New gene that makes common bacteria resistant to last-line antibiotic found in animals and patients in China

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A new gene (mcr-1) that enables bacteria to be highly resistant to polymyxins, the last line of antibiotic defence we have left, is widespread in Enterobacteriaceae taken from pigs and patients in south China, including strains with epidemic potential, according to new research published in *The Lancet Infectious Diseases*.

The mcr-1 gene was found on plasmids, mobile DNA that can be easily copied and transferred between different bacteria, suggesting an alarming potential to spread and diversify between different bacterial populations.

"These are extremely worrying results. The polymyxins (colistin and polymyxin B) were the last class of antibiotics in which resistance was incapable of spreading from cell to cell. Until now, colistin resistance resulted from chromosomal mutations, making the resistance mechanism unstable and incapable of spreading to other bacteria," explains author Professor Jian-Hua Liu from South China Agricultural University in Guangzhou, China.

"Our results reveal the emergence of the first polymyxin resistance gene that is readily passed between common bacteria such as *Escherichia coli* and *Klesbsiella pneumoniae*, suggesting that the progression from extensive drug resistance to pandrug resistance is inevitable."

During routine testing of food animals for antimicrobial resistance in China, Liu and colleagues isolated an E coli strain (SHP45) from a pig on an intensive pig farm in Shanghai that showed resistance to colistin that could be transferred to another strain. This prompted the researchers to collect bacteria samples from pigs at slaughter across four provinces, and from pork and chicken sold in 30 open markets and 27 supermarkets across Guangzhou between 2011 and 2014. They also analysed bacteria samples from patients presenting with infections to two hospitals in Guangdong and Zhejiang provinces. Samples were tested for antibiotic susceptibility and the mcr-1 gene using polymerase chain reaction (PCR) and sequencing.

The researchers found a high prevalence of the mcr-1 gene in E coli isolates from animal (166 of 804) and raw meat samples (78 of 523). Worryingly, the proportion of positive samples increased from year to year (table 2). mcr-1 was also found in 16 E coli and K pneumoniae isolates taken from 1322 hospitalised patients.

Importantly, the transfer rate (rate at which the mcr-1 gene is copied and transferred between different bacteria) was very high between *E. coli* strains. Moreover, the researchers found that the mcr-1 gene has the potential to spread into other epidemic pathogenic bacterial species such as *K. pneumoniae* and *Pseudomonas aeruginosa*, which can cause a variety of diseases from pneumonia to serious blood infections, suggesting that mcr-1 is likely to spread rapidly into human pathogens.

"Because of the relatively low proportion of positive samples taken from humans compared with animals, it is likely that mcr-1 mediated colistin resistance originated in animals and subsequently spread to humans," says co-author Professor Jianzhong Shen from China Agricultural University in Beijing, China. "The selective pressure imposed by increasingly heavy use of colistin in agriculture in China could have led to the acquisition of mcr-1 by *E. coli*."

China is one of the world's largest users and producers of colistin for agriculture and veterinary use. Worldwide, the demand for colistin in

agriculture is expected to reach almost 12000 tonnes per year by the end of 2015, rising to 16500 tonnes by 2021.

Provided by Lancet

According to the authors, "The emergence of mcr-1 heralds the breach of the last group of antibiotics. Although currently confined to China, mcr-1 is likely to emulate other resistance genes such as blaNDM-1 and spread worldwide. There is a critical need to re-evaluate the use of polymyxins in animals and for very close international monitoring and surveillance of mcr-1 in human and veterinary medicine."

Professor Shen adds, "In response to the rapid increase in colistin resistant bacteria from animals in China, the Ministry of Agriculture, China, has immediately responded by launching a risk assessment on use of colisitin in animal feed additives. This responsible and positive reaction is a reflection on how seriously the Chinese government are taking these findings. We are also working very closely with the Government to assess the impact of mcr-1. It should be also be noted that China is not the only country to use colisitin in farming but there are many countries, including in Europe, that use polymixins in agriculture, and therefore the responsibility to acknowledge and address the use of antibiotics across human and veterinary sectors must be also global."

Writing in a linked Comment, David Paterson and Patrick Harris from the University of Queensland, Brisbane, Australia say, "The links between agricultural use of colistin, colistin resistance in slaughtered animals, colistin resistance in food, and colistin resistance in human beings are now complete. One of the few solutions to uncoupling these connections is limitation or cessation of colistin use in agriculture. This will require substantial political will and we call upon Chinese leaders to act rapidly and decisively. Failure to do so will create a public health problem of major dimensions."

More information: *The Lancet Infectious Diseases*, www.thelancet.com/journals/lan … (15)00424-7/abstract