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## **EUROTRAVNET SCIENCE WATCH : September 2010**

**Scientific advances** Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological and epidemiological study. Kumarasamy KK et al , *The Lancet Infectious Diseases* 2010 (10); 9: 597-602

**Scientific advances:** Spiroindolones, a Potent Compound Class for the Treatment of Malaria. Rottmann M et al. *Science* 2010, Vol. 329. no. 5996, pp. 1175 - 1180

**Scientific Advances** – Neglected tropical diseases outside the tropics.

Norman FF et al. *PLoS Negl Trop Dis*. 2010 Jul 27;4(7):e762

**Scientific Advances** – Extensive Drug Resistance in Malaria and Tuberculosis. Wongsrichanalai C et al, *Emerg Infect Dis* [serial on the Internet]. 2010 Jul [date cited]. <http://www.cdc.gov/EID/content/16/7/1063.htm>

**Scientific advance : Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological and epidemiological study.**

Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, Chaudhary U, Doumith M, Giske C, Irfan S, Krishnan P, Kumar AY, Maharian S, Mushtaq S, Noorie T, Paterson DL, Pearson A, Perry C, Pike R, Roa, B, Ray U, Sarma JB, Sharma M, Sheridan E, Thirunarayan MA, Turton J, Upadhyay S, Warner M, Welfare W, Livermore DM, Woodford N.

**The Lancet Infectious Diseases 2010 (10); 9: 597-602**

**Link to the article : <http://www.ncbi.nlm.nih.gov/pubmed/20705517>**

**Description:** Gram-negative Enterobacteriaceae with resistance to carbapenem conferred by New Delhi metallo- $\beta$ -lactamase 1 (NDM-1) were identified in isolates from India (Chennai, Haryana and other sites), the UK and Pakistan. NDM-1 was found mostly among *Escherichia coli* and *Klebsiella pneumoniae* which were resistant to all antibiotics except tigecycline and colistin. Many of the UK NDM-1 positive patients had travelled to India or Pakistan in the past year or had been admitted to a hospital in these countries for procedures ranging from bone marrow transplant to cosmetic surgery.

**ECDC comment:** The increase in resistance of Gram-negative bacteria is mainly due to mobile genes on plasmids that can spread rapidly through bacterial populations. This paper shows how human air travel and migration allows rapid global transport of such genes. The superbug spectre of Gram-negative Enterobacteriaceae bacteria resistant to conventional antibiotics is a frightening scenario and this report received widespread media coverage.

**Public Health Significance:** The potential of NDM-1 to be a worldwide public health problem is great and co-ordinated international surveillance is needed. Development of new antibiotics active against Gram-negative bacteria is an urgent priority.

**Keywords :** Gram-negative Enterobacteriaceae, NDM-1, resistance,

This paper was selected by Dr Patricia Schlagenhaut (pat@ifspm.uzh.ch) from Zürich, Switzerland.

## **Scientific Advances – Spiroindolones, a Potent Compound Class for the Treatment of Malaria**

Matthias Rottmann, Case McNamara, Bryan K. S. Yeung, Marcus C. S. Lee, Bin Zou, Bruce Russell, Patrick Seitz, David M. Plouffe, Neekesh V. Dharia, Jocelyn Tan, Steven B. Cohen, Kathryn R. Spencer, Gonzalo E. González-Páez, Suresh B. Lakshminarayana, Anne Goh, Rossarin Suwanarusk, Timothy Jegla, Esther K. Schmitt, Hans-Peter Beck, Reto Brun, Francois Nosten, Laurent Renia, Veronique Dartois, Thomas H. Keller, David A. Fidock, Elizabeth A. Winzeler, Thierry T. Diagana

**Science 2010: Vol. 329. no. 5996, pp. 1175 - 1180**

**Link to the paper:** <http://www.ncbi.nlm.nih.gov/pubmed/20813948>

**Description:** This paper identifies a new class of compounds, spiroindolones, that show promise as anti-malarials. These potent drugs kill the blood stages of *Plasmodium falciparum* and *Plasmodium vivax* clinical isolates at low concentrations. Spiroindolones rapidly inhibit protein synthesis in *P. falciparum*. Studies in a rodent malaria model show that spiroindolone NITD609 has pharmacokinetic properties compatible with once-daily oral dosing and has single-dose efficacy in a rodent malaria model.

**ECDC comment:** This new, fully synthetic drug is active against the blood stages of *P. falciparum* and *P. vivax* including a range of drug resistant strains. The preliminary data suggest that the safety profile is acceptable. Clinical trials will now test the efficacy and tolerability of this class of anti-malarial to evaluate the transfer .

**Public health significance :** In SE Asia, there have been recent reports of signs of resistance to artemisinin, the current, most potent anti-malarial drug. New pipeline anti-malarial drugs that can overcome the challenges of resistance are essential to combat malaria, a disease which affects almost half of the world's population, causes more than 800,000 deaths annually and kills more under-5-year-olds than any other infectious disease.

**Keywords :** Malaria, spiroindolones,

This paper was selected by Dr Patricia Schlagenhauf (pat@ifspm.uzh.ch) from Zürich, Switzerland.

## **Scientific Advances – Neglected tropical diseases outside the tropics.**

Norman FF, Pérez de Ayala A, Pérez-Molina JA, Monge-Maillo B, Zamarrón P, López-Vélez R.

PLoS Negl Trop Dis. 2010 Jul 27;4(7):e762

**Description:** The neglected tropical diseases (NTDs) cause significant morbidity and mortality worldwide. Due to increased human mobility, NTDs are increasingly diagnosed in countries of the western world outside of their usual geographic area of endemicity. This paper describes a mixed cohort of 6168 immigrants and travelers diagnosed with one of the 13 core NTDs at a Tropical Medicine Referral Unit in Spain. The main NTDs diagnosed in immigrants were onchocerciasis acquired mainly in sub-Saharan Africa, Chagas disease in immigrants from South America, and ascariasis found mainly in immigrants from sub-Saharan Africa. Most frequent NTDs in travelers were: schistosomiasis, onchocerciasis and ascariasis - all mainly acquired in sub-Saharan Africa.

### **Link to the article:**

<http://www.plosntds.org/article/info%3Adoi%2F10.1371%2Fjournal.pntd.0000762>

**ECDC comment:** The neglected tropical diseases (NTDs) are a group of chronic diseases normally seen in distinct geographic regions amongst the world's poorest populations. International travel and immigration have blurred the geography of disease.

**Public health significance.** Imported NTDs have an important impact on public health. For example, Chagas Disease, seen increasingly in Spain, may become an important cause of cardiomyopathy in the future. In some countries national legislation for the screening of blood donations needs to be established. Considering the changing demographic profiles in European countries, health professionals attending immigrants and travellers from tropical regions should consider appropriate protocols for screening of NTDs in their everyday practice.

**Keywords :** Neglected tropical diseases, screening

This paper was selected by Prof. Rogelio Lopez Vélez (Madrid, Spain) and Dr Patricia Schlagenhauf (pat@ifspm.uzh.ch) from Zürich, Switzerland.

## **Scientific Advances** – Extensive Drug Resistance in Malaria and Tuberculosis

Chansuda Wongsrichanalai, Jay K. Varma, Jonathan J. Juliano, Michael E. Kimerling, and John R. MacArthur

Emerg Infect Dis. 2010 Jul;16(7):1063-7

**Description:** This perspective addresses the terminology used for drug resistance in tuberculosis (TB) and malaria and suggests the creation of a new category of malaria resistance, namely, „*extensively drug resistant*“ malaria. Recent declines in the clinical effectiveness of antimalarial drugs, including artemisinin-based combination therapy, have prompted the need to revise the definitions of and/or to recategorize antimalarial drug resistance to include « *extensively drug-resistant* » malaria.

**Link to the article:**

[http://www.cdc.gov/eid/content/16/7/1063\\_cme\\_activity.htm](http://www.cdc.gov/eid/content/16/7/1063_cme_activity.htm)

**ECDC comment:** Drug resistance in TB and malaria arises from inadequate or inappropriate use of antimicrobial agents; however, the definitions used to classify drug resistance, as well as the public health control measures, vary. These pathogens are increasingly resistant to more drugs, and new descriptive terms such as multidrug resistant (MDR) and, for TB, extensively drug-resistant (XDR) have been introduced to describe these changes. For TB, definitions of these new terms are now widely accepted. For malaria, recent changes in clinical effectiveness of antimalarial drugs, in particular the emergence of artemisinin resistance, are forcing malaria experts to consider revising the definitions of drug resistance for *Plasmodium falciparum*. For malaria, the geographic location in which infection is acquired is the primary determinant of the risk of having a drug-resistant infection and geography will guide treatment options. For TB, the geographic area in which infection is acquired is not a reliable determinant of treatment choice and here the most reliable predictors of MDR risk are a history of prior treatment or known exposure to another case-patient.

**Public health significance** Applying precise case definitions to different levels of drug resistance in malaria and TB is useful for individual patient care and therapeutic decisions. From the public health perspective, information on malaria drug resistance and use of appropriate definitions are central for strategic planning and the formulation of policy guidelines.

**Keywords** : malaria, tuberculosis, resistance,

This paper was selected by Prof. Philippe Parola (Marseille, France) and Dr Patricia Schlagenhauf (pat@ifspm.uzh.ch) from Zürich, Switzerland.