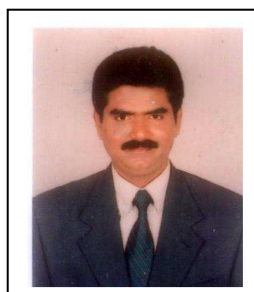


REVIEW ARTICLE

MICROBIOLOGY

BAD BUGS NO DRUGS-A REVIEW ON NDM-I



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ABSTRACT

A dangerous new mutation that makes some bacteria resistant to almost all antibiotics has become increasingly common throughout the world. Experts in antibiotic resistance called the gene mutation, named NDM-1(New Delhi Metallo-beta-lactamase), "worrying" and "ominous" and they feared it would spread globally. The spreading of this is increasing day by day. So, the scarcity of the antibiotics and the need of these in the present condition show the target to the world. The potential of NDM-1 to be a worldwide public health problem is great, and co-ordinated international surveillance is needed.

KEYWORDS

NDM-1, Antibiotics, bacteria and superbug.

INTRODUCTION

Homo sapiens is an alien species on earth. This planet belongs to bacteria. There are more bacteria on earth than all other living organisms. The human body contains more number of bacteria than human cells themselves. We lived with arrogant optimism that we had conquered infections, at least the bacterial infections, if not the viruses. How wrong we were! Bacteria have finally reclaimed their premier status and superiority and won the war against humans. They are literally mocking our intellect, knowledge and antibiotic weaponry¹.

When we are called to manage patients with severe infections due to pan resistant bugs, we do really wonder whether we are living in pre-Alexander Fleming years without antibiotics and then with a shock, but no surprise, realize that we have reached the end of antibiotic era². Still, the Indian medical community remains in a state of denial. We have not yet taken the issue of antibiotic resistance seriously. We believe that Dr. Fleming has discovered penicillin only early this morning and consider antibiotic resistance a problem of next century where in fact antibiotics are dead and the foul smell of decay is already around us, It is too late to save antibiotics,

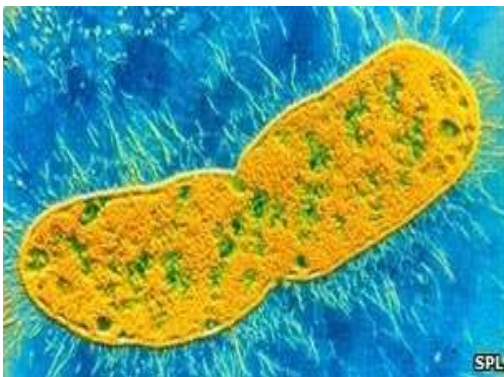
unless we have divine powers to bring the dead back to the life³.

The new superbug

Experts have warned that a new type of drug resistant super bug, they have called NDM-1 and it could spread worldwide.

*New Delhi Metallo-beta-lactamase (NDM-1)*⁴

is a gene that makes bacteria resistant to antibiotics of the carbapenem family¹². It encodes a type of beta-lactamase enzyme called a carbapenemase¹⁰. It is found on plasmids - DNA structures that can be easily copied and transferred between different bacteria - suggesting "an alarming potential to spread and diversify among bacterial populations"⁵. Bacteria that carry this gene are often referred to by news reporters as "super bugs"⁶. There are currently no new drugs in the research pipelines that aim to stop NDM-1. Some strains of E.coli and Klebsiella pneumonia⁸ are known carriers of the gene, but the gene can be transmitted from one strain of bacteria to another through horizontal gene transfer.



**Function**

The gene produces a metallo-beta-lactamase, an enzyme that hydrolyzes and inactivates antibiotics in the beta-lactam family⁷. This modification makes bacteria completely resistant to all known antibiotics—even to the “WEAPON OF LAST RESORT”, a group of drugs called the CARBAPENEMS, which are usually held in reserve for grave emergencies and infections by highly-resistant bacteria such as MRSA⁸. Those antibiotics were, until recently, capable of killing most bacteria by inhibiting the synthesis of one of their cell wall layers. The resistance conferred by this gene therefore aids the expansion of bacteria that carry it throughout a human host, since they will face less opposition/competition from populations of antibiotic-sensitive bacteria, which will be diminished by the original antibacterial treatment.

Regular queries regarding this issue**What is ndm-1?**

New Delhi metallo-β-lactamase-1⁴ is a gene carried by bacteria that makes the strain resistant to carbapenem antibiotics. This is concerning because these antibiotics are some of the most powerful ones, used on hard-to-treat infections that evade other drugs.

Why is this a problem?

NDM-1⁴ (or more precisely the DNA code for this enzyme) is “extremely mobile” can easily now jump from one strain of bacteria to another & it may end up in another bacterium which is already resistant to many other antibiotics. Ultimately, it could produce dangerous infections that would spread rapidly from person to person and be almost impossible to treat.

What are all the bacterial strains bearing this?

K pneumoniae⁸, Escherichia coli, Citrobacter freundii, Enterobacter cloacae, and Morganella morganii⁹. Other classes of carbapenemases have already been found in K

pneumoniae, E cloacae, Pseudomonas aeruginosa, and Acinetobacter baumannii¹⁰.

Can it be treated?

Other treatment options are available to fight these infections but they present major challenges for clinicians and will often demand combinations of antibiotics are used. Scientists have identified some strains that have been resistant to all known antibiotics.

How would I know if I had it?

The infections have ranged from mild to severe - and some have been fatal. Two types of bacteria have been host to NDM-1: the gut bacterium E.coli and another that can invade the lungs called Klebsiella pneumoniae⁸. Both can lead to urinary tract infections and blood poisoning.

Can its spread be stopped?

Experts say the way to stop it is through surveillance, rapid identification and isolation of any hospital patients who are infected. Normal infection control measures, such as disinfecting hospital equipment and doctors and nurses washing their hands with antibacterial soap, can stop the spread. And they say we now need new drugs to treat resistant strains.

Are there new antibiotics that could help?

While there is a great deal of investment in research to find new antibiotics, experts say that most of the drugs currently in the pipeline will be useless for treating NDM-1 positive patients. This is because the bacteria that carry NDM-1 are Gram-negative, while most of the work is being carried out for Gram-positive bugs like MRSA¹¹. The Health Protection Agency says "multi-resistant Gram-negative bacteria pose a notable public health risk and it remains important that the pharmaceutical industry continues to work towards developing new treatment options".

**What will happen now?**

The government said HPA (health protection agency) would continue to monitor the situation and would regularly review the data and the need for further action. In the meantime, hospitals should ensure they continue to provide good infection control to prevent any spread, and consider whether patients have recently been treated abroad and send samples to HPA for testing if necessary.

What you can do to protect yourself?

So what steps can you take to minimise the risk?

Simply, don't get it that's your best bet. Wearing a mask or respirator like the Critical Cover Micro breathe Mask and the Critical Cover PFL N-95 Particulate Respirator will go very far to keep you from contacting the virus.

- Use an antibacterial body wash/shampoo such as Hibiscrub before, during and after a hospital stay.
- If you're fitted with a catheter, ask for it to be removed as soon as clinically possible, says Professor Mervyn Bibb, a molecular microbiologist at the John Innes Institute, Norwich. 'It is a potential source of infection.'
- Ask hospital staff and visitors to use antiseptic hand gel.
- Take your antibiotics as prescribed: If you don't finish the course or take them at reduced dose there is a risk you won't kill all the bacteria, says Professor Bibb. 'Finishing the course will ensure all pathogens are killed. Taking less than the prescribed amount could lead to incrementally resistant strains developing.'
- Watch for signs of redness, swelling and pain around wounds and report it to medical staff.
- At home, practice good hand hygiene. Wash your hands after going to the loo and before preparing food. Regularly clean door handles, light switches and flushes on loos. Avoid sharing towels. Be vigilant about food hygiene: E. coli can colonise meat products,

such as burgers, so make sure you cook them thoroughly and they are not left bloody.

Ndm-1, is it a global scare

Already 40 types of bugs similar to NDM-1 are existing globally, that also includes the German Imipenem Resistant Metallurgical Strain. The Indian variant is just the 41st strain.

A day after the Lancet report⁵ on a drug-resistant super bug NDM-1 created a global scare, It's quite concerning because there are very limited treatment options. "The risk is that we have an enzyme with very major resistant and if it combined with a particularly nasty bacterium, then that would be a concern". As it is spreading alarmingly i.e. several cases are identified 44 isolates with NDM-1 in Chennai, 26 in Haryana, 37 in the UK, and 73 in other sites in India and Pakistan⁵. NDM-1 was mostly found among *Escherichia coli* (36) and *Klebsiella pneumoniae* (111), which were highly resistant to all antibiotics except to tigecycline and colistin. *K pneumoniae* isolates from Haryana were clonal but NDM-1 producers from the UK and Chennai were clonally diverse. The potential of NDM-1 to be a worldwide public health problem is great, and co-ordinate international surveillance is needed.

It is a wakeup call for microbiologists, an extremely serious situation and our health authorities are not able to realize the gravity of it¹⁹.

Linking india to superbug is unfair and wrong¹⁵

The Ministry of Health protested against the British study blaming India for exporting a drug-resistant super bug to the rest of the world. "India strongly refutes the naming of this enzyme as New Delhi metallo beta lactamase (NDM-1) and also refutes that hospitals in India are not safe for treatment, including medical



tourism," read a statement from the Union Health ministry²⁴.

"It is ridiculous to call it NDM-1 when none of the samples that tested positive were picked in New Delhi," it is a commercially motivated campaign to hurt India's Rs 1,200-crore medical tourism industry.

The Indian health ministry has disputed the conclusion that the gene originated in India or Pakistan, describing this conclusion as "unfair" and stating that Indian hospitals are perfectly safe for treatment^{13, 14}. Indian politicians have described linking this new drug resistance gene to India as "malicious propaganda" and blamed multinational corporations for what they describe as selective malignancy^{20, 21}. The Indian Ministry of Health released a statement "strongly refuting" naming the enzyme "New Delhi"²².

The primary author of the 2010 Lancet study, who is based in the University of Madras, has stated that he does not agree with the part of the article that advises people to avoid elective surgeries in India¹⁷.

Bajaj described the statements by British medical experts as being politically motivated. 'They might have been alarmed by the prospect of losing business to Indians'. Medical tourism in India is expected to be worth \$2.3 billion by 2012, according to an estimate²⁵.

Health experts said it was politically motivated as Western doctors were alarmed at the prospect of losing business to India's booming health tourism. As the 'Indian surgeons

are the world's best in liver transplantation and also at the very top in endoscopic procedures. In fact American doctors are coming here to learn the procedure from us.

Several super bugs are surviving in nature and they have been reported from countries like Greece, Israel, the US, Britain, Brazil, Puerto Rico and many others and it is unfair to link the super bug to India,' said V.M. Katoch, director general, Indian Council of Medical Research (ICMR).

CONCLUSION

We have a bleak window of may be ten years, where we are going to have to use the antibiotics very wisely, but also grapple with the reality that we have nothing to treat these infections with. It is the first time it has got to this stage with these types of bacteria. 'Every time we throw enough antibiotics at enough people, we encourage the evolution of drug-resistant mutants.' So, now there're no antibiotics in the pipeline to treat this.

Ultimately, we will need new antibiotics - and even completely new ways of killing bacteria. Professor Enright's team at Biocontrol Ltd is working on a new take on an old idea - using natural viruses to attack bacteria instead of antibiotics.

Clinical trials are under way and we could have a new weapon in our armory within a few days.

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