class, tetracyclines, and the corresponding resistance genes. This will help to perform comprehensive analysis and discussion of the antibiotic discovery and usage, the corresponding antibiotic resistance mechanisms that emerged, and evolutionary and ecological aspects of antibiotics/resistance mechanisms. The general concepts derived from these analyses would be apparently applicable to other classes of antibiotics and the corresponding antibiotic resistance genes.

23.4 First-Generation Tetracyclines: Discovery and Usage

Chlortetracycline (Aureomycin®) was the first antibiotic of this class discovered by the researchers at Lederle Laboratories Division of American Cyanamid Company (Duggar 1948). Another antibiotic of this class, oxytetracycline (Terramycin®), was discovered in a collaborative drug discovery project between Pfizer and Harvard University (Hochstein et al. 1953). But even before these discoveries, there are indications that tetracyclines have been used well before the modern antibiotic era (Bassett et al. 1980; Hummert and Van Gerven 1982; Cook et al. 1989; Nelson et al. 2010). The tetracycline traces have been found on several occasions as incorporated into human skeletal remains, presumably because of diet containing the biomass of antibiotic-producing strains.

The clinical evaluation of the newly discovered chlortetracycline was almost immediately examined for the treatment of various human infections, and it was found to be equal in potency to penicillin (Wright and Schreiber 1949). Since then tetracyclines have been extensively used in the therapy of many human infections due to their efficiency and low incidences of side effects.

Another property of chlortetracycline that has been discovered accidentally at Lederle Laboratories Division of American Cyanamid Company is the growth-promoting effects of Aureomycin on animals (Duggar 1948; Aminov 2017). Following the confirmation of this effect, the company started producing animal feed with this additive, and many other companies and countries worldwide followed this example. Since then the antibiotics of this class became the drugs of choice for the use in animal production. In the United States, for example, tetracyclines comprise a large proportion of all antibiotics used in food animals; the quantity sold to the industry in 2013 reached an astounding 6 514 779 kg of active ingredient (FDA 2015). Proportionally, tetracyclines accounted for 71% of all antibiotics sold for the use in food-producing animals in the United States. The main route of tetracycline consumption by the livestock is via medicated feed, which accounted for most domestic sales and distribution of medically important antimicrobials approved for the use in food-producing animals. Tetracyclines were also the leading antibiotics to be administered via drinking water (FDA 2015). In China tetracyclines are also