

ANTIBIOTIC USE IN POULTRY: CROSSROADS OF RESISTANCE, PUBLIC HEALTH, AND POLICY GAPS

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Article Received on
06 March 2025,

Revised on 27 March 2025,
Accepted on 16 April 2025

DOI: 10.20959/wjpr20259-36420



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ABSTRACT

In this paper explore about antibiotic impact on chicken, mechanism of antimicrobial resistance, antibiotic impact on poultry worker while using antibiotic in animal for therapeutic and non therapeutic, antibiotic impact on human through environment and animal food, antibiotic impact on children enter through the animal food and vegetables from infected soil and impact of antibiotic to cause cancer. Over the half century almost all known antibiotics are increasingly losing their activity against pathogenic microorganisms. In worldwide more than 60 % of all antibiotics that are used in animal production for both therapeutic (Prophylaxis) an non therapeutic (growth promoters) purposes. Furthermore, antibiotics are widely used to prevent bacterial diseases in plants also. Adequate cooking generally destroy the pathogenic bacteria in food, if hygiene measures are inadequate in food outlets, and it may be that such cross-contamination occurs with other bacteria as well, including resistant strains, but again there is no direct information. In particular, with overuse or prolonged exposure of main antibiotic classes associated with an excess of incident cancer.

Antibiotic impact on chicken

Poultry is defined as a group of domesticated birds raised for animal products (e. g., meat, eggs, manure), fiber (e. g., feathers), entertainment (e. g., racing, exhibition, hunting, etc.), or

work (e. g., messenger pigeons). Most poultry species encompass a few avian orders that include Galliformes (chickens, turkeys, quail, pheasants, grouse, guinea fowl), Anseriformes (ducks, geese, swans), and Columbiformes (pigeons and doves), and Ratites (ostriches, emus) The use of Antibiotics in Poultry production increases the selection pressure of antibiotic-resistant bacteria (Diarra and Malouin 2014). The antibiotics are used in the poultry industry for prevention and treatment of disease and also act as growth promoters. In all large poultry producing countries are permits usage of antibiotics in poultry industries. The antibiotic used in the poultry industry not only prevention of disease and it is also used to make them grow faster (WHO/CDS/CPE/ZFK/204.) The antibiotic which are used to growth promotion is compared to small amount as that of therapeutic use. However the one of the adverse effect of excessive use of antimicrobial drugs is that they get accumulated in the tissues and organs of treated animals as residues and eventually become part of the food pyramid [Oyarzapal. et. al, Goetting. V. et. al, Rokka. M et. al and Yunus. A. W. et. al] hence excessive usage has been recognized as illegal and prohibited by the food regulatory and health authorities (Oyarzapal. et. al, Rokka. M et. al, Seri. H. I. et. al).

The following diseases which is caused due to modern approaches apply to efficient chicken production, there are typhoid, mycotoxicosis, *E. coli* infections, coccidiosis, Salmonellosis, enteritis, ascites, Newcastle disease, Marek's disease, hydropericardium syndrome, and Gumboro disease (Yunus. A. W. et. al, Chapman. H. et. al, Bera. A. K. et. al). These diseases are not only causes poultry growth and production, but these are also affect considerably to the economic losses due to a high mortality among the flocks (Bera. A. K. et. al, Zakeri. B. et. al).

In developing countries, the use of antibiotics is quite common. The most commonly used antibiotics are: tetracycline (Filazi. A. et. al), gentamicin (Alheni. A. B. et. al), neomycin, tylosine, erythromycin (Sarkozy. G. et. al), virginiamycin, ceftiofur, and bacitracin which are usually helpful in the reduction and prevention of respiratory diseases and necrotic enteritis infections; flouroquinolones and/or quinolone compounds are used for treating gastroenteritis, skin, or soft tissue infections; (Soni. K. et. al, Kolaczek. et. al) sulfonamide compounds are administered as preventive and chemotherapeutic agents against coccidiosis, fowl typhoid, coryza, and pullorum disease; (Kolaczek. et. al, Beyene. T. et. al) while, piperazine, oxytetracycline, amoxicillin, amprolium, ciprofloxacin, and sulfa drugs are used

to treat coccidiosis (**Tags:** Antibiotic Residues in Chicken, CSE, Antibiotics in Chicken, Centre for Science and Environment (CSE), Antibiotics in Food Industry,).

Mechanisms for Antimicrobial Resistance Spread and Evolution

AMR bacteria are naturally found in the environment because many antibiotics are produced by other organisms such as fungus (e. g., penicillin) and soil bacteria (e. g., streptomycin, chloramphenicol, and tetracycline) (Banin. E. et. al).

Acquired bacterial resistance is caused by four general mechanisms including inactivation, target alteration, decreased permeability, and increased efflux [ibner. J. J. et. al]. First, target site changes typically occur from spontaneous mutation of a bacterial gene with selection pressure of antibiotics [Lambert. P. et. al]. Two examples consist of mutations in RNA polymerase and DNA gyrase which facilitate resistance in rifamycins and quinolones, respectively [Peterson. E. et. al]. Second, target alteration uses a strategy to make the antibiotic ineffective through enzymatic degradation, commonly occurring among aminoglycosides, chloramphenicol, and beta-lactams [Meria-Netos. et. al]. Third, Gram-negative bacteria can decrease permeability to selectively filter antibiotics from entering the cell membrane [Blair. J. M. et. al]. Fourth, efflux pumps function mainly to release toxic substances from the bacterium and many of these pumps can transport an extensive variety of compounds [Blair. J. M. et. al, Mageiros. L. et. al].

CSE study conducted in chicken sample for Growing antibiotic-resistance in humans also because of large-scale indiscriminate use of antibiotics in poultry industry

Indians are developing resistance to antibiotics — and hence falling prey to a host of otherwise curable ailments. Some of this resistance might be due to large-scale unregulated use of antibiotics in the poultry industry, says a new study released here today by Centre for Science and Environment (CSE), the New Delhi-based research and advocacy think-tank.

Releasing the findings of the study which has been conducted by CSE's Pollution Monitoring Laboratory (PML), Sunita Narain, director general, CSE, said: "Antibiotics are no more restricted to humans nor limited to treating diseases. The poultry industry, for instance, uses antibiotics as a growth promoter. Chickens are fed antibiotics so that they gain weight and grow faster. " The CSE lab study found residues of antibiotics in 40 per cent of the samples of chicken that were tested.

Speaking on the occasion, Chandra Bhushan, CSE's deputy director general and head of the lab, said: "Public health experts have long suspected that such rampant use of antibiotics in animals could be a reason for increasing antibiotic resistance in India. But the government has no data on the use of antibiotics in the country, let alone on the prevalence of antibiotic resistance. Our study proves the rampant use and also shows that this can be strongly linked to growing antibiotic resistance in humans in India."

CSE Study

- 70 chicken samples from Delhi-NCR region tested for six commonly used antibiotics.
- 40 per cent samples test positive; residues of more than one antibiotic found in 17 per cent samples.
- Points to large-scale unregulated use of antibiotics as growth promoters by the poultry industry.
- Antibiotics that are important to treat diseases in humans, like ciprofloxacin, being rampantly used by the industry. This is leading to increased cases of antibiotic resistance in India. For instance, ciprofloxacin resistance is growing rapidly in the country.
- India has no regulation on controlling antibiotic use in the poultry industry, or to control sales of antibiotics to the industry. It is free for all.
- India has not set any limits for antibiotic residues in chicken.
- India will have to implement a comprehensive set of regulations including banning of antibiotic use as growth promoters in the poultry industry. Not doing this will put lives of people at risk.

The test results

PML tested 70 samples of chicken in Delhi and NCR: 36 samples were picked from Delhi, 12 from Noida, eight from Gurgaon and seven each from Faridabad and Ghaziabad. Three tissues - muscle, liver and kidney were tested for the presence of six antibiotics widely used in poultry: oxytetracycline, chlortetracycline and doxycycline (class tetracyclines); enrofloxacin and ciprofloxacin (class fluoroquinolones) and neomycin, an aminoglycoside. This is the biggest study done in India to test residues of antibiotics in chicken.

Residues of five of the six antibiotics were found in all the three tissues of the chicken samples. They were in the range of 3.37-131.75 µg/kg. Of the 40 per cent samples found tainted with antibiotic residues, 22.9 per cent contained residues of only one antibiotic while the remaining 17.1 per cent samples had residues of more than one antibiotic. In one sample

purchased from Gurgaon, a cocktail of three antibiotics — oxytetracycline, doxycycline and enrofloxacin — was found. This indicates rampant use of multiple antibiotics in the poultry industry.

CSE has recommended the following to the government

1. Ban use of antibiotics as growth promoters and for mass disease prevention. Antibiotics critical for humans should not be allowed in the poultry industry.
2. Antibiotics should not be used as a feed additive; the government should regulate the poultry feed industry.
3. Unlicensed and unlabeled antibiotics should not be sold in the market.
4. The government should promote development of alternatives and good farm management practices.
5. Set standards for antibiotics in chicken products.
6. Set up systems for monitoring and surveillance of antibiotic use and antibiotic resistance in humans and animals.
7. Set pollution control standards for the poultry industry.

About Centre for Science and Environment and its Pollution Monitoring Lab

New Delhi-based Centre for Science and Environment (CSE) is one of the foremost research and advocacy bodies working in the South Asian region on issues of environment and development. CSE's Pollution Monitoring Lab has conducted some seminal studies on health and environment, and its work has had immense impact in driving policy as well as public opinion in India.

Antibiotic impact on Poultry workers

Poultry workers in the United States are 32 times more likely to carry *E. coli* bacteria resistant to the commonly used antibiotic, gentamicin, than others outside the poultry industry, according to a recent study conducted by researchers at the Johns Hopkins Bloomberg School of Public Health. While drug-resistant bacteria, such as *E. coli*, are common in the industrial broiler chicken environment, this is the first U. S. research to show exposure occurring at a high level among industrial poultry workers.

The study was conducted with poultry workers and community residents in the eastern shore regions of Maryland and Virginia, and it confirms similar studies in Europe showing that poultry farmers and workers are at risk of exposure to drug resistant *E. coli* bacteria. The

Maryland and Virginia regions on the Delmarva Peninsula are among the top broiler chicken producing regions in the U. S., producing more than 600 million chickens annually.

In the study, researchers conducted in-depth analyses of 49 study participants, 16 working within the poultry industry and 33 community residents. Stool samples from the participants were tested for resistance to the antimicrobials ampicillin, ciprofloxacin, ceftriazone, gentamicin and tetracycline. Findings showed that poultry workers had 32 times greater odds of being colonized with gentamicin-resistant *E. coli* than other members of the community.^[29]

An international team of scientists has determined how harmless *E. coli* gut bacteria in chickens can easily pick up the genes required to evolve to cause a life-threatening infection. Their study, published in *Nature Communications*, warns that such infections not only affect the poultry industry but could also potentially cross over to infect humans.

E. coli is a common bacterium that lives in the intestines of most animals, including humans. It is usually harmless when it stays in the gut, however it can become very dangerous if it invades the bloodstream, causing a systemic infection that can even lead to death.

Avian pathogenic *E. coli* (APEC) is most common infection in chickens reared for meat or eggs. It can lead to death in up to 20 per cent of cases and causes multi-million pound losses in the poultry industry. The problem is made worse by increasing antibiotic resistance and infections also pose a risk of causing disease in humans. (John Hopkins University. *et. al*).

Antibiotic impact on human

Current evidence indicates that **there is no direct impact of antibiotic residues in meat on human health**, but the risk of generating antibiotic-resistant bacteria in animals poses a potential risk to humans.

Much of the evidence relating to the potential for transfer of a resistance problem from animals to man comes from a consideration of the epidemiology of zoonoses, mainly salmonella and campylobacter infection, and of what have become known as ‘indicator organisms’—enterococci and *Escherichia coli*, which cause no disease in animals (the animal-pathogenic *E. coli* are excluded) but can cause disease in man and which might be zoonotic. The epidemiology of these diseases is far from simple since there are many possible sources other than food animals and many routes of transmission other than food of animal origin.

The important antibiotic-resistant strains in this context are the multiply antibiotic-resistant salmonellae, macrolide- or fluoroquinolone-resistant campylobacters, glycopeptide- or streptogramin-resistant enterococci and multiply antibiotic-resistant *E. coli*. In all cases, the hypothesis is that the food chain is the main means of transmission. The hypothesis is intuitively attractive, and there can be no doubt of the existence of a hazard, but neither of these considerations means that the hypothesis is correct or of universal significance.

Transfer of resistant bacteria from chicken to humans

It is well known that antibiotic-resistant bacteria that have been selected in chicken may contaminate meat derived from those animals and that such contamination also declines when the selecting antibiotics are not used. However, most of the studies of the food chain ignore the fact, already noted, that there are potential sources of resistant enterococci and Enterobacteriaceae other than farm animals given antibiotics. Humans themselves as well as other animals may be a source of resistant bacteria subsequently isolated from food animals, since commensals and pathogens (including resistant strains) can reach the general environment via sewage. [Harwood. V. J. et. al] Wild animals, especially rodents, and birds, especially gulls, can acquire these environmental contaminants and pass them on via their excreta to grazing land or to the foodstuffs of food animals. VRE have been found in wild rodents [Mallon. D. J. et. al, Devriese. L. A. et. al] and in pet animals. [Devriese. L. A. et. al] Vegetables may also be contaminated from sewage, especially in countries in which human faeces is used as a fertilizer. Multiply antibiotic-resistant *E. coli* strains were found to be widespread contaminants of market vegetables in London during the investigation of a community outbreak of *E. coli* O15 infection, although we failed to find the epidemic strain among them. Phillips. I. et. al, Riley. P. A. et. al], Fish farming involves the use of antibiotics (although this is diminishing in Europe), and fish as food may be contaminated with resistant bacteria. Furthermore, antibiotics are widely used to prevent bacterial diseases in plants: tetracyclines and aminoglycosides are used to protect fruit trees from fire blight. [Viaver. A. K. et. al] Streptogramin-resistant *E. faecium* have been isolated from bean sprouts from sources yet to be identified. [Bager. F. et. al 199 & 2002] Genetic engineering in plants involves the use of a variety of antibiotics including vancomycin. [Teixeira da silva. J. A. et. al] We are aware of no rigorous epidemiological studies of such potential reservoirs, and the assumption that they make negligible contributions to human enteric pathogen resistance is unfounded.

Animals that carry, or in certain cases are infected by, resistant organisms are a hazard to those who work with them since the organisms can be transferred by direct contact. This is the probable explanation of the rare but well publicized finding of indistinguishable glycopeptide-resistant enterococci—for example, in the faeces of a Dutch turkey farmer and his flock, Van den Bogerd. *et. al*] and of streptogramin-resistant *E. faecium* in the faeces of a Dutch chicken farmer and his chickens. [Jansen. L. B. *et. al*] Even in these cases, we cannot exclude the possibility that both animals and humans acquired the strains from a common source, or even that the organisms were transferred from man to his animals. The recent description of an outbreak in China of virulent but not antibiotic-resistant *E. faecium* infection in pigs and those in close contact with them seems too unusual for us to learn much about the epidemiology of ‘normal’ enterococci. [La, H-Z. *et. al*] Isolates of enterococci from human and animal faeces that have no evidence of close conventional epidemiological links are often different on molecular testing, depending on the sensitivity of the method used, although in these studies, indistinguishable strains have sometimes been found among human and animal faecal enterococci. [Descheemaeker. P. R. *et. al*, Hammerum. A. M. *et. al*, Simonsen. G. S. *et. al*, Roberdo. B. *et. al*, Manson. J. M. *et. al*] Recent work from Bruinsma *et al.* suggests that whereas human and pig faecal isolates of *E. faecium* have genetic similarities, those from poultry faeces are different. Others have not found such similarities, and clearly more work needs to be done.

It is generally accepted that adequate cooking destroys bacteria in food. No evidence indicates that antibiotic-resistant strains are more refractory to cooking than are the largely susceptible strains on which the original research was conducted. Although most of the work was done on salmonellae, we are aware of no specific investigation of antibiotic-resistant campylobacters or the ‘indicator organisms’ *E. coli* and enterococci. We must also assume that as with salmonellae, inadequate cooking fails to decontaminate food. We also know that salmonella cross-contamination between uncooked and cooked food may occur if hygiene measures are inadequate in food outlets, and it may be that such cross-contamination occurs with other bacteria as well, including resistant strains, but again there is no direct information. We know nothing of the degree, if any, of contamination of food on the plate just before its ingestion, by any of these organisms.

There is experimental evidence for host-species specificity among enterococci: ingestion of heavy inocula of strains from humans by animals [Qai Yumi. S. *et. al*] or of animal strains by

humans[Sorenson. *et. al*] does not result in their permanent establishment. In the experiment of Sørensen *et al.*, ingestion of pig or chicken strains resulted in their excretion for a very limited period of time: in only one experimental subject out of 12 was the same organism detected at 15 days after ingestion but in none thereafter. As already noted, enterococci from chickens do not closely resemble those in human faeces, although those from pigs may have similar molecular characteristics to those from humans, but this does not mean that humans acquire their faecal enterococci from pigs. However, on the basis of analyses of *vanX* variants on Tn1546 in *E. faecium* from chickens and pigs and humans, Jensen *et al.* [Jensen. L. B. *et. al*] argue that spread is indeed from animals to man and not vice versa. The frequency of inter-host-species spread of faecal enterococci remains unknown.

The same host–animal specificity appears to apply to *E. coli*: van den Bogaard *et al.* [Vanden bogard. *et. al.* 2001] give a good account of the history of the disagreement as to whether or not resistant *E. coli* from animals colonize and infect humans. In a study carried out by Parsonnet & Kass, women working in a chicken abattoir, when they developed urinary tract infections (UTI), rarely yielded isolates that resembled (in terms of antibiotic resistance patterns) those from the chicken carcasses unless the woman developing UTI had been treated with antibiotics. A recent study from the Netherlands reported that among three poultry and five farmer/slaughterer populations, the PFGE patterns of ciprofloxacin-resistant *E. coli* in the faecal flora were ‘quite heterogeneous’, but three farmers each had a faecal isolate of *E. coli* with PFGE patterns that were indistinguishable from those of some of the poultry isolates. [Vanden bogard. *et. al.* 1997] As with enterococci in farmers and their animals, it seems likely that transmission was not via animal-derived food.

Zoonoses such as salmonella and campylobacter infection, undoubtedly can reach humans via the food chain, but their immediate source may not be the animal faecal flora. In each case, reports of infection traced from a farm to a human non-epidemic infection are uncommon. Furthermore, campylobacter strains from chickens, their commonly assumed source for humans, are often genetically different from strains isolated from humans (see *Campylobacter* below).

The evidence that ‘indicator’ bacteria reach and persist in the human faecal flora via the food chain is increasingly contradictory. Although it may seem highly plausible that the VRE or streptogramin-resistant *E. faecium* found in animal faeces, on meat derived from them and in human faeces in non-hospitalized patients (the prevalence varying widely in part because of

differences in microbiological technique) are the same, (Parsonnet. et. al) the fact is that isolates from human faeces are usually different from those in animals (except occasionally in the case of the farmers mentioned above) and on food. [Van en bogerd. et. al, Jensen. L. B. et. al] Even when those who report studies claim that all these enterococci belong to the same pool of organisms, there is evidence of segregation in their results, although some authors have not commented on this. [Werner. G. et. al] As already noted, a recent study shows that chicken enterococci do indeed belong to a different pool from those of humans and pigs. [Bruinsman. N. et. al] Thus, in the absence of adequate conventional and molecular epidemiological studies, we are aware of no evidence of the extent to which resistant enterococci or *E. coli* from food animals are able to colonize the human intestinal tract.

Ian Phillips, Mark Casewell, Tony Cox, Brad De Groot, Christian Friis, Ron Jones, Charles Nightingale, Rodney Preston, John Waddell.

Antibiotic impact on Children

Infants and children are affected by transmission of [antibiotic-resistant, disease-causing pathogens] through the food supply, direct contact with animals, and environmental pathways. For most [food-borne] infections, incidence was highest among children younger than 5 years. And when antibiotics fail, these children are in a fight for their lives.

Children, who are especially vulnerable to pathogens, can be exposed to antibiotic-resistant bacteria through contact with raw meat or farm animals. Treat all meat as if it is contaminated: keep it away from kids, cook it thoroughly and avoid cross-contamination in the kitchen.

When shopping for meat, look for labels that confirm no antibiotics have been used on healthy animals. These labels include.

- USDA Certified Organic
- Certified Humane
- Animal Welfare Approved
- American Grassfed Association
- Food Alliance Certified – Grassfed
- Global Animal Partnership

Infants and children are affected by antibiotic-resistant bacteria in the food supply, direct contact with animals and exposure in the environment, the researchers report.

For most infections, incidence was highest among children under age five, according to data the researchers cited from Center for Disease Control and Prevention's Food borne Diseases Active Surveillance Network.

Parents and other consumers may also help discourage the use of antibiotics in livestock feed by choosing to buy only organic products or foods labeled as "raised without antibiotics," said Urvashi Rangan, executive director of the Consumer Reports Food Safety and Sustainability Center.

Impact on Antibiotic in chicken to cause cancer

Current there are no concrete scientific studies that establish the link to cancer. But it is important to pay attention to the quality of meat that we eat.

A systematic review and meta-analysis of observational studies to assess the association between antibiotic use and risk of cancer.

antibiotic use may be associated with an excess of incident cancer diagnoses and lymphomas, in particular, with overuse or prolonged exposure of main antibiotic classes (e. g., beta-lactams, cephalosporins and fluoroquinolones). These data derive from a large number of patients included in observational studies. (Fausto Petrelli. et. al]

CONCLUSION

Several bacterial species are the major causes of infections in Poultry. Most of these infections are linked to food borne outbreaks, live animal contact, poor hygiene an environmental exposure. With the increasing antimicrobial resistance, the pathogenicity and virulence of these organisms have increased and treatment options are reduced and also more expensive. Multidrug resistant bacteria have been found in poultry, poultry products, litter an fecal matter of birds and these pose a risk to both handler, consumers and thread to global and public health. The above information increase the calls of surveillance measure and monitoring of antibiotic usage in both animal husbandry and human throughout the world.

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