

# Medical tourists in India and Pakistan might be at risk for new NDM-1 “superbug”

A multi-national team of researchers reported in the online August issue of *Lancet Infectious Diseases* that some British residents who travelled to India or Pakistan for medical procedures have apparently picked up multi-drug resistant (MDR) enterobacteria there and carried the pathogens home.

NDM-1 multi-drug resistance factor (RF) was found expressed in bacterial isolates (of *E. coli*, *Klebsiella pneumoniae*, and other enterobacteria species) in 37 people in Britain. 17 of the 37 had been in India or Pakistan in the past year; and 14 of the 37 had been hospitalised there (several for cosmetic or transplant surgery). The NDM-1 enterobacteria (“superbugs”) were found in patients hospitalised in two Indian cities >1,000 miles apart. This suggests that the “superbugs” are widely distributed in the region. The “superbugs” resisted all antibiotics except for tigecycline (marketed by Wyeth) and colistin.

The researchers stated that this finding was disturbing, because UK patients sometimes opt for surgery in India with the aim of saving money, but the cost of treating a highly resistant infection would cancel short-term savings. They warned that the NDM-1 RF would likely spread worldwide, as medical tourism to South Asia is also popular with Europeans and Americans. The authors found the potential for international spread “clear and frightening”.

NDM-1 is a beta-lactamase enzyme. (NDM refers to New Delhi beta-metallolactamase, described in a Swedish national who apparently fell ill in December 2009 with antibiotic resistant infection while in New Delhi, and was subsequently repatriated home – Yong

D et al.) Characterisation of a new metallo-beta-lactamase gene, bla(NDM-1), and a novel erythromycin esterase gene carried on a unique genetic structure in *Klebsiella pneumoniae* sequence type 14 from India. {Antimicrobial Agents and Chemotherapy, 53 (12): 5046-54. doi:10.1128/AAC.00774-09.} It inactivates a range of common antibiotics. The gene for it is often carried on bacterial nuclei plasmids that could be easily acquired by other pathogens. In late June, the US CDC reported that NDM-1 had been found in the US for the first time, in three isolates identified in three separate state laboratories, in three different species.

The multi-national team of researchers wanted to investigate the prevalence of NDM-1 in India, Pakistan and the UK. Enterobacteriaceae isolates (including *E. coli*, *K. pneumoniae*, *Enterobacter cloacae*, two *Proteus* species, and others) were studied from two major centres in India – Chennai in South India and Haryana in North India, and those referred to the UK’s national reference laboratory. Case data for UK patients were reviewed for evidence of travel and recent admission to hospitals in India or Pakistan.

Of 3,521 isolates from the southern Indian city of Chennai, 4% (44) carried NDM-1. Of 198 isolates collected in the northern state of Haryana, nearly 25% (26) were positive. There were also 73 NDM-1 positive isolates from other locations in India and Pakistan.

In the UK, samples from facilities across the country, including Scotland and Northern Ireland, there were 37 NDM-1 positive isolates. The first was discovered in 2008. Of all 180 NDM-1 positive isolates found in the study,

111 were

*K. pneumoniae*

and 36 were *E. coli*.

Most NDM-1 positive

isolates came from patients with

urinary tract infections, bacteraemia, or pneumonia.

The NDM-1 positive isolates in Haryana were genetically identical, and the NDM-1 gene was not easily transferred to other species. On the other hand, the positive samples from elsewhere were clonally diverse, and the gene was carried on plasmids that could readily move





among different enterobacteria species.

Laboratory testing indicated that the NDM-1 isolates were resistant to all beta-lactam antibiotics, fluoroquinolones, and aminoglycosides; except for two isolates that were killed by gentamicin.

All but 39 were sensitive to minocycline; only 19 were resistant to tigecycline, and 3 were resistant to colistin. One *K. pneumoniae* isolate was resistant to both tigecycline and colistin.

The authors predicted that the appearance of NDM-1 might potentially herald the end of treatment with beta-lactams, fluoroquinolones, and aminoglycosides, which collectively form the backbone of therapy for gram-

negative infections. They state that in contrast to the previous decade, MDR gram-negative bacteria would pose the greatest risk to public health.

The study was funded by the EU, the Wellcome Trust, and Wyeth. The lead author received a travel grant from Wyeth. Another author holds or manages shares in some pharmaceutical companies.

An accompanying editorial states that the appearance of NDM-1 in multiple locations merits very close monitoring and worldwide, internationally funded, multi-centre surveillance studies – especially in countries that promote medical tourism. The editorial author from the University of Calgary recommended that individuals having medical procedures in India should be actively screened for MDR bacteria before they received medical care in their home country. **SMA**

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Sources: (1) Kumarasamy K, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study. *Lancet Inf Diseases* 2010; DOI: 10.1016/S1473-3099(10)70143-2. (2) Pitout J. The latest threat in the war on antimicrobial resistance. *Lancet Inf Diseases* 2010; DOI: 10.1016/S1473-3099(10)70143-2.

**Note:**

- (1) New insights into the mechanism of topoisomerase action suggest a platform for structure-based drug design of a new class of antibacterial agents for use MDR pathogens -- <http://en.wikipedia.org/wiki/NDM-1> - cite\_ref-13#cite\_ref-13Bax BD et al. Type IIA topoisomerase inhibition by a new class of antibacterial agents. *Nature* (4 August 2010). doi:10.1038/nature09197.
- (2) The Indian Health Ministry has disputed the conclusions of the Lancet report – India rejects UK scientists' superbug claim. BBC News 12 August 2010. <http://www.bbc.co.uk/news/world-south-asia-10954890>.