QUINOLONE ANTIMICROBIAL AGENTS 3rd Edition
CONTENTS

Contributors • vii
Preface • xi
Introduction • xiii

I. Mechanisms and Spectrum of Antibacterial Activity and Resistance

1. Structure-Activity Relationships of the Quinolone Antibacterials in the New Millennium: Some Things Change and Some Do Not • 3
John M. Domagala and Susan E. Hagen

2. Mechanisms of Quinolone Action • 19
Karl Drlica and David C. Hooper

3. Mechanisms of Quinolone Resistance • 41
David C. Hooper

4. Quinolones and Eukaryotic Topoisomerases • 69
Thomas D. Gootz and Neil Osheroff

5. Activity In Vitro of the Quinolones • 91
C. Thauvin-Eliopoulos and G. M. Eliopoulos

II. Pharmacology

6. Pharmacokinetics of Fluoroquinolones • 115
Michael N. Dudley

7. Drug-Drug Interactions • 133
Roula Qaqish and Ronald E. Polk

8. Pharmacodynamics of Quinolone Antimicrobial Agents • 147
William A. Craig and David R. Andes

III. Clinical Applications

9. Treatment of Urinary Tract Infections • 159
Kalpana Gupta, Kurt Naber, and Walter Stamm

10. Use of Quinolones for Treatment of Sexually Transmitted Diseases • 171
Rosanna W. Peeling and Allan R. Ronald

11. Treatment and Prophylaxis of Gastroenteritis • 193
Michael L. Bennish

12. Treatment of Intra-Abdominal Infections • 217
Joseph S. Solomkin

13. Treatment of Community-Acquired Respiratory Tract Infections • 227
Peter Ball and Lionel Mandell

14. Treatment of Infections of the Ears, Nose, and Throat and Nasal Carriage • 245
Jennifer Rubin Grandis and Victor L. Yu

15. Treatment of Osteomyelitis and Septic Arthritis • 251
Louis Bernard, Francis Waldvogel, and Daniel Lew

16. Treatment of Experimental and Human Bacterial Endocarditis with Quinolone Antimicrobial Agents • 259
Thuan P. Le, Michael R. Yeaman, and Arnold S. Bayer

17. Treatment of Bacterial Meningitis and Other Central Nervous Systems Infections • 275
Allan R. Tunkel and W. Michael Scheld
18. Treatment of Eye Infections • 291
   Michael H. Miller and Martin Mayers

19. Treatment of Skin and Soft Tissue Infections • 311
   Adolf W. Karchmer

20. Treatment of Intracellular Infections • 323
    Jean-Marc Rolain and Didier Raoult

21. Fluoroquinolones in Intensive Care Unit Infections • 337
    Ethan Rubinstein

22. Quinolones in Pediatrics • 343
    Faryal Ghaffar and George H. McCracken, Jr.

23. Quinolone Resistance and Its Clinical Relevance • 355
    Donald E. Low

24. Veterinary Use of Quinolones and Impact on Human Infections • 387
    Henrik C. Wegener and Jørgen Engberg

IV. Adverse and Other Effects

25. Adverse Effects • 407
    Hartmut Lode and Ethan Rubinstein

26. QT Prolongation with Quinolone Antimicrobial Agents • 421
    Yee Guan Yap and A. John Camm

27. Effects on Connective Tissue Structures • 441
    Ralf Stahlmann

28. Phototoxicity Due to Fluoroquinolones • 451
    James Ferguson

29. Central Nervous System Toxicity • 461
    S. Ragnar Norrby

30. Effects of Quinolones on the Immune System • 467
    Lowell S. Young

Index • 475
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The quinolone class of antimicrobial agents has emerged as one of the most widely used classes of antimicrobials in clinical medicine. For this reason, the first edition of *Quinolone Antimicrobial Agents* was organized to bring together in a single volume information about their chemistry, antimicrobial activity, pharmacology, and clinical uses. As their use and numbers increased, additional information was covered in the second edition. Now with the substantial amount of new information on these agents that has become available since the publication of the second edition of *Quinolone Antimicrobial Agents* in 1993, an expanded third edition has been organized in a single, convenient volume to include comprehensive coverage of current information on a larger number of compounds, their clinical applications, and the limitations to their use, including updates on the important and expanding data on bacterial resistance and profiles of adverse effects. Like the first and second editions, this edition is designed for use by clinicians, clinical microbiologists, pharmacologists, pharmacists, basic scientists, and others needing information about these drugs.

The third edition of *Quinolone Antimicrobial Agents* now includes 30 chapters organized into sections on mechanisms and spectrum of activity and resistance (5 chapters), pharmacology (3 chapters), clinical applications (16 chapters), and adverse and other effects (6 chapters). All chapters are either new or completely updated. The area of greatest expansion has been in the section on adverse and other effects because of the substantial body of new information in this area that has become available since the second edition.

We are grateful for all of the considerable efforts of the authors of the individual chapters and the assistance and patience of the editors at the American Society for Microbiology ASM Press. Particular thanks are due to our families for their patience, support, and inspiration during this project.

David C. Hooper
Ethan Rubinstein
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INTRODUCTION

The quinolones (also called fluoroquinolones, 4-quinolones, and quinolone carboxylic acids) are analogs of the earlier developed agent nalidixic acid. Although nalidixic acid is a related naphthyridone, this chemical group is now generally included within the quinolone class. Nalidixic acid, the first member of the class, was originally isolated by Lesher and associates (1) from a distillate during chloroquine synthesis and thus was a by-product of antimalarial research (2). Additional older analogs include oxolinic acid, pipemidic acid, and cinoxacin. These older or first-generation analogs are not considered further in this book, except for purposes of comparison with the newer agents.

The second generation of quinolones, about which we have considerable information, includes norfloxacin, ciprofloxacin, ofloxacin, enoxacin, and pefloxacin. These agents are substantially more potent in vitro and have broader antibacterial spectra than nalidixic acid but maintain the favorable property of being absorbed after oral administration. Additional advantageous pharmacologic properties include relatively long half-lives due to slow of elimination that allow twice-daily dosing, excellent distribution into many tissues and body fluids, and penetration into human cells, resulting in antimicrobial activity in so called “sanctuaries” as well as against some intracellular pathogens. Although differences in spectra of activity exist, this generation of quinolones in general exhibits striking potency against enteric gram-negative bacilli; additional lesser activity against nonenteric, gram-negative bacilli and some staphylococci; and generally marginal activity against streptococci and anaerobes.

The third generation of quinolones that followed maintained many of the favorable properties of the second generation and added increases in potency against gram-positive bacteria and, in some cases, against anaerobes and mycobacteria and in many cases also added longer half-lives of elimination that supported once-daily dosing. A few compounds in the second generation (e.g., lomefloxacin and fleroxacin) also had long half-lives and once-daily dosing, and others (e.g., sparfloxacin, and tosfloxacin) had enhancements of activity against gram-positive and anaerobic bacteria, but none became widely used in the United States and in Europe. The earliest of the third third-generation compounds was temafloxacin, and later in succession levofloxacin, trovafloxacin, gatifloxacin, and moxifloxacin became members of this group.

In general, the tolerability of many of the marketed quinolones has been good and comparable to that of other commonly used classes of antimicrobials, and with many of the second-generation agents and some of the third-generation agents have been given to millions of patients. Some adverse effects related to particular structural properties were recognized among second-generation agents, e.g., the photosensitivity caused by lomefloxacin and sparfloxacin due to a halide substituent at position 8, were recognized. Other adverse effects were unexpected and incompletely recognized until after drug release, e.g., a hemolytic uremic syndrome with temafloxacin and severe hepatotoxicity with trovafloxacin, were unexpected and incompletely recognized until after drug release, resulting in part because of the rarity of their occurrence. The mechanisms of some of these rare reactions are still incompletely understood, and thus the tolerability of each member of the quinolone class must be considered individually.

The information provided in the third edition of Quinolone Antimicrobial Agents is organized into sections on mechanisms and spectrum of activity and resistance (5 chapters), pharmacology (3 chapters),
clinical applications (16 chapters), and adverse and other effects (6 chapters). All chapters are either new or completely updated. The area of greatest expansion has been in the section on adverse and other effects because of the substantial body of new information in this area that has become available since the second edition.

REFERENCES


INDEX

Absorption of fluoroquinolones
  drug interactions involving, 133–138
  factors influencing, 115–116, 118
  mechanisms of, 115
Acinetobacter
  in CNS infections, 282–284
  in intensive care unit infections, 340–341
  in vitro activity against, 93
AcrAB-TolC pump, 52–53
Actinobacillus actinomycetemcomitans, 268
Activity, antimicrobial. See also Pharmacodynamics, specific drugs
  animal studies, 148, 149–151
  human studies, 148, 151–152
  time course, 147–148
  in vivo studies, 148
Acute renal failure, 412
Acute tubular necrosis, 412
Adherence, effect on, 468
Adverse effects
  allergic reactions, 413–414
  bone marrow, 409–410
  candidiasis, 416
  central nervous system, 461–464
  connective tissue, 441–447
  drug withdrawals due to, 408
  frequency of, 407–409
  hepatic, 412–413
  immune system, 410–411
  laboratory test abnormalities, 413
  most common, list of, 407–408
  ocular toxicity, 304–305
  in pediatrics, 345–346
  phototoxicity, 451–458
  in pregnancy, 414
  QT interval prolongation, 421–436
  renal, 411–412
  acute renal failure, 412
  acute tubular necrosis, 412
  allergic interstitial nephritis, 411
  crystalluria, 412
  granulomatous interstitial nephritis, 411–412
  interstitial nephritis, 411
  temafloxacin syndrome, 412
  structure of drug, relationship to, 407, 408
  structure relationship to, 3–13
Aeromonas, 205
AIDS patients, fluoroquinolone pharmacokinetics in, 126
Allergic interstitial nephritis, 411
Allergic reactions, 413–414
Amifloxacin, 260, 261, 262, 265–266
Anaerobes. See also specific species
  resistance to quinolones, 222–223
  in vitro activity against, 99, 100
Animals, use in, 387–399
  in cattle, 389
  in companion animals, 390
  in fish, 390
  indications for use, 389
  in poultry, 389–390
  proprietary quinolones licensed for animal use, 388
  resistance in zoonotic bacteria, 392–396
Campylobacter, 395–396, 397–399
  control measures, 399
Escherichia coli, 396
  human quinolone use and, 398–399
Salmonella, 393–394, 396–397, 398
  transfer to humans, 396–398
resistance of animal pathogens, 390–392
Campylobacter, 391
Escherichia coli, 390
  mechanism of, 392
mycoplasmas, 392
Pasteurellaceae, 392
Salmonella, 390
  staphylococci, 391–392
  streptococci, 391–392
  in swine, 389
Antacids, effect on fluoroquinolone absorption, 133–137
Antimalarials, QT interval prolongation from, 430
Antineoplastic drugs, topoisomerase II-targeted, 72
Antiparasitic activity of fluoroquinolones, 82–83
Antitumor activity of fluoroquinolones, 82
Arthritis, septic, 251–258
Arthropyathy, 196, 442–443, 445–446
AUC (area under the curve)/MIC ratio, 148–153
Azole antifungals, QT interval prolongation from, 430
Bacillus anthracis
  in skin and soft tissue infections, 318
  in vitro activity against, 99
Bacillus cereus
  in CNS infections, 282
  in eye infections, 303, 305
Bacillus subtilis, resistance in, 50, 56, 57
Bacteremia, in intensive care unit infections, 340
Bacterial vaginosis, 186-187
Bactericidal action of quinolones, 31-34, 103
Bacteriostatic action of quinolones, 24-31
Bacteroides fragilis
intra-abdominal infections, 217, 219-223
resistance in, 42-43, 44, 56, 222-223
in skin and soft tissue infections, 311, 314-315
in vitro activity against, 99
Bacteroides thetaiotaomicron, resistance in, 50, 56
Balofloxacin
allergic reactions, 414
for eye infections, 297-298
structure, 11
Bartonella
treatment for intracellular pathogens, 329-330
in vitro activity against, 102
Bay 3118
adverse effects, 407, 408
photosensitivity from, 455-458
structure, 453
Benzodiazepines, drug interactions with, 141-142
Binding sites, quinolone, 26-28
Bit efflux system, 57
Bmr efflux system, 57
Bone infections. See also Osteomyelitis
in pediatrics, 347-348
Bone marrow, adverse effects on, 409-410
Bordetella pertussis, 96
Borrelia burgdorferi, 101-102
Bronchitis
acute, 235
chronic, acute exacerbation of, 235-238
cost, 238
severe, 237
third-generation quinolones for, 236
treatment duration and response, 236-237
Brucella, 268, 329
Campylobacter fetus, 42
Campylobacter jejuni
gastrointestinal infections, 197, 201-202
resistance in, 42, 44, 55, 194, 196-197, 201-202, 348,
367-369, 391, 395-396, 397-399
clinical relevance, 368
drivers of resistance, 367
prevalence of resistance, 367-368
in vitro activity against, 95
Candidiasis, after antibiotic treatment, 416
Cardiototoxicity
QT interval prolongation, 421-436
as a quinolone class effect, 424-426
Cardiovascular hemodynamic responses, 470
Cartilage, effects on, 196, 441-443, 445-446
in pediatrics, 345-346
Central nervous system (CNS) infections
brain abscess, 284-285
carriage of meningococcus, prophylaxis for, 285
cerebrospinal fluid penetration of fluoroquinolones,
277-280
efficacy of fluoroquinolones
in animal models, 280-282
in humans, 282-285
meningitis
efficacy of fluoroquinolones in, 282-284
epidemiology and etiology, 275-276
in vitro activity of fluoroquinolones, 276-277
in pediatrics, 349
pharmacodynamics, 280
Central nervous system (CNS) toxicity, 461-463
Cerebrospinal fluid, distribution into, 120
Cervicitis, 182
Chancroid (Haemophilus ducreyi), 183-184
Children. See Pediatrics
Chlamydia pneumoniae
bronchitis, treatment for, 235
intracellular pathogens, treatment for, 328-329
in vitro activity against, 96
Chlamydia psittaci
treatment for intracellular pathogens, 328-329
in vitro activity against, 96
Chlamydia trachomatis
resistance in, 43, 46, 361
treatment of infection, 173-176
clinical studies, 175-176
intracellular pathogens, 328-329
microbiological studies, 174-175
in vitro activity against, 96, 101, 174
Cholesteatoma, 246-247
Ciprofloxacin
adverse effects, 409-413, 428, 443-447, 462
allergic reactions, 414
for CNS infections, 276-279, 281-286
drug interactions, 136-143
for ear diseases, 245-247
for endocarditis, 260-264, 266-269
for eradication of nasal carriage of bacteria, 248
for eye infections, 291-305
for gastrointestinal infections, 194, 196-208
immune effects of, 469
for intensive care unit infections, 337-341
for intra-abdominal infections, 219-221
pharmacodynamics, 148, 151-153
pharmacokinetics, 115, 117-120, 122-128
photosensitivity from, 452, 455, 458
in pregnancy, 415, 416
for respiratory tract infections, 232-233, 235-238
for skin and soft tissue infections, 312-318
structure, 24, 116, 453
Citrobacter diversus, 283-284
Citrobacter freundii, resistance in, 42, 44, 48, 55
Clinafloxacin
adverse effects, 407, 408, 410, 462
for CNS infections, 277, 282
drug interactions, 139, 140, 141, 142
immune effects of, 469
for intensive care unit infections, 341
for intra-abdominal infections, 221–222
pharmacokinetics, 117, 119, 126
photosensitivity from, 455, 458
for skin and soft tissue infections, 312–313, 316
structure, 24, 116, 453
Clostridium difficile
resistance in, 43, 45
treatment of pseudomembranous colitis, 341
in vitro activity against, 99
Clozapine, drug interactions with, 143
Colitis, pseudomembranous, 341
Colonization, effect on, 468
Combinations of antimicrobials, 104–105
Community-acquired pneumonia (CAP), treatment of,
227–234
Conjunctivitis, 291
Connective tissue, effects on, 441–447
clinical data, 445–447
arthropathy, 445–446
tendinopathy, 446–447
experimental data, 441–445
epiphyseal growth plate, 443
joint cartilage, 442–443
mechanism, 441–442
pharmacokinetics, 442
tendons, 443–444
Corynebacterium, in vitro activity against, 99
Coxiella burnetii
in endocarditis, 266–267, 269
treatment for intracellular pathogens, 328
Crystalluria, 410
Cyclosporine, drug interactions with, 142
Cystic fibrosis, 124–125, 346–347
Cystitis, 161–162
Deasquin, 414
Desfluoroquinolones, pharmacodynamics of, 149, 150
Diabetic foot infections, 317
Diarrhea, 193–208
empiric therapy, 197–200
traveler's, 197–200
Aeromonas, 205
Campylobacter jejuni, 201–202
Escherichia coli, 202
Plesiomonas shigelloides, 205
prophylaxis, 201
Salmonella, 204–205, 206–207
Shigella, 203
treatment, 200–201
Vibrio cholerae, 202–203
Yersinia enterocolitica, 205
Difloxacin
for endocarditis, 260, 262, 265–266
structure, 4
Distribution of fluoroquinolones
in cerebrospinal fluid, 120
methods for describing, 118–119
in normal versus infected tissue, 119–120
in ocular tissues, 120
protein binding, 118
DNA gyrase, 21–34
description, 21–22
quinolone action on, 23–34
topoisoromerase II compared, 69
DNA synthesis, inhibition of, 29–30, 32–34
DNA topoisoromases, 19–24
bacteriostatic action of quinolones and, 24–31
gyrase, 21–34
lethal action of quinolones and, 31–34
targets, fluoroquinolone, 22–24
topoisoromerase I, 20, 74
topoisoromerase II
antineoplastic drugs, 72
bacterial DNA gyrase compared, 69
catalytic cycle, 70–71
evolutionary conservation of quinolone interaction
domain, 78–79
isoforms of, 70
physiological roles, 70
quinolone effects on, 73–78
quinolone enhancement of DNA cleavage, 75–77
regulation, 70
topoisoromerase III, 21
topoisoromerase IV, 22–24, 25–26, 28–30, 32
Drug interactions, 133–143
CNS toxicity potentiated by, 462–463
involving absorption, 133–138
involving metabolism, 138–143
Ear disease
auricular perichondritis, 246
chronic, 246–247
malignant (necrotizing) external, 245–246
otitis media in pediatrics, 349
Efflux systems
in gram-negative bacteria, 50, 51–56
AcrAB-ToIC pump, 52–53
EmrAB and MdfA pumps, 53
Mex-Opr, 53–55
in gram-positive bacteria, 50, 56–58
Bmr and Blt, 57
NorA, 56–57
PmrA, 57–58
in mycobacteria, 58
Ehrlichia
treatment for intracellular pathogens, 328
in vitro activity against, 101
Elderly
adverse effects in, 408–409, 442
fluoroquinolone pharmacokinetics in, 125–126
urinary tract infections in, 164
EmrAB pump, 53
Enantiomeric forms, of fluoroquinolones, 116
Endocarditis, 259–270
efficacy of quinolones against
Coxiella burnetii, 266–267
Enterobacter, 264–265
enterococci, 266
Escherichia coli, 265
Pseudomonas aeruginosa, 263–264
Staphylococcus aureus, 260–262
Staphylococcus epidermidis, 262–263
viridans group streptococci, 265–266
tissue penetration of quinolones, 259–260
use of quinolones against
Coxiella burnetii, 269
Pseudomonas aeruginosa, 268
Staphylococcus aureus, 267–268

Endophthalmitis, 291–305
Endotoxin, 469–470
Enoxacin
adverse effects, 428
for CNS infections, 278, 285
drug interactions, 136, 139, 141, 142
for endocarditis, 262, 265
for eye infections, 296–297
pharmacokinetics, 115, 118, 119
for pharyngitis, 235
photosensitivity from, 452
in pregnancy, 415
structure, 6
Enteric fever. See Typhoid fever
Enteric pathogens. See also Gastrointestinal infections
resistance, 361–369
Enterobacter
in CNS infections, 283–284
in endocarditis, 264–265
in intensive care unit infections, 340
resistance in, 44, 48, 55
in vitro activity against, 93
Enterobacteriaceae
in intensive care unit infections, 337–340
osteomyelitis, 251–252, 254, 256
resistance in, 193–194
in skin and soft tissue infections, 312, 315
in vitro activity against, 91–93, 160
Enterococcus
in endocarditis, 266
in intensive care unit infections, 341
resistance in, 42, 45, 46, 47, 49, 50
in skin and soft tissue infections, 313
in vitro activity against, 98–99
Epididymitis, 186
Epiphyseal growth plate, effect on, 443
Escherichia coli
in CNS infections, 276, 278, 280–282, 284
in endocarditis, 265
in gastrointestinal infections, 197, 200, 202
in intensive care unit infections, 340
resistance in, 41, 42, 44, 47, 48, 50, 52, 58, 338, 369–372, 390, 396
Shiga toxin producing (STEC), 197, 200, 202
in vitro activity against, 91, 103
Excretion of fluoroquinolones, 121–122
Eye infections, treatment of, 291–305
ocular pharmacology, 292–295
outcome studies
in animals with endophthalmitis, 302–303
in animals with external eye disease, 301–302
in humans, 303
pharmacodynamics, 295–296
pharmacokinetics
with intravitreal administration, 298
with systemic administration, 297–298, 299
with topical administration, 296–297, 298
toxicity, ocular, 304–305

Fandofloxacin, 4
Febrile neutropenia, 347
Fleroxacin
adverse effects, 407, 462
allergic reactions, 414
for CNS infections, 278
for endocarditis, 260–261, 264
for eye infections, 294, 298, 301
for gastrointestinal infections, 200, 206
pharmacokinetics, 120, 124
photosensitivity from, 452
in pregnancy, 415
for skin and soft tissue infections, 316–317
structure, 116, 453
Fluoroquinolones. See also specific drugs
drug-drug interactions, 133–143
pharmacodynamics, 147–152
pharmacokinetics, 115–129, 133–143
phototoxicity due to, 451–458
structure–activity relationships, 6–8, 33–34
targets of action, 22–24
Francisella, 331
GABA receptors, quinolone interaction with, 462
Gardnerella vaginalis
treatment of infection, 187
in vitro activity against, 99
Garenoxacin
drug interactions, 143
for intensive care unit infections, 341
pharmacodynamics, 149
for skin and soft tissue infections, 312–314
structure, 8
Gastrointestinal infections, 193–208
diarrhea
empiric therapy, 197–200
traveler’s, 197–200
in pediatrics, 347–348
pharmacologic properties important in treatment of, 194–196
in vitro activity against pathogens, 94–95, 193–194
Gatifloxacin
adverse effects, 409, 413, 414, 416, 426–429
allergic reactions, 414
for CNS infections, 280, 282
drug interactions, 135, 136, 139, 142
for intensive care unit infections, 340
pharmacodynamics, 149, 150, 152, 153
pharmacokinetics, 117, 120–123, 125, 127–128
for respiratory tract infections, 228, 230–233
for skin and soft tissue infections, 312–314, 316
structure, 24, 116
Gemifloxacin
for CNS infections, 282
drug interactions, 135, 136, 139, 141
pharmacodynamics, 149, 150
pharmacokinetics, 118, 122
for respiratory tract infections, 227
for skin and soft tissue infections, 312–314
structure, 5, 9, 24, 116
Genital pathogens
sexually transmitted diseases (STDs), 171–187
in vitro activity against, 99–101
Genotoxicity, 80–82
Glyburide, drug interactions with, 142
Gonococcal infection, 176–182
clinical studies, 176–178
duration of treatment, 173
epidemiology of resistance, 178–179
mechanisms of resistance, 179–180
microbiological studies, 176
QRNG (quinolone-resistant Neisseria gonorrhoeae),
176, 179, 182
resistance in Neisseria gonorrhoeae, 44, 48, 56
clinical relevance, 361
drivers of resistance, 360
prevalence of resistance, 360–361
treatment of
keratoconjunctivitis, 304
pharyngitis, 234–235
sexually transmitted disease, 176–182
in vitro activity against pathogen, 99
Gram-positive infections, quinolones and, 471
Granulocyte-macrophage colony-stimulating factor
(GM-CSF), 411
Granuloma inguinale (Donovanosis), 184
Granulomatous interstitial nephritis, 411–412
Grepafloxacin
adverse effects, 345, 407–409, 416, 425, 427–429
allergic reactions, 414
for CNS infections, 276
drug interactions, 139, 141, 142
pharmacodynamics, 148
pharmacokinetics, 117, 119–127, 129
for respiratory tract infections, 230, 232, 236–237
structure, 6, 116
Group A β-hemolytic streptococcus (GABHS), 234
Gyrase. See DNA gyrase
Haemophilus ducreyi, 173, 183–184
clinical studies, 184
microbiological studies, 183–184
Haemophilus influenzae
bronchitis, treatment for, 236–237
in eye infections, 304
resistance in, 42, 44, 48, 359
in vitro activity against, 95
Helicobacter pylori
resistance in, 42, 44
in vitro activity against, 95
Hemolytic-uremic syndrome (HUS), 197, 200, 202
Hepatic disease, fluoroquinolone pharmacokinetics in,
127, 129
Hepatic system, adverse effects on, 412–413
Hyposxanthine-guanine phosphoribosyl transferase gene
(HGPRT) assay, 81
Immune system, effects on, 83, 467–472
adverse, 409–411
cytokine network, impact on, 469–470
experiments needed, 471–472
gram-positive infections, 471
intra-abdominal infections, 470–471
mechanism of, 467–469
In vitro activity, 91–105
anaerobic bacteria, 99, 100
assessment of, factors influencing, 102
Bartonella, 102
Borrelia burgdorferi, 101–102
Chlamydia trachomatis, 101
combinations of antimicrobials, 104–105
genital pathogens, 99–101
gram-negative bacteria, 91–96, 97
Enterobacteriaceae, 91–93
gastrointestinal pathogens, 94–95
Pseudomonas, 93–94
respiratory tract pathogens, 95–96
gram-positive bacteria, 96–99, 100
enterococci, 98–99
Listeria monocytogenes, 99
staphylococci, 96–98
streptococci, 98
mycobacteria, 101–102
mycoplasmas and ureaplasmas, 101
rickettsia, 101
Intensive care unit infections, 337–341
bacteremia, 340
overview, 337–339
pharmacokinetics/pharmacodynamics of fluoroquinolone use, 339
pseudomembranous colitis, 341
sinusitis, 341
urinary tract infections, 341
wound infections, 341
Interferon γ (IFN-γ) induction, 410, 469
Interleukin-2 (IL-2) induction, 410
Interstitial nephritis, 411
Intra-abdominal infections, 217–223
ciprofloxacin-metronidazole versus imipenem-cilastatin, 219
ciprofloxacin-metronidazole versus piperacillin-tazobactam, 220–221
clinofloxacin for, 221–222
clinical trials, 217–218
microbiology of community-acquired, 217, 218
outcomes of treatment, 219–220
pefloxacin-metronidazole versus gentamicin-metronidazole, 218
postoperative, use of quinolones in, 223
resistance by anaerobes to quinolones, 222–223
trovafloxacin for, 222

Intracellular pathogens, 323–332
activity of antibiotics, studies on
animal models, 326
cell culture models, 325–326
results of, 326–327
uptake and subcellular localization, 323–325
behavior of, 323
treatment for
Bartonella, 329–330
Brucella, 329
chlamydial diseases, 328–329
Coxiella burnetii, 328
Franciscella, 331
Legionella pneumophila, 331
rickettsia, 327–328
Salmonella, 330
Shigella, 330
Yersinia enterocolitica, 330–331

Joint infections
arthropathy, 196, 442–443, 445–446
in pediatrics, 347–348
septic arthritis, 251–258

Keratitis, 291–292

Klebsiella pneumoniae
in CNS infections, 276, 282–284
in intensive care unit infections, 338–340
pharmacodynamics of killing, 148, 150, 153
resistance in, 44, 48, 55, 58, 369–372
in vitro activity against, 91, 93, 103

Laboratory test abnormalities, 411

Legionella pneumophila, 234, 331

Levofloxacin
adverse effects, 409, 426
allergic reactions, 414
for CNS infections, 276–277
drug interactions, 135, 136, 137, 139, 141
for endocarditis, 269
for eye infections, 291, 294, 297–298, 300–302, 305
for intensive care unit infections, 338, 340
pharmacodynamics, 148, 151–153
pharmacokinetics, 116, 117, 118, 120–128
in pregnancy, 415
for respiratory tract infections, 227–233, 236–238
for skin and soft tissue infections, 312–314, 316
structure, 24, 116

Lipoteichoic acid, 471, 472

Listeria monocytogenes, 349
in CNS infections, 277, 280–281
in vitro activity against, 99

Lomefloxacin
adverse effects, 407
allergic reactions, 414
drug interactions, 136, 139
for eye infections, 302–304
pharmacodynamics, 148
pharmacokinetics, 118, 119, 122
photosensitivity from, 455, 457, 458
structure, 116, 453

Macrolides, QT interval prolongation from, 429–430

Mechanism of quinolone action, 19–34
bacteriostatic, 24–31
lethal, 31–34

Meningitis
efficacy of fluoroquinolones in, 282–250
epidemiology and etiology, 275–276
in vitro activity of fluoroquinolones, 276–277
Meningococcal carriage, prevention of, 248, 350

Metabolism
drug interactions involving, 138–143
of fluoroquinolones, 120–121

Methylxanthines, drug interactions with, 138

Mex-Opr efflux system, 53–55
MIC, 147–153. See also in vitro activity
Moraxella catarrhalis, 359

Morganella morganii, 282

Moxifloxacin
adverse effects, 409, 413–414, 425–429, 443
allergic reactions, 414
for CNS infections, 276, 281–282
drug interactions, 135, 136, 137, 139, 141
pharmacodynamics, 153
pharmacokinetics, 117, 119–123, 128, 129
for respiratory tract infections, 228, 230–233, 236–237
for skin and soft tissue infections, 312–314, 316
structure, 11, 12, 24, 116, 453

Mutation prevention concentration (MPC), 153

Mycobacteria
in pediatrics, 350
in vitro activity against, 101–102

Mycobacterium avium, blockage of adherence, 468

Mycobacterium leprae, 350

Mycobacterium smegmatis, resistance in, 43, 45, 50, 58

Mycobacterium tuberculosis
in pediatrics, 350
resistance in, 43, 45, 47, 48, 58
in vitro activity against, 101–102, 103

Mycoplasma hominis
resistance in, 392
in vitro activity against, 101, 182

Mycoplasma hominis, bronchitis, treatment for, 235
genital infections, 182–183
resistance in, 392
in vitro activity against, 101, 182

Mycoplasmas

Nalidixic acid
  adverse effects, 304, 410, 445
  for gastrointestinal infections, 193, 194, 203, 204–205
  resistant organisms, 205, 348
  structure, 453
Narcotics, drug interactions with, 142–143
Nasal carriage of bacteria, 248
Neisseria gonorrhoeae
  resistance in, 44, 48, 56
  clinical relevance, 361
  drivers of resistance, 360
  prevalence of resistance, 360–361
  treatment of
    keratoconjunctivitis, 304
    pharyngitis, 234–235
    sexually transmitted disease, 176–182
  in vitro activity against, 99
Neisseria meningitidis
  carriage of, 248, 350
  in CNS infections, 275–276, 280, 284–285
Nervous system toxicity, 461–464
Neutropenia, febrile, 347
NMDA receptors, quinolone interaction with, 462
Nonspecific urethritis, 182
Nonsteroidal anti-inflammatory drugs (NSAIDs), drug interactions with, 143
Nor A efflux system, 56–57
Norfloxacin
  adverse effects, 409, 410, 412, 443, 446
  allergic reactions, 414
  drug interactions, 136, 139, 141
  for eye infections, 291, 297–300, 304
  for gastrointestinal infections, 198, 200–201, 203–206
  pharmacokinetics, 119, 122
  photosensitivity from, 452
  in pregnancy, 414–415
  structure, 6, 24
Ocular pharmacology, 292–295. See also Eye infections, treatment of
Ocular tissue, distribution into, 120
Ofloxacin
  adverse effects, 409, 410, 412, 444–446
  allergic reactions, 414
  for CNS infections, 276–281
  drug interactions, 136, 139
  for endocarditis, 260–261, 264, 266–267, 269
  for eye infections, 291, 294–305
  for gastrointestinal infections, 194, 196, 199–200, 202, 204–208
  immune effects of, 469
  pharmacokinetics, 115–116, 118, 119, 120, 121, 122
  photosensitivity from, 452
  in pregnancy, 415, 416
  for respiratory tract infections, 236
  for skin and soft tissue infections, 314, 317
  structure, 11
Olamufloxacin, 10
Osteomyelitis, 251–256
  experimental, 252–255
  chronic osteomyelitis, 254
  clinical studies, 254
  comparative studies, 254–255
  concentration of quinolones in bone, 253–254
  diabetic osteomyelitis, 255
  fractures and, 253, 255
  models with presence of foreign implant, 253
  nonprospective and open studies, 254–255
  penetration of quinolones, 253
  rabbit model, 252
  rat model, 252–253
  microbial aspects of, 251
  overview of, 251
Otitis. See Ear disease
Pasteurellaceae, resistance in, 392
Pazufloxacin
  allergic reactions, 414
  structure, 11
Pediatric patients, fluoroquinolone pharmacokinetics in, 126–127
Pediatrics, quinolone use in, 343–350
  adverse effects, 345–346
  clinical uses, 346–350
    bone and joint infections, 347–348
    CNS infections, 349
    cystic fibrosis, 346–347
    febrile neutropenia, 347
    gastrointestinal infections, 196, 208, 347–348
    meningococcal carriage, prevention of, 350
    mycobacterial infections, 350
    otitis media, 349
    pneumococcal infections, resistant, 350
    urinary tract infections, 347
  pharmacokinetics, 344–345
  pharmacology, 344
  resistance, 343–344
  spectrum of activity, 343
Pefloxacin
  adverse effects, 409, 410, 412, 442, 444, 446
  allergic reactions, 414
  for CNS infections, 276–279, 281–283, 285
  drug interactions, 136, 139
  for endocarditis, 260–262, 264–269
  for eye infections, 295, 297–298, 300, 304
  for gastrointestinal infections, 206
  for intra-abdominal infections, 218
  pharmacodynamics, 149
  pharmacokinetics, 118, 119, 120–121, 122
  photosensitivity from, 452
  in pregnancy, 415
  structure, 116
Pelvic inflammatory disease (PID), 185–186
Pentamidine, QT interval prolongation from, 431
Pentavalent antimonials meglumine, QT interval prolongation from, 431
Persistent effects, 147–148
Pharmacodynamics, 147–153
   applications of, 153
   CNS infections, 280
   efficacy, requirements for, 148–152
   of eye infection treatment, 295–296
   of fluoroquinolone use for intensive care unit infections, 339
   resistance, emergence of, 152–153
   in respiratory tract infection, 228–229
   skin and soft tissue infections, 311–312
   time course, 147–148
   in urinary tract, 160
Pharmacokinetics
   absorption, 115–116, 118
   central nervous system, 461
   connective tissue, effects on, 442
   distribution, 118–120
   drug interactions, 133–143
   excretion, 121–122
   of eye infection treatment
      with intravitreal administration, 298
      with systemic administration, 297–298, 299
      with topical administration, 296–297, 298
   of fluoroquinolones, 115–129
   in intensive care unit infections, 339
   metabolism, 120–121
   in pediatrics, 344–345
   skin and soft tissue infections, 311–312
   in special populations, 122, 124–129
   summary table of, 117
   in urinary tract, 160–161
Pharyngotonsilitis, 247–248
Pharyngitis, 234–235
Phenytoin, drug interactions with, 142
Phototoxicity due to fluoroquinolones, 79–80, 451–458
   comparison of drugs, 458
   eye effects, 454
   human studies, 454–458
   laboratory studies, 454
   overview, 451–453
   in pediatrics, 345
   skin and soft tissue infections, 311–312
   in special populations, 122, 124–129
   summary table of, 117
   in urinary tract, 160–161
Phenytoin, drug interactions with, 142
Phototoxicity due to fluoroquinolones, 79–80, 451–458
   comparison of drugs, 458
   eye effects, 454
   human studies, 454–458
   laboratory studies, 454
   overview, 451–453
   in pediatrics, 345
   skin and soft tissue infections, 311–312
   in special populations, 122, 124–129
   summary table of, 117
   in urinary tract, 160–161
PID (pelvic inflammatory disease), 185–186
Pseudomonas shigelloides, 205
PmrA efflux system, 57–58
Pneumococcal infections, in pediatrics, 350
Pneumonia, community-acquired (CAP), 227–234
Postantibiotic effects, 147–148
Pregnancy, use in, 414
Prostatitis, 165–166
Protein binding, of fluoroquinolones, 118
Proteus vulgaris, resistance in, 55
Prulifloxacin, 414
Pseudomembranous colitis, 341
Pseudomonas aeruginosa
   in bone and joint infections, 348
   in CNS infections, 276, 278, 280–284
   in cystic fibrosis patients, 346
   in ear disease, 245–247
   in endocarditis, 263–264, 268
   in eye infections, 291–292, 301–305
   in intensive care unit infections, 337–340
   osteomyelitis, 251–256
   in otitis media, 349
   pharmacodynamics of killing, 148–149, 151, 153
   resistance in, 44, 48, 50, 52, 53–55, 372–374
   in skin and soft tissue infections, 315–316
   in vitro activity against, 93–94, 103
Pyelonephritis, 163–164
Q fever. See Coxiella burnetii
QT interval prolongation, 421–436
   cardiotoxicity as a quinolone class effect, 424–426
   drug involvement
      antimalarials, 430
      azole antifungals, 430
      list of, 432–433
      macrolides, 429–430
      mechanism, 421–422
      pentamidine, 431
      pentavalent antimonial meglumine, 431
      prevention and treatment, 431, 433
      quinolones, 424–428
   measurement of QT interval, 423
   mechanism of acquired, 422–423
   regulatory perspective in drug development, 433, 435, 436
   risk with quinolone use, 424–426
RecA, 31–32
Renal adverse effects, 411–412
   acute renal failure, 412
   acute tubular necrosis, 412
   allergic interstitial nephritis, 411
   crystalluria, 412
   granulomatous interstitial nephritis, 411–412
   interstitial nephritis, 411
   temafloxacin syndrome, 412
Renal dysfunction, fluoroquinolone pharmacokinetics in, 127, 128
Renal excretion of fluoroquinolones, 121
Resistance, 355–375
   by anaerobes, 222–223
   of animal pathogens, 390–392
      Campylobacter, 391
      Escherichia coli, 390
   mechanism of, 392
   mycoplasmas, 392
   Pasteurellaceae, 392
   Salmonella, 390
   staphylococci, 391–392
   streptococci, 391–392
   Campylobacter, 367–369
   clinical relevance, 368
   drivers of resistance, 367
   prevalence of resistance, 367–368
   Chlamydia trachomatis, 361
   in endocarditis pathogens, 261–262
   in enteric pathogens, 193–197, 201–202, 205, 361–369
   Escherichia coli, 369–372
frequencies of, 103–104

*Haemophilus influenzae*, 359

in intensive care unit infections, 337–341

*Klebsiella*, 369–372

*Moraxella catarrhalis*, 359

*Mycoplasma*, 359

in *Neisseria gonorrhoeae*, 176, 178–182

in pediatrics, 343–344

PK/PD parameters and emergence of, 152–153

*Pseudomonas aeruginosa*, 372–374

repeated passage and, 104

respiratory tract pathogens, 355–359

*Salmonella*, 362–367

clinical relevance, 365–367

drivers of resistance, 364–365

prevalence of resistance, 364–365

*Sexually transmitted diseases*, 360–361

clinical relevance, 361

drivers of resistance, 360

prevalence of resistance, 360–361

*Shigella*, 369

*Staphylococcus*, 374

*Streptococcus pneumoniae*, 355–359

clinical relevance, 355–359

drivers of resistance, 355–356

prevalence of resistance, 356–358

*Streptococcus pyogenes*, 359

viridans group streptococci, 374–375

in zoonotic bacteria, 392–396

*CAMPYLOBACTER*, 395–396, 397–399

control measures, 399

*Escherichia coli*, 396

human quinolone use and, 398–399

*Salmonella*, 393–394, 396–397, 398

transfer to humans, 396–398

Resistance mechanisms, 41–59

due to altered access to target enzymes, 51–58

altered permeation in gram-negative bacteria, 51–56

altered permeation in gram-positive bacteria, 56–58

altered permeation in mycobacteria, 58

due to altered drug target enzymes, 41–51

gyrase A subunit changes, 43–47

gyrase B subunit changes, 47

models for, 50–51

topoisomerase IV ParC subunit changes, 47–49

topoisomerase IV ParE subunit changes, 49–50

in *Neisseria gonorrhoeae*, 179–180

plasmid mediated, 58–59

Respiratory tract infections

bronchitis, acute, 235

bronchitis, acute exacerbation of chronic, 235–238

cost, 238

severe, 237

third-generation quinolones for, 236

treatment duration and response, 236–237

community-acquired pneumonia (CAP), treatment of, 227–234

gatifloxacin, 231–232

gemifloxacin, 232

gleofloxacin, 229–230

moxifloxacin, 230–231

pharmacoeconomic analysis of fluoroquinolone use, 232–233

PK-PD parameters and therapy, 228–229

role of fluoroquinolones in, 233–234

pharyngitis, 234–235

resistance, 355–359

in vitro activity against pathogens, 95–96

Rickettsia

treatment for intracellular pathogens, 327–328

in vitro activity against, 101

Rifampin, drug interactions with, 142

RNA synthesis, inhibition of, 30–31

Rosoxacin, for eye infections, 296–298

Rufloxacin

for CNS infections, 280

drug interactions, 136

effectiveness of, 471

*Salmonella*

in arthritis, septic, 348–349

in CNS infections, 282–285

gastrointestinal infections, 197, 200, 204–205, 206–207, 347–348

resistance in, 42, 44, 47, 48, 53, 362–367, 390, 393–394, 396–397, 398

clinical relevance, 365–367

drivers of resistance, 363–364

prevalence of resistance, 364–365

treatment for intracellular pathogens, 330

in vitro activity against, 95

Sexually transmitted diseases (STDs), 171–187

bacterial vaginosis, 186–187

chancre (Haemophilus ducreyi), 183–184

*Chlamydia trachomatis*, 173–176

clinical manifestations, 172

duration of treatment, 173

epididymitis, 186

gonococcal infection, 176–182

granuloma inguinale (Donovanosis), 184

ideal drugs for, 171–173

mycoplasmas, 182–183
	nonspecific urethritis and cervicitis, 182

overview, 171

pelvic inflammatory disease (PID), 185–186

resistance, 360–361

clinical relevance, 361

drivers of resistance, 360

prevalence of resistance, 360–361

syphilis, 186

treatment guidelines, 173

Shiga toxin producing *Escherichia coli* (STEC), 197, 200, 202

*Shigella*

gastrointestinal infections, 200, 203, 347–348

resistance in, 42, 44, 369

treatment for intracellular pathogens, 330

in vitro activity against, 95

Side effects. See *Adverse effects*
Sinusitis, 341

Sitafloxacin
  adverse effects, 405
  allergic reactions, 412
  pharmacodynamics, 149, 150
  structure, 4, 10

Skin and soft tissue infections, 311–319
  fluoroquinolone treatment, clinical evaluation of, 315–318
  complicated infections, 316–317
  cutaneous anthrax, 318
  diabetic foot infections, 317–318
  uncomplicated infections, 315–316
  microbiology of, 312–315
  pharmacokinetics and pharmacodynamics, 311–312

Sparfloxacin
  adverse effects, 345, 407–410, 425–429
  allergic reactions, 414
  for CNS infections, 277, 280
  drug interactions, 136, 139
  for endocarditis, 260, 262, 266
  for eye infections, 294, 297–298, 300–303, 305
  for intensive care unit infections, 340
  pharmacokinetics, 115, 117, 119, 120, 122
  photosensitivity from, 452, 458
  for skin and soft tissue infections, 312–314
  structure, 6, 11, 24, 116, 453

Staphylococci
  resistance in, 374, 391–392
  in vitro activity against, 96–98

Staphylococcus aureus
  in CNS infections, 276, 278, 280, 282–283
  in endocarditis, 260–262, 267–268
  in eye infections, 291, 301–304
  in intensive care unit infections, 337–339
  nasal carriage of, 248
  osteomyelitis, 251–256
  resistance in, 42, 44, 46–51, 56–59, 261–262, 374
  in skin and soft tissue infections, 311–319
  in vitro activity against, 96–98, 103

Staphylococcus epidermidis
  in endocarditis, 262–263
  in eye infections, 291–293, 296, 302–303
  in intensive care unit infections, 340

STDS. See Sexually transmitted diseases

Stenotrophomonas maltophilia
  in intensive care unit infections, 338
  resistance in, 50, 55
  in vitro activity against, 94

Streptococci
  resistance in, 355–359, 374–375, 391–392
  viridans group streptococci in endocarditis, 265–266
  in vitro activity against, 98

Streptococcus agalactiae, 277

Streptococcus mitis
  in endocarditis, 265
  resistance in, 45, 48, 49

Streptococcus pneumoniae
  in CNS infections, 275–276, 280, 282, 349
  in otitis media, 349
  pharmacodynamics of killing, 147–153
  resistance in, 42, 45, 46, 48–50, 57–58, 355–359
  clinical relevance, 358–359
  drivers of resistance, 355–356
  prevalence of resistance, 356–358
  respiratory tract infection, treatment of, 227–234, 236, 350
  in vitro activity against, 96–98, 103

Streptococcus pyogenes
  resistance, 359
  in skin and soft tissue infections, 311–312
  treatment of pharyngitis, 234
  in vitro activity against, 96–98

Streptococcus sanguis
  in endocarditis, 262–263
  in eye infections, 291–293, 296, 302–303
  in intensive care unit infections, 340

Tendinopathy, 443–445, 446–447

Topoisomerases. See DNA topoisomerases

Torsades de pointes. See also QT interval prolongation
  drugs linked to, 424–426, 429–433, 435
  mechanisms of, 421–424
  risk from quinolones, 424–426

Tosufloxacin
  adverse effects, 407, 409
  allergic reactions, 414
  for skin and soft tissue infections, 313
  structure, 5

Toxicity. See Adverse effects; specific organs or drugs involved

Traveler’s diarrhea. See Diarrhea

Treponema pallidum, 172, 186

Trovanloxacin
  adverse effects, 407–409, 413, 416, 462
  allergic reactions, 414
  for CNS infections, 276, 280–285
  drug interactions, 135, 136, 139, 141
  pharmacodynamics, 148, 149
  in pregnancy, 415
  for respiratory tract infections, 236, 237
  structure, 3

Tendonopathy, 443–445, 446–447

Topoisomerases. See DNA topoisomerases

Torsades de pointes. See also QT interval prolongation
  drugs linked to, 424–426, 429–433, 435
  mechanisms of, 421–424
  risk from quinolones, 424–426

Tosufloxacin
  adverse effects, 407, 409
  allergic reactions, 414
  for skin and soft tissue infections, 313
  structure, 5

Toxicity. See Adverse effects; specific organs or drugs involved

Traveler’s diarrhea. See Diarrhea

Treponema pallidum, 172, 186

Trovafloxacin
  adverse effects, 407–409, 413, 416, 462
  allergic reactions, 414
  for CNS infections, 276, 280–285
  drug interactions, 135, 136, 139, 141
  pharmacodynamics, 148, 149
  for endocarditis, 260, 262–263, 265–266, 269
  for eye infections, 291, 293, 297–298, 302
  for intensive care unit infections, 340
  for intra-abdominal infections, 222
  pharmacodynamics, 148
  pharmacokinetics, 117–120, 122–123, 126
  for respiratory tract infections, 230–233, 237–238
  for skin and soft tissue infections, 312–318
  structure, 3, 4, 24, 116
Tumor necrosis factor α (TNF-α), 411, 469, 470
Typhoid fever, 204–205, 206–207

Unscheduled DNA synthesis (UDS) assay, 80

Ureaplasma
- genital infections, 182–183
- in vitro activity against, 101, 182

Urinary fluoroquinolone concentration, 121–122
Urinary tract infections, 159–167
- clinical definitions, 159–160
- epidemiology, 159
- in intensive care unit, 341
- in pediatrics, 347
- pharmacology of quinolones, 160
- quinolone agents in prevention of, 166–167
- catheter-associated UTI, 167
- recurrent UTI, 166
- urological surgery, 166–167
- quinolone agents in treatment of, 161–166
- acute pyelonephritis, 163–164
- acute uncomplicated cystitis, 161–162
- complicated UTI, 164–165
- prostatitis, 165–166
- UTI in elderly, 164

Vaginitis, after antibiotic treatment, 416
Veterinary use of quinolones, 387–399

Vibrio cholerae
- gastrointestinal infections, 202–203
- resistance in, 50, 55

Vibrio parahaemolyticus, resistance in, 42, 44, 48, 50, 55

Viridans group streptococci
- in endocarditis, 265–266
- resistance in, 374–375

Warfarin, drug interactions with, 140
Wound infections, in intensive care unit, 341

Yersinia enterocolitica
- gastrointestinal infections, 205
- treatment for intracellular pathogens, 330–331

Zoonotic bacteria, resistance in, 392–396

Campylobacter, 395–396, 397–399
- control measures, 399

Escherichia coli, 396
human quinolone use and, 398–399
Salmonella, 393–394, 396–397, 398
- transfer to humans, 396–398