

none (or few) have actual evidence of infection. Often this involves mass medication of large numbers of animals at the same time (e.g. an entire herd), a situation termed *metaphylaxis*. In some instances, such antibiotics are added to feed or water at low concentrations, a situation analogous to what often occurs with use for growth promotion.

Growth promotion: antibiotics are added to feed or water, usually at low concentrations, to increase growth rates or increase the efficiency of feed conversion into animal mass.

It is likely that much more than half of the total volume of antibiotics used in the world, are given to food animals (Van Boeckel *et al.*, 2015; JETACAR, 1999; FDA, 2014; FDA, 2012; CIPARS, 2013; DANMAP, 2014; EFSA and ECDC, 2015; ECDC *et al.*, 2015; UCUSA, 2004). The majority of use is for growth promotion and as mass prophylaxis, areas in which there is little current evidence for any major ongoing economic benefit for farmers or health benefits for food animals. The antibiotics are added to feed or water and are often given for the entire life of the food animals. This usage does not appear to help malnourished people achieve better protein intake (Collignon *et al.*, 2005).

Despite its importance, data regarding agricultural antibiotic usage remain limited. In the United States, Australia, Canada, Denmark, and other countries where some data are available on antibiotic usage, the proportion used in food animals may be as high as 80% of total volumes used (JETACAR, 1999; FDA, 2014; FDA, 2012; CIPARS, 2013; DANMAP, 2014; EFSA and ECDC, 2015; ECDC *et al.*, 2015). Estimates from developing countries are more difficult to obtain, but in China it appears that over half of all antibiotics used are in food animals. Usage volumes in humans and animals also appear to be much higher than in developed countries. This is likely to be similar to what happens in other rapidly developing countries with large populations, such as India, Vietnam, and Brazil. Usage in food animals is likely to escalate rapidly in the next decades and at a much more rapid rate than antimicrobial usage in people (Van Boeckel *et al.*, 2015; Collignon and Voss, 2015; Krishnasamy *et al.*, 2015; Zhang *et al.*, 2015).

Many classes of antibiotics used in food animals are the same as used in people. This includes groups classified as “critically important” for human use by the WHO (WHO, 2011; WHO, 2013; Collignon *et al.*, 2009). Although many antibiotics can be the same as those used in humans (e.g. ampicillin), others are in the same class but are not used in people. These agents often have unfamiliar names to medical workers but nevertheless are from similar drug classes as agents used in human health. For example, ceftiofur is a commonly used third-generation cephalosporin in animal production but in fact is very similar to ceftriaxone (see Chapter 27, Ceftriaxone). Similarly, tylosin is a high-volume usage macrolide administered only in animals, and avoparcin is a glycopeptide similar to vancomycin (see

Chapter 43, Vancomycin), which was used as an animal growth promoter.

Table 2.1 lists all the antibiotics and their classes that have been registered for use (or there is evidence for their use) in food animals and aquaculture in the United States, EU and Australia since 2000 (JETACAR, 1999; FDA, 2012; DANMAP, 2014; APVMA, 2014; ECDC, 2015). However, there is likely to be off-label use of other antibiotics not on this list. Many of these agents are critically important or last-line antibiotics (or compounds that are chemically similar to antibiotics) that are also used for serious human infections (WHO, 2011; WHO, 2013; Collignon *et al.*, 2009; Aarestrup *et al.*, 2008).

Antibiotics have been used since the 1950s as growth promoters in food animals, with the perceived benefit thought to be the result of altering the gut bacterial flora (particularly Gram-positive organisms). Some animals then achieve a larger weight gain over a set period of time and may consume less feed to achieve the same weight (JETACAR, 1999; Collignon *et al.*, 2005; Aarestrup *et al.*, 2008; Engster *et al.*, 2002). In most Scandinavian countries, all antibiotic use for growth promotion was banned 15 to 20 years ago. Sweden was the first to do so. Denmark followed in 1999. This ban followed a series of actions that started in May 1995 when Denmark banned the antimicrobial growth promoter avoparcin (WHO, 2003). This was in response to concerns that avoparcin use contributed to the creation of an animal reservoir of glycopeptide-resistant enterococci (vancomycin-resistant enterococci; VRE), which posed a potential risk to public health. In December 1997 the Commission of the European Union banned avoparcin in all EU member states. In December 1999 the Danish swine industry voluntarily stopped the use of all antimicrobial growth promoters in pigs under 35 kg (weaners). A subsequent detailed analysis by the WHO of the effects of this termination, showed no major economic or major deleterious health effects in food animals following this ban. There continues to be a substantial decrease in total antibiotic usage in food animals in Denmark, compared to the 1990s (DANMAP, 2014). Following the Scandinavian lead, The EU and its member states subsequently adopted a ban on the use of antibiotics as growth promoters (FAOSTAT, 2015).

Other studies have reported similar findings as the WHO’s in terms of the magnitude of the economic benefits attributed to antibiotic growth promoters. In some studies, very small or no benefits with antibiotics were observed; in some cases there were even negative economic effects (Engster *et al.*, 2002; Graham *et al.*, 2007). The largest benefits were observed in animals that were stressed, exposed to large doses of pathogenic bacteria or were raised under non-ideal conditions. The value to farmers or consumers does not appear to be very large—for instance, in chickens the calculated benefit in Australia was approximately 3 cents per chicken for the producer (JETACAR, 1999). In the United States, estimates (in 1981) of the likely increase in retail price if antibiotics were not used as growth promoters were 3 to 6 cents per pound for pork and 1.3 to 2.6 cents per pound for chickens (CAST,