

Antibiotic resistance in human *Salmonella* isolates are related to animal strains

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Comment

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In my opinion, the conclusions given in the recent paper published on antimicrobial-resistant *Salmonella* in your *Journal* [1] are erroneous and opposite to what emerges from any objective analysis of the data. In contrast to their conclusions, there seems an obvious and clear association between antibiotic-resistant *Salmonella* isolates in animal and human ones.

Their major antibiotic resistance profiles were types 3, 4, 17, 20 and 24. These involved more than 4000 of their isolates and were clearly commonly found in both animals and humans. All had the same resistance phenotype in both humans and animals. Overall, more than 95 per cent of the human isolates were also found in animal isolates.

There are many methodological limitations in this paper. The most important is that they have selectively given similar weights to resistance phenotypes with just single isolates as to phenotypes containing hundreds of isolates or more. Importantly, other limitations are that it is based on data from only sick animals in Scotland. This means they were likely causing disease in animals (probably calves) and are unlikely to reflect what is being carried in other food animals asymptotically.

The authors early on appropriately acknowledge and reference papers that show *Salmonella* DT104 is predominantly spread to humans from food animals via foods. However, they then seem very ambivalent on this issue. The deleterious effects of the spread of non-typhoidal *Salmonella* isolates to people from food animals were established decades ago. In Britain, in the 1960s, hundreds of people were infected with antibiotic-resistant *Salmonella* from cattle with six deaths [2]. In Denmark, the vast majority of *Salmonella* infections are clearly linked to food animals mainly poultry and pigs [3].

By using only isolates from Scottish animals, the authors have assumed that nearly all *Salmonella* that infect people in Scotland have come from foods that are locally produced and hence captured by their sampling. This is clearly very unlikely.

Another bias is that their animal isolates predominantly came from cattle (80%). Only 20 per cent of meat consumed in Scotland is beef [4] and only 62 per cent of raw beef purchased in Scotland is of Scottish origin (and thus about 12% of meats consumed there). Thus, the vast majority of food animals that are the source of foods for people in Scotland (foods imported from England or elsewhere) were not sampled.

I believe that their abstract and conclusions are very misleading. They found 65 different resistant phenotypes, most of which were unique to humans and very few common to both animals and people. The numbers are presented in a manner that states that shared *Salmonella* isolates (i.e. humans and animals) were very few and only five phenotypes were likely derived from food animals (or less than 10%). This is then presented as the evidence that the problem of antimicrobial resistance in *Salmonella* isolates infecting people is much more to do with human antibiotic use and not associated with antibiotic use in animals.

It is inappropriate to look only at resistance phenotypes. Nowhere in the paper do they give the numbers of isolates with these different phenotypes. This is found only in the supplementary material of Mather *et al.* [1]. While there were large numbers of resistance profiles only seen in humans isolates (30), this mainly involved single isolates. Only two of these 30 ‘unique human’ profiles had more than three isolates. In contrast, their most common profile (profile ID 3) had 2192 animal isolates and 1934 human isolates. Overall, the 30 phenotypes on which they based their conclusions involved less than a few per cent of the total *Salmonella* isolates.

While it may be true that some resistant *Salmonella* phenotypes seen in people may not be associated with animals, these in absolute numbers are very small. Humans are more likely to be tested than animals when sick. Thus, having large numbers of different human resistance phenotypes, but for most of which there are only very small numbers, is meaningless if this is just used for comparisons. Many may also have been derived from food animals. However, as the authors did not sample many animals other than cattle and there was no testing of either imported or local foods, their sampling method would have missed many animal-derived but resistant *Salmonella* isolates.

The authors show many clear associations between animal isolates and human ones. They point out in their paper with fig. 3 that with nearly all the resistant phenotypes they studied were interconnected. In the electronic supplementary material, figure S1 there is a clear temporal association between number of DT104 seen in people and animals, with large and similar peaks from 1994 to 1996. Electronic supplementary material, figure S4 shows that for nearly all antimicrobials, when resistance was seen in isolates from people for the first time, it occurred at the same time in animals or was seen early in animals.

The overwhelming evidence around the world is that the spread of *Salmonella* is predominantly from food animals to

humans, in countries that have good water supplies. I think their data also strongly support that understanding.

Antibiotic resistance is rapidly rising in bacteria, both in people and in animals [5,6]. Many of these bacteria (e.g. *Salmonella* and *Escherichia coli*) spread to people via the food chain, and many are resistant to 'critically important antimicrobials' for humans [6,7]. The overuse and misuse of antibiotics in food animals, especially third-generation cephalosporins and fluoroquinolones, result in many multi-resistant bacteria developing and spreading in food animals and in the foods produced from these animals [8]. Bacteria such as resistant *E. coli* and *Salmonella* cause serious infections in people and cause more deaths and increased lengths of hospital stay when they are also antimicrobial resistant [9,10].

I think the conclusions by the authors will have misled some readers, and they, unfortunately, have already been misused by some [11] to try and obfuscate what is a clear link between animal use of antibiotics and serious infections caused by antibiotic-resistant bacteria in people.

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