HALF OF ALL ANTIBIOTICS FAIL DUE TO 'SUPERBUGS'



GPs are increasingly handing out antibiotics that turn out to be useless, as up to half of courses of the drugs 'fail' and result in further treatment, a study has found.

Groundbreaking research has analyzed 11m courses of antibiotics prescribed to British patients over the last 22 years covering the most common diseases areas including tonsilitis, pneumonia and ear infections.

Scientists said the findings were 'bleak' with one in six courses of antibiotics failing in 2012 but for some drugs this was more than one in two.

Experts and governments have warned that antibiotic resistance is one of the greatest threats to modern health care yet prescriptions of the drugs by family doctors continues to increase.

GPs have admitted prescribing antibiotics to 'get rid of' patients.

It comes after the Telegraph revealed that GPs in some areas of the country are prescribing twice as many antibiotics as in others, with rates lowest in London and highest in the north of the country.

Cardiff University researchers found that as GP prescriptions of antibiotics rose in recent years so did the proportion of the treatment courses that ended in failure.

This was defined as when patients needed another course of drugs within a month, were admitted to hospital with an infection within 30 days, had other complicating factors relating to infection or died from conditions relating to the infection.

They looked at common antibiotics prescribed for upper respiratory tract infections such as sinisitus and tonsilitis; lower respiratory tract infections, such as bronchitis and pneumonia; skin and soft tissue infections, and middle-ear infection.

Between 1991 and 2012 overall antibiotic failures increased from 13.9 per cent to 15.4 per cent.

Failure rates for lower respiratory tract infections such as bronchitis and pneumonia were worse with more than one in three courses resulting in further complications or treatment.

One drug, trimethoprim, an antibiotic normally used in the treatment of upper respiratory tract infections such as tonsilitis and listed on the World Health Organisations's register of 'essential medicines', failed up to 70 per cent of the time when used to treat bronchitis or pneumonia. This compared with the more commonly prescribed amoxicillin which failed 18 per cent of the time for those diseases.

Rise of the superbugs

How antibiotic-resistant bacteria evolve and how they can infect people.

WHAT THEY ARE



Usually, only some bacteria are naturally resistant to drugs. But in the absence of antibiotics, these germs typically are at a disadvantage.



But when **antibiotics** kill non-resistant bacteria...



These drug- resistant bacteria can then grow and take over.

HOW THEY SPREAD

Chickens receive antibiotics routinely, which can kill off weaker bacteria and promote antibiotic resistant bacteria. Resistant bacteria can leave the farm through:



Contact with animals



The spreading of manure contaminated with bacteria onto crops as fertilizer



Human mishandling of contaminated meat.

Staff, 15/09/2014

The researchers, writing in the *British Medical Journal*, warned that the failure rates might even be an underestimate because if antibiotics were prescribed spuriously for viral disease and no follow-up treatment required then it would not have registered as a 'failure'.

Professor Craig Currie from Cardiff University's School of Medicine, said: "There is a strong link between the rise in antibiotic treatment failure and an increase in prescriptions.

"Between 2000 and 2012, the proportion of infections being treated with antibiotics rose from 60 per cent to 65 per cent which is the period in which we see the biggest increase in antibiotic failure rates. These episodes of failure were most striking when the antibiotic selected was not considered first choice for the condition treated.

"Given the lack of new antibiotics being developed, the growing ineffectiveness of antibiotics delivered through primary care is very worrying indeed.

"There is a mistaken perception that antibiotic resistance is only a danger admitted to hospital patients, but recent antibiotic use in primary care is the single most important risk factor for an infection with a resistant organism. "Furthermore, what happens in primary care impacts on hospital care and vice versa.

"Antibiotic resistance in primary care needs to be more closely monitored, which is actually quite difficult given that primary care clinicians seldom report treatment failures. The association between antibiotic resistance and antibiotic treatment failure also needs to be further explored. From the general level of feverish debate, it's not quite the "cliff" we would have imagined, but clearly this is worrying."

David Cameron has set up an antibiotic resistance task force and has warned the issue threatens to send medicine 'back to the Dark Ages'.

Increasing numbers of infections are now resistant to all common antibiotics making them almost impossible to treat and few new drugs are in the pipeline.

Professor Currie added: "We need to ensure that patients receive the appropriate medication for their condition and minimize any unnecessary or inappropriate treatment which could be fuelling microbial resistance to antibiotics, prolonging illness and in some cases killing people."

The research was only possible because the team had access to anonymous medical records of more than 14m people from more than 700 GP practices in the UK.

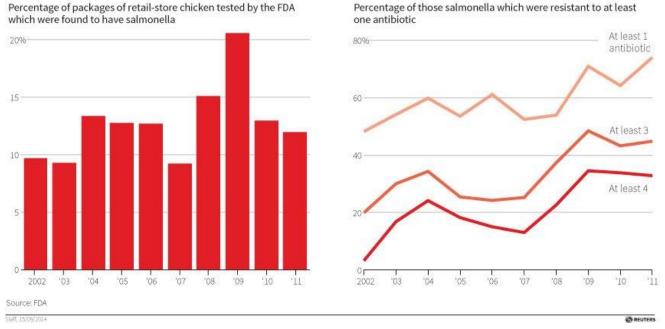
Dr Richard Stabler, Senior Lecturer in Molecular Bacteriology at the London School of Hygiene & Tropical Medicine, said: "The overall picture presented is bleak but not unexpected, with rises in drug resistance rising in most categories.

"The increase in resistance is possibly lower than expected, certainly in comparison to hospital based studies, but without action and a continual increase in resistance, antimicrobial resistance is still a real threat.

"Treatable infections becoming untreatable is a real possibility with several important infections, for example Tuberculosis and gonorrhoea, having already been documented to be almost totally resistant to all known classes of antimicrobials in some cases."

Salmonella superbugs on the rise

Public health officials fear that antibiotic use on poultry farms is boosting the rise of antimicrobial-resistant salmonella. The U.S. government does not require meat companies to automatically recall chicken products that test positive for salmonella.



Reuters

Prof Mark Woolhouse, Professor of Infectious Disease Epidemiology at University of Edinburgh, said: "Though antimicrobial resistance is a huge concern both nationally and internationally there is a worrying paucity of hard data that could inform health policy.

"The study does suggest that large numbers of patients require further medical attention within 30 days of being prescribed an antibiotic. That's obviously a worry. Moreover, the study shows that this fraction is rising, albeit slowly, over the past 20 years.

"This study confirms that that GPs are prescribing antibiotics as frequently if not more frequently than ever and that the problem of antimicrobial resistance continues to grow. The upshot is that we are increasingly reliant on a dwindling arsenal of drugs. That supports calls to develop new drugs but also, and probably even more importantly in the long term, to reduce usage and develop alternative therapies."

Prof Mark Fielder, Professor in Medical Microbiology at Kingston University, said: "There is a continued need for education across the spectrum with both patients and medical professionals being aware of the importance of this issue.

"This is due to the fact that with good guidelines for treatment and rigorous adherence we can help maintain effective antimicrobial therapies for longer. So ensuring that an antimicrobial is required, clearly relaying that information to patients and then making sure the prescribing guidelines are followed, do this and it can help preserve drug efficacy for longer. The authors make the point that primary care physicians can play an important role in containing antibiotic treatment failures by careful management of patient expectation whilst also adhering to approved treatment guidelines."

Public Health England is due to publish a report on variation in GP antibiotic prescribing nex month.

Dr Susan Hopkins, a healthcare epidemiologist at Public Health England said: "Public Health England have published national infection guidelines on which antibiotic is the most appropriate first-line treatment for a range of infections including those described in the BMJ paper.

"The rates of treatment failure for these recommended antibiotics are stable. What the paper shows is that where these guidelines are not followed treatment failures are increasing for both respiratory tract (e.g. bronchitis, pneumonia) and skin and soft tissue infections (e.g. cellulitis).

"Antibiotic resistance is an increasing problem, we strongly recommend that all clinicians follow the advice given in the PHE guidelines to limit the likelihood of treatment failure in their patients. Antibiotics are not recommended for coughs and colds."

Increased GVHD-related mortality with broad-spectrum antibiotic use after allogeneic hematopoietic stem cell transplantation in human patients and mice

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Antibiotics for allogeneic transplant—A double-edged sword

Patients undergoing allogeneic hematopoietic stem cell transplantation often receive antibiotics for infections, which can also unfortunately kill intestinal bacteria. These symbiotic bacteria in the gut generally do not cause disease and are thought to suppress inflammation. In a new study, Shono *et al.* examined the records of 857 transplant patients and found that certain antibiotics were linked with development of graft-versus-host disease (GVHD), which can cause severe intestinal inflammation. Using a mouse model, the authors showed that these antibiotics may select for bacteria that consume intestinal mucus and lead to loss of this important layer of protection for the gut, thus exacerbating GVHD in the intestine. This study suggests that not all antibiotic regimens are appropriate for treating transplant patients.

Abstract

Intestinal bacteria may modulate the risk of infection and graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Allo-HSCT recipients often develop neutropenic fever, which is treated with antibiotics that may target anaerobic bacteria in the gut. We retrospectively examined 857 allo-HSCT recipients and found that treatment of neutropenic fever with imipenem-cilastatin and piperacillin-tazobactam antibiotics was associated with increased GVHD-related mortality at 5 years (21.5% for imipenem-cilastatintreated patients versus 13.1% for untreated patients, P = 0.025; 19.8% for piperacillintazobactam-treated patients versus 11.9% for untreated patients, P = 0.007). However, two other antibiotics also used to treat neutropenic fever, aztreonam and cefepime, were not associated with GVHD-related mortality (P = 0.78 and P = 0.98, respectively). Analysis of stool specimens from allo-HSCT recipients showed that piperacillin-tazobactam administration was associated with perturbation of gut microbial composition. Studies in mice demonstrated aggravated GVHD mortality with imipenem-cilastatin or piperacillin-tazobactam compared to aztreonam (P < 0.01and P < 0.05, respectively). We found pathological evidence for increased GVHD in the colon of imipenem-cilastatin-treated mice (P < 0.05), but no difference in the concentration of shortchain fatty acids or numbers of regulatory T cells. Notably, imipenem-cilastatin treatment of mice with GVHD led to loss of the protective mucus lining of the colon (P < 0.01) and the

compromising of intestinal barrier function (P < 0.05). Sequencing of mouse stool specimens showed an increase in *Akkermansia muciniphila* (P < 0.001), a commensal bacterium with mucus-degrading capabilities, raising the possibility that mucus degradation may contribute to murine GVHD. We demonstrate an underappreciated risk for the treatment of allo-HSCT recipients with antibiotics that may exacerbate GVHD in the colon.

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