

rates among infected infants of 25–30% in the UK.^{2,3} Untreated neonatal HSV infection has a high mortality of 80%,⁴ and prospective studies from the USA³ report that at least 2% of all women who were negative for HSV IgG, and therefore susceptible to primary genital HSV, acquired it during pregnancy; most of these infections were asymptomatic.

The diagnosis of maternal genital herpes is crucial in preventing neonatal HSV acquisition, especially since transmission is influenced by whether the infection is first-episode (primary) or recurrent and by the duration of membrane rupture at delivery, mode of delivery, and use of invasive fetal monitoring. Current UK guidelines for management of genital HSV in pregnancy state that first-episode genital herpes carries a higher risk for neonatal HSV infection than recurrent HSV in pregnancy.³

Over the past few months, two HSV infections of neonates have been diagnosed in our hospital. The mothers had developed vaginal discharge at around 36 weeks' gestation and samples had been sent only for *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and candida testing with no request for HSV testing since there were no vesicular lesions. However, retrospective testing showed HSV type 2 IgG seroconversion at 36 weeks' gestation along with reactive HSV type 2 IgM, confirming HSV type 2 infection.

Samples from pregnant women with vaginal discharge might only be sent for detection of bacteria and fungi, unless vesicular lesions are present on examination. Some reports on the management of vaginal discharge focus mainly on chlamydia and gonorrhoea infection, and HSV infection might not be considered as part of the differential diagnosis.⁵ Moreover, subclinical first-episode mucocutaneous HSV infection might occur and

viral shedding has been described in more than 80% of HSV type 2 infected individuals who report no lesions.⁶

Provisional data from the British Paediatric Surveillance Unit² indicate that although neonatal HSV infection remains rare, there has been a near doubling in the reported annual rate of cases in 2006–07 compared with 1986–91, when the incidence was reported to be one in 60 000 live births per year.

The neonatal HSV infections that we have seen recently highlight the issue of testing maternal genital samples for HSV DNA, especially when the mother presents late in pregnancy with vaginal discharge and no obvious herpetic genital lesions. HSV DNA testing must be considered when there are maternal symptoms suggestive of genital tract infection during the antenatal period, especially during the later stages of pregnancy.

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- 1 Senior K. Herpes simplex type 2 infects one in ten globally. *Lancet Infect Dis* 2009; **9**: 15.
- 2 Tookey P, Peckham CS, Lynn R, Brown D. British paediatric surveillance unit 21st annual report 2006–2007. London: British Paediatric Surveillance Unit, Royal College of Paediatrics and Child Health, 2007. http://bpsu.inopsu.com/publications/annual_reports/BPSU%20Annual%20report%202006-7.pdf (accessed April 20, 2009).
- 3 Royal College of Obstetricians and Gynaecologists. Management of genital herpes in pregnancy. Green-top guideline No 30. London: Royal College of Obstetricians and Gynaecologists, 2007. <http://www.rcog.org.uk/files/rcog-corp/uploaded-files/GT30GenitalHerpes2007.pdf> (accessed April 20, 2009).
- 4 Chantal Caviness A, Demmler GJ, Selwyn BJ. Clinical and laboratory features of neonatal herpes simplex virus infection. *Paed Inf Dis J* 2008; **27**: 425–30.
- 5 H Mitchell. Vaginal discharge—causes, diagnosis and treatment. *BMJ* 2004; **328**: 1306–08.
- 6 Wald A, Zeh J, Selke S, et al. Reactivation of genital herpes simplex virus type 2 infection in asymptomatic seropositive persons. *N Engl J Med* 2000; **342**: 844–50.

European Union conference on poverty-related diseases research

The European Commission (EC) organised a conference on poverty-related diseases (PRDs) in Brussels, Belgium (Nov 13–14, 2008), entitled *Challenges for the future: research on HIV/AIDS, malaria and tuberculosis*. It brought together more than 350 representatives from 63 countries, including a broad swathe of disease-

endemic countries. "AIDS, malaria, and tuberculosis kill 5 million people each year. We have not forgotten the importance of battling the diseases that affect the poorest among us the hardest. We are here to define the specific priorities for research in this field", said Janez Potočnik, EC Commissioner for Science and

Research. HIV/AIDS, malaria, and tuberculosis became a specific research focus in the European Union's Sixth Framework Programme (FP6), which ran from 2002 to 2006.¹ Over the course of the 4 years of FP6, the EC allocated more than €450 million to research and development into new drugs, vaccines, and clinical investigations for PRDs. The results were striking. There are now more than 80 collaborative projects involving more than 250 research groups. European Union money helped to set up the European AIDS Treatment Network, the first pan-European network for clinical trials that focuses on finding the best combination therapies for HIV treatment. European Union money has also been used to set up tuberculosis and malaria projects.

TBVAC is an EC-funded project to design and test tuberculosis vaccines. Three new tuberculosis vaccine candidates are now in clinical trials, two live tuberculosis vaccines are entering clinical development, and new preclinical models and immunity biomarkers have been discovered and validated. The European Malaria Vaccine Development Association set up a standardised preclinical assay package, in close cooperation with WHO and the US National Institutes of Health, where candidate vaccines are comparatively evaluated, such that eventually three vaccine candidates can go into trials.²

The aim of the conference was to develop views on how to focus PRD research under the Seventh Framework Programme. Throughout the meeting, four overarching aspects of European-Union-supported PRD research surfaced: science (quality and thematic priorities), impact (new tools to treat and prevent PRDs), partnerships (within and beyond Europe), and the European Research Area including the European and Developing Countries Clinical Trials Partnership (EDCTP) (how to best organise European PRD research). Separate breakout sessions focused on each of the three diseases. Full details will soon be available on the EC website.³

HIV/AIDS continues to cause substantial morbidity and mortality in resource-poor countries.⁴ Current vaccines and microbicides have failed in clinical trials, and HIV is becoming increasingly resistant to treatment. Conference participants felt that the top research priorities for vaccines should be to gain a better understanding of the host proteins involved in viral transmission and functional immune activities, and to step up basic research into mucosal and innate immunity



A patient receiving antiretroviral treatment for HIV, Chikwawa, Malawi

and B-cell biology. A call was made for a renewed focus on vector insert design for T-cell vaccines. Other priorities included validating new intervention targets to broaden the pipeline of microbicides, exploring combined prevention modalities for both vaccines and microbicides, and developing fast-track approaches to human clinical trials.⁵ For treatment, more fundamental research into the pathogenesis of HIV/AIDS is needed to identify new avenues to develop novel drugs against viral and cellular targets.⁶ Addressing long-term drug toxicity, multidrug resistance, continuity of treatment, drug-combination methods, and the management of coinfections, were recognised as vital for the future of antiretroviral treatment in developing countries. Immediate public-health strategies must also focus on reducing transmission by non-medical means and on investigating the effect on transmission of limited access to biomedical intervention, especially for minorities, migrants, and poor communities.^{4,7}

Although new drug treatments for malaria and conventional malaria control measures show promise, millions still die of the disease.⁸ Development of highly effective and safe malaria vaccines still requires substantial advances in our understanding of the antigenic targets in malaria and how the parasite evades and disables the immune system. Several vaccine candidates are currently in development, each based on a rationale from our current, partial understanding of these mechanisms. Participants felt that more basic

research is needed to gain a thorough understanding of immune responses to the parasite, which should feed into antigen selection criteria and preclinical assays. As *Plasmodium falciparum* and *Plasmodium vivax* are coprevalent in many places, the search for an antivivax component in combination vaccines would be useful and challenging.⁹ Research for new antimalaria drugs should make use of chemical libraries and promising leads in ethnic pharmacology. Malaria drug development should also include medicinal chemistry, and structure–activity relations should be pursued.¹⁰ Treatment without prevention is not a sustainable approach to malaria control. In addition to vaccines, effective vector-control tools are greatly needed. Research should span the range from vector and population biology to new insecticides and implementation strategies.¹¹ Operational research into malaria control and eradication should include rapid diagnostics and a comparative assessment of interventions and strategies.

Worldwide, nearly 10 million people develop active tuberculosis every year and about 1.7 million die from the disease.¹² Improved diagnostics are crucial to tuberculosis care and control, and there is a great need for serious investment in tuberculosis diagnostics and biomarkers, with priority for point-of-care diagnostics.¹³ The rich pipeline of new tuberculosis vaccines requires more investment in worldwide partnerships for evaluation in clinical trials spanning different geographical sites.¹⁴ Research must continue into second-generation tuberculosis vaccines, combined (first and second

generation antigens, both lipid and protein) vaccines, pre-exposure vaccines, latency vaccines, and vaccines against a broader range of mycobacterial strains. Centralised facilities for animal models, including new imaging technologies and postexposure models were thought important. Further investment in capacity for phase IIb and III clinical trials of vaccines is needed. The current tuberculosis drug pipeline is scanty and only two candidates are in the final clinical evaluation phase.¹⁵ Encouragement was shown for the development of new antituberculosis drugs, short duration drug regimens, and adjunct immunotherapy to reduce the duration of chemotherapy and to treat drug-resistant tuberculosis. The current restriction of EDCTP funding to phase III drug trials should be extended to include phase I, II, and IV. Furthermore, it is important to narrow the gap between preclinical and clinical development, good clinical laboratory practice (GCLP)-compliant sites, phenotypic screening, and to increase access to diversified compound libraries.

Participants agreed that current leads must be moved forward to clinical trials, good manufacturing practice production, and marketing. For this purpose, the EDCTP is now established and widely recognised as a key instrument of the European Union's PRD programme.¹⁶ In addition to boosting clinical trial capacity, participants felt it would be useful and achievable to establish a network of GCLP-compliant PRD reference laboratories in endemic countries and to coordinate and harmonise ongoing cohort studies. All three breakout groups also shared the view that there is need to go back to basic research, as there are still huge gaps in our understanding of the biology, immunology, and pathophysiology of the three diseases. One scientific black box is the mechanisms of latent infection, which affects all three diseases. Fundamental knowledge is essential to find more rational approaches to exploring and designing new drug and vaccine candidates (and adjuvants), better diagnostics, and biomarkers. The dynamics and control of transmission, including the effect of human behaviour, remain largely unknown for all three diseases and should attract more attention.

The European Union's PRD research programmes have contributed to advancing science and developing new tools, not least thanks to the strong emphasis on intra-European and extra-European cooperation in designing the funding schemes.¹⁷ For these efforts to pay off,



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A child being vaccinated in Gulu, Uganda

momentum must be maintained and accelerated in the future. Work must be well coordinated and aligned to relevant PRD research programmes in European Union member states and associated countries, other major global research funders, and public-private partnerships. This requires innovative health-financing mechanisms. The current global economic recession should not prevent this from happening. Lastly, new tools and practices are useless unless they can be brought to the patients and communities in need. While continuing to explore the frontiers of science and bring new discoveries to fruition, the European scientific community working on PRDs will therefore not tire of advocating universal access to quality health care and a fairer global distribution of welfare in general.

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- 1 Communication from the Commission to the Council and the European Parliament—a European programme for action to confront HIV/AIDS, malaria and tuberculosis through external action (2007–2011). <http://europa.eu/scadplus/leg/en/lvb/r12537.htm> (accessed April 20, 2009).
- 2 European Commission. Combatting deadly diseases: EU funded projects on poverty-related diseases HIV/AIDS, malaria, tuberculosis, 3rd edn. Luxembourg: Office for official publications of the European Communities, 2006. http://ec.europa.eu/research/health/infectious-diseases/poverty-diseases/doc/catalogue-3rdcall_en.pdf (accessed April 20, 2009).
- 3 European Commission—research health. Challenges for the future: research on HIV/AIDS malaria and tuberculosis. http://ec.europa.eu/research/conferences/2008/poverty-related-diseases/index_en.html (accessed April 20, 2009).
- 4 Merson MH, O'Malley J, Serwadda D, Apisuk C. The history and challenge of HIV prevention. *Lancet* 2008; **372**: 475–88.
- 5 Girard MP, Bansal GP. HIV/AIDS vaccines: a need for new concepts? *Int Rev Immunol* 2008; **27**: 447–71.
- 6 Dau B, Holodniy M. Novel targets for antiretroviral therapy: clinical progress to date. *Drugs* 2009; **69**: 31–50.
- 7 Hirsch JS. Gender, sexuality, and antiretroviral therapy: using social science to enhance outcomes and inform secondary prevention strategies, *AIDS* 2007; **21** (suppl): S21–29.
- 8 Laufer MK. Monitoring antimalarial drug efficacy: current challenges. *Curr Infect Dis Rep* 2009; **11**: 59–65.
- 9 Galinski MR, Barnwell JW. *Plasmodium vivax*: who cares? *Malar J* 2008; **7** (suppl): S9.
- 10 Jenwitheesuk E, Horst JA, Rivas KL, Van Voorhis WC, Samudrala R. Novel paradigms for drug discovery: computational multitarget screening. *Trends Pharmacol Sci* 2008; **29**: 62–71.
- 11 Black WC 4th, Gorrochategui-Escalante N, Randle NP, Donnelly MJ. The yin and yang of linkage disequilibrium: mapping of genes and nucleotides conferring insecticide resistance in insect disease vectors. *Adv Exp Med Biol* 2008; **627**: 71–83.
- 12 WHO. Global tuberculosis control—epidemiology, strategy, financing: WHO report 2009. Geneva: World Health Organization, 2009. http://www.who.int/tb/publications/global_report/en/ (accessed April 20, 2009).
- 13 Wallis RS, Doherty TM, Onyebujoh P, et al. Biomarkers for tuberculosis disease activity, cure, and relapse. *Lancet Infect Dis* 2009; **9**: 162–72.
- 14 Hoft DF. Tuberculosis vaccine development: goals, immunological design, and evaluation. *Lancet* 2008; **372**: 164–75.
- 15 Global alliance for TB drug development. Pathway to patients: charting the dynamics of the global TB drug market. New York: Global alliance for TB drug development, 2007. http://www.bvgh.org/documents/TB_Alliance_Pathway_to_Patients_FINAL.pdf (accessed April 20, 2009).
- 16 Communication from the Commission to the European Parliament and the Council on the progress report on the 'European and Developing Countries Clinical Trials Partnership' Programme. COM/2008/688/. <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SEC:2008:2724:FIN:EN:PDF> (accessed April 20, 2009).
- 17 Annual Report on research and technological development activities of the European Union in 2007. Brussels: European Commission, 2008. http://ec.europa.eu/research/reports/2008/index_en.html (accessed April 20, 2009).