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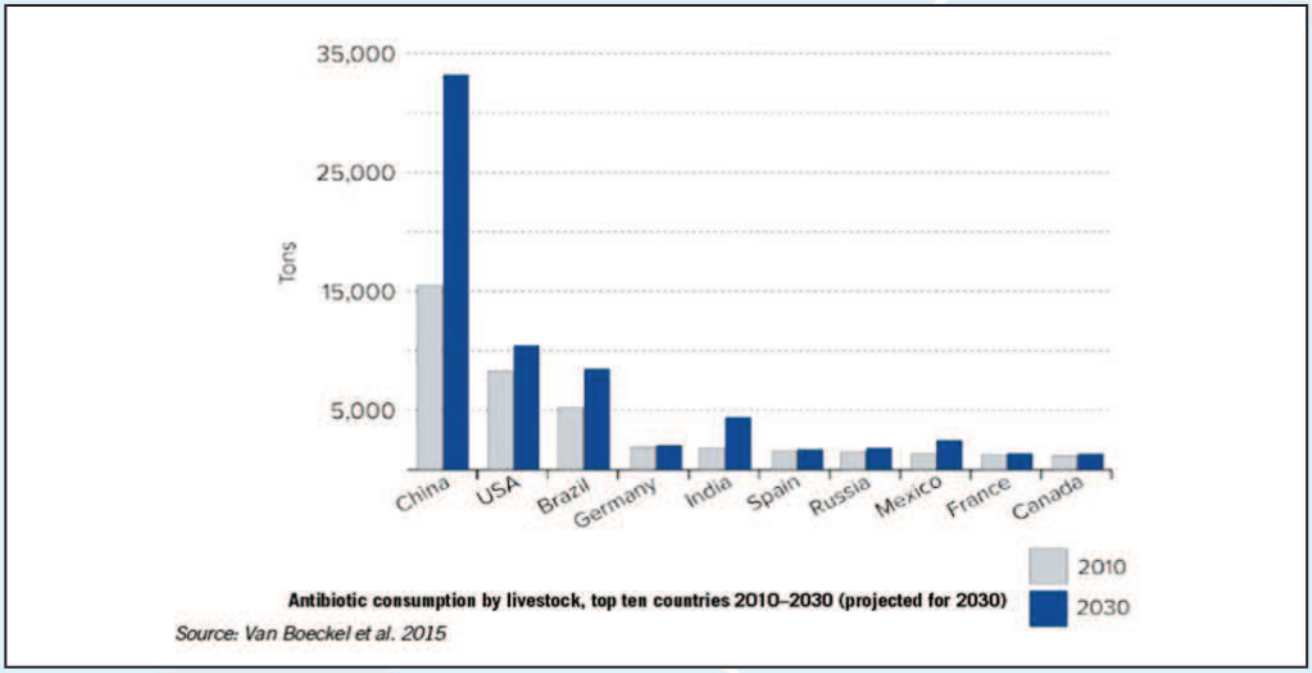
Technical Bulletin

NOVEMBER , 2016

ANTIBIOTICS IN FOOD: A global Concern

The discovery of antimicrobials is one of the most significant achievements of modern medicine and has substantially contributed to a reduction in the burden of common infectious diseases of humans and livestock globally.

The term “antibiotic growth promoter” is used to describe any medicine that destroys or inhibits bacteria and is administered at a low, sub-therapeutic dose. According to the National Office of Animal Health (NOAH, 2001), antibiotic growth promoters are used to “help growing animals, digest their food more efficiently, get maximum benefit from it and allow them to develop into strong and healthy individuals”. The use of antibiotics for growth promotion has arisen with the intensification of livestock farming. Infectious agents reduce the yield of farmed food animals and, to control these, continous administration of sub-therapeutic antibiotics and antimicrobial agents has been shown to be effective.



Antibiotic consumption by livestock, top ten countries 2010–2030 (projected for 2030)

Source: Van Boeckel et al. 2015

However, the widespread use of antimicrobials in human medicine and livestock farming has created selection pressure and fostered the emergence and spread of antimicrobial resistant pathogens worldwide. Resistant microbes and resistant genes can circulate between humans, animals, food, water and the environment. Since many antimicrobials commonly used in livestock are the same as or similar to antimicrobials used in human medicine, there is global concern that drug-resistant organisms may present a serious threat to public health. This phenomenon has already started occurring in our hospitals, where compromised patients and over-use of antibiotics create an optimal environment for promoting resistance in susceptible strains of bacteria.

Two years ago, independent studies by the Centre for Science and Environment (CSE), New Delhi, reported high level of antibiotic residues in chicken meat samples collected from various outlets in Delhi and the national capital region. This report brought lot of media attention and public debate at that time.

Recently, Dr Vinod Paul, Chief of Pediatrics at the All India Institute of Medical Sciences (AIIMS), New Delhi, who along with his team has been working on models to prevent hospital acquired infections soon after birth and rapid diagnostics was quoted saying "We are now staring at the overwhelming evidence of rampant antibiotic resistance, across all ages, all over the country. This worrying epidemic like situation is a result of overuse of antibiotics in humans, agriculture and livestock."

Ban on use of AGPs in livestock farming: Global Status

The use of antibiotics in animal feeds has been prevalent for about 60 years in the United States and other countries. The United States Food and Drug Administration (FDA) approved the use of antimicrobials as feed additives without veterinary prescription in 1951 (Jones and Ricke, 2003). In the 1950s and 1960s, each European state approved the use of antimicrobials in animal feed in its own national regulations.

In Australia a range of growth promoters are employed. Pig farmers use arsenical compounds,

THE HINDU

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TODAY'S PAPER

NEW DELHI, September 16, 2016

Babies fall victim to antibiotic resistance

VIDYA KRISHNAN

Major Delhi study identifies superbugsbehind untreatable sepsis, pneumonia

A PUBLIC HEALTH SCARE

DeNIS study looked at 13,530 infants in ICUs

- Multi-drug resistance to Acinetobacter was found in 82 per cent of the newborns
- Resistance to Klebsiella was found in 54 per cent and E. coli in 38 per cent
- 56,524 newborns in India die each year from microbial resistant bacteria
- Three 'superbugs' (pic) were linked with more than half the infections in the infants

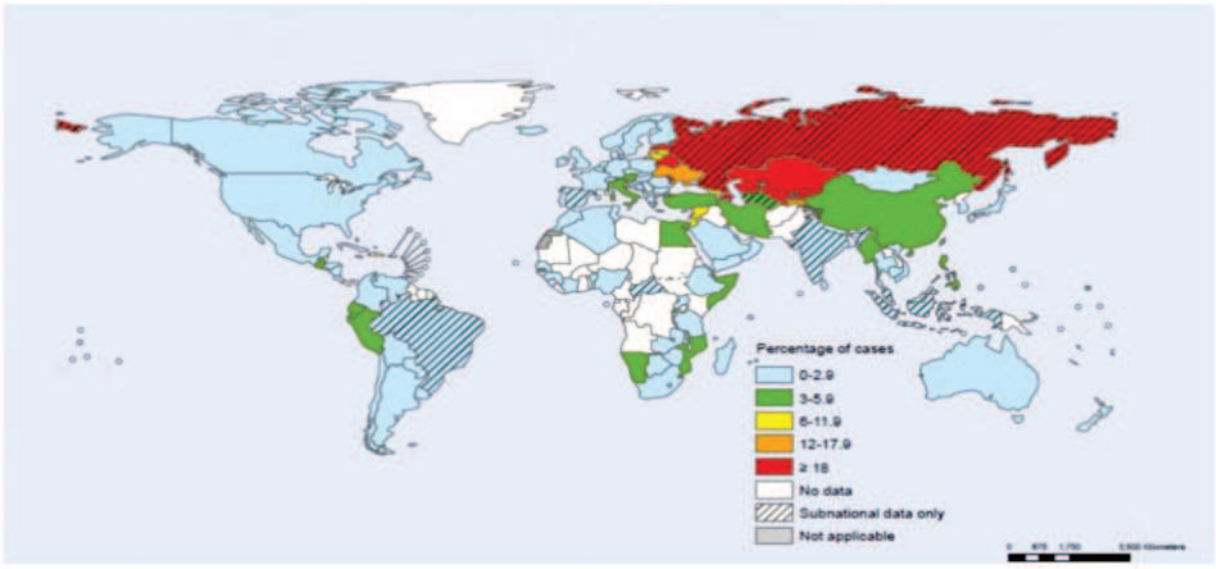
Klebsiella Acinetobacter E. coli

Source: Lancet Delhi Neonatal Infection Study

Infected with 'superbugs' in birth facilities within 72 hours of being born, thousands of Indian babies are dying due to an 'alarming degree' of drug resistance, a major study has found. The researchers found that nearly 26 per cent of babies with sepsis died, as multi-drug resistance made the ailment untreatable.

The findings, published in the journal *The Lancet* , said that despite early detection and appropriate medical attention, neonates with sepsis and pneumonia (both common ailments in newborns) died, because none of the drugs worked. The lead author of the study, Dr. Vinod Paul, chief of pediatrics at the All India Institute of Medical Sciences (AIIMS), said this was a manifestation of drug resistant bacteria in the Indian population. Dr. Paul's team is working on models to prevent hospital-acquired infections soon after birth, and rapid diagnostics.

Cases of drug resistant microbes are on the rise around the world, especially bacteria resistant to antibiotics. This map of WHO (April, 2014) shows the proportion of cases of Tuberculosis that are resistant to multiple drugs



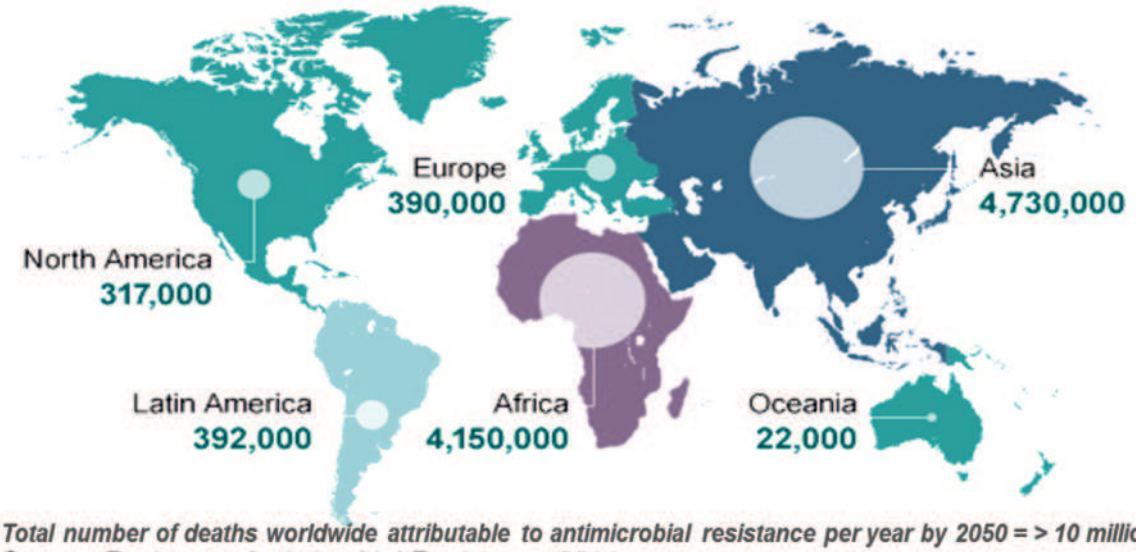
Numbers are based on the most recent year for which data have been reported, which varies among countries.

flavophospholipol, the macrolides kitasamycin and tylosin, the quinoxaline olaquindox, and also virginiamycin, a streptogramin. Poultry producers use arsenical compounds, flavophospholipol, bacitracin and virginiamycin. Australian cattle farmers employ a range of ionophores, namely lasalocid, monensin, narasin and salinomycin. They also employ flavophospholipol and the macrolide oleandomycin. The glycopeptide avoparcin is still used in pig and poultry farming and in rearing cattle in Australia.

USA uses a wide range of antibiotics, including some considered to be "medically important". Pigs are exposed to the greatest range of growth promoters. Though the figure is based on incomplete data, an estimated 80% of all antibiotics consumed in USA are used in food animals (U.S. FDA, 2010). In the USA, for example, pigs are exposed to B-lactam antibiotics, including penicillins, lincosamides and macrolides, including erythromycin and tetracyclines. All these groups have members that are used to treat infections in humans. Pigs in the USA are exposed to a range of other compounds intended for growth promotion. These include bacitracin, flavophospholipol, pleuromutilins, quinoxalines, virginiamycin and arsenical compounds. In the USA, compounds used as growth promoters for cattle include flavophospholipol and virginiamycin, both also used as growth promoters in poultry. Cattle are also exposed to ionophores such as monensin to promote growth. Poultry are given arsenical compounds.

The cattle industry in the USA is, perhaps, the most dependent on growth promoters as cattle have energy requirements that are high and that cannot be met easily without the use of growth promoters. High energy rations increase muscle growth and fat deposition in beef cattle, and help to improve milk productivity in dairy cattle. Unfortunately, the use of such rations is associated with side-effects, such as bloat and lactic acidosis, which can be debilitating or even fatal. These conditions are not a problem in Europe, where cattle diets contain more forage. To counteract this, monensin is used and, in addition to preventing the aforementioned conditions, it also significantly reduces ammonia and methane emissions (Mbanzamihigo et al.,

Deaths attributable to antimicrobial resistance every year by 2050

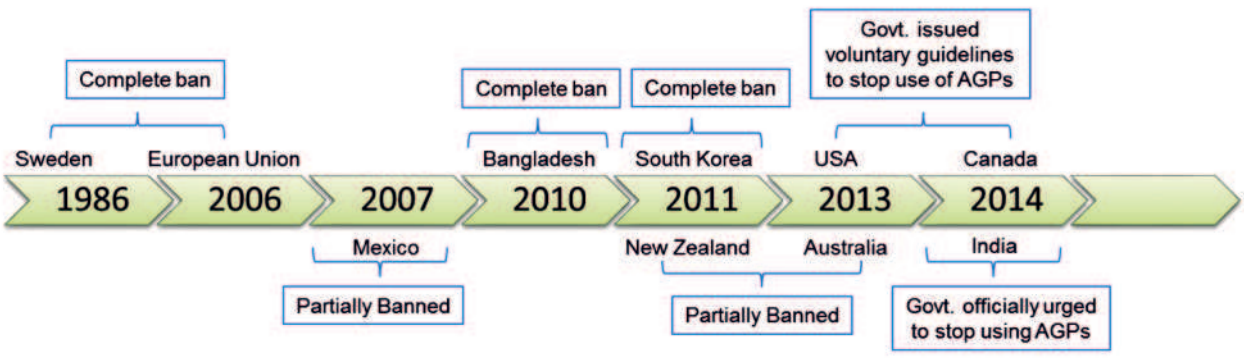


Total number of deaths worldwide attributable to antimicrobial resistance per year by 2050 = > 10 million
Source: Review on Antimicrobial Resistance 2014
(Jim O'Neill)

1995). It does not belong to a class of medically important antibiotics and is not associated with any major resistance problems.

About 20 years ago, the use of feed antibiotics and some other antimicrobial compounds used as performance enhancers became the target of increasing public criticism and political controversy (particularly in the EU countries). Sweden was the first state to prohibit the use of antibiotic additives in feed and its ingredients in 1986. Avoparcin was banned in Denmark in 1995 and Germany in 1996 arguing that this glycopeptide antibiotic produces resistance to glycopeptides used in human medicine (Castanon, 2007). These different national restrictions led to the EU Regulation No. 1831/2003 on additives for use in animal nutrition which stated that "antibiotics, other than coccidiostats and histomonostats, might be marketed and used as feed additives only until 31 December 2005; as from 1 January 2006, those substances shall be deleted from the Register" (European Union, 2003). In the United States, the use of AGPs was not banned, but the FDA recently issued voluntary guidelines for the industry to withdraw the use as growth promoters of medically important antibiotics (US Food and Drug Administration, 2013). In 2014, the Canadian government published a strategy mimicking the voluntary FDA approach on phasing out AGPs. Some OECD (Convention on the Organisation for Economic Co-operation and

Chronological development on AGP Ban



Regulation of antimicrobial use in livestock in OECD countries

OECD country	Legislative status of various countries in terms of antimicrobial usage in animal production	
	Ban on antimicrobial growth promoters	Prescription requirement to use antimicrobials in animals
Australia	No, but some AGPs are banned (fluoroquinolones, avoparcin, virginiamycin, etc.) (Australian Commission on safety and quality in health care, 2013).	Nearly all veterinary antimicrobials can only be sold on a veterinarian prescription.
Canada	No. The Canadian government issued in April 2014 a notice to stakeholders mimicking the FDA approach to voluntary phase out use of medically important antibiotics as growth promoters (Government of Canada, 2014).	No. Plan to develop options to strengthen the veterinary oversight of antimicrobial use in food animals in line with the FDA approach.
Chile	No data	No data
E.U. Member States	Yes. All AGP banned in 2006 (European Union, 2003).	Yes
Israel	No data	No data
Japan	No (Maron et al., 2013)	Yes
Mexico	Yes, AGP were banned in 2007 with some exceptions (avoparcin, vancomycin, bacitracin, tylosin, virginiamycin, etc.) (Maron et al., 2013).	Yes
New Zealand	Yes, for the critically and highly important antibiotics listed by both WHO and OIE (MAF New Zealand, 2011).	Yes for antibiotics identified with the potential for resistance problem.
South Korea	Yes, since 2011 the use AGP has been discontinued until a veterinary oversight system can be put in place (USDA, 2011)	Yes, the veterinary oversight system is currently being developed.
Turkey	No data	No data
United States	No. The FDA released voluntary guidelines for the industry to withdraw the use as growth promoters of medically important antibiotics (US Food and	No. Under the new FDA guidance for industry, use of medically important antibiotics will be under

Development) countries have a ban on AGPs (Mexico, South Korea, New Zealand), while AGPs are authorized in other countries (for instance Japan). AGPs are not banned in most of the non-OECD countries which are major meat (poultry, pig and cattle) producers, such as China, Brazil, Russia Federation, Argentina, Indonesia, Philippines, and South Africa.

In India, it has been stated in a letter (No. 102-74/2014) dated 3rd June, 2014 issued by the Department of Animal Husbandry, Dairying & Fishery, Ministry of Agriculture, that the State Governments and Union Territories are requested to advise the State Veterinarians, feed manufacturers and the persons involved in treating animals for judicious use of antibiotics and hormones for the treatment of ailing food producing animals. An awareness program at the consumer and farmer level may also be arranged. **At the same time use of antibiotics and hormones in animal feed should be stopped.** However Indian meat and poultry farmers are continuing the use of antibiotics even though authorities have urged them to stop the practice.

In Nepal, it is not banned, nor has the Government given any voluntary guidelines for the industry to withdraw the use of AGPs. In Bangladesh, it is banned officially through "Fish Feed And Animal Feed Act, 2010".

World's top restaurant chains committed to cut antibiotics

On February 25, Consumers International – a global federation of over 240 consumer groups – published a report entitled "Antibiotics Off The Menu". Specifically, the report says

- **McDonald's** has committed to sourcing chicken raised without the routine use of antibiotics important for human medicine in

the USA by 2017 and in Canada by 2018.

- **Subway** has made a strong time bound commitment that it will be sourcing antibiotic free chicken (2016), turkey (2019), beef (2025) and pork (2025) in the USA.

According to a report, in 2014, Chick-Fil-A of USA became the first quick-service restaurant chain to commit to a "100 percent raised-without-antibiotics" standard for poultry. Since then, several quick-service restaurant chains have followed suit. Tyson Foods Inc. announced in June 2007 that it would produce all of its retail Tyson brand chicken from birds raised without antibiotics. The company later on realized that the demand for poultry produced and labeled "raised without antibiotics" increased. Perdue, the third largest chicken producer in the USA and amongst the top ten in the world, announced in February 2016 that all of Perdue's value-added chicken products will soon be carrying the label "No Antibiotics Ever".

Worried about Antibiotics in Your Food and Antibiotic-Resistant Bacteria?

It is of utmost importance to preserve the efficacy of antimicrobials for future use. Medically important antibiotics must be prohibited from use in a growth promotional role as a matter of immediacy. The use of antibiotics should principally be the last resort rather than a substitute for these methods. Antibiotics are not needed to promote growth, but they are essential to treat infectious diseases and maintain animal health. In order to start a reformation of the Industry as a whole, it is essential that attitudes to the use of antibiotic growth promoters be changed. The use of antibiotics in feed for growth promotion has long been debated, but there has been a lot of research activity looking at possible alternative compounds. There is a huge potential for feed additives such as organic acids, probiotics, prebiotics, essential oils and other natural growth promoters to improve performance in poultry and swine, without inducing any drug resistance and without posing any challenge to food safety.

Their efficacy is primarily based on antimicrobial effects, their ability to influence the composition and overall concentration of intestinal microflora and support to the overall health of the digestive tract. Taking this into consideration, we can see how various new and some traditional feed additives claim to affect the health of the intestine and composition or activity of the intestinal microbiota. In recent years, some of those products have been described by the general term 'eubiotics', which is related to the Greek term 'eubiosis', referring to an optimal balance of microflora in the gastrointestinal tract. The main purpose of using such products is to maintain the eubiosis and general health of the tract, which will result in an improved health status and performance in farm animals.

Demand for meat and poultry products from animals and birds raised without any antibiotic growth promoter is steadily increasing. Irrespective of change in the current policy and regulatory framework of antibiotic usage, the consumer demand for such safer products along with an active and vociferous media is likely to drive the market in this direction sooner than one expects.

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