assay targeting the *lytA* gene. ເຕັກນິກການກວດແບບໃໝ່ດ້ວຍ real-time PCR ທີ່ໄດ້ຮັບການພັດທະນາຢູ່ໃນລາວ ແມ່ນໄດ້ຖືກນຳໃຊ້ເພື່ອຄັດແຍກຊະນິດສາຍພັນຂອງເຊື້ອ.

ໃນຈຳນວນຄົນເຈັບ 10799 ຄົນທີ່ໄດ້ຮັບການປູກເລືອດ ແລະ 353 ຄົນທີ່ມີຕົວຢ່າງນ້ຳໄຂສັນຫຼັງ, ແມ່ນຖືກກວດພົບເຊື້ອ *S. pneumoniae* ຢູ່ 0.21 % ແລະ 5.4% ຕາມລຳດັບ (n=35). ໃນນີ້ມີເຊື້ອ 2 ຕົວທີ່ ກວດພົບ ແລະ ມີສ່ວນກ່ຳໃຫ້ເກີດເຍື່ອຫຸ້ມສະໝອງອັກເສບແມ່ນຕ້ານຕໍ່ຢາ penicillin ເຊິ່ງມີ MICs 0.39 µg/mL 0.125 µg/mL. ສ່ວນເຊື້ອ *S. pneumoniae* ທີ່ເຫຼືອແມ່ນຖືກກັບຢາ Ceftriaxone.

ສາຍພັນທີ່ພົບຫຼາຍທີ່ສຸດແມ່ນ ສາຍພັນທີ 1, ຕ່ຳມາແມ່ນ ສາຍພັນ 5, 6A /B/C, 14 ແລະ 23F. ມີພຽງ 39% ຂອງສາຍພັນທີ່ພົບເຫັນໃນລາວຖືກບັນຈຸໃນວັກແຊງ PCV-7, ແຕ່ຈະພົບສາຍພັນຂອງລາວໃນວັກແຊງ PCV-10 ເຖິງ 73% ແລະ ໃນວັກແຊງ PCV-13 ເຖິງ 76%. ສະນັ້ນ ເຖິງວ່າຂະໜາດຕົວຢ່າງ ໃນການສຶກສານີ້ຈະໜ້ອຍ ແຕ່ຂໍ້ມູນນີ້ຊີ້ໃຫ້ເຫັນວ່າ ວັກແຊງ PCV-7 ອາດມີປະສິດທິພາບຕ່ຳໃນປະເທດລາວ, ກົງກັນຂ້າມ ວັກແຊງ PCV-13 ອາດມີປະສິດທິພາບສູງກ່ວາໜ່ວ.

ເຊື້ອໄວຣັສທີ່ກ່ຳໃຫ້ເກີດອັກເສບສະໝອງຍີ່ປຸ່ນ (JEV) ແລະ ນະໂຍບາຍການສັກຢາວັກແຊງປ້ອງກັນ

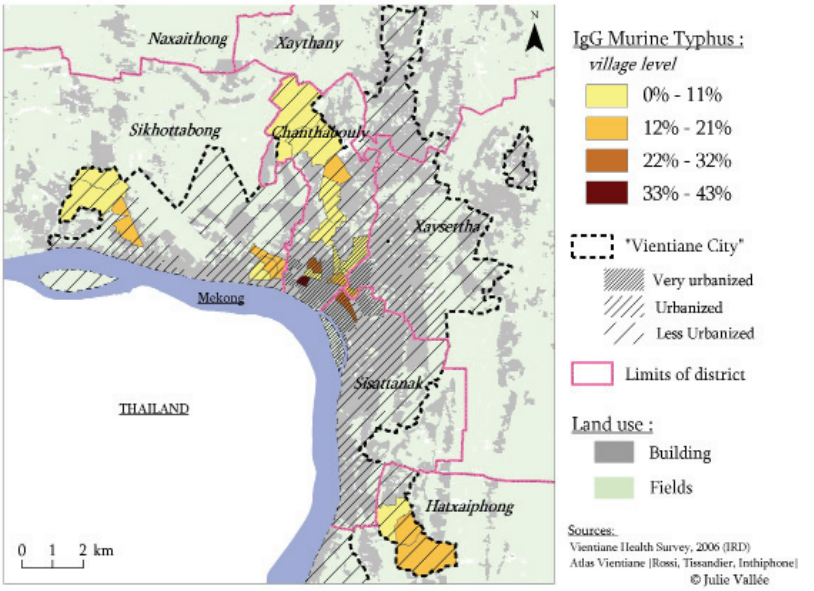
ເຖິງວ່າບໍ່ມີຂໍ້ມູນກ່ຽວກັບເຊື້ອສາເຫດທີ່ກ່ຳໃຫ້ເກີດອັກເສບສະໝອງຢູ່ໃນລາວ, ເຊື້ອໄວຣັສທີ່ກ່ຳໃຫ້ເກີດອັກເສບສະໝອງຍີ່ປຸ່ນອາດເປັນສາເຫດຫຼັກເນື່ອງຈາກມັນພົບເຫັນຢູ່ປະເທດອ້ອມຂ້າງຂອງລາວ. ການບົ່ງມະຕິ JEV ແມ່ນຍາກຫຼາຍ ເພາະວ່າ ມັນບໍ່ສາມາດຈຳແນກເບິ່ງຄວາມແຕກຕ່າງທາງດ້ານອາການສາດກັບເຊື້ອອື່ນໆທີ່ເປັນສາເຫດຂອງອັກເສບສະໝອງຮຸນແຮງ ແລະ ມີປະຕິກິລິຍາໄຂ່ວ ກັນທາງດ້ານເຊຣອມວິທະຍາກັບທາດກາຍຕ້ານຕ່ຳກັບໄຂ້ເລືອດອອກ ແລະ ທາດກາຍຕ້ານຕ່ຳ flavivirus ອື່ນໆ. ການກວດຫາໄວຣັສຈາກນ້ຳໄຂສັນຫຼັງ ແມ່ນບໍ່ສູ້ໄດ້ຜົນ ດັ່ງນັ້ນ ພວກເຮົາຈຶ່ງເຮັດການສຳຫຼວດໂດຍໃຊ້ ELISA ເພື່ອກວດຫາ anti-JEV IgM ໃນນ້ຳໄຂສັນຫຼັງເພື່ອເບິ່ງວ່າເຊື້ອ JEV ແມ່ນເປັນບັນຫາສຳຄັນຢູ່ໃນລາວຫຼືບໍ່, (ເບິ່ງ Moore *et al.* 2012). ຈາກການສຶກສາໃນຄົນເຈັບ 515 ຄົນ ທີ່ເຂົ້າມານອນຢູ່ໃນໂຮງໝໍ ມະໂຫສົດ (2003-2008) ແລະ ສົງໃສວ່າມີການຊຶມເຊື້ອຂອງລະບົບປະສາດສຸນກາງພົບວ່າ 234 (45%) ມີໝວດອາການອັກເສບສະໝອງ, 256 (50%) ມີໝວດອາການເຍື່ອຫຸ້ມສະໝອງອັກເສບແລະ 157 (31%) ແມ່ນມີທັງສອງໝວດອາການ.

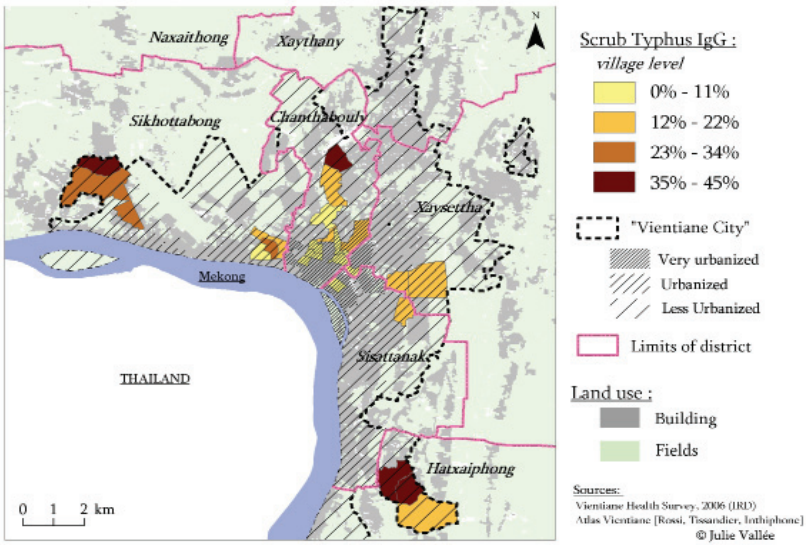
ອາຍຸສະເລ່ຍຂອງຄົນເຈັບ (median age (IQ; range)) ແມ່ນ 24 (8-38; 0.05-85) ປີ ແລະ 32% ແມ່ນມີອາຍຸຕ່ຳກ່ວາ 15 ປີ. ຈຳນວນນ້ຳໄຂສັນຫຼັງທີ່ກວດພົບ anti-JEV IgM ມີ 14.5% ໃນຄົນເຈັບທີ່ມີໝວດອາການອັກເສບສະໝອງ ແລະ 10.1% ໃນຄົນເຈັບທີ່ມີທັງໝວດອາການອັກເສບສະໝອງ ແລະ ໝວດອາການເຍື່ອຫຸ້ມສະໝອງອັກເສບ. ໃນຈຳນວນຄົນເຈັບທີ່ກວດພົບ anti-JEV IgM ໃນນ້ຳໄຂສັນຫຼັງ, 42% ຂອງຄົນເຈັບດັ່ງກ່າວມີອາການຊັກ, 63% ມີຄະແນນ Glasgow Coma Score ຫຼຸດລົງຕ່ຳກ່ວາຄ່າປົກກະຕິ, ຄ່າ median (range) ຂອງເມັດ ເລືອດຂາວໃນນ້ຳໄຂສັນຫຼັງແມ່ນ 125 (0-653) /µL, ຄ່າ median (range) ຂອງເປີເຊັນຂອງ lymphocytes ແມ່ນ 37 (0-90)%. ສ່ວນໃຫຍ່ຂອງຄົນເຈັບແມ່ນມາຈາກ ພາກເໜືອຂອງລາວ ແຕ່ກ່ຳຍັງມີຫຼັກຖານການຕິດເຊື້ອ JEV ຈາກທົ່ວປະເທດເນື່ອງຈາກ JEV ເປັນພະຍາດທີ່ ສາມາດປ້ອງກັນໄດ້, ສະນັ້ນ ການນຳໃຊ້ເຕັກນິກການກວດ ELISA ຢ່າງກ້ວາງຂວາງອາດສາມາດຊ່ວຍກຳນົດຂະໜາດ ຂອງບັນຫາທີ່ເກີດຈາກພະຍາດດັ່ງກ່າວ. ຂໍ້ມູນເຫຼົ່ານີ້ໄດ້ຊີ້ໃຫ້ເຫັນເຖິງຄວາມສຳຄັນທີ່ຈະຕ້ອງໄດ້ພິຈາລະນາການສັກຢາວັກແຊງປ້ອງກັນ JEV.

ການສຳພັດກັບພະຍາດ **Typhus** ແລະ ປັດໃຈສ່ຽງຂອງການຕິດເຊື້ອພະຍາດດັ່ງກ່າວໃນນະຄອນຫລວງວຽງຈັນ

Scrub typhus (ໄຂ້ແມງແດງ) ແລະ Murine typhus (ໄຂ້ໝັດໝູ) ເປັນສາເຫດຂອງການໄຂ້ ທີ່ພົບຫລາຍໃນ ນະຄອນຫລວງວຽງຈັນ. ແຕ່ປັດໃຈສ່ຽງໃນການຕິດເຊື້ອເຫຼົ່ານີ້ແມ່ນຍັງບໍ່ທັນຊັດເຈັນເທື່ອ. ຈາກພາກສ່ວນໜຶ່ງຂອງໂຄງການສຳຫລວດຕົວເມືອງຂອງນະຄອນຫລວງວຽງຈັນ, ພວກເຮົາໄດ້ທຳການກວດທາງເຊຣອມວິທະຍາ ເພື່ອຊອກຫາທາດພາຍຕ້ານຊະນິດ G (IgG) ຕໍ່ເຊື້ອ *Orientia tsutsugamushi* (ໄຂ້ແມງແດງ) ແລະ *Rickettsia typhi* (ໄຂ້ໝັດໝູ) ໃນຜູ້ໃຫຍ່ ທີ່ອາໃສຢູ່ເຂດຕົວເມືອງ ແລະ ເຂດອ້ອມແອ້ມຕົວເມືອງຂອງນະຄອນ ຫຼວງວຽງຈັນ ໂດຍການສຸ່ມເອົາ (ຜູ້ໃຫຍ່ອາຍຸ 35 ປີ ຈຳນວນ 2002 ຄົນ) (Vallee *et al.* 2010). ໃນການສຶກສາຄັ້ງນີ້, ພວກເຮົາໄດ້ທຳການກວດ ELISA ຈາກແຜ່ນຊັບເລືອດ ທີ່ໄດ້ຮັບການເຈືອຈາງ. ໄຂ້ແມງແດງທີ່ມີຜົນບວກທາງດ້ານເຊຣອມວິທະຍາ (IgG ບວກ) (ແຜນທີ່ດ້ານລຸ່ມ) ຖືກພົບໃນຜູ້ໃຫຍ່ທີ່ອາໃສຢູ່ເຂດອ້ອມແອ້ມຕົວເມືອງ (28.4%) ຫລາຍກວ່າຢ່າງຊັດເຈນເມື່ອປຽບທຽບໃສ່ຜູ້ໃຫຍ່ທີ່ອາໃສຢູ່ເຂດໃຈກາງເມືອງ (13.1%) ຂອງນະຄອນຫລວງວຽງຈັນ. ແຕ່ໃນທາງກົງກົນຂ້າມ, ສຳລັບ ໄຂ້ໝັດໝູ (ແຜນທີ່ດ້ານລຸ່ມ) ທີ່ມີຜົນບວກທາງດ້ານເຊຣອມວິທະຍາ (IgG ບວກ) ແມ່ນພົບຫຼາຍກວ່າຢ່າງຊັດເຈນໃນຜູ້ໃຫຍ່ທີ່ອາໃສຢູ່ເຂດໃຈກາງເມືອງ (30.8%) ເມື່ອປຽບທຽບໃສ່ ຜູ້ໃຫຍ່ທີ່ອາໃສຢູ່ເຂດອ້ອມແອ້ມຕົວເມືອງ (14.4%). ອີງຕາມການວິເຄາະທາງດ້ານສະຖິຕິທີ່ສົມທຽບຫຼາຍໆປັດໃຈສ່ຽງຂອງພະຍາດໃສ່ນຳກັນພົບວ່າ: ຄົນທີ່ອາໃສຢູ່ ໃນນະຄອນຫຼວງວຽງຈັນເປັນເວລາດົນນານ ແມ່ນຈະມີຄວາມສ່ຽງຕໍ່ການທີ່ເຄີຍສຳຜັດກັບເຊື້ອພະຍາດໄຂ້ໝັດໝູ (IgG ບວກ) ສູງ ແລະ ມີຄວາມສ່ຽງທີ່ເຄີຍສຳຜັດກັບເຊື້ອພະຍາດໄຂ້ແມງແດງ (IgG ບວກ) ຕ່ຳກ່ວາ.

ສຳລັບກຸ່ມຄົນທີ່ບໍ່ຮູ້ໜັງສື (ກືກໜັງສື), ມີລາຍຮັບຕ່ຳ, ອາໃສຢູ່ໃນເຂດທີ່ມີສຸຂະອະນາໄມບໍ່ດີ, ຄອບຄົວໃຫຍ່ ແລະ ເປັນຊາວໄຮ່ນາ ແມ່ນມີປັດໃຈສ່ຽງຕໍ່ພະຍາດໄຂ້ແມງແດງສູງກວ່າ ແລະ ກຸ່ມຄົນທີ່ອາໃສຢູ່ບໍລິເວນໃກ້ຄຽງກັນ ທີ່ມີຄວາມໜາແໜ້ນຂອງອາຄານບ້ານເຮືອນ ແລະ ຢູ່ໃກ້ກັບຕະຫລາດແມ່ນມີປັດໃຈສ່ຽງຕໍ່ ການທີ່ເຄີຍສຳຜັດກັບພະຍາດໄຂ້ໝັດໝູສູງກວ່າ ແລະ ມີປັດໃຈສ່ຽງເຄີຍຕິດ ພະຍາດໄຂ້ແມງແດງຕ່ຳ.
ຄວາມສຳພັນລະຫວ່າງໄຂ້ໝັດໝູທີ່ມີຜົນບວກທາງດ້ານເຊຣອມວິທະຍາ (IgG ບວກ) ກັບການທີ່ມີເຮືອນຢູ່ໃກ້ກັບຕະຫຼາດ ຊີ້ໃຫ້ເຫັນວ່າການກຳຈັດຂີ້ເຫຍື້ອ ແລະ ຄວບຄຸມພວກສັດກັດແທ້ນ ອາດຈະຊ່ວຍຫຼຸດຜ່ອນການເກີດພະຍາດໄດ້. ໂດຍທົ່ວໄປ ແລ້ວ ໄຂ້ແມງແດງ ບໍ່ເປັນພະຍາດທີ່ພົບ ໃນຕົວເມືອງ. ເຖິງແນວໃດກໍ່ຕາມພະຍາດໄຂ້ແມງແດງ ສາມາດພົບໃນຄົນທີ່ເຮັດວຽກຢູ່ສວນປາມ, ຢູ່ໃນປ່າຕຶບ, ຢູ່ຊາຍຫາດ ແລະ ຢູ່ສວນສາທາລະນະໃນຕົວເມືອງ ແລະ ຄຳສັບ Scrub ຫຼື ປ່າຫຍ້າອາດພາໃຫ້ເຂົ້າໃຈຜິດວ່າເປັນພະຍາດທີ່ພົບໃນປ່າ. ອາດຈະເປັນໄປໄດ້ວ່າ ຄົນທີ່ອາໃສຢູ່ໃນຕົວເມືອງວຽງຈັນອາດຈະຕິດເຊື້ອໃນເວລາທີ່ເຂົາເຈົ້າເດີນທາງໄປເຂດຊົນນະບົດ; ຕົວຢ່າງເຊັ່ນການໄປຫາໜໍ່ໄມ້ ຫຼື ຫາປາ ຫຼື ເຂົ້າໄປສວນຄົວ ຫຼື ສວນສາທາລະນະໃນຕົວເມືອງ.





ຢາຕ້ານເຊື້ອທີ່ກວດພົບໃນນ້ຳຍ່ຽວ

ການຕ້ານ (ດື້) ຕໍ່ຢາຕ້ານເຊື້ອເປັນບັນຫາສຳຄັນທາງສາທາລະນະສຸກໃນໂລກ, ເຊິ່ງມີຜົນກະທົບຕໍ່ການຕັດສິນໃຈໃນການປິ່ນປົວ, ຕໍ່ຜົນການປິ່ນປົວ, ຕໍ່ຄ່າໃຊ້ຈ່າຍໃນການຮັກສາ ແລະ ເຮັດໃຫ້ທັດສະນະຄະຕິຂອງປະຊາຊົນຕໍ່ການບໍລິການສາທາລະນະສຸກບໍ່ດີ. ການນຳໃຊ້ຢາຕ້ານເຊື້ອແບບຊະຊາຍຢ່າງກວ້າງຂວາງ, ການໃຫ້ຢາໃນປະລິມານທີ່ບໍ່ພຽງພໍ, ບໍ່ກິນຢາຕາມຄຳສັ່ງຂອງແພດໝໍ ແລະ ການສະໜອງຢາທີ່ບໍ່ມີຄຸນນະພາບ ແມ່ນມີສ່ວນກ່ຽວຂ້ອງກັບການເພີ້ມຂຶ້ນຂອງການຕ້ານ (ດື້) ຕໍ່ຢາຕ້ານເຊື້ອ.

ພວກເຮົາໄດ້ປະເມີນອັດຕາສ່ວນຂອງຄົນເຈັບນອນໃນໂຮງໝໍ ແລະ ຄົນເຈັບມາກວດເຂດນອກທີ່ໄດ້ຮັບຢາຕ້ານເຊື້ອກ່ອນມາປຶກສາແພດໂດຍການຊອກຫາລິດຂອງຢາຕ້ານເຊື້ອໃນນ້ຳຍ່ຽວ ດ້ວຍການເອົານ້ຳຍ່ຽວໃສ່ພຸມປູກທີ່ມີເຊື້ອ (*Bacillus stearothermophillus, Escherichia coli* and *Streptococcus pyogenes*). ຖ້ານ້ຳຍ່ຽວມີຢາຕ້ານເຊື້ອຈະສາມາດຂ້າເຊື້ອແບັກທີເຣັຍໄດ້. ໃນການສຶກສາຢ້ອນຫລັງ (N = 2,058) ແລະ ສຶກສາໄປໜ້າ (N = 1,153), ພົບວ່າ 49.7% ແລະ 36.2% ຕາມລຳດັບ, ຂອງຄົນເຈັບໃນນະຄອນຫລວງວຽງຈັນ ມີຢາຕ້ານເຊື້ອໃນນ້ຳຍ່ຽວ. ກຸ່ມຄົນເຈັບທີ່ໄດ້ຮັບຢາຕ້ານເຊື້ອຫຼາຍທີ່ສຸດແມ່ນຄົນເຈັບທີ່ສົງໃສວ່າເປັນຊຶມເຊື້ອລະບົບປະສາດສູນກາງ ແລະ ຊຶມເຊື້ອເລືອດຈາກຊຸມຊົນ (ທັງສອງ 56.8%). ໃນນະຄອນຫລວງວຽງຈັນ, ຄົນເຈັບເດັກນ້ອຍແມ່ນໄດ້ຮັບຢາຕ້ານເຊື້ອກ່ອນການປິ່ນປົວຫລາຍກວ່າຜູ້ໃຫຍ່ (60.0% ທຽບກັບ 46.5%, P < 0.001). ການນຳໃຊ້ຢາຕ້ານເຊື້ອ ໂດຍອີງຕາມການສອບຖາມປະຫວັດແມ່ນໜ້ອຍກວ່າການກວດພົບຢາຕ້ານເຊື້ອໃນນ້ຳຍ່ຽວ. ເຖິງວ່າ ສປປ ລາວຈະເປັນປະເທດທີ່ມີລະດັບການຕ້ານຕ່ຳຢາຕ້ານເຊື້ອຕ່ຳເມື່ອສົມທຽບກັບບັນດາປະເທດໃກ້ຄຽງ, ແຕ່ ESBL positive *E. coli* (ເບິ່ງໜ້າ 8) ແລະ ESBL positive *Klebsiella pneumoniae* ແມ່ນພົບເຫັນໃນນະຄອນຫລວງວຽງຈັນ. ເມື່ອເສດຖະກິດມີການຂະຫຍາຍຕົວ; ໂອກາດທີ່ຈະມີການນຳໃຊ້ຢາຕ້ານເຊື້ອທາງດ້ານປະລິມານ ແລະ ຄວາມຫຼາກຫຼາຍກໍ່ຈະເພີ່ມຂຶ້ນເຊັ່ນກັນ. ອັດຕາການນຳໃຊ້ຢາຕ້ານເຊື້ອທີ່ສູງໃນຊຸມຊົນທົ່ວໄປຄືດັ່ງທີ່ສະແດງອອກໃນຜົນການກວດຢ່ຽວນີ້ ອາດເຮັດໃຫ້ສະພາບການຕ້ານ (ດື້) ຕໍ່ຢາຕ້ານເຊື້ອໜັກໜ່ວງຂຶ້ນຕື່ມ. ສະນັ້ນ ຈຳເປັນຕ້ອງມີການຄວບຄຸມກ່ຽວກັບການນຳໃຊ້ຢາຕ້ານເຊື້ອ ແລະ ມີການອອກລະບຽບການຄວບຄຸມຮ້ານຂາຍຢາໃຫ້ຮັດກຸມຫຼາຍຂຶ້ນກວ່າເກົ່າ.

ລະວັງໜາກ້ອຍປ່າ!

ຫວ່າງບໍ່ດົນມານີ້ມີລາຍງານຄົນເຈັບ 6 ຄົນທີ່ແຂວງຫຼວງນ້ຳທາ ເຊິ່ງເຂົ້າມາໂຮງໝໍດ້ວຍອາການລຳໃສ້ອຸດຕັນເນື່ອງຈາກກິນໜາກ້ອຍປ່າ (Slesak *et al.* 2011). ທັງ 6 ຄົນແມ່ນຈຳເປັນຕ້ອງໄດ້ຜ່າຕັດລຳໃສ້ຍ້ອນກ້ອນໜາກ້ອຍປ່າອຸດຕັນ. ຈາກການສອບຖາມຄົນເຈັບອື່ນໆ/ພີ່ນ້ອງຈຳນວນ 227 ຄົນ, ພົບວ່າ 46% ແມ່ນເຄີຍກິນແກ່ນຫມາກ້ອຍປ່າ, ໃນນັ້ນ 45% ແມ່ນຮູ້ເຖິງຜົນສະທ້ອນຂອງມັນ ເຊັ່ນທ້ອງຜູກ (38%), ໃສ້ຕັ່ງອັກເສບ/ເຈັບທ້ອງ/ຮາກ (3% ໃນແຕ່ລະຢ່າງ) ແລະ ທ້ອງເບັ່ງ/ເສຍຊີວິດ (1% ໃນແຕ່ລະຢ່າງ). ລາວກາງ/ລາວສູງມີໂອກາດກິນກ້ອຍປ່າຫຼາຍກວ່າ, ເພດຊາຍ ແລະ ຜູ້ທີ່ບໍ່ຮູ້ຜົນຮ້າຍຂອງການກິນໜາກ້ອຍປ່າຈະມີໂອກາດກິນຫຼາຍກວ່າ. ອີງຕາມການສອບຖາມທ່ານໝໍຜ່າຕັດ 44 ທ່ານ ພົບວ່າທ່ານໝໍທີ່ພົບກໍລະນີຄົນເຈັບໃສ້ອຸດຕັນເນື່ອງຈາກກິນໜາກ້ອຍປ່າມີ 33 ທ່ານ, ເຊິ່ງຄົນເຈັບສ່ວນຫຼາຍແມ່ນຄົນໜຸ່ມ, ເພດຊາຍຊົນເຜົ່າລາວສູງ. ປີ 2009 ທົ່ວປະເທດ, ມີລາຍງານກໍລະນີຄົນເຈັບໃສ້ຕັນຍ້ອນກິນກ້ອຍປ່າຈຳນວນ 46 ຄົນ (ອຸບັດການເກີດ 0.8/100 000) ແລະ ທຸກກໍລະນີແມ່ນໄດ້ກິນກ້ອຍປ່າທີ່ມີແກ່ນ. ໃນລາວ, ລຳໃສ້ອຸດຕັນເນື່ອງຈາກກິນ ໜາກ້ອຍປ່າທີ່ມີແກ່ນແມ່ນແຜ່ຫຼາຍ ໂດຍສະເພາະແມ່ນເພດຊາຍຜູ້ທີ່ກິນກ້ອຍປ່າທີ່ມີແກ່ນ ຕອນທ້ອງຫວ່າງເວລາເຂົ້າປ່າ. ຮູບແບບການປິ່ນປົວແບບພື້ນເມືອງຂອງຊາວບ້ານ ກໍລະນີລຳໃສ້ອຸດຕັນຍ້ອນກິນໜາກ້ອຍປ່າ ອາດເປັນອັນຕະລາຍ ເຊັ່ນ: ການໃຊ້ໄມ້ແຫຍ່ເຂົ້າຮູທວານ ແລະ ການໃຊ້ນ້ຳມັນຢ່ອງໃສ່ທໍ່ເຂົ້າທາງຮູທະວານ. ສະນັ້ນມີຄວາມຈຳເປັນທີ່ຈະຕ້ອງໃຫ້ສຸຂະສຶກສາແກ່ປະຊາຊົນ ເພື່ອໃຫ້ຮັບຮູ້ກ່ຽວກັບຄວາມສ່ຽງ ແລະ ອັນຕະລາຍຂອງການກິນໜາກ້ອຍປ່າ.

Phytobezoars ຂອງໜາກ້ອຍປ່າຈາກລຳໃສ້ຂອງຄົນເຈັບ. ຄວາມຍາວສູງສຸດ 5 ຊມ.

Extended-spectrum beta-lactamase (ESBL) bacteria

ນັບຕັ້ງແຕ່ປີ 2004 ເປັນຕົ້ນມາ ພວກເຮົາເຫັນວ່າມີການເພີ່ມຂຶ້ນຂອງຄົນເຈັບທີ່ຕິດເຊື້ອ *Escherichia coli* ແລະ *Klebsiella pneumoniae* ທີ່ມີການຜະລິດ ESBL ໃນໂຮງໝໍມະໂຫສົດ, ເຊິ່ງເພີ້ມຄວາມຫຍຸ້ງຍາກໃນການປິ່ນປົວເພາະ ເຊື້ອດັ່ງກ່າວຕ້ານຕໍ່ຢາໃນກຸ່ມcephalosporins ແລະ ສ່ວນຫຼາຍແມ່ນຕ້ານຕໍ່ຢາ gentamicin ແລະ ຢາໃນກຸ່ມ fluoroquinolones ນຳ. ໄດ້ມີການສຶກສາດ້ານລະບາດວິທະຍາ-ພັນທຸກຳ ໂດຍການເອົາເຊື້ອ *E.coli* ທີ່ຜະລິດ ESBL ຈຳນວນ 54 ຕົວຢ່າງມາສຶກສາ ເຊິ່ງສ່ວນໃຫ່ຍຂອງເຊື້ອ(76%)ໄດ້ມາຈາກເລືອດ ແລະ ລະບົບຖ່າຍເທ, ອີກ 20% ແມ່ນໄດ້ຈາກນ້ຳໝອງ.

ຜົນການສຶກສາພົບວ່າສາຍພັນທີ່ມີຢີນ CTX-M ແມ່ນພົບໃນທຸກຕົວຢ່າງ *ESBL-E. coli* ທີ່ໄດ້ມາໃນຊ່ວງປີ 2004-2009, ເຊິ່ງຄ້າຍກັນກັບສາຍ ພັນທີ່ພົບໃນປະເທດໃກ້ຄຽງເຊັ່ນ: ປະເທດຈີນ ແລະ ໄທ (CTX-M-14, -15 ແລະ 55-like, CTX-M-27). ນອກນັ້ນຍັງມີລັກສະນະການຕ້ານຮ່ວມກັບຢາ ciprofloxacin / gentamicin ເຖິງ 68%. ໃນທົ່ວໂລກ *ESBL-E. coli* ສາຍພັນທີ່ພົບຫລາຍແມ່ນ (ST-131,ST-405), ແຕ່ວ່າສາຍພັນ ST-648 ເຊິ່ງຜ່ານມາຖືກພົບໃນຈຳພວກນົກ ແມ່ນເປັນສາຍພັນທີ່ພົບຫລາຍເປັນອັນດັບສອງ ເຊິ່ງອາດເປັນຍ້ອນອັດຕາການລ້ຽງສັດປີກຢູ່ຕາມເດີ່ນບ້ານໃນລະດັບສູງພາຍໃນລາວ (ເບິ່ງ Stoesse *et al* 2011). ຂໍ້ມູນເຫຼົ່ານີ້ຊີ້ໃຫ້ເຫັນຄວາມສຳຄັນໃນການເຝົ້າລະວັງ ແລະ ຕິດຕາມການນຳໃຊ້ຢາຕ້ານເຊື້ອ, ໂດຍສະເພາະຢາໃນກຸ່ມ cephalosporins ແລະ ຊອກຫາຢາຕ້ານ ເຊື້ອຊະນິດອື່ນທີ່ມີລາຄາບໍ່ແພງ ເພື່ອມາທົດແທນເຂົ້າໃນການປິ່ນປົວ.

Chromoblastomycosis and Myiasis

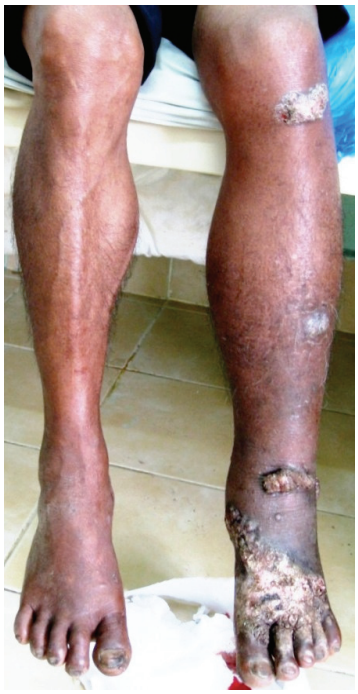
Chromoblastomycosis ແມ່ນການຕິດເຊື້ອແບບຊໍ້າເຮື້ອ ຂອງຜິວໜັງ ແລະ ຊັ້ນໃຕ້ຜິວໜັງ ເຊິ່ງພົບເຫັນໃນທົ່ວໂລກ ພົບເຫັນຫລາຍກ່ວາໝູ່ແມ່ນໃນເຂດຮ້ອນ ແລະ ເຂດໃກ້ເຂດຮ້ອນ ເກີດຈາກເຊື້ອເຫັດຈຳ ພວກ *Fonsecaea*, *Phialophora* ແລະ *Cladophialophora* ທີ່ມີຊີວິດຢູ່ໃນດິນແລະ ພືດຜັກ. ສ່ວນໃຫຍ່ແມ່ນຈະຕິດເຊື້ອຢູ່ບໍລິເວນຂາພາກສ່ວນລຸ່ມ ແລະ ກ້ອນຕຸດ ແລະ/ຫຼື ແຜ່ນຫຸດ ອາດຂະຫຍາຍຕົວອ້ອມບາດແຜ. ອາການສິນທີ່ພົບເຫັນເລື້ອຍແມ່ນການຕິດເຊື້ອແບັກເທີເລຍແຊກຊ້ອນ, ມະເຮັງຜິວໜັງ ກໍ່ອາດເປັນໄປໄດ້.

ຄົນເຈັບອາຊີບຊາວນາອາຍຸ 72 ປີ, ໄດ້ເຂົ້ານອນປິ່ນປົວຢູ່ໂຮງ ໝໍແຂວງຫລວງນ້ຳທາ, ພາກເໜືອຂອງປະເທດລາວ, ດ້ວຍອາການໃຫຍ່ຂຶ້ນຂອງສ່ວນລຸ່ມຂາຂວາໄດ້ 1 ອາທິດ, ຫລັງຈາກທີ່ຖືກປີ່ງກັດບໍລິເວນໜັງຕີນ 10 ປີກ່ອນໜ້ານີ້. ມີຕຸ່ມຄ້າຍຄືກະລຳປີດອກ ແລະ ມີບາດແຜຊຶມເຊື້ອຢູ່ບໍລິເວນຂາພາກສ່ວນລຸ່ມ ແລະ ຢູ່ສົນນ່ອງຕີນເບື້ອງຊ້າຍມີການອັກເສບຈຸລັງຊັ້ນໃຕ້ຜິວໜັງ, ບວມ, ມີໜອງ.

ເບື້ອງຕົ້ນທ່ານໝໍຄິດວ່າ ລາວເປັນຂີ້ທູດ ຫຼື ມະເຮັງຜິວໜັງ ແຕ່ວ່າໜັງທີ່ຊຸດໄດ້ຈາກພາກສ່ວນດັ່ງກ່າວ ແມ່ນມີລັກສະນະສະເພາະຄືເປັນສີນ້ຳຕານ, ກົມ ແລະ ໜາ, ມີ multiseptate sclerotic cells ເຊິ່ງເຫັນໄດ້ຈາກການຊ່ອງ ພາບສິດ, ຢືນຢັນດ້ວຍເຕັກນິກ ການໃຊ້ Potassium hydroxide 10%.

ໃນໄລຍະທີ່ກຳລັງລ້າງບາດແຜ, ໄດ້ພົບເຫັນໜອນ 22 ໂຕຢູ່ບໍລິເວນແຜສົ້ນນ່ອງ ເປັນໂຕອ່ອນໄລຍະສາມຂອງ Old World screwworm fly, *Chrysomya bezziana*. ອາດຈະເປັນໄປໄດ້ວ່າແມງວັນວາງໄຂ່ໃນແຜເປີດ.

PCR ຈາກເນື້ອເຍື່ອທີ່ໄດ້ເອົາຈາກ nodule ຂາຊ້າຍສະແດງໃຫ້ເຫັນ *Fonsecaea pedrosoi*, *monophora* ຫຼື *F. nubica*, ລາວໄດ້ຮັບການປິ່ນປົວຫາຍດີດ້ວຍຢາ terbinafin ບວກກັບໃຫ້ itraconazole ແບບ pulse-therapy (ການໃຫ້ຢາໃນປະລິມານທີ່ສູງ ແຕ່ໃຫ້ເປັນໄລຍະ ຈຸດປະສົງແມ່ນເພື່ອເພີ່ມປະສິດທິພາບຂອງຢາ ແລະ ຫຼຸດຜົນຂ້າງຄຽງຂອງຢາ) ນອກນັ້ນກໍ່ມີການຕັດເນື້ອຕາຍອອກ (ເບິ່ງ Slesak *et al.* 2011).



ຮູບຊ້າຍ: ຂາເບື້ອງລຸ່ມຂອງຄົນເຈັບມີບາດແຜຕິດເຊື້ອບໍລິເວນໜ້າຕີນລາມຫາຫົວເຂົ່າ.

ຮູບດ້ານລຸ່ມ: **screwworm fly *Chrysomya bezziana*** ໜອນຈາກສົ້ນນ່ອງຂອງຄົນເຈັບ ໜອນຍາວ ~ **1cm**

ການບົ່ງມະຕິໄຂ້ທໍລະພິດແບບງ່າຍດາຍ ແຕ່ເປັນເຕັກນິກທີ່ມີຄວາມແມ່ນຢຳ

ເຖິງວ່າເຊື້ອແບກທີເລຍທີ່ກໍ່ໃຫ້ເກີດພະຍາດໄຂ້ທໍລະພິດ, *Salmonella enterica* serovar Typhi ຖືກຄົ້ນພົບມາໄດ້ 132 ປີ ແລ້ວ ກໍ່ຕາມ, ຄົນເຈັບທີ່ເປັນພະຍາດໄຂ້ທໍລະພິດ ສ່ວນໃຫ່ຍໃນທົ່ວໂລກຍັງບໍ່ສາມາດເຂົ້າເຖິງການບົ່ງມະຕິດ້ານການກວດວິເຄາະທີ່ໜ້າເຊື່ອຖືໄດ້. ມັນມີຄວາມຈຳເປັນອັນຮີບດ່ວນທີ່ຕ້ອງມີເຄື່ອງມືທາງຫ້ອງວິເຄາະໃນການບົ່ງມະຕິພະຍາດໄຂ້ທໍລະພິດທີ່ວ່ອງໄວ, ລາຄາບໍ່ແພງ ແລະ ງ່າຍດາຍ ສາມາດເຄື່ອນຍ້າຍໄປໃນຫ້ອງຖິ່ນທີ່ຫ່າງໄກສອກຫຼີກ ເຊິ່ງເປັນບ່ອນທີ່ຂາດເງື່ອນໄຂໃນການບົ່ງມະຕິພະຍາດ ແລະ ມີພະຍາດຫຼາຍທີ່ສຸດ. ການບົ່ງມະຕິພະຍາດໄຂ້ທໍລະພິດ ສາມາດຍົກລະດັບຂຶ້ນໂດຍເຮັດໃຫ້ການປູກເລືອດຊອກຫາເຊື້ອ *S.* Typhi ງ່າຍຂຶ້ນ, ໃນລາຄາບໍ່ແພງ ແລະ ໄວຂຶ້ນ. ພວກເຮົາໄດ້ເຮັດການສຶກສາແບບປະສົມປະສານລະຫວ່າງເຊື້ອທີ່ເກີດໃນແກ້ວປູກເລືອດ ແລະ ການນຳໃຊ້ແຜ່ນຈຸ່ມແບບໄວໃນການບົ່ງມະຕິ *S.* Typhi antigen ແບບໄວວາ (rapid diagnostic test)ໂດຍການນຳໃຊ້ຕົວຢ່າງຈາກຫຼອດແກ້ວປູກເລືອດ ເຊິ່ງອາດເປັນເຕັກນິກທີ່ແມ່ນຢຳ, ລາຄາບໍ່ແພງ ແລະ ເຮັດໃຫ້ການບົ່ງມະຕິໃນຄົນເຈັບທີ່ເປັນພະຍາດໄຂ້ທໍລະພິດໃຫ້ໄວຂຶ້ນໃນລາວ (ເບິ່ງໃນ Castonguay-Vanier *et al.* 2013). ແຜ່ນຈຸ່ມທີ່ໃຊ້ໃນການບົ່ງມະຕິແບບໄວວານີ້ຖືກປະດິດຂຶ້ນມາເພື່ອກວດຫາເຊື້ອ *S.* Typhi ໃນອາຈົມ ແຕ່ພວກ ເຮົາ ໄດ້ປັບເອົາແຜ່ນຈຸ່ມດັ່ງກ່າວມາກວດຊອກຫາເຊື້ອ *S.* Typhi ໃນຕົວຢ່າງຈາກຫຼອດແກ້ວປູກເລືອດທີ່ມີສີຂຸ້ນ.

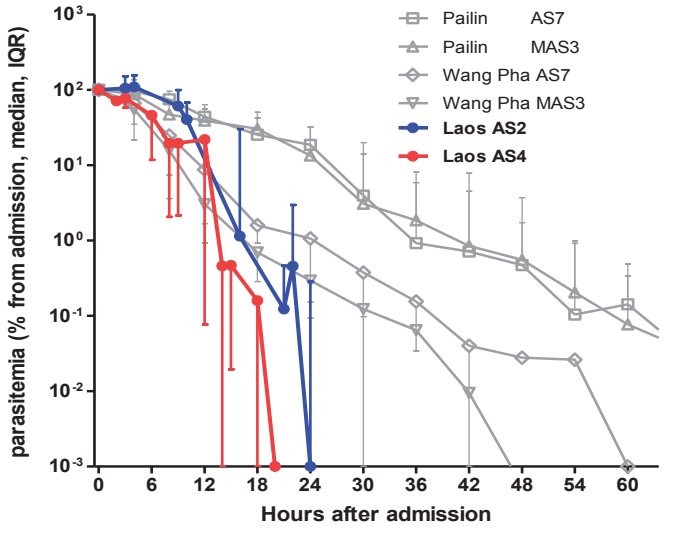
ເຮົາໃຊ້ສາຍພັນແບກທີເລຍ gram ລົບ ເປັນຕົວອ້າງອີງ, ແຜ່ນຈຸ່ມທີ່ໃຊ້ບົ່ງມະຕິຢ່າງໄວວາສາມາດກວດພົບສະເພາະແຕ່ Group D *Salmonella enterica* ແລະ *S.* Typhi ເທົ່ານັ້ນ. ຈາກການສຶກສາໄປຂ້າງໜ້າ, 6456 ແກ້ວປູກເລືອດຈາກຄົນເຈັບ 3028 ຄົນ ເປັນເວລາຫຼາຍກວ່າ 15 ເດືອນ ພົບວ່າ 392 (6.1%) ແກ້ວປູກເລືອດຈາກຄົນເຈັບ 221 ຄົນ (7.3%) ມີແບກທີເລຍ gram ລົບໃນແກ້ວປູກເລືອດ. ຄວາມ ໄວ, ຄ່າພະຍາກອນລົບ, ຄວາມຈຳເພາະ, ແລະ ຄ່າພະຍາກອນບວກຂອງເຄື່ອງກວດແມ່ນ 96.7%, 99.5%, 97.9% ແລະ 87.9% ຕາມ ລຳດັບ ສຳລັບຄົນເຈັບທີ່ມີເຊື້ອ *S.* Typhi. ສຳລັບຄົນເຈັບທີ່ຕິດເຊື້ອ Group D Salmonella ແມ່ນ 91.2%, 98.4%, 98.9% ແລະ 93.9% ຕາມລຳດັບ. ການກວດດ້ວຍແຜ່ນຈຸ່ມ (RDT) ແມ່ນເຮັດໃຫ້ການບົ່ງມະຕິໄວຂຶ້ນ ໂດຍສະເລ່ຍແມ່ນໜຶ່ງມື້ ແລະ ມີລາຄາບໍ່ແພງ ແລະ ປະຢັດແຮງງານກວ່າການໃຊ້ແຍກເຊື້ອໂດຍການປູກເລືອດ.

ເຖິງແນວໃດກໍ່ຕາມວິທີການດັ່ງກ່າວນີ້ກໍ່ບໍ່ໄດ້ແກ້ໄຂບັນຫາຂອງການປູກເລືອດທີ່ສາມາດກວດພົບເຊື້ອ *S.* Typhi ໄດ້ພຽງແຕ່ ~40-80 % ຂອງຄົນເຈັບທີ່ເປັນໄຂ້ທໍລະພິດທັງໝົດ. ແຕ່ມັນກໍ່ສະແດງໃຫ້ເຫັນວ່າການກວດດ້ວຍ RDT ຮ່ວມກັນການປູກເລືອດ ແມ່ນເຮັດໃຫ້ການບົ່ງມະຕິໄວຂຶ້ນ, ເປັນຊຸດກວດທີ່ມີລາຄາບໍ່ແພງ ແລະ ແມ່ນຢຳ. ພວກເຮົາຄາດວ່າມັນຈະຖືກນຳໄປທົດລອງໃຊ້ໃນຫ້ອງຖິ່ນອື່ນໆ ແລະ ເປັນປະໂຫຍດສຳລັບການບົ່ງມະຕິໃນຫ້ອງວິເຄາະທີ່ຫ່າງໄກສອກຫຼີກ ແລະ ຊ່ວຍສືບຫາການລະບາດຂອງພະຍາດທີ່ສົງໃສວ່າເປັນຍ້ອນໄຂ້ທໍລະພິດ.

ເຊື້ອໄຂ້ຍຸງທີ່ດື້ (ຕ້ານ) ຕໍ່ຢາ Artemisinin ມາຮອດລາວແລ້ວບໍ?

ຖືເປັນເລື່ອງບໍ່ດີ ທີ່ໄດ້ມີຫລັກຖານຊີ້ໃຫ້ເຫັນວ່າ ໄດ້ມີເຊື້ອໄຂ້ຍຸງຟານຊີປາຣອມ ດື້ຕໍ່ຢາ Artemisinin ຢູ່ປະເທດກຳປູເຈຍ, ຫວຽດນາມ ແລະ ຊາຍແດນໄທ-ພະມ້າ ແລ້ວ. ພວກເຮົາ ໄດ້ເຮັດການສຶກສາຄົ້ນຄວ້າແບບ Randomized clinical trial ເພື່ອປະເມີນເບິ່ງໄລຍະເວລາທີ່ເຊື້ອໄຂ້ຍຸງໝົດໄປຈາກກະແສເລືອດ ແລະ ປະເມີນເບິ່ງປະສິດທິພາບຂອງຢາ Artesunate ຊະນິດກິນ ໃນປະລິມານ 4 mg/kg ແລະ 2 mg/kg ເປັນເວລາ 3 ມື້ ແລ້ວ ຕາມດ້ວຍຢາ Artemether-lumefantrine ໃນຄົນເຈັບທີ່ເປັນໄຂ້ຍຸງຟານຊີປາຣອມທີ່ບໍ່ມີອາການສົມ ທີ່ເມືອງ ເຊໂປນ ແຂວງສະຫວັນນະເຂດ (Mayxay *et al.*, 2012). ຜົນການຄົ້ນ ຄວ້າພົບວ່າ ໄລຍະເວລາສະເລ່ຍ ທີ່ເຊື້ອໄຂ້ຍຸງໝົດໄປຈາກກະແສເລືອດ [Mean (range)] ແມ່ນ 23.2 (12-46) ຊົ່ວໂມງ. ມີຄົນເຈັບ 10 ຄົນ (23%) ຍັງມີເຊື້ອໃນກະແສເລືອດ ໃນມື້ທີ 1 ຫລັງການປິ່ນປົວ ແຕ່ບໍ່ມີຄົນເຈັບຜູ້ໃດທີ່ມີເຊື້ອໃນກະແສເລືອດ ໃນມື້ທີ 2 ຫລື 3 ຫລັງປິ່ນປົວ. ອັດຕາການປິ່ນປົວຫາຍຂາດພາຍໃນ 42 ມື້ ແມ່ນ 100%. ສະຫລຸບ: ຍັງບໍ່ ທັນມີຫລັກຖານຊີ້ໃຫ້ເຫັນວ່າ ເຊື້ອໄຂ້ຍຸງຟານຊີປາຣອມໃນພາກໃຕ້ຂອງລາວ ດື້ຕໍ່ຢາ Artesunate ໃນຄົນເຈັບເທື່ອ, ແຕ່ເຮົາ ຈະຕ້ອງໄດ້ມີການຕິດຕາມຢ່າງເປັນປະຈຳ.

ເສັ້ນສີແດງ ແລະ ສີຟ້າ ສະແດງເຖິງໄລຍະເວລາທີ່ເຊື້ອໄຂ້ຍຸງຫາຍຈາກກະແສເລືອດ ພາຍຫລັງປິ່ນປົວດ້ວຍຢາ Artesunate ໃນປະລິມານ 2 mg/kg (AS2) ແລະ 4 mg/kg (AS4) ສ່ວນເສັ້ນສີຂີ້ເຖົ່າ ແມ່ນຂໍ້ມູນຈາກ ເຂດໄພລິນ (ຊາຍແດນໄທ-ກຳປູເຈຍ) ແລະ ເຂດວັງຜາ (ຊາຍແດນໄທ-ພະມ້າ)



ແຜນທີ່ຂ້າງຊ້າຍມືນີ້ ສະແດງໃຫ້ເຫັນຂົງເຂດອາຊີຕາເວັນອອກຊ່ຽງໃຕ້ ເຊິ່ງສີຟ້າບົ່ງບອກເຖິງນະຄອນຫລວງຂອງປະເທດ ແລະ ຈຸດທີ່ພົບໄລຍະເວລາທີ່ເຊື້ອ ໄຂ້ຍຸງໝົດໄປຈາກກະແສ ເລືອດແກ່ຍາວກວ່າ ປົກກະຕິພາຍຫລັງປິ່ນປົວດ້ວຍຢາ Artemisinin (ສີແດງ) ລວມທັງ ສະຖານທີ່ທຳການສຶກສາຄົ້ນຄວ້າ ໃນລາວ ທີ່ ເມືອງເຊໂປນ (ສີຂຽວ) ເຊິ່ງໄລຍະເວລາ ທີ່ເຊື້ອໝົດໄປຈາກກະແສເລືອດແມ່ນຍັງສັ້ນຢູ່.

Typhus, fluoroquinolones ແລະ ການປິ່ນປົວ

ໄຂ້ແມງແດງ (*Orientia tsutsugamushi*) ແມ່ນບັນຫາທາງດ້ານສາທາລະນະສຸກສຳລັບພົນລະເມືອງຫຼາຍກວ່າພັນລ້ານຄົນໃນອາຊີ ແລະ ອົດສະຕາລີ ເຊິ່ງຄາດວ່າມີອຸບັດການໜຶ່ງລ້ານກໍລະນີຕໍ່ປີ. ເຖິງວ່າຢາ doxycyline ແມ່ນຢາປິ່ນປົວມາດຕະຖານ ແຕ່ວ່າຢາ fluoroquinolones ກໍ່ນຳໃຊ້ໄດ້ຜົນດີໃນບາງກໍລະນີ. ແຕ່ມີຫຼັກຖານຢັ້ງຢືນທາງຄລີນິກໃຫ້ເຫັນວ່າ ຢານີ້ບໍ່ມີປະສິດທິພາບໃນການປິ່ນປົວໄຂ້ແມງແດງ. ເພື່ອໃຫ້ຄວາມກະຈ່າງແຈ້ງຕໍ່ກັບບັນຫານີ້ ພວກເຮົາໄດ້ເຮັດການທົດສອບເບິ່ງການຕອບສະໜອງໃນຫ້ອງທົດລອງຂອງເຊື້ອ *O. tsutsugamushi* (ສາຍພັນ Kato) ຕໍ່ຢາ ciprofloxacin ແລະ ສຶກສາທາງ Sequence ເພື່ອເບິ່ງຈຸດທີ່ພາໃຫ້ຕ້ານຕໍ່ quinolone (quinolone - resistance - determining - region ຫຼື QRDR) ຂອງ gyrA gene. ໃນຄົນເຈັບລາວ 18 ຄົນ (ເບິ່ງໃນ Tantibhedhyangkul *et al.* 2009). ເຊື້ອ *O. tsutsugamushi* ແມ່ນຕ້ານຕໍ່ຢາ ciprofloxacin ແລະ ofloxacin ໃນຫ້ອງທົດລອງ (MIC = 8µg/ml) ແລະ Sequences ທີ່ໃຈ້ແຍກມາໄດ້ທັງໝົດ ລວມທັງ genomes ຂອງເຊື້ອ *O. tsutsugamushi* ສອງສາຍພັນ (ສາຍພັນ Boryong and Ikeda) ແມ່ນມີ Ser83Leu ທີ່ກາຍພັນໃນຈຸດ QRDR ເຊິ່ງເປັນທີ່ຮູ້ກັນວ່າມີຄວາມສຳພັນກັບການຕ້ານຂອງເຊື້ອຕໍ່ຢາ fluoroquinolone. ຜົນການທົດລອງ ນີ້ໄດ້ຊີ້ໃຫ້ເຫັນວ່າເຮົາບໍ່ຄວນໃຊ້ຢາ fluoroquinolones ເພື່ອປິ່ນປົວໄຂ້ແມງແດງ. ພວກເຮົາບໍ່ຮູ້ວ່າປະສິດທິພາບຂອງຢາ fluoroquinolones ສາມາດປິ່ນປົວໄຂ້ໝັດໝູໄດ້ຫຼືບໍ່. ເຊັ່ນດຽວກັນຍັງບໍ່ມີຄວາມຊັດເຈນກ່ຽວກັບປະສິດທິພາບຂອງ azithromycin ໃນການປິ່ນປົວໄຂ້ແມງແດງ ຫຼື ໄຂ້ໝັດໝູໃນລາວ. (ຕິດຕາມຂໍ້ມູນເພີ່ມໃນວາລະສານຫ້ອງວິເຄາະຈຸລິນຊີວິທະຍາສະບັບໜ້າ).

ປັດຈຸບັນຍັງບໍ່ທັນມີປຶ້ມຄູ່ມືທີ່ເປັນທີ່ເປັນເອກະພາບ ກ່ຽວກັບນິຍາມຂອງໄຂ້ແມງແດງ ຫຼື ໄຂ້ໝັດໝູຮ້າຍແຮງ. ໃນທາງທົດສະດີຢາ doxycyc-line ແລະ chloramphenicol ໜ້າຈະໄດ້ຜົນດີແຕ່ການປິ່ນປົວທີ່ດີທີ່ສຸດນັ້ນຍັງບໍ່ມີຄວາມຊັດເຈນ. ສຳລັບຜູ້ທີ່ມີຄະແນນ Glasgow Coma Score ຕ່ຳ ຫຼື ບໍ່ສາມາດກືນຢາໄດ້, ແມ່ນມີຄວາມຈຳເປັນໃຫ້ຢາທາງເສັ້ນເລືອດ (ເຖິງແມ່ນວ່າເຮົາບໍ່ມີຢາ doxycycline ທີ່ສັກເຂົ້າໃນເສັ້ນເລືອດໃນລາວ) ຫຼື ອາດຈະໃຫ້ຢາທາງທໍ່ກະເພາະອາຫານໂດຍໃຊ້ຢາ doxycycline ແລະ chloramphenicol (ໜ້າ 11).

ແນວທາງການປິ່ນປົວ
ກະລຸນາກວດເບິ່ງແນວທາງການປິ່ນປົວເດັກເກີດໃໝ່ ແລະ ເດັກນ້ອຍ ແລະ ພິຈາລະນາກວດເບິ່ງການຖືພາ

ຂໍ້ແນະນຳໃນໜ້າຕໍ່ໄປນີ້ແມ່ນຄັດມາຈາກຂໍ້ມູນການຕ້ານຕໍ່ຢາຂອງເຊື້ອທີ່ເຊື້ອທີ່ພົບຢູ່ໃນໂຮງໝໍມະໂຫສົດ. ກະລຸນາຮັບຮູ້ໄວ້ວ່າ ນີ້ພຽງແຕ່ເປັນແນວທາງໃນການປິ່ນປົວເທົ່ານັ້ນ ແລະ ຄວນພິຈາລະນາຕາມສະພາບຂອງຄົນເຈັບເປັນສ່ວນບຸກຄົນ, ຕາມໜ້າທີ່ການໝາກໄຂ່ຫຼັງ ແລະ ໜ້າທີ່ການຂອງຕັບ, ຂໍ້ຫ້າມໃຊ້ ແລະ ການແພ້ຢາກ່ອນທີ່ຈະສັ່ງຢາໃຫ້ຄົນເຈັບ. ກະລຸນາກວດເບິ່ງປະລິມານຢາກ່ອນການສັ່ງຢາໃຫ້ຄົນເຈັບ. ສຳລັບເດັກ ກະລຸນາກວດເບິ່ງແນວທາງການປິ່ນປົວສຳລັບເດັກນ້ອຍ. ພວກເຮົາຈະບໍ່ຮັບຜິດຊອບການນຳໃຊ້ຂໍ້ແນະນຳຕໍ່ໄປນີ້.

ການປິ່ນປົວພະຍາດໄທຟັສ (typhus)

ໃຫ້ **Doxyxycline** 4 mg/kg ທາງປາກຄັ້ງທຳອິດ ຕາມດ້ວຍ 2 mg/kg ທຸກໆ 12 ຊົ່ວໂມງ, ປິ່ນປົວ 7 ມື້
(ປະລິມານປົກກະຕິທີ່ໃຫ້ໃນຜູ້ໃຫຍ່ແມ່ນ 200 mg ຄັ້ງທຳອິດ ຕາມດ້ວຍ 100 mg ທຸກໆ 12 ຊົ່ວໂມງ ປິ່ນປົວ 7 ມື້)
ຫຼື
ໃຫ້ **Chloramphenicol** 50-70 mg/kg/ມື້ ທາງປາກ ເປັນເວລາ 7 ມື້
(ປະລິມານປົກກະຕິທີ່ໃຫ້ໃນຜູ້ໃຫຍ່ແມ່ນ 500 mg ທຸກໆ 6 ຊົ່ວໂມງ ປິ່ນປົວ 7 ມື້)

ຄວາມສ່ຽງທີ່ໃຫ້ **Doxycycline** 7 ມື້ ໃນເດັກນ້ອຍ < 8 ປີ ອາດຈະຕ່ຳກວ່າຄວາມສ່ຽງທີ່ບໍ່ໃຫ້ doxycycline. ໃນແມ່ຍິງຖືພາ, ການໃຫ້ **Azithromycin** ໃນການປິ່ນປົວ ເປັນເວລາ 7 ມື້ ອາດເປັນທາງເລືອກທີ່ດີທີ່ສຸດ.

ຕ້ອງກວດເບິ່ງການຖືພາໃນແມ່ຍິງໄວຈະເລີນພັນກ່ອນການໃຫ້ຢາ doxycycline. ຕ້ອງເຕືອນຄົນເຈັບລ່ວງໜ້າກ່ຽວກັບອາການເຈັບກະເພາະທີ່ອາດເກີດຈາກການກິນຢາ

ການປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບ

ໜ້າຕໍ່ໄປແມ່ນແນວທາງການປິ່ນປົວພະຍາດເຍື່ອຫຸ້ມສະໝອງອັກເສບ (ໃນເວລາທີ່ຍັງບໍ່ທັນຮູ້ຈັກເຊື້ອສາຍເຫດ ແລະ ຜົນຂອງການທົດສອບເຊື້ອໃສ່ກັບຢາຕ້ານເຊື້ອ), ແລະ ພວກເຮົາຕ້ອງການເນັ້ນໜັກບາງຈຸດດັ່ງລຸ່ມນີ້ :

* ຖ້າສົງໃສເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອຈຸລິນຊີ ຄວນປິ່ນປົວດ້ວຍຢາຕ້ານເຊື້ອ ກ່ອນເຈາະນ້ຳໄຂສັນຫຼັງ ຫລື ພາຍຫລັງເຈາະນ້ຳໄຂ ສັນຫລັງໃນທັນທີໂລດ (ຈະໃຫ້ຢາຕ້ານເຊື້ອກ່ອນ ຫລື ຫລັງການເຈາະນ້ຳໄຂສັນຫລັງ ແມ່ນອີງຕາມສະພາບຂອງຄົນເຈັບ).
* ຖ້າສົງໃສເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອ *R. Typhi* ຫຼື *O. tsutsugamushi* ແນະນຳໃຫ້ຕື່ມຢາ Doxycycline ຮ່ວມກັບຢາຕ້ານເຊື້ອຕົວອື່ນ ທີ່ໃຊ້ປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບທົ່ວໆໄປ (ບໍ່ແມ່ນຈະໃຊ້ແຕ່ຢາ Doxycycline ຢ່າງດຽວ).
* ຢາ Ceftriaxone ອາດໄດ້ຜົນດີສຳລັບເຍື່ອຫຸ້ມສະໝອງອັກເສບຈາກເຊື້ອ Leptospirosis ເຊັ່ນກັນ.
* ເຊື້ອ *Listeria monocytogenes* ເປັນເຊື້ອທີ່ບໍ່ຄ່ອຍພົບໃນນະຄອນຫຼວງວຽງຈັນ. ເຊື້ອດັ່ງກ່າວນີ້ ແມ່ນຕ້ານ (ດື້) ຕໍ່ຢາ Cephalosporins ລຸ້ນທີສາມ.
* ພວກເຮົາເຄີຍພົບເຊື້ອ *S. pneumoniae* ທີ່ຕ້ານ (ດື້) ຕໍ່ຢາ Penicillin, ສະນັ້ນພວກເຮົາບໍ່ແນະນຳປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບດ້ວຍຢາ penicillin (ໃນເວລາຍັງບໍ່ທັນຮູ້ຈັກເຊື້ອ ແລະ Antibiogram ເທື່ອ), ພວກເຮົາແນະນຳໃຫ້ໃຊ້ cephalosporin ລຸ້ນທີສາມເຊັ່ນ : Ceftriaxone.
* ມີຂໍ້ມູນວ່າການໃຊ້ຢາ steroids ອາດມີຜົນດີໃນການປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອ *M. tuberculosis*, ແຕ່ຍັງບໍ່ທັນມີຂໍ້ມູນຈະແຈ້ງເທື່ອວ່າ ການໃຊ້ຢາ steroids ຈະມີຜົນດີໃນການປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອ *Haemophilus influenzae b* ຫຼື *S. pneumoniae* ໃນແຖບອາຊີຕາເວັນອອກສ່ຽງໃຕ້.

ທິດທາງໃນການປິ່ນປົວເຍື່ອຫຸ້ມສະໝອງອັກເສບ

ຂໍ້ແນະນຳການໃຊ້ຢາຕ້ານເຊື້ອ

Ceftriaxone

80-100 mg/kg/ມື້ IV (Cephalosporins ລຸ້ນທີ3 ເປັນຢາທີ່ເລືອກໃຊ້ກ່ອນຈະໄດ້ຮັບຜົນກວດທາງວິເຄາະ)
ແບ່ງເປັນ 2 ເທື່ອຕໍ່ມື້

(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນປະມານ 2g IV ທຸກໆ 12 ຊົ່ວໂມງ)

ຫຼື ໃນເດັກເກີດໃໝ່

Cefotaxime

ອາຍຸ 0-7 ມື້ 100- 150 mg/kg/ມື້ IV (ທຸກໆ 8- 12 ຊົ່ວໂມງ) ຫຼື
ອາຍຸ 8-28 ມື້ 150- 200 mg/kg/ມື້ IV (ທຸກໆ 6-8 ຊົ່ວໂມງ)

ຖ້າສົງໃສວ່າມີການຕິດເຊື້ອ Listeria (ປົກກະຕິຈະພົບໃນເດັກ < 1 ເດືອນ)ໃຫ້ສົມທົບກັບ

Ampicillin

ອາຍຸ:	0-7 ມື້	8-28 ມື້	<15 ປີ	>15 ປີ
ປະລິມານຕໍ່ມື້ IVD:	150mg/kg/ມື້	200mg/kg/ມື້	300mg/kg/ມື້	12g/ມື້
ໄລຍະຫ່າງ:	ທຸກໆ 8 ຊົ່ວໂມງ	ທຸກໆ 6-8 ຊົ່ວໂມງ	ທຸກໆ 6 ຊົ່ວໂມງ	ທຸກໆ 4 ຊົ່ວໂມງ

ຫຼື ຖ້າບໍ່ມີ Ceftriaxone ຫຼື ບໍ່ມີຢາໃນກຸ່ມ Cephalosporins ລຸ້ນທີ 3

Chloramphenicol

ອາຍຸ:	0-7 ມື້	8-28 ມື້	<15 ປີ	>15 ປີ
ປະລິມານຕໍ່ມື້ IVD:	25mg/kg/ມື້	50mg/kg/ມື້	75-100mg/kg/ມື້	4-6g/ມື້
ໄລຍະຫ່າງ:	24 ຊົ່ວໂມງ	12-24 ຊົ່ວໂມງ	6 ຊົ່ວໂມງ	6ຊົ່ວໂມງ

(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນ 1.5g ທຸກໆ 6 ຊົ່ວໂມງ)

ສົມທົບກັບ

Ampicillin

ອາຍຸ:	0-7 ມື້	8-28 ມື້	<15 ປີ	>15 ປີ
ປະລິມານຕໍ່ມື້ IVD:	150mg/kg/ມື້	200mg/kg/ມື້	300mg/kg/ມື້	4-6g/ມື້
ໄລຍະຫ່າງ:	ທຸກໆ 8 ຊົ່ວໂມງ	ທຸກໆ 6-8 ຊົ່ວໂມງ	ທຸກໆ 6 ຊົ່ວໂມງ	ທຸກໆ 4 ຊົ່ວໂມງ

ຖ້າສົງໃສ Rickettsia ໃຫ້ຕື່ມ Doxycycline ກິນ 4mg/kg ຕອນທຳອິດ, ຈາກນັ້ນ 2mg/kg ທຸກໆ 12 ຊົ່ວໂມງ ເປັນເວລາ 1 ອາທິດ. ຜູ້ໃຫຍ່ແມ່ນຈະໄດ້ປະລິມານ 200mg ຕອນທຳອິດ, ຕໍ່ມາແມ່ນ 100mg ທຸກໆ 12h ເປັນເວລາ 1 ອາທິດ. ຄວາມສ່ຽງຂອງຢາ Doxycycline ໃນເດັກ <8 ປີ ສຳລັບການປິ່ນປົວ ແມ່ນມີໜ້ອຍກວ່າການທີ່ບໍ່ໃຫ້ຢາປິ່ນປົວດ້ວຍ Doxycycline. ໃນແມ່ຍິງຖືພາ, ຢາ Azithromycin ອາດເປັນຢາທີ່ໃຊ້ໄດ້ຜົນດີທີ່ສຸດ ແລະ ອາດມີປະສິດທິພາບດີໃນເດັກເຊັ່ນກັນ.

ເວລາທີ່ທ່ານເຮັດ PL, ໃຫ້ທ່ານສົ່ງເລືອດໄປປຸກ ນຳເພາະຈະມີໂອກາດພົບ ເຊື້ອທີ່ພາໃຫ້ເປັນພະຍາດ ຫຼາຍຂຶ້ນກວ່າເກົ່າ.

ຖ້າຫາກທ່ານສົງໃສວັນນະ ໂລກເຍື່ອຫຸ້ມສະໝອງ ກະລຸນາສົ່ງຕົວຢ່າງນ້ຳໄຂ ສັນຫຼັງຫຼາຍເທົ່າທີ່ຈະໄດ້

ການກວດຫາ IgM ຕໍ່ ເຊື້ອພະຍາດໃດໜຶ່ງແລ້ວ ໃຫ້ຜົນບວກນັ້ນອາດສະ ແດງເຖິງການຕິດເຊື້ອຜ່ານ ມາແລ້ວ,ແຕ່ບໍ່ແມ່ນອາ ການເຈັບເປັນໃນຄັ້ງນີ້! ສະນັ້ນທ່ານຄວນແປຜົນ ກວດຢ່າງລະມັດລະວັງ. ໃນຂະນະນີ້ ເຮົາຍັງບໍ່ທັນ ມີວິທີການກວດຫາ DNA ຫຼື Antigen ຂອງເຊື້ອພະຍາດ Typhus ແລະ Rickett-sia ເທື່ອ, ສະນັ້ນ ເຮົາຄວນສົມມຸດຖານວ່າ ຄົນເຈັບອາດເປັນເຍື່ອ ຫຸ້ມສະໝອງອັກເສບ ຍ້ອນເຊື້ອຈຸລິນຊີອື່ນໆ ນຳ ແລະ ຄວນໃຫ້ການ ປິ່ນປົວດ້ວຍຢາ Cepha-losporins ລຸ້ນທີ 3 ນຳ.

ສຳລັບການປິ່ນປົວອັກ ເສບສະໝອງຍີ່ປຸ່ນ ຫຼື ອັກເສບສະໝອງຈາກໄຂ້ ເລືອດອອກນັ້ນ ແມ່ນບໍ່ ທັນມີຢາປິ່ນປົວສະເພາະ ເທື່ອ.

ແນວທາງການປິ່ນປົວພະຍາດ Melioidosis ຮ້າຍແຮງ

ການປັບປະລິມານຢາ ceftazidime ໃນຄົນເຈັບທີ່ມີໜ້າທີ່ການໄຂ່ຫຼັ່ງຊຸດໂຊມ

ເນື່ອງຈາກວ່າຄົນເຈັບເປັນ melioidosis ມັກພົບວ່າມີໜ້າທີ່ການທຳງານຂອງໄຂ່ຫຼັ່ງຊຸດໂຊມ ພວກເຮົາຂໍແນະນຳລະບົບການປິ່ນປົວໂດຍອີງໃສ່ປະລິມານຂອງ creatinine ໃນກະແສເລືອດຂອງຄົນເຈັບສຳລັບຜູ້ໃຫຍ່ນ້ຳໜັກປະມານ 50 kg.

Serum creatinine		**Ceftazidime Dose**
µmol/L	**mg/dL**	
ຕ່ຳກ່ວາ 176	ຕ່ຳກ່ວາ 2	2g ທຸກໆ 8 ຊົ່ວໂມງ
176 - 352	2-4	1g ທຸກໆ 8 ຊົ່ວໂມງ
353 -528	4-6	1g ທຸກໆ 12 ຊົ່ວໂມງ
ສູງກ່ວາ 528	ສູງກ່ວາ 6	1g ທຸກໆ 24 ຊົ່ວໂມງ

<u>Melioidosis ຊະນິດຮ້າຍແຮງ</u>: ປິ່ນປົວດ້ວຍຢາສັກ-ຕໍ່ດ້ວຍຢາກິນ

Ceftazidime IV 120mg/kg/ມື້ ແບ່ງເປັນ 3 ເທື່ອ, ເປັນເວລາຢ່າງນ້ອຍ 10 ມື້
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນປະມານ 2g IV ທຸກໆ 8 ຊົ່ວໂມງ)

ຫຼື

Amoxicillin-clavulanate IV 150mg/kg/ມື້ ແບ່ງເປັນ 6 ເທື່ອຕໍ່ມື້, ເປັນເວລາຢ່າງໜ້ອຍສຸດ 10 ມື້
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນປະມານ 1.2g IV ທຸກໆ 4 ຊົ່ວໂມງ)

ຈາກນັ້ນໃຫ້ກິນຢາຕໍ່ຄື:

Co-trimoxazole ກິນ 2 ເທື່ອຕໍ່ມື້, ເປັນເວລາ 12-20 ອາທິດ - ປະລິມານຂອງຢາແມ່ນປັບຕາມນ້ຳໜັກຂອງຄົນເຈັບ.
ເບິ່ງດ້ານເທິງຂອງໜ້າທີ 14.

<u>ສົມທົບກັບ</u>

Doxycycline 4 mg/kg/ມື້ ມື້ລະເທື່ອ, ເປັນເວລາ 12-20 ອາທິດ
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນປະມານ 2 ເມັດຂອງ 100mg ທຸກໆ 24 ຊົ່ວໂມງ)

ຫຼື ໃຫ້ຢາດຽວຄື:

Amoxicillin-clavulanate 60/15 mg/kg/ມື້ ແບ່ງເປັນ 3 ເທື່ອຕໍ່ມື້, ເປັນເວລາ 20 ອາທິດ
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນປະມານ 2 ເມັດຂອງ 500/125mg ທຸກໆ 8 ຊົ່ວໂມງ)

ແນວທາງການປິ່ນປົວພະຍາດ Melioidosis ດ້ວຍຢາຊະນິດກິນ

ການໃຫ້ຢາ Co-trimoxazole ໂດຍອີງໃສ່ນ້ຳໜັກຂອງຄົນເຈັບ (ເບິ່ງ Dance 2011)

ນ້ຳໜັກຮ່າງກາຍເປັນ kg	ປະລິມານຢາ Co-trimoxazole (TMP/SMX) mg ທຸກໆ 12 ຊົ່ວໂມງ
< 40	160/800 mg
40 - 60	240/1200 mg
> 60	320/1600 mg

<u>Melioidosis ທີ່ເປັນຢູ່ຈຸດໃດຈຸດໜຶ່ງ-ການປິ່ນປົວດ້ວຍຢາຊະນິດກິນ</u>

<u>(ຄົນເຈັບທີ່ເປັນ Melioidosis ຢູ່ສະເພາະທີ່ໃດໜຶ່ງ ໂດຍບໍ່ມີການຊຶມເຊື້ອໃນເລືອດ)</u>

Co-trimoxazole ກິນ 2 ຄັ້ງຕໍ່ມື້ ເປັນເວລາ 12-20 ອາທິດ - ປະລິມານການໃຫ້ຢາແມ່ນປັບຕາມນ້ຳໜັກ ຂອງຄົນເຈັບ. ເບິ່ງດ້ານເທິງ.

<u>ສົມທົບກັບ</u>

Doxycycline 4 mg/kg/ມື້ ມື້ລະເທື່ອ ເປັນເວລາ 12-20 ອາທິດ
(ປະລິມານປົກກະຕິສຳລັບຜູ້ໃຫຍ່ ນ້ຳໜັກ 50kg ແມ່ນປະມານ 2 ເມັດຂອງ 100mg ທຸກໆ 24 ຊົ່ວໂມງ)

<u>ການປິ່ນປົວດ້ວຍຢາດ່ຽວ</u>

Amoxicillin - clavulanate 60/15 mg/kg/ມື້ ແບ່ງເປັນ 3 ເທື່ອຕໍ່ມື້ ເປັນເວລາ 20 ອາທິດ
(ປະລິມານປົກກະຕິສຳລັບຜູ້ໃຫຍ່ ນ້ຳໜັກ 50kg ແມ່ນ 2 ເມັດຂອງ 500/125mg ທຸກໆ 8 ຊົ່ວໂມງ)

ປະລິມານສູງສຸດແມ່ນ 1500/375mg ຕໍ່ເທື່ອ, ທຸກໆ 8 ຊົ່ວໂມງ.

ການປິ່ນປົວໄຂ້ທໍລະພິດ (typhoid)

<u>ໄຂ້ທໍລະພິດທີ່ບໍ່ມີອາການສິນ</u> ປິ່ນປົວດ້ວຍ ofloxacin 15 mg/kg/ມື້ ແບ່ງກິນ 2 ຄັ້ງຕໍ່ມື້ ເປັນເວລາ 3 ມື້

<u>ໄຂ້ທໍລະພິດຮ້າຍແຮງ</u>
ຕົວຢ່າງ: ຄວາມດັນເລືອດຕ່ຳ, ເຈັບທ້ອງ, ເລືອດໄຫຼທາງລະບົບລະລາຍອາຫານ ຫຼື ລຳໄສ້ຊອດ, encephalopathy, ຊັກ, ອັກເສບປອດ. ໃຫ້ປຶກສາທ່ານໝໍຜ່າຕັດ ພ້ອມທັງໃຫ້ຢາ ceftriaxone 60 mg/kg/ມື້ IV/IM 1 ຄັ້ງຕໍ່ມື້ ເປັນເວລາ 10-14 ມື້

ພິຈາລະນາໃຫ້ dexamethasone 3mg/kg ທາງເຊໂລມ(ເສັ້ນເລືອດ) ປ່ອຍໃຫ້ໝົດພາຍໃນ 30 ນາທີ ຕາມດ້ວຍ 1mg/kg ໃຫ້ໝົດພາຍໃນ 30 ນາທີ ທຸກໆ 6 ຊົ່ວໂມງ ເປັນເວລາ 8 ຄັ້ງ.

ການໃຫ້ຢາ ofloxacin 3 ມື້ ໃນເດັກນ້ອຍອາຍຸຕ່ຳກ່ວາ 8 ປີ ແມ່ນມີຄວາມສ່ຽງນ້ອຍກ່ວາການບໍ່ໃຫ້ຢາດັ່ງກ່າວ.

ໝາຍເຫດ: ການປິ່ນປົວດ້ວຍຢາ fluoroquinolone ແມ່ນຂາດໄຂ້ໄວກ່ວາການປິ່ນປົວດ້ວຍ ceftriaxone ທາງເສັ້ນເລືອດ ແລະ ຄົນເຈັບອາດຈະຂາດໄຂ້ຫຼັງຈາກຢຸດຢາ fluoroquinolone ໄດ້ 1 ມື້.

ການປິ່ນປົວຊຶມເຊື້ອເລືອດໂດຍບໍ່ມີຜົນຢັ້ງຢືນທາງຫ້ອງວິເຄາະ

ການຊຶມເຊື້ອເລືອດ ທີ່ເກີດຈາກເຊື້ອຢູ່ນອກໂຮງໝໍ

Gentamicin IV 5 - 7 mg/kg ມື້ລະເທື່ອ

(ປະລິມານປົກກະຕິສຳລັບຜູ້ໃຫຍ່ ນ້ຳໜັກ 50 ກິໂລ ~ 240-360mg IV ມື້ລະເທື່ອ)
(ໃຫ້ລະວັງໄຂ່ຫຼັງຊຸດໂຊມ ຖ້າໃຫ້ຫຼາຍມື້ຕໍ່ມາ)

ສົມທົບກັບ

Ampicillin 25-100mg/kg IV ທຸກໆ 6 ຊົ່ວໂມງ
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນ 1g IV ທຸກໆ 6 ຊົ່ວໂມງ)

ຫຼືອາດໃຊ້ຢາທີ່ມີລາຄາແພງກວ່ານີ້ ແຕ່ຄອບຄຸມໄດ້ຫຼາຍເຊື້ອເຊັ່ນ:

Ceftriaxone IV ຫຼື IM 50-100mg/kg ທຸກໆ 24 ຊົ່ວໂມງ
(ປະລິມານປົກກະຕິສຳລັບຄົນເຈັບຜູ້ໃຫຍ່ 50kg ແມ່ນ 2-4g IV ທຸກໆ 24 ຊົ່ວໂມງ)

ຖ້າຫາກສົງໃສວ່າມີການຊຶມເຊື້ອຊ່ອງທ້ອງ, ແນະນຳໃຫ້ຕື່ມຢາ metronidazole (500 mg ທຸກໆ 8 ຊົ່ວໂມງ)

ກະລຸນາເອົາທຸກຕົວຢ່າງໄປກວດທາງດ້ານຈຸລິນຊີວິທະຍາ ແລະ ເອົາຕົວຢ່າງເລືອດ ຫຼາຍຊຸດໄປປູກຊອກຫາເຊື້ອກ່ອນການໃຫ້ຢາຕ້ານເຊື້ອ

ກໍລະນີພິເສດ

ຖ້າຫາກທ່ານສົງໃສອັກເສບເຍື່ອຫຸ້ມໃນຫົວໃຈ:

ແນະນຳໃຫ້ເອົາຕົວຢ່າງເລືອດໄປປູກ 6 ຊຸດ ໃນເວລາທີ່ແຕກຕ່າງກັນ ແລະ ແຈ້ງທ່ານໝໍຊ່ຽວຊານດ້ານຫົວໃຈ

ຖ້າຫາກທ່ານສົງໃສ melioidosis, ໃນຊ່ວງລໍຖ້າຜົນກວດ:

ໃຫ້ co-amoxiclav ຫຼື ຖ້າຫາກທ່ານສົງໃສ melioidosis ຫຼາຍ ກໍໃຫ້ປິ່ນປົວດ້ວຍ ceftazidime

ຖ້າຫາກຄົນເຈັບຫາກເປັນເດັກນ້ອຍຕ່ຳກ່ວາ 1 ປີ:

ໃຫ້ຕື່ມ cloxacillin

ຖ້າຫາກທ່ານສົງໃສເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອຈຸລິນຊີ ຮ່ວມກັບຊຶມເຊື້ອເລືອດ:

ແນະນຳໃຫ້ປິ່ນປົວດ້ວຍ ceftriaxone ທຸກໆ 12 ຊົ່ວໂມງ ແທນທີ່ຈະໃຫ້ທຸກໆ 24 ຊົ່ວໂມງ

ຖ້າຫາກທ່ານສົງໃສເຍື່ອຫຸ້ມສະໝອງອັກເສບຍ້ອນເຊື້ອ pneumococci ຮ່ວມກັບຊຶມເຊື້ອເລືອດ:

ແນະນຳໃຫ້ປິ່ນປົວດ້ວຍ ceftriaxone ທຸກໆ 12 ຊົ່ວໂມງ, ແທນທີ່ຈະໃຫ້ penicillin

ບົດຄົ້ນຄວ້າທາງດ້ານການແພດທີ່ຖືກຕີພິມເຜີຍແຜ່ຈາກປະເທດລາວ

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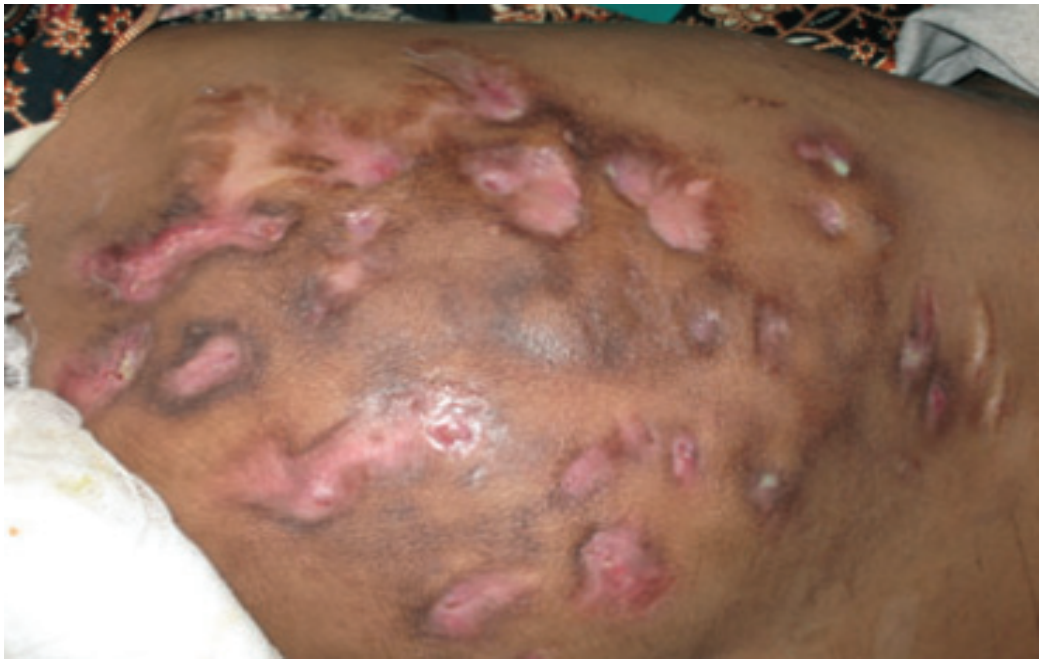
ຝີຢູ່ກົ້ນ

ຄົນລາວ ອາຍຸ 18 ປີ ອາຊີບນັກສຶກສາແລະເຮັດນາ ມາຈາກແຂວງ ສາລະວັນ ເຂົ້ານອນ ໂຮງໝໍມະໂຫສົດ ດ້ວຍອາການເປັນຝີແຜ່ລາມ ແລະ ມີຮອຍແປ້ວຢູ່ກະໂພກ ເບື້ອງຊ້າຍເປັນໄລຍະເວລາ 3 ປີ . ທຳອິດເລີ້ມເປັນຕຸ່ມໝອງນ້ອຍໆໂນນຂຶ້ນ ບໍ່ເຈັບ, ບໍ່ໄດ້ຖືກກະທົບຫຼືສັກຢາມາກ່ອນ, ຕໍ່ມາມັນເປັນບາດແຜໃຫ່ຍຂຶ້ນ ແລະ ໄດ້ປິ່ນປົວດ້ວຍການເຈາະລະບາຍໝອງອອກ ແລະ ໄດ້ຮັບຢາ **Ampicillin** ໜຶ່ງອາທິດ. ເຖິງວ່າການປຸກເລືອດຈະບໍ່ເກີດເຊື້ອ, ໝອງທີ່ໄດ້ຈາກກະໂພກເກີດເຊື້ອ ***Burkholderia pseudomallei***. ການກວດເລືອດຊອກຫາພະຍາດເບົາຫວານ ແລະ **thalassaemia** ແມ່ນບໍ່ພົບ. ການຊ່ອງໄຟຟ້າຜີ້ງເອີກແມ່ນປົກກະຕິ, ການກວດສ່ອງຜີ້ງທ້ອງດ້ວຍຄື້ນສຽງ **abdominal ultrasound** ພົບວ່າລາວມີຝີຢູ່ປ້າງ. ສ່ວນການກວດຊອກຫາຮູຊຶມ **(A fistulogram)** ແມ່ນພົບວ່າ ມັນເປັນພຽງບາດແຜຢູ່ບໍລິເວນກົ້ນຂອງລາວ ບໍ່ໄດ້ມີຮູຊອດຫາອະໄວຍະວະພາຍໃນຜີ້ງທ້ອງ. ລາວໄດ້ຮັບການປິ່ນປົວດ້ວຍຢາ **ceftazidime** ທາງເສັ້ນເປັນເວລາ 3 ອາທິດ ແລະ ກິນຢາ **doxycycline and co-trimoxazole 16** ອາທິດ ແລະ ຕໍ່ມາຄົນເຈັບກໍ່ມີອາການດີຂຶ້ນຢ່າງຊັດເຈນ.



ການວິເຄາະທີ່ເຮັດໄດ້ ທີ່ພະແນກວິເຄາະຈຸລິນຊີວິທະຍາ, ໂຮງໝໍມະໂຫສົດ

ໝາຍເຫດ: ຕົວເລກສີແດງ ແມ່ນຈຳນວນມື້/ອາທິດ ທີ່ພວກເຮົາພະຍາຍາມຈະລາຍງານຜົນການກວດໃຫ້ທ່ານໄວເທົ່າທີ່ຈະໄວໄດ້

ປູກເລືອດ - ຄົນເຈັບທີ່ສົງໃສເປັນຊຶມເຊື້ອເລືອດ (ຊຸດປູກເລືອດ - UI-2) 8 ມື້
ໝອງ - ສົງໃສຕິດເຊື້ອຈຸລິນຊີ (ໃຊ້ໄມ້ປັ່ນຝ້າຍອະເຊື້ອແລ້ວ - sterile swab) 3 ມື້
ຍ່ຽວ - ສົງໃສຕິດເຊື້ອລະບົບຖ່າຍເທ - UTI (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
(ກະລຸນາສົ່ງຕົວຢ່າງໃນກໍລະນີທີ່ຄົນເຈັບມີອາການ ຂອງ UTI ເທົ່ານັ້ນ, ຍົກເວັ້ນແມ່ມານ)
ຕົວຢ່າງຈາກຮູຄໍ - ສົງໃສເປັນ Melioidosis (ໄມ້ປັ່ນຝ້າຍທີ່ອະເຊື້ອແລ້ວສຳລັບຕ້ອຍຮູຄໍ - sterile swab) 4 ມື້
ອາຈົມ - ສົງໃສຕິດເຊື້ອລະບົບລະລາຍຈາກເຊື້ອຈຸລິນຊີ/ອາມິບ (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
ນ້ຳເຍື່ອຫຸ້ມປອດ - ສົງໃສການຕິດເຊື້ອໃນປອດຈາກເຊື້ອຈຸລິນຊີ ຫລື Paragonimus (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
ນ້ຳເຍື່ອຫຸ້ມທ້ອງ - ສົງໃສນ້ຳໃນຜົ້ງທ້ອງຕິດເຊື້ອຈຸລິນຊີ (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
ນ້ຳເຍື່ອຫຸ້ມຫົວໃຈ - ສົງໃສອັກເສບເຍື່ອຫຸ້ມຫົວໃຈຈາກເຊື້ອຈຸລິນຊີ (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
ນ້ຳຈາກການລ້າງຫລອດປອດ - ສົງໃສການຕິດເຊື້ອໃນປອດຈາກເຊື້ອຈຸລິນຊີ (ຫລອດຝາສີຂາວອະເຊື້ອແລ້ວ) 3 ມື້
ພຕພ (STI) - ຕົວຢ່າງຕ້ອຍຈາກຊ່ອງຄອດ, ທໍ່ຍ່ຽວ, ລົ້ງຂາວ - Direct microscopic wet mount ແລະ Gram stain exam 1 ມື້
Weber test - stool - ສົງໃສເລືອດໄຫລທາງລະບົບລະລາຍອາຫານ 1 ມື້

ນ້ຳໄຂສັນຫລັງ (CSF) - ສົງໃສຊຶມເຊື້ອລະບົບປະສາດສູນກາງ ຫລື ພະຍາດໃນກະໂຫລກຫົວ - ກະລຸນາໂທຫາຫ້ອງວິເຄາະຈຸລິນຊີ
- ຫລອດຝາສີຂາວອະເຊື້ອ 3 ຫລອດ ແລະ ຫລອດ Fluoride ສຳລັບໃສ່ CSF
- ໃຫ້ເຈາະເລືອດໄປປູກນຳພ້ອມ (UI-2) ຖ້າສົງໃສຊຶມເຊື້ອລະບົບປະສາດສູນກາງ
- ພວກເຮົາຈະນັບຈຸລັງໃນ CSF, ປູກຫາເຊື້ອຈຸລິນຊີ, ຍ້ອມ Gram stain, Indian Ink stain 1 ມື້.
ປູກໃສ່ພຸ້ມປູກ LJ ເພື່ອຫາເຊື້ອວັນນະໂລກ 6 ອາທິດ
- ກວດເຊໂຣໂລຊີ ພະຍາດໄຂ້ເລືອດອອກ ແລະ JE 7 ມື້
- ກວດຫາ Scrub typhus and murine typhus ດ້ວຍແຜ່ນຈຸ່ມ 1-2 ມື້
- ກວດ PCR ຫາເຊື້ອຈຸລິນຊີ (*S. pneumoniae, H. influenzae* b, *and N. meningitidis*)
ຈະເຮັດໃຫ້ໄວເທົ່າທີ່ຈະເຮັດໄດ້
- ກວດ PCR ຫາເຊື້ອໄວຣັສ CMV, Enterovirus, HSV, VZ, JEV, dengue, mumps, measles, influenza, West Nile, tick-borne encephalitis and Nipah viruses ຈະເຮັດໃຫ້ໄວເທົ່າທີ່ຈະເຮັດໄດ້
- ປູກຫາເຊື້ອໄວຣັສ 3 ອາທິດ

+ ຖ້າຄົນເຈັບຕ້ອງໄດ້ຮັບການກວດ CT ສະໝອງ ກ່ອນການເຮັດ LP ແຕ່ບໍ່ມີເງື່ອນໄຂ, ກະລຸນາແຈ້ງພະແນກວິເຄາະຈຸລິນຊີວິທະຍາ

ປູກຫາເຊື້ອ Leptospires - ເຮັດໃຫ້ໂດຍອັດຕະໂນມັດ ໂດຍໃຊ້ຕົວຢ່າງເລືອດເຫລືອຈາກຫລອດຝາສີຂາວໃນຊຸດ UI-2 4 ອາທິດ
ເຊໂຣໂລຊີ Rickettsia - ເຮັດໃນມື້ທີ່ກວດ Scrub typhus and murine typhus ດ້ວຍແຜ່ນຈຸ່ມ (ແລະ ກວດດ້ວຍເຕັກນິກ IFA ຕາມຫຼັງ) ຖ້າສົງໃສຄົນເຈັບເປັນ Typhus (ສຳລັບຄົນເຈັບທີ່ໄດ້ເຮັດ LPພວກເຮົາຈະເຮັດໃຫ້ໂດຍອັດຕະໂນມັດ)
ປູກຫາເຊື້ອ Rickettsia - ພວກເຮົາຈະເຮັດໃນຄົນເຈັບທຸກຄົນທີ່ມີຜົນກວດ scrub and murine typhus ໃຫ້ຜົນບວກດ້ວຍແຜ່ນຈຸ່ມ ຫລື ຖ້າສົງໃສຕິດເຊື້ອ Spotted fever group (ຫລອດຝາສີບົວ) 8 ອາທິດ
ກວດ Dengue/JEV IgM/IgG/NS1 ELISAs - ຈະເຮັດໂດຍອັດຕະໂນມັດໃນຄົນເຈັບທຸກຄົນທີ່ສົງໃນຊຶມເຊື້ອລະບົບປະສາດສູນກາງ ແລະ ໃນຊ່ວງລະດູການຂອງພະຍາດໄຂ້ເລືອດອອກ ເຊິ່ງຈະກວດໃນທຸກໆວັນພຸດ 7 ມື້
ພະຍາດມື ຕີນ ແລະ ປາກ - ຕົວຢ່າງຕ້ອຍຮູຄໍ, ນ້ຳຈາກຕຸ່ມໃສ, ອາຈົມ ແລະ ເລືອດ. ກະລຸນາໂທພ້ອພັນຫ້ອງວິເຄາະ

ຖ້າພົບເຫັນເຊື້ອທີ່ພາໃຫ້ເປັນພະຍາດພາຍຫລັງການປູກ/ກວດ, ພວກເຮົາຈະໂທແຈ້ງພະແນກຂອງທ່ານໃນທັນທີ ແຕ່ຍັງຈະບໍ່ສາມາດລາຍງານໃຫ້ໄດ້ຢ່າງຄົບຖ້ວນເທື່ອ. ກະລຸນາໝາຍຊື່ຄົນເຈັບ, ອາຍຸ, ພະແນກ, ເລກທີເຂົ້ານອນໂຮງໝໍ ໃນຫລອດຕົວຢ່າງທີ່ສົ່ງໄປກວດ ແລະ ຂຽນ ຊື່ຂອງທ່ານໝໍທີ່ສັ່ງກວດຢ່າງຈະແຈ້ງ ໃນໃບສັ່ງກວດ (ບໍ່ແມ່ນພຽງແຕ່ລາຍເຊັນເທົ່ານັ້ນ). ຂໍຂອບໃຈ

Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU)

Mahosot Microbiology Review

Issue No. 7

January 2013

Inside this issue:

The extended Microbiology Laboratory at Mahosot Hospital looking SE

We are very grateful to the Minister of Health, His Excellency Prof. Dr. Eksavang Vongvichit, the Director of the Curative Department, Assoc. Prof. Dr. Chanphomma Vongsamphanh and the Director of Mahosot Hospital, Assoc. Prof. Dr. Bounthaphany Bounexouai for facilitating and supporting this project. With very many thanks to all the staff of Mahosot Hospital, those who checked this newsletter, CMPE, NCLE, UHS, IFMT, IRD, MORU, Fondation Merieux, Institut Pasteur, WPRO, WHO-Vientiane, Health Frontiers, Luang Nam Tha, Salavan & Phonsavan Hospitals, SFE, HPA-UK, Natural History Museum-London, LSHTM, MRC Human Nutrition, Royal Brompton Hospital-London and the Universities of Oxford. Aix-Marseille and Paris Ouest.

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This newsletter summarizes the results of the collaborative infectious disease & tropical medicine research carried out by the Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit. A Lao language version is available at the website below. Please let us know any suggestions for improvement or comment and distribute to all who are interested. A pdf file is available from the e-mail addresses above. Due to delays in publication there are many new Lao relevant papers included (pages 16-28) so that we can catch up with these lists. We hope to publish MMR-8 in February 2014.This newsletter is available from http://www.tropmedres.ac/study-sites/asia/laos/links-and-publications.html.

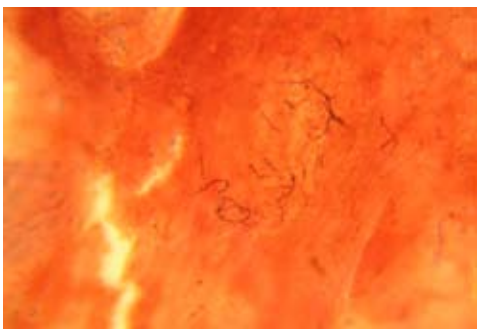
Medical literature relevant to Laos

A dramatic increase in the volume of published scientific literature relevant to public health in Laos continues

Actinomycosis

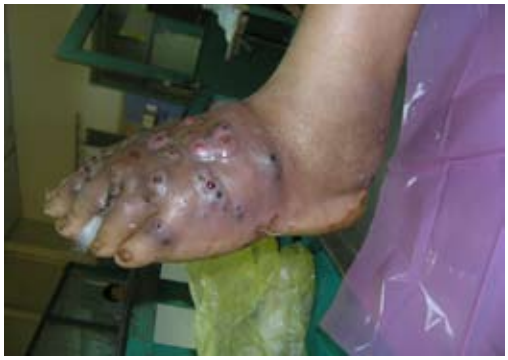
Mycetomas, commonly known as Madura foot, are chronic, localized, slowly progressing infections of the cutaneous and subcutaneous tissues caused either by true fungi (eumycetoma) or by aerobic actinomycetes (actinomycetoma). They are acquired by traumatic implantation, especially in rural tropical agriculture communities. Although well recognized elsewhere in Asia, it has not been reported from Laos before (see Rattanavong *et al*. 2012).

A 30 year-old school teacher and rice farmer from Xieng Khouang was admitted to Mahosot Hospital with a massive growth on her left foot, without a history of trauma. The swelling had progressed slowly but painlessly over 5 years with multiple draining sinuses. Ten days before admission the foot had increased considerably in size, preventing her from walking. Gram stain and bacterial culture of tissue biopsies revealed a branching filamentous Gram-positive bacterium that was subsequently identified as *Actinomadura madurae* by 16S-rRNA sequencing. Foot X-ray demonstrated extensive osteolysis of the left metatarsal bones. She was treated with long-term co-trimoxazole and multiple 3-week cycles of amikacin with a good therapeutic response. As ~78% of Lao people work in agriculture and there are, as elsewhere in the rural tropics, few microbiology laboratories, it is likely that the condition is under-diagnosed.



Left - Gram stain of smear from left foot tissue biopsy revealed branching, filamentous Gram positive bacteria.

Right - Left foot of patient before treatment



Infantile beriberi

Infantile beriberi, or clinical thiamin (vitamin B_1) deficiency in infants, is a forgotten disease in Asia. In the late 19th century with the advent of mechanical rice milling, which removed rice husk containing thiamin, beriberi became a major public health problem in Asia, responsible for considerable mortality. Children aged ~ 2-3 months present in cardiac failure but usually rapidly improve if given thiamin injections. It remains relatively common in Vientiane, with 50-90 infants admitted with a clinical diagnosis of beriberi/ year at Mahosot Hospital, probably resulting from prolonged intra- and post-partum food avoidance behaviours. A case control study [Soukaloun *et al.* 2003] suggested that, compared with control mothers, mothers of infants with beriberi had significantly less diet diversity, soaked glutinous rice significantly longer or were more likely to pour off excess water from non-glutinous rice, had fewer years of schooling, were more likely to report that income was inadequate for basic needs, were more likely to perform hard physical labour and to be married to farmers.

There has been very little recent research on the best diagnostic techniques to confirm the diagnosis. A case controlled study of 47 infants with beriberi and age-matched afebrile and febrile controls in Vientiane (see Soukaloun *et al*. 2011) addressed this. Contrary to the situation in adults, basal erythrocyte transketolase activity (ETK) was a better biochemical marker of infantile beriberi than the activation coefficient. Plasma troponin T may be a useful indicator of infantile beriberi in babies at risk. This holds promise as there are now rapid diagnostic tests for troponin.

Clinical disease may be the tip of an iceberg with subclinical thiamin deficiency also contributing to illness. To investigate this 778 sick infants were recruited during one year at Mahosot Hospital, without clinical evidence of beriberi, and ETK assays performed - 13.9 % of infants had basal ETK levels suggesting biochemical thiamin deficiency (see Khounnorath *et al.* 2011). Mortality was 5.5% but, among infants >2 months old, mortality was higher in those with low basal ETK (3/48, 6.3%) than in those with normal basal ETK (P=0.048, relative risk=9.06 (95%CI 0.97 - 85.1)). However, caution is required as the mortality difference is based on only 4 deaths among 197 infants aged >2 months with basal ETK data with borderline relative risk and significance. Clinically unapparent thiamin deficiency may contribute to mortality and a low clinical threshold for providing thiamin to sick infants is needed. Only a clinical trial will answer which groups of infants should receive supplementation. For sick infants thiamin should be given parenterally to increase tissue levels rapidly. There is evidence that gastrointestinal absorption of thiamin is saturated at doses of >5 mg, suggesting that oral doses above this give limited, if any, benefit.

'Hua wan' from Pakse - the root inside the bamboo container is used to make tea for the mother to drink to ward off harm when she does not properly observe post-partum food avoidance behaviour.

Burkholderia pseudomallei, water and soil

Melioidosis (caused by *Burkholderia pseudomallei*) is an important cause of sepsis in SE Asia and N Australia, especially in Thailand and Laos. We still do not understand the spatial distribution of the pathogen in soil and water and there has been relatively little work to understand this and what chemical, physical or biological aspects of the environment are important. In Laos, *B. pseudomallei* is a significant cause of sepsis around Vientiane capital and has been isolated in soil around the city in the Mekong River valley. We see patients who appear to have been infected elsewhere in the Mekong Valley but very few who we are sure have lived all their lives in the highlands. Two studies have tried to shed light on *B. pseudomallei* in the environment.

First, we explored whether *B. pseudomallei* occurs in Lao soil distant from the Mekong River, drawing three axes across northwest, northeast and southern Laos to create 9 sampling areas in 6 provinces (see Rattanavong *et al.* 2011). Within each sampling area a rice field was selected at random and holes, in a grid of 100 sampling points each 5m apart, dug. Soil was obtained from a depth of 30 cm and cultured for *B. pseudomallei*. Four of 9 sites (44%) were culture positive. The highest isolation frequency was in east Saravan, where 94% of soil samples were *B. pseudomallei* positive with a very high (the world record) geometric mean (range) concentration of ~464 (25-10,850) CFU/g soil. At Luang namtha, only one sample (1%) was culture positive. Therefore, *B. pseudomallei* occurs in Lao soils beyond the immediate vicinity of the Mekong River in southern Laos. Health workers in NE and NW Laos may be able to put melioidosis lower on their differential diagnosis than in southern Laos.

Second, we used Moore's swabs. made of gauze (see Vongphayloth e*t al.* 2012), to sample paddy field, lake, river, borehole and storage tank water. Thirty-six and six percent of water samples collected around East and West Saravane, respectively, were swab culture positive. Low pH and high turbidity were independently associated with culture of *B. pseudomallei*. Most positive water samples were from the Sedone River, downstream of the East Saravane site. Could river *B. pseudomallei* culture provide an index of *B. pseudomallei* soil density in the watershed ?

This work suffers from uncertainty as to whether *B. pseudomallei* can be present and viable in soil/water but is not culturable by current techniques. Comparisons of molecular assays with culture are needed. Culture is extremely labour intensive and in beeastern Lao the abundant UXO means that digging sites have to checked first for ordnance.

Top - The distribution of *B. pseudomallei* at 9 sampling sites in Laos, 2009; star = culture positive and circle = negative. The blue line represents the course of the Mekong River.

Bottom - A Moore's gauze swab being lowered into a small well, retaining any *B. pseudomallei* present, in Salavan.

Pneumoccoci and vaccination policy

Invasive pneumococcal disease (IPD) is a major cause of morbidity and mortality globally with an estimated 1.6 million people dying of pneumococcal disease each year. Of these 0.7–1 million are children under the age of 5 years living in the developing world. IPD has been described from Vientiane but there are no data on the local serotypes - important to guide planned Lao vaccination policies. A prospective hospital-based study of the circulating serotypes in Laos was conducted (see Moore *et al.* 2009). IPD was defined as patients culture positive for *S. pneumoniae* in blood and/or cerebrospinal fluid (CSF), and/or positive for *S. pneumoniae* in CSF using a real-time PCR assay targeting the *lytA* gene. A novel real-time PCR assay, developed in Laos, was used to determine serotypes.

Of 10,799 patients with haemocultures and 353 patients with CSF samples, 0.21% and 5.4%, respectively, were positive for *S. pneumoniae* (n=35). Two isolates associated with meningitis were penicillin-nonsusceptible, with MICs of 0.39 and 0.125 µg/mL. All *S. pneumoniae* tested were susceptible to ceftriaxone.

The most frequent serotype was 1, followed by serotypes 5, 6A/B/C, 14 and 23F. Serotype represented in the PCV-7 vaccine infected 39% of patients, with 73% and 76% coverage for the PCV-10 and PCV-13 vaccine, respectively. Although the sample size is small, these data suggest that the PCV-7 vaccine may have relatively low efficacy in Laos and that PCV-13 would be optimal.

Japanese encephalitis virus and vaccination policy

Although there has been no information on the causes of encephalitis in Laos, the Japanese encephalitis virus (JEV) is likely to be important as it occurs in all adjacent countries. Diagnosis of JEV is difficult because it is clinically indistinguishable from other causes of acute encephalitis and there are serological cross-reactions with dengue and other flavivirus antibodies. Detection of the virus in cerebrospinal fluid (CSF) is rarely successful so we use ELISAs to detect anti-JEV IgM in CSF confirming the importance of JEV in Laos (see Moore *et al.* 2012). CSF from 515 patients admitted at Mahosot Hospital (2003-2008) with suspected central nervous system infections were tested; 234 (45%) with acute encephalitis, 256 (50%) with meningitis and 157 (31%) with both syndromes.

The median (IQR; range) age of patients was 24 (8-38; 0.05-85) years and 32% were <15 years. CSF from 14.5% of patients with encephalitis and 10.1% from those with encephalitis and meningitis were positive for anti-JEV IgM. Of JEV IgM positive patients, 42% had convulsions, 63% had a reduced Glasgow Coma Score, the median (range) CSF white cell count was 125 (0-653)/µL with a median percentage of lymphocytes of 37 (0-90)%. Patients came from northern Laos and there is also evidence from sera of JEV throughout the country. As JEV is an important preventable disease, the expanded use of ELISA assays would help define the burden of disease. These data suggest that JEV vaccination should be considered.

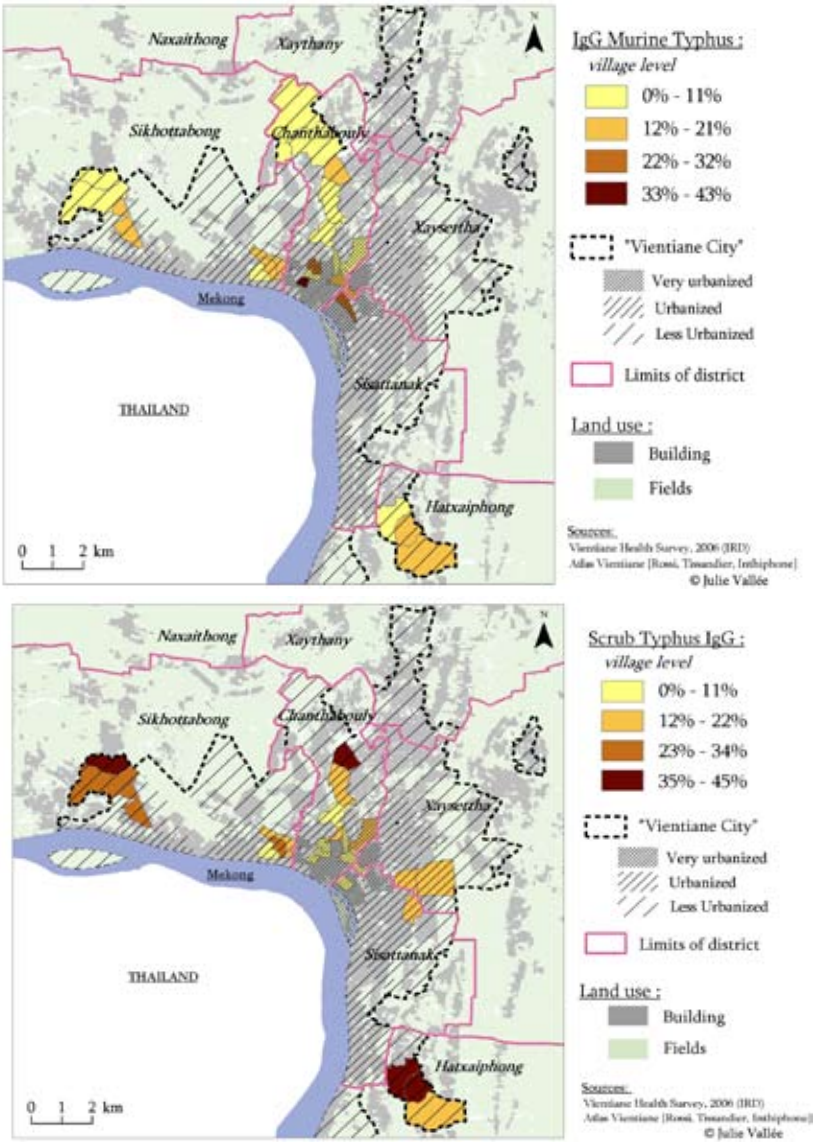
Typhus exposure and risks in Vientiane

Both scrub typhus and murine typhus are common causes of fever in Vientiane. Comparative risk factors for infection are unclear. As part of a large project examining urbanisation in Vientiane, we therefore determined the frequency of IgG seropositivity against *Orientia tsutsugamushi* (scrub typhus) and *Rickettsia typhi* (murine typhus), as indices of prior exposure to these pathogens, in randomly selected adults in urban and peri-urban Vientiane City (n=2,002, adults ≥ 35 years)(see Vallée *et al*. (2010). We performed ELISAs on eluates from filter paper blood spots.

Scrub typhus seropositivity (bottom map) was significantly higher among adults living in the periphery (28.4%) than in the central zone (13.1%) of Vientiane. In contrast, seroprevalence of murine typhus IgG antibodies (top map) was significantly higher in the central zone (30.8%) as compared to the periphery (14.4%). In multivariate analysis, adults with a longer residence in Vientiane were at significant greater risk of past infection with murine typhus and at lower risk for scrub typhus.

Those with no education, living on low incomes, living on plots of land with poor sanitary condition, living in large households and farmers were at higher risk of scrub typhus and those living in neighborhoods with high building density and close to markets were at greater risk for murine typhus and at lower risk of scrub typhus past infection.

The association of murine typhus seropositivity with homes close to markets suggest that enhanced market rubbish disposal and rodent control may help reduce the incidence of the disease. Scrub typhus is not conventionally thought of a disease of cities. However, it infects people in palm plantations, primary forest, beaches and in city gardens and the term ‘scrub’ is misleading. It is possible that Vientiane city dwellers are infected during residence in rural areas, visits to the countryside - for example to collect bamboo shoots or to fish-or in gardens and parks within the city.



Antibiotic activity in urine !

Antibiotic resistance is a major global public health problem, affecting treatment decisions, patient outcome, health care expenditure and public perceptions of health care. Widespread unregulated provision of antibiotics, dispensing of insufficient doses, reduced adherence to complete dose regimens and the poor quality of the drug supply are thought to contribute to the spread of antibiotic resistance.

We estimated the proportion of Lao in- and out-patients who had taken antibiotics before medical consultation by detecting antibiotic activity in their urine added to lawns of reference organisms (*Bacillus stearothermophillus, Escherichia coli* and *Streptococcus pyogenes*). Urine containing antibiotics kills the bacteria. In the retrospective (N=2,058) and prospective studies (N=1,153), 49.7% and 36.2%, respectively, of Vientiane patients had urinary antibiotic activity detected. The highest frequency of estimated antibiotic pre-treatment was found in patients recruited with suspected central nervous system infections and community-acquired septicaemia (both 56.8%). In Vientiane, children had a higher frequency of estimated antibiotic pre-treatment than adults (60.0% v 46.5%; P<0.001). Antibiotic use based on patients histories was significantly less frequent than when estimated from urinary antibiotic activity. Although Laos appears to have lower levels of antibiotic resistance in comparison to adjacent countries, ESBL positive *E. coli* (see page 8) and *Klebsiella pneumoniae* clinical isolates are common in Vientiane. It is likely that as the economy improves a greater volume and diversity of antibiotics will be consumed. The high frequency of antibiotic use in the community, as revealed by urinary antibiotic activity, may engender worsening drug resistance. This suggests that enhanced antibiotic stewardship and pharmacy regulation are required.

Beware the wild banana !

Six patients with bowel obstruction after eating wild bananas (BOWB) were recently described from Luang Namtha (see Selsak *et al.* 2011). Six required enterotomy for phytobezoars. On asking 227 other patients/relatives, 46% had eaten wild banana seeds. 45% knew of complications, including constipation (38%), appendicitis/abdominal pain/vomiting (3% each) and bloated stomach/death (1% each). Middle/highland Lao ethnicity was associated with wild banana consumption and male sex with consumption and unawareness. Of 44 doctors at all surgically-equipped hospitals in Laos, 33 knew of BOWB, describing patients as usually young, adult middleland Lao males. Countrywide, 46 patients with BOWB are known to have been operated on in 2009 (incidence ~0.8/100,000). All consumed WB seeds. BOWB is widespread in Laos, especially among men consuming WB seeds on an empty stomach in the forest. Alarming modes of local treatment were described, including the insertion of sticks and the piping of gasoline into the rectum. More engagement and education are needed to warn people of

WB phytobezoars from bowel of Lao patient.
Max length 5 cm

Extended-spectrum beta-lactamase (ESBL) bacteria

Since 2004 we have seen increasing numbers of patients infected with Extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* and *Klebsiella pneumoniae* at Mahosot Hospital. These can be extremely difficult to treat as they are resistant to cephalosporins and often also to gentamicin and fluoroquinolones. The molecular epidemiology of ESBLs from Laos was investigated in 54 *E. coli* isolates; the majority of isolates (76%) were from bloodstream and urinary tract infections, with a further 20% from pus samples.

CTX-M genotypes were found in all ESBL-*E. coli* clinical isolates from 2004-2009, with variants similar to those seen in neighbouring China and Thailand (CTX-M-14,-15 and -55-like, CTX-M-27). There was common concomitant ciprofloxacin/gentamicin resistance (68%). Global ESBL-*E. coli* lineages (ST-131, ST-405) were common, but ST-648, previously identified amongst birds, was the second most common sequence type, possibly related to the high frequency of backyard poultry farming in Laos (see Stoesser *et al*. 2011). These data suggest that it will be very important to enhance antibiotic stewardship measures in Laos, especially for cephalosporins, and investigate afforable alternative antibiotics for therapy.

Chromoblastomycosis and Myiasis

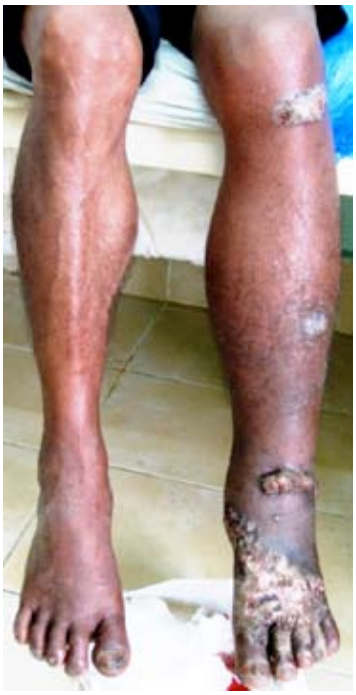
Chromoblastomycosis is a worldwide chronic infection of the skin and subcutaneous tissue, most commonly found in tropical and subtropical areas. It is mainly caused by the fungal genera *Fonsecaea*, *Phialophora* and *Cladophialophora* that are saprophytes in soil and plants. The lower limbs are most commonly infected and the nodular and/or verrucous plaques can develop centripetal satellite lesions. The most frequent complication is bacterial secondary infection, but malignancies have also been recorded.

A 72 year-old farmer was admitted to Luang Namtha Provincial Hospital, northern Laos, with a growth on the left lower leg which began 1 week after a forefoot leech bite 10 years previously. He presented with a cauliflower-like mass and plaque-like lesions on his lower leg/foot and cellulitis with a purulent tender swelling of his left heel.

He was thought initially to have leprosy or skin cancer, but skin scrapings from the left lower leg lesions revealed typical brownish, round, thick-walled, multiseptate sclerotic cells in a wet film, confirmed with the 10% potassium hydroxide technique.

During wound dressing, 22 maggots were discovered in the heel wound and identified as third instar larvae of the Old World screwworm fly, *Chrysomya bezziana*. Presumably flies laid eggs in the open wound.

PCR of a biopsy of a left lower leg nodule demonstrated *Fonsecaea pedrosoi*, *F. monophora*, or *F. nubica*. He was successfully treated with long term terbinafin plus itraconazole pulse-therapy and local debridement (see Slesak *et al*.



Left - Lower leg of the patient at presentation with typical lesions on his foot that spread centripetally up to his knee.

Below - Contaminating screwworm fly *Chrysomya bezziana* maggots from patient's heel. They are ~1 cm long

Simple but accurate diagnosis of typhoid

Although the bacterium causing typhoid, *Salmonella enterica* serovar Typhi, was first described 132 years ago, most typhoid patients globally do not have access to reliable laboratory diagnosis. There remains an urgent need for inexpensive, rapid, portable, and simple techniques for diagnosing typhoid in locations away from sophisticated hospital settings, where the burden of diseases is the greatest. Typhoid diagnosis could be enhanced by making the identification of *S*. Typhi in blood cultures simpler, less expensive and faster. We investigated whether the combination of blood culture bacterial growth with an *S*.Typhi antigen rapid diagnostic test (RDT) on the blood culture fluid could be an accurate and inexpensive tool for the accelerated diagnosis of patients with acute typhoid in Laos (see Castonguay-Vanier *et al*. 2013). These RDTs were developed for detecting *S*. Typhi in stools. We adapted them for detecting *S*. Typhi in blood culture fluid when the fluid becomes turbid.

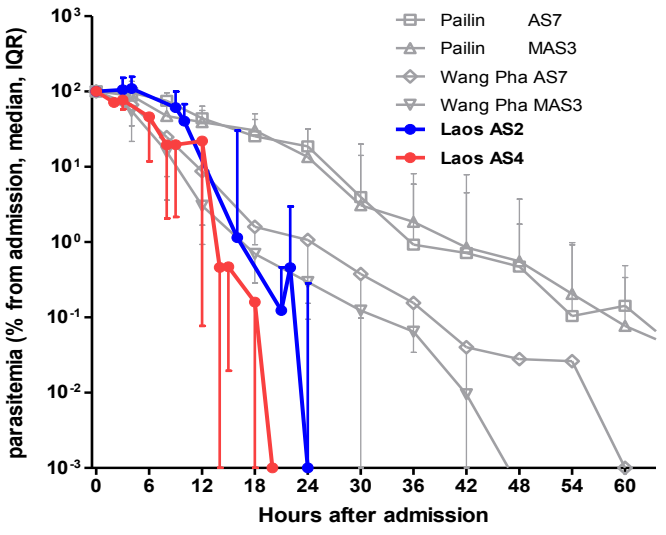
Using reference strains of Gram negative bacteria, the RDT was only positive for Group D *Salmonella enterica,* including *S*. Typhi. In a prospective study of 6,456 blood culture bottles from 3,028 patients over 15 months, 392 blood culture bottles (6.1%) from 221 (7.3%) patients had Gram negative rods (GNR) seen in the blood culture fluid. The sensitivity, negative predictive value, specificity and positive predictive value were 96.7%, 99.5%, 97.9% and 87.9%, respectively, for patients with proven *S*. Typhi bacteremia and 91.2%, 98.4%, 98.9% and 93.9% for patients with Group D Salmonella. The RDT accelerated diagnosis by a median of one day and were less expensive and labour intensive than conventional reference assays.

Although, this does not address the problem that blood cultures only detect *S*. Typhi in ~40-80 % of patients with typhoid, it suggests that the combination of blood cultures with RDTs are promising as accurate tools for accelerated, inexpensive diagnosis. We hope that they will be trialed in other locations and be useful for diagnosis in peripheral diagnostic labs and in investigation of suspected typhoid outbreaks.

Has artemisinin resistance arrived in Laos ?

There is now, sadly, evidence for *Plasmodium falciparum* artemisinin resistance in Cambodia, Vietnam and the Thai/Burma border. We conducted a randomized clinical trial to assess parasite clearance times (PCT) and the efficacy of 4mg/kg and 2mg/kg oral artesunate for 3 days followed by artemether-lumefantrine in patients with uncomplicated falciparum malaria at Xepon, Savannakhet Province (see Mayxay *et al*. 2012). The mean (range) PCT was 23.2 (12-46) h. Ten patients (23%) remained parasitemic on day 1 after treatment but no patient had patent asexual parasitemia on day 2 or 3. The 42-day PCR-corrected cure rate was 100%. In conclusion, no evidence of *P. falciparum* in vivo resistance to artesunate was found in southern Laos. However, this will need to be checked regularly.

Red & blue lines are Lao parasite clearance at 2 (AS2) and 4 (AS4) mg/kg artesunate whilst grey lines are for Pailin (Thai/Cambodia border) and Wang Pha (Thai/Burma border)



The map, left, shows mainland SE Asia with capitals (blue) and sites with evidence for prolonged artemisinin treatment parasite clearance (red) and the Lao study site of Xepon that still has fast parasite clearance (green).

Typhus, fluoroquinolones and treatment

Scrub typhus (*Orientia tsutsugamushi*) is a public health concern for a population of over a billion humans in Asia and Australia with an estimated incidence of one million cases/year. Although doxycycline remains the standard therapy, fluoroquinolones have been used successfully in a few patients. However, there is also clinical evidence that these compounds are ineffective in the treatment of scrub typhus. In order to clarify this, we determined the *in vitro* susceptibility of *O. tsutsugamushi* strain Kato to ciprofloxacin and sequenced the quinolone-resistance-determining-region (QRDR) of the *gyrA* gene, the target of fluoroquinolones, from 18 Lao patients (see Tantibhedhyangkul *et al.* 2009). *O. tsutsugamushi* were resistant to ciprofloxacin and ofloxacin *in vitro* (MIC = 8µg/ml) and all sequences obtained, including those from the two available genomes of *O. tsutsugamushi* (strains Boryong and Ikeda), had a Ser83Leu mutation in their QRDR domain that is known to be associated with fluoroquinolone resistance. These results suggest that fluoroquinolones should not be used in the treatment of scrub typhus. We do not know how effective fluoroquinolones are for murine typhus. Similarly, it is unclear how effective azithromycin is for treatment of either scrub typhus or murine typhus in Laos (more data in next MMR).

There are no consensus guidelines for the definition of severe scrub typhus or murine typhus. In theory doxycycline and chloramphenicol should be efficacious but the optimum treatment is unclear. For those with reduced Glasgow Coma Score or unable to swallow, intravenous therapy (although we do not have intravenous doxycycline in Laos) or nasogastric tube administration of doxycycline and chloramphenicol would be required (see Page 11).

Treatment Guidelines

Please check paediatric guidelines for neonates and children and consider pregnancy testing

The recommendations in these pages are derived from the latest drug resistance data from the pathogens isolated in Mahosot Hospital. Please note that these are only guidelines and the condition of the individual patient, renal and liver function, drug contraindications and allergies need to be considered before prescribing. Please check these doses before prescribing. For children please consult paediatric guidelines. We take no responsbility for their use.

Treatment of typhus

Oral **Doxycycline** 4mg/kg stat followed by 2mg/kg every 12 hours for 7 days
[Usual dose in adults 200mg stat followed by 100mg every 12 hours for 7 days

OR

Oral **Chloramphenicol** 50–75mg/kg/day for 7 days
[Usual dose in adults 500mg every 6 hours for 7 days]

The risks to children <8 years of 1 week doxycycline therapy are likely to be less than the risks of not giving doxycycline. In pregnant women, oral azithromycin for **7 days** is probably the best option.
Do pregnancy test before giving doxycycline to women of childbearing age. Suggest to warn patients of gullet pain

Treatment of meningitis

On the following page we give provisional guidelines for the treatment of meningitis. We would like to emphasise:

* if bacterial meningitis is suspected please give empirical antibiotic therapy before LP or immediately after LP, depending on the clinical situation.

* if *R. typhi* or *O. tsutsugamushi* are suspected, suggest to add (not replace) doxycyline to an antibiotic that will counter conventional bacterial meningitis.

* ceftriaxone should also be active against leptospiral meningitis

* *Listeria monocytogenes* appears to be rare in Vientiane. This organism is resistant to third-generation cephalosporins.

* we have found *S. pneumoniae* resistant to penicillin - therefore we do not recommend penicillin for empirical therapy - suggest a 3rd generation cephalosporin such as ceftriaxone.

* There is evidence that steroids may be beneficial in *M. tuberculosis* meningitis but the evidence for benefit in those with *Haemophilus influenzae* b or *S. pneumoniae* meningitis in SE Asia remains unclear

Guidelines : Treatment of Meningitis

Antibiotic Recommendations

Ceftriaxone (a third generation cephalosporin is the preferred empirical therapy)

80-100 mg/kg/day IV divided into 2 daily doses
[Usual dose for 50 kg adult ~2 g IV every 12h]

OR in neonates

Cefotaxime
Aged 0-7 days 100–150 mg/kg/day IV (dose interval every 8–12h) or aged 8-28 days 150–200 mg/kg/day IV (dose interval every 6–8h)

AND IF *Listeria* is suspected (usually in infants < 1 month old)

Ampicillin

Age	0-7 days	8-28 days	<15 years	>15 years
Daily dose IV	150mg/kg/day	200mg/kg/day	300mg/kg/day	12 g/day
Dose Interval	every 8 h	every 6-8 h	every 6 h	every 4h

If ceftriaxone (or other 3rd generation cephalosporin) is not available

Chloramphenicol

Age	0-7 days	8-28 days	<15 years	>15 years
Daily dose IV	25mg/kg/day	50mg/kg/day	75-100mg/kg/day	4-6g/day
Dose Interval	24h	12-24h	6h	6h

[Usual dose for 50kg adult chloramphenicol 1.5g six hourly]

AND

Ampicillin

Age	0-7 days	8-28 days	<15 years	>15 years
Daily dose IV	150mg/kg/day	200mg/kg/day	300mg/kg/day	12 g/day
Dose Interval	every 8 h	every 6-8 h	every 6 h	every 4h

If suspect rickettsial disease add in: oral **Doxycycline** 4mg/kg stat followed by 2mg/kg every 12 hours for 1 week. In adults this will normally be 200mg stat followed by 100mg every 12 hours for 1 week. The risks to children <8 years of doxycycline therapy are likely to be less than the risks of not giving doxycycline. In pregnant women, oral azithromycin for 7 days is probably the best option and may also be efficacious in children.

Please always send blood cultures to the laboratory when you do a lumbar puncture. We then have a greater chance of finding the causative organism.

If you suspect TB meningitis please send as much CSF as you can

Tests for IgM antibodies against pathogens may represent recent infections before the presenting illness ! Therefore, please always treat these results with some suspicion. Until we have better DNA or antigen detection tests for typhus and rickettsia please assume that patients may have 'conventional' bacterial meningitis and treat with a 3rd generation cephalosporin.

Please ensure haemoculture, and other relevant samples such as urine, throat swab, are taken before commencing antibiotics.

Guidelines : Treatment of Severe Melioidosis

Dosage adjustment for ceftazidime in patients with renal impairment

As patients with melioidosis often have impaired renal function we give here a suggested dose regime for different ranges of serum creatinine for adults of about 50 kg.

Serum creatinine µmol/L	Serum creatinine mg/dL	Ceftazidime Dose
Less than 176	Less than 2	2g every 8 hours
176 - 352	2-4	1g every 8 hours
353 -528	4-6	1g every 12 hours
Greater than 528	>6	1g every 24 hours

SEVERE MELIOIDOSIS - PARENTERAL FOLLOWED BY ORAL THERAPY

Ceftazidime IV 120 mg/kg/day in 3 divided doses for minimum of 10 days
[Usual dose for 50 kg adult ~ 2 g iv every 8 hours]

OR

Amoxicillin-clavulanate IV 150 mg/kg/day in 6 divided doses for minimum of 10 days
[Usual dose for 50 kg adult ~ 1.2 g iv every 4 hours]

THEN oral eradication treatment of:

Co-trimoxazole in 2 divided doses for 12-20 weeks - dose adjusted for body weight. See top of Page 14.

COMBINED WITH

Doxycycline 4 mg/kg/day in 1 daily dose for 12-20 weeks
[Usual dose for 50 kg adult ~ 2 x 100 mg capsules every 24 hours]

OR, AS LONE THERAPY

Amoxicillin-clavulanate 60/15 mg/kg/day in 3 divided doses for 20 weeks
[Usual dose for 50 kg adult 2 x 500/125 mg capsules every 8 hours]

Guidelines : Oral Treatment of Melioidosis

Co-trimoxazole dose based on body weight (see Dance 2011)

Body weight/kg	Dose (TMP/SMX) mg every 12 hours
< 40	160/800 mg
40-60	240/1200 mg
> 60	320/1600 mg

LOCALISED MELIOIDOSIS – ORAL TREATMENT

For patients with melioidosis at ONE site WITHOUT septicaemia

Co-trimoxazole in 2 divided doses for 12-20 weeks - dose adjusted for body weight. See above.

WITH

Doxycycline 4 mg/kg/day in 1 daily dose for 8 - 20 weeks
[Usual dose for 50 kg adult ~ 2 x 100 mg capsules every 24 hours]

OR, AS LONE THERAPY

Amoxicillin-clavulanate 60/15 mg/kg/day in 3 divided doses for 20 weeks

[Usual dose for 50 kg adult 2 x 500/125 mg capsules every 8 hours]

Treatment of typhoid

Uncomplicated typhoid Ofloxacin 15mg/kg/day po in 2 divided doses for 3 days

Severe typhoid
eg. hypotension, abdominal pain, intestinal hemorrhage/perforation, encephalopathy, seizures, pneumonia
Ask for surgical review plus ceftriaxone 60mg/kg/day iv/im in single dose/day for 10-14 days

Consider dexamethasone 3mg/kg infusion iv over 30 mins followed by 1mg/kg over 30 mins every 6 hours for eight additional doses.

The risks to children <8 years of 3 days ofloxacin are likely to be less than the risks of not giving oxfloxacin.

NB Fever clearance is usually shorter with flouroquinolones than iv ceftriaxone and fever may disappear ~ one day after fluoroquinolones are stopped

Empirical treatment of Septicaemia

COMMUNITY –ACQUIRED SEPTICAEMIA

Gentamicin IV 5 - 7 mg/kg once a day

[Usual dose for 50 kg adult ~ 240 – 360 mg IV once a day]
[beware renal impairment for doses subsequent to the first]

WITH EITHER

Ampicillin IV 25 - 100mg/kg every 6 hours
[Usual dose for 50kg adult = 1 g IV every 6 hours]

OR ALTERNATIVE, MORE EXPENSIVE, REGIMEN WITH WIDER COVERAGE

Ceftriaxone IV or IM 50-100mg/kg every 24 hours
[Usual dose for 50kg adult = 2 - 4 g every 24 hours]

If intra-abdominal sepsis suspected, suggest adding metronidazole (500 mg every 8 hours)

Please try to take all microbiology samples and multiple blood cultures before starting antibiotics

SUGGESTIONS FOR SPECIAL SITUATIONS

If you suspect endocarditis:
Suggest taking six seperate blood culture sets and inform cardiologist

If you suspect melioidosis, while you wait culture results:
Use co-amoxiclav or, if you very strongly suspect melioidosis, use ceftazidime

If the patient is an infant:
Add cloxacillin

If you suspect bacterial meningitis plus septicaemia:
Ceftriaxone is recommended to be given every 12 hours rather than every 24 hours

If you suspect pneumococcal meningitis plus septicaemia:
Suggest using ceftriaxone every 12 hours, rather than a penicillin

Recent Medical Papers From Laos [Copies available from the Microbiology Laboratory]

2009 - since last newsletter

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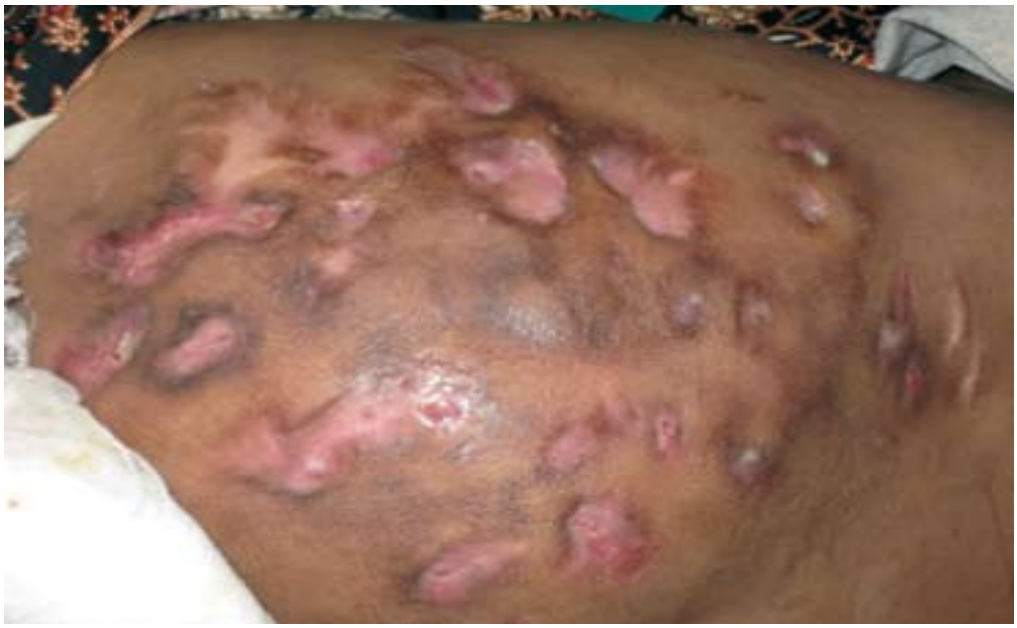
THE TAIL END

An 18-year-old Lao student and rice farmer from Saravan Province presented at Mahosot Hospital with widespread abscess formation and significant scarring of her left buttock of three years duration (see Wootton *et al.* 2012). Initially starting as a small painless pustule, without antecedent trauma or injection, the lesion had grown and been treated with incision and drainage and a week's course of ampicillin. Although blood cultures were negative, pus from the buttock grew *Burkholderia pseudomallei*. Tests for diabetes and thalassaemia were negative. Chest XR was normal but she had splenic abscesses visible on abdominal ultrasound. A fistulogram showed no connection with internal organs but she had a large collection in her buttock that was drained. She was treated with iv ceftazidime for three weeks and then oral doxycycline and co-trimoxazole for 16 weeks with significant improvement.



Microbiology tests available at the Microbiology Laboratory, Mahosot Hospital

The superscript number is the number of days/weeks we will try to issue the final report by.
asap = as soon as possible

Blood culture - for suspected septicaemia [blood culture set for UI-2]. [8 days]

Pus - for suspected bacterial infection [sterile swab]. [3 days]

Urine - for suspected UTI [sterile white capped tube]. [3 days]
please only send if patient has UTI symptoms, except in pregnancy

Throat swab - for suspected melioidosis [sterile swab]. [4 days]

Stool - for suspected bacterial/amoebic GI infection [sterile white capped tube]. [3 days]

Pleural fluid - for suspected bacterial or *Paragonimus* lung infection [sterile white capped tube]. [3 days]

Ascitic fluid - for suspected bacterial ascitis [sterile white capped tube]. [3 days]

Pericardial fluid - for suspected bacterial pericarditis [sterile white capped tube]. [3 days]

Broncho-alveolar lavage - for suspected lung bacterial infection [sterile white capped tube]. [3 days]

STI - vaginal/urethral discharge swab - direct microscopic wet mount and Gram stain exam. [1 day]

Weber test - stool - for suspected gastrointestinal tract bleeding. [1 day]

CSF - for suspected CNS infection or other intracranial pathology - please call Lab +
- sterile white capped tube x 3 & fluoride tube for CSF
- please always do blood culture (UI-2) set if CNS Infection suspected
- CSF cell count, bacterial culture, Gram stain, Indian Ink stain.[1 day]LJ culture -TB. [6 weeks]
- dengue/JEV serology. [7 days]
- scrub typhus & murine typhus rapid tests. [1-2 days]
- bacterial PCR for *S. pneumoniae, H. influenzae* b. *S. suis* and *N. meningitidis.* [asap]
- viral PCR for CMV, Enterovirus, HSV, VZ, JEV, dengue, mumps, measles, influenza, West Nile, tick-borne encephalitis and Nipah viruses. [asap]
- viral culture. [3 weeks]

+ if patient needs a CT brain before LP but cannot afford cost please inform Microbiology Laboratory

Leptospiral culture - automatically performed on all white capped tubes in UI-2 set. [4 weeks]

Rickettsial serology - scrub typhus & murine typhus rapid tests same day (and subsequent IFA) for suspected typhus. Automatically performed on all who have LP

Rickettsial culture - we do for all patients who are rapid test positive for scrub or murine typhus or if the patient is suspected as gaving Spotted Fever Group infection [EDTA pink capped tube]. [8 weeks]

Dengue/JEV IgM/IgG/NS1 ELISAs - we will do automatically for all patients with suspected CNS Infection and during the 'dengue season' will run samples every Wednesday. [7 days]

Hand, Foot and Mouth Disease - throat swab, vesicle fluid, stool and serum. Please phone Lab.

We will phone the ward if we grow a clinically significant organism but cannot issue a full report yet. Please always label specimens and form with patient's name, age, phone number, ward, Hospital Number and requesting doctors name (not just the signature !).

Laos Oxford

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