of *tet*(X) are the older tetracyclines that are widely available without prescription in these communities.

The use of the third-generation tetracyclines such tigecycline in animals is not authorized, and it can be used only under exceptional circumstances in companion animals since *the Cascade* rule allows the use of human-approved drugs in certain situations (EMA 2013). The use of tigecycline in clinical medicine also remains limited because it is an antibiotic of last resort and reserved for treatment of infections that are not susceptible to other antibiotics (although its use is continuously increasing (Huttner et al. 2012)). The observed extensive dissemination of *tet*(X) in agriculture and low-income communities, however, is driven by other factors than the direct selection by glycylcyclines. Since the gene confers cross-resistance to tetracyclines of all generations, the most likely selective pressure for its widespread dissemination is the extensive use of older tetracyclines in agriculture and its unrestricted availability in low-income communities. Co-selection by other antimicrobials such as coccidiostats, arsenicals (and other heavy metals), and other antibiotics may also play a role in the dissemination.

Thus, the examples given above, which are derived from the history of tetracycline antibiotic use and the consequent emergence of resistance, allow us to synopsize some general concepts that are apparently applicable to other classes of antibiotics and the corresponding antibiotic resistance genes. These concepts could be applicable for designing the corresponding strategies to limit the spread of antibiotic resistance. But first we need to reveal the roles played by antibiotics in nature. This background evidence is crucial for understanding what is happening when the antibiotic producers are taken from the environmental context, optimized for a large-scale antibiotic production, and the resulting antibiotics are extensively used for the purposes unrelated to their role in nature.

23.13 Antibiotics and Antibiotic Resistance as Integral Parts of Microbial Diversity

The common perception of antibiotics, which is based on clinical practice of using them for clearing bacterial infectious agents, categorizes antibiotics as killing chemical compounds. In this role, antibiotics perfectly fit the idea of a weaponry used by some bacteria against others in competition for limited resources. These aspects have been studied in detail and resulted in characterization of almost all antibiotics for the MICs *in vitro* and their pharmacokinetic/pharmacodynamic (PK/PD) properties *in vivo*. The antibiotic concentrations in natural ecosystems are generally low, and they have been consistently measured only in few occasions involving the symbiotic relationships, with the antibiotic production by symbionts to defend their hosts from fungal pathogens