

Portrait of the superbug

The controversy about the New Delhi Super Bug can do with a look at some of the facts, says S.Ananthanarayanan.

The controversy is about a paper in *Lancet*, the reputed medical journal, about resistance to antibiotics arising in Gram negative bacteria, as opposed to Gram positive bacteria, which have displayed the most resistance so far. What is more, the resistance seen is to the most powerful category of antibiotics to date, and is hence of great concern. And the instances studied in the Lancet paper indicated that the cellular factor responsible seemed to start from Haryana and Chennai, in India.

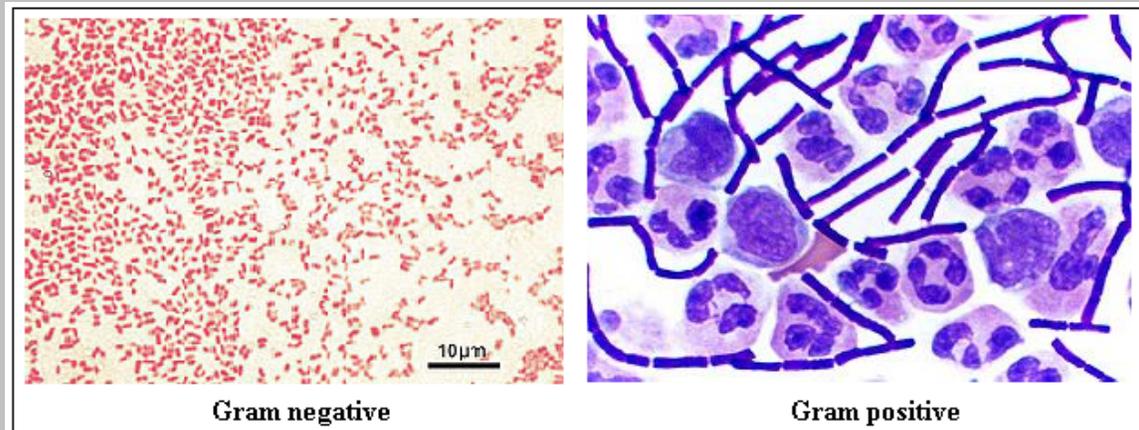
The paper also said that with close historical and current contacts between UK and India, this was of concern to the UK and the world. “Several of the UK source patients had undergone elective, including cosmetic, surgery while visiting India or Pakistan. India also provides cosmetic surgery for other Europeans and Americans, and *bla*NDM-1, which is the gene that provides bacteria with resistance, will likely spread worldwide.”

The mention of India being a risk location for surgery has sparked off protests from India and the validity of the research about the gene has been questioned. The team of 31 doctors and scientists who authored the report includes 17 from the Indian subcontinent.

Gram negative bacteria

Bacteria can be classed as Gram negative or Gram positive, and this classification is one that depends on the surface features of different bacteria. The name of the classification comes from Hans Christian *Gram*, the Danish scientist who devised this method of staining bacteria and classifying them according to the colour they took.

Gram positive bacteria have a thick, mesh-like cell wall, which stains purple in the Gram stain test. Gram negative bacteria have a thinner cell wall that contains lipids, which consist of molecules like those of oils or waxes and they stain pink. Gram negative bacteria also carry on their surface some scraps of DNA, called *plasmids*, which can readily pass from one to another and thus spread any resistance that one bacterium may develop.



The rising resistance of gram negative bacteria is hence of great concern. Unprecedented human air travel can rapidly transfer such features world-wide, the spread getting detected only when the bacterium produces some disease, which then resists control. One such factor, which promotes the production of a gene which confers resistance to penicillin and many other antibiotics, was first detected in Indian hospitals in the 1990s and has since spread world-wide. This factor is now found to be present in a large proportion of gram negative bacteria found in India and the use of a reserved category of antibiotic, the *carbopenems*, is getting necessary in most places.

Gram negative bacteria are involved in respiratory and gastrointestinal diseases, meningitis, urinary tract infections and some STDs. Gram positive bacteria are involved in pneumonia, diphtheria, scarlet fever and mild respiratory infections.

The New Delhi enzyme

The new resistance giving factor, called *New Delhi metallo-beta-lactamase* (NDM), that has been detected, is deadly, it gives resistance to even the carbopenems. The way bacteria manage to evade antibiotics is by the generation of an enzyme, *beta-lactomase*. Carbopenems are less sensitive to inactivation by beta-lactamase and have hence been the answer to bacteria which are resistant to other antibiotics.

But the *NDM-1 gene*, produces NDM-1, an enzyme that is able to inactivate even the carbopenems. Another version of this kind of enzyme, the *Klebsiella pneumoniae carbapenemase* (KPC) is currently the most common type of this enzyme, which was first detected in North Carolina, USA in 1996 and has spread worldwide.

NDM-1 was first detected in Dec 2009, in a Swedish patient who had fallen ill in New Delhi and did not respond to treatment. When the patient was transferred to Sweden, it was found that he had a carbapenem resistant KCP strain with the newly discovered gene. In March 2010, a group of doctors in Mumbai found that the majority of carbapenem resistant bacteria isolated from patients carried the NDM-1 gene.

The study reported in *Lancet*, of August 2010 is of large numbers of affected patients in Chennai and Haryana and a large proportion of affected patients in the UK having history of travel to India, and undergoing surgery, within the last one year.

The NDM-1 bacteria, however, are still susceptible to the antibiotics, *tigecycline* and *colistin*. Only early in August 2010 a chemical compound called GSK 299423 has been found to significantly fight against bacteria by making such bacteria unable to reproduce, which may be a likely treatment of the NDM-1 strain.

Implication for India

Whatever the effect on so called ‘medical tourism’ of patients from western countries coming to India for treatment, the effect of spreading NDM-1 is likely to have far-reaching effects on the load of indigenous patients who begin to resist antibiotics. An editorial in the March 2010 issue of the *Journal of Association of Physicians of India* and also the study in Mumbai in the same month had noted the free use of antibiotics in India, resulting in rising resistance. The implications are serious as there are few antibiotics that act against Gram negative bacteria in the pharmaceutical pipeline and none that work with those that carry NDM-1.
