

INDEX

Note: Page numbers in *italics* indicate figures.

Page numbers followed by a “t” indicate tables.

2012 ACR guidelines for Management of Gout, 331-368. See also
ACR 2012 guidelines.

2015 ACR/Eular Classification of Gout, 105, 147-165. See also
Classification of gout.

ABCG2, 29, 35, 35t, 36, 37, 40t, 57

functional significance of gene variants, 39-41, 57

small intestinal, 42-43

Achilles tendon, tophus development in, 91, 93, 98

ACR 2012 guidelines for management of gout, 331-368

acute gout attack, management of, 358-360

acute gouty arthritis, 357

attack features, 357

combination therapy for, 361t

management in NPO patient, 365

pharmacologic monotherapy for, 362-364

allopurinol and uricosuric ULT, core recommendations, 333t

anti-inflammatory prophylaxis, 332, 366-367

assumptions in, 334, 339t

baseline recommendations and strategic plan, 345, 346-349

case scenarios, 336-337, 340-341

acute gouty arthritis, 357

CTGA, 340, 342-344

escalation of ULT, 347, 354-355, 356t

gout, 340

refractory disease, 354-355, 356t

combination therapy, 332, 362t

committee to develop, 333

comorbidity checklist, 350t

conflicts of interest, management of, 338

consensus methodology, 334-335

core expert panel (CEP) in, 335

“domains” in gout management, 333

grading of evidence, 334-336

health, diet, and lifestyle recommendations, 351-352

hotlinks to, 331

hyperuricemia definition, 337

level of evidence (Level A, B, or C), 336

long-term management, 348

Part 1, 331-332

Part 2, 331, 332-334

pegloticase in, 332

pharmacologic therapeutic agents, definitions of, 337-338

project design, 334-336

ACR 2012 guidelines for management of gout (*continued*)

RAND/UCLA Appropriateness Method, 334

RAND/UCLA consensus methodology, 334-335

ratings (Inappropriate, Uncertain, or Appropriate), 335-336

refractory disease, 354-355, 356t

risk-benefit ratios, 333

significance and innovations, 331-334

summary of, 345

systematic review, 336

targets for serum urate in, 331

task force panel (TFP), 335, 337

urate-lowering therapy (ULT) in, 285, 286, 287

escalation of, and refractory disease, 347, 354-355, 356t

ACR/Eular Classification of Gout (2015), 105, 147-165. See also
Classification of gout.

ACTH, 170t, 185-186, 323, 374t

dose recommendations, 186

for gout management in NPO patient, 365

Acute gout, 53, 86-90, 87t

classic description and symptoms, 87, 87t

combination therapy approach, 361t

common sites of involvement, 91, 97-98

polyarthritis, 99

inflammation and, 49-56, 52, 53, 87t

length of time in this stage, 54, 89

management of, 288t, 304-305

ACR 2012 guidelines, 358-360, 361t

ACTH, 185-186

colchicine, 179-180, 358

monotherapy, 362-364

necessity for, 89

NSAIDs, 358

systemic corticosteroids, 358

ULT, 358

pain of, 86, 87, 87t, 289, 374t

pathogenesis of, 21-22, 23t, 49-56, 52

recurrence rates, 88-89

refractory, 304-305

self-limiting aspect of attacks/flare, 54, 87-88, 87t

time to treat (first 24 hours), 332

Acute intermittent gout. See *Acute gout.*

Acute polyarticular gout. See *Polyarticular gout.*

Adherence. See *Patient adherence.*

Advanced gout, 51, 90-92, 92t

advanced gouty arthritis, with tophi, 92, 92, 92t

pain and urate burden in, 86

African Americans, eGFR value in, 300, 302t

Age. See also *Elderly population; Menopause.*

gout in the aged/elderly, 65, 81

at onset of gout, 86

Age, at onset of gout (*continued*)

early-onset gout, 94, 98, 218
in women, 86-87

AGREE trial, 181, 184

AHRQ (Agency for Healthcare Research and Quality)

assessment of gout, 113-114, 375
primary conclusions of, 374t
systematic effectiveness reviews, 371

AHS. See *Allopurinol hypersensitivity syndrome*.

Alcohol, 73t, 194-201, 207

gout and, 23, 71, 194, 196t, 199t, 200t, 207, 254
gout flares and, 23, 23t, 73t, 195, 200t, 254
historical aspects of, 194t
hyperuricemia and, 47, 73t, 194, 199t
recommendations for, 71
relative gout risk of different alcoholic beverages, 199, 254
beer, 194, 195, 199
liquor, 199
wine, 199, 199t
as risk factor for gout, 194, 196t, 199

Allantoin, 28, 238

Allopurinol, 220-229

in ACR 2012 guidelines, 332, 337, 347
core recommendations, 333t
action mechanism, 30, 48, 220, 221t, 222
adverse events, 223-224
AHS (allopurinol hypersensitivity syndrome), 227, 227t, 228t, 230
discontinuance due to, 229
DRESS syndrome, 224, 228t
HLA allele variants/ethnicity, 226-227, 226
mortality of, 226
rash, 223-224, 229, 244
Stevens-Johnson Syndrome (SJS), 223-224, 225
chemical structure of, 222
in CKD/renal disease, 300-301, 302t
combined therapy, with probenecid, 291t
CONFIRMS trial, 231-232, 231, 233, 258, 261, 303t, 324
contraindications and cautions, 229
dosage, 221t, 227-229, 229, 243, 353t
based on creatinine clearance (CrCl), 353t
correlation with serum urate level, 223
maintenance dose, 228
to prevent SJS, TEN, and DRESS/AHS, 224-227, 225
renally-adjusted, 227-228, 230, 301, 324, 331-332
starting dose, 228-229, 243, 331-332
upward titration of, 243
drug-drug interactions, 224t
FDA approval of, 220-223
hypersensitivity syndrome (AHS), 227, 227t
indications, 243, 331

Allopurinol (*continued*)

response to, gene variants and, 39
vs febuxostat, 232-233

Allopurinol hypersensitivity syndrome (AHS), 224, 226-227, 226, 227t
American College of Rheumatology (ACR). See *ACR*.

Amlodipine, 293t

AMPK inhibition, 255

Analgesia. See *Pain reduction*.

Anti-inflammatory therapies. See *Inflammation, anti-inflammatory therapies*.

Arhalofenate, 269-270, 311-313

Arthritis, 22, 98

chronic, 92t, 98
gouty, 22t, 92, 92t, 98. See also *Gout; Gouty arthritis*.
management of, 167-192
infectious (septic), 104, 106t, 107
osteoarthritis, 92, 106t, 107-109, 108-109
posttraumatic, 106t, 107-109
reactive (psoriatic), 106t
rheumatoid, 92
differential diagnosis of, 106t, 110

Ascorbate (vitamin C), 204-205

urate-lowering properties of, 293t

Asians

gout prevalence among, 63-64
HLA allele variants, 332
allopurinol and, 226, 226, 244, 353t

Aspirin

contraindications and cautions, 175t
high-dose, 175, 188
not recommended for acute gout, 175, 175t, 188
low-dose, 254
gout flares and, 254

Asymptomatic hyperuricemia, 22, 25, 51, 65-66, 85-86

Atherosclerosis, 72t

Atorvastatin, urate-lowering properties of, 293t

ATP (adenosine triphosphate), 47

Axial skeleton gout, 95, 96

Azathioprine, interactions with allopurinol, 322

Azithromycin

dosing with concomitant colchicine use, 267t
safety with colchicine, 265, 271

Bacterial cellulitis, 110

Benzbromarone, 237, 337

Birefringence, 117, 118, 142

of CPPD crystals, 118-121, 124

of urate crystals, 118, 123

BMI

gout risk and, 68t, 206, 207t
optimizing, 289

- Bone destruction, 89
- Bouchard's nodes, 92, 92, 98, 107
- Bursae. See also *Olecranon bursa*.
crystal deposition in, 89
- Caffeine, 203-204
- Calcineurin inhibitors. See *Cyclosporine*; *Tacrolimus*.
- Calcitonin, 293t
- Calcium oxalate urolithiasis, 56
- Calcium pyrophosphate dihydrate. See *CPPD*.
- Canakinumab, 178, 187, 269
- Cardiovascular (CV) disease
gout associated with, 24, 56, 75
hyperuricemia associated with, 24, 56, 75-79, 77, 81
myocardial infarction (MI) risk model, 76-79, 78
xanthine oxidase inhibitors and, 75, 77
- Cardiovascular (CV) safety, NSAIDs and COX-2 inhibitors, 175
- Celecoxib, 171-175
- Cellulitis, 106t, 110
- Charlemagne, *xviii*
- Cherry products, 197t, 205-206, 255
- CHF. See *Congestive heart failure*.
- Cholesterol crystals, 121, 126
- Chondrocalcinosis, 124
- Chronic kidney disease (CKD), 71, 203t, 300-304. See also *Renal disease*.
colchicine use/dosage, 261-262, 262t, 303
corticosteroid use in, 170, 170t
defined by GFR, 200
in elderly, cautions for, 81
NSAID cautions for, 301-303
prevalence of, 372-373
as risk factor for gout, 71, 72t
in women, 94, 100
stages of, 300-301
treatment implications, 81, 300-303, 302t, 303t
treatment-refractory gout in, 203t, 300-304, 324
- Chronic tophaceous gouty arthropathy (CTGA), 340, 342-344
- Cigarettes/smoking, 204
- CK. See *Creatine kinase*.
- CKD. See *Chronic kidney disease*.
- Clarithromycin
dose adjustment with colchicine, 266t
interactions with colchicine, 263, 271
- Classification of gout (2015 ACR/Eular Classification Criteria), 105, 147-165
classification criteria, 158-161
definitions and domains, 148t-150t
entry criteria, 147, 154t
- Classification of gout (2015 ACR/Eular Classification Criteria)
(*continued*)
performance characteristics of various classification criteria, 151, 162t-163t
take-away messages, 164-165
- Clinical features of gout, 85-101, 86. See also *Diagnosis of gout*:
Natural course of gout.
acute intermittent gout, 86-90, 87t
advanced gout, 90-92, 92t
asymptomatic hyperuricemia, 85-86
initial gout attack, classic description, 87, 87t
nonclassic presentations, 94-95
acute polyarticular gout, 94-95
axial skeleton gout, 95, 96
early-onset, 94, 98
organ transplant, 94
women, 94, 100
in renal disease, 95-96, 97t, 98, 99
Tumor Lysis Syndrome and, 95-96, 100t
stages of gout, 51, 85-92, 86
take-away messages, 97-100
- Coffee, 197t, 203-204
- Colchicine, 72t-74t, 111, 167, 168, 178-188, 194, 205, 217, 218, 249, 250t, 253, 269-271, 280t, 281t, 288t, 294, 299t, 302t, 322t, 322, 324, 360
ACR 2012 guidelines on, 332-333, 358, 362
action mechanism, 178-179, 258
adverse events/side effects, 181-184, 185t, 261
colchicine overdose, 181-184, 185t
GI symptoms, 186
neuromyopathy, 263
AGREE trial, 181, 184
best practice for use in gout, 179, 180t
in chronic kidney disease (CKD), 261-262, 262t
clinical pharmacology, 262-268, 264, 265
combination therapy, 186
with corticosteroids, 361t
with NSAIDs, 186, 361t
contraindications/cautions, 180t, 259t
in ERSD/hemodialysis, 303-304, 304t
in gout diagnosis, 142-143
macrolide antibiotics, 263-265
metabolism changed by cyclosporine, 323
dosage, 179-181, 180t, 188-189, 290t
for acute gout, 179-181, 180t, 362
adjustments for renal impairment, 182t-183t, 261-262, 262t, 325, 332-333
adjustments for use with other therapies, 266t-267t
FDA-approved regimen, 180t
for gout flare prophylaxis, 258, 259t, 261

- Colchicine, dosage (*continued*)
- high-dose, 179-180, 184
 - low-dose, 181, 184, 243, 291t, 374t
 - for gout flare prophylaxis, 258, 259t
 - reduction after organ transplant, 323
 - drug-drug interactions, 180t, 182t, 262-268, 264, 265
 - for gout flare prophylaxis, 187, 200, 258-268
 - indications for, 170, 170t, 188, 243
 - acute gout attack, 358
 - acute gouty arthritis, 361t, 362
 - gout-flare prophylaxis, 258, 259t, 291, 366-367
 - pain reduction, 374t
 - metabolism, 264-265
 - oral, 290t, 332-333
 - as frontline therapy choice, 170t, 290t
 - indications for, 170t
 - monotherapy with, 362-364
 - pharmacokinetics, 184, 261
 - primary care shortfalls in prescribing, 370
- Combinations of therapies, 332, 362t
- Comorbid conditions, 71-75, 72t-74t
- checklist for (in ACR 2012 guidelines), 350t
 - control of, 287-288, 289, 289t, 298t
 - in elderly, treatment considerations, 299t
- Compensated polarized light microscope, 117-121, 118, 119, 120-123
- Comprehensive management plan. See *Management of gout*.
- Computed tomography (CT), 128-129, 141
- dual-energy. See *DECT*.
- CONFIRMS trial, 231-232, 231, 233, 258, 261, 303t, 324
- Congestive heart failure (CHF), 72t
- Corticosteroids, 168, 169-170, 176-178
- ACR 2012 guidelines on, 332, 358, 361t
 - adverse effects, 176t
 - rebound flares, 178
 - combination with colchicine, 361t
 - for gout management in NPO patient, 365
 - indications for, 170t
 - acute gout attack, 258
 - acute gouty arthritis attack, 363
 - gout management in NPO patient, 365
 - intra-articular, 125, 170-171, 170t, 184-185, 361t, 363
 - systemic, 169-170, 176-178, 290t
 - for acute gout attack, 358
 - dosage, 176, 177t, 188
 - as frontline therapy for gout, 170t, 290t
 - for pain reduction, 374t
 - parenteral (IV), 178, 189
 - rebound gout flares after discontinuation, 178, 188
- Costs of gout, 79-80, 80t, 81, 369
- chronic refractory gout, 80
- COX-2 inhibitors, 171-175, 175t
- agents
 - celecoxib, 171-175
 - etoricoxib and lumiracoxib, 171
 - indications for
 - acute gouty arthritis attack, 362
 - for gout-flare prophylaxis, 268
 - monotherapy with, 362
- CPPD (calcium pyrophosphate dihydrate), 21
- crystal deposition disease, 21, 104, 136-137, 143
 - crystals, 21, 104, 118-121
 - microscopic features of, 118-121, 124
 - ultrasound imaging of, 104, 124-135, 128, 136-137
 - in pseudogout, 107
- Creatine kinase (CK), monitoring, 261, 271
- Creatinine clearance (CrCl), 181, 259t
- Crystal-deposition diseases, 21, 104, 136-137, 143
- Crystals. See also *CPPD crystals*; *MSU crystals*; *Urate crystals*.
- gout progression and, 49, 51, 52
 - in gouty nephropathy, 95-96, 99
 - microscopic features of, 118-121, 120-123
 - types and deposition of, 21, 48-49, 50, 53, 56, 86
 - “beach ball” appearance, 121, 126
 - in gout diagnosis, 104, 110, 113t, 117-121, 120-123
 - “Maltese cross” appearance, 121
- Cyclosporine, 74t, 94, 317, 323, 325
- dose adjustment with colchicine, 266t
 - gout development associated with, 74t, 94
 - hyperuricemia and, 74t
 - interactions with colchicine, 263, 271
 - tophus development and, 89
- Cytochrome P-450 3E4 (CYP3A4) inhibitors, 266t-267t
- Cytokines, 50, 169
- DECT (dual-energy computed tomography), 25, 104-105, 129, 135-141, 138-139
- performance measures, 140t
 - pros and cons of, 105, 140t
 - reference standard, 153
- Definitions
- of gout, 22-24, 22t
 - of hyperuricemia, 24-28, 26-27
- Dehydration
- avoiding, 206, 254
 - involved in seasonal gout flares, 23
 - as trigger of gout flares, 23, 23t, 206, 250t, 255, 270
- Diabetes mellitus, 74t
- gout and, 74t
 - risk, 79, 79

Diagnosis of gout, 103-145
 assessment of (2016 AHRQ), 113-114
 assessments involved in, 103-104
 initial assessment, 143
 criteria for, 105-114
 2015 ACR/Eular Classification of Gout, 105, 147-165
 2016 AHRQ assessment, 113-114
 ACR, 112, 112t
 EULAR ladder approach, 112-113, 113t
 “gold standard” (joint aspiration), 104, 110, 111t, 134, 142
 limitations of, 111-113
 tophi, palpable, 105
 definitive, 104, 142-143
 crystal identification, 104, 110, 113t, 117-121, 120-123
 differential diagnosis, 105-110, 106t
 vs rheumatoid arthritis, 92, 106t
 doubt in, joint aspiration for, 104, 142
 early, benefits of, 103
 in the elderly, 298-299
 imaging, 121-142, 149t-150t, 152, 153. See also *Imaging of gout*.
 comparison of methods, 126-134, 128-129, 135-141
 computed tomography (CT), 128-129, 141
 DECT (dual-energy CT), 104-105, 129, 138-139, 140t, 153
 hyperechoic “double contour,” 125-126, 128, 130-131, 132-133, 136, 153
 magnetic resonance imaging (MRI), 129, 141
 plain radiography, 123-124, 127, 128
 polarized light microscopy, 117-121, 118, 119, 120-123, 134
 reference standards, 153
 ultrasound, high-resolution, 104, 124-135, 128, 134t, 136-137, 153
 in-office, 142-143
 integrating clinical, lab, and imaging information, 110-114
 joint aspiration and examination, 104, 110, 111t, 134
 laboratory examinations, 114-121
 24-hour urine uric acid excretion, 104
 cholesterol or starch crystals, 121, 126
 CPPD crystals, 118-121, 124
 glucocorticoid crystals, 121, 125
 joint fluid examination, 104, 110, 111t, 117-121, 118, 119, 120-123, 134
 leukocyte count, 115
 serum urate values, 114, 115, 142, 149t
 synovial fluid analysis, 114-117, 116, 116t, 142, 149t
 with polarized light microscopy, 117-121, 118, 119, 120-123
 urate crystals, 117-118, 120-121, 122, 123, 153
 misdiagnosis, 111, 112
 reexamination of, 304, 324
 tophi, clinical evidence of, 149t, 151, 152, 159
 take-away messages, 142-143, 164-165
 Diagnosis of gout flares, 252-253
 Dialysis, for end-stage renal disease, 303-304, 304t
 Diclofenac, 171
 Diet, 193-216. See also *Alcohol; Obesity*.
 ACR 2012 guidelines, 351-352
 alcohol and gout, 194-206, 196t, 199t, 207, 254
 ascorbate (vitamin C), 204-205
 carbohydrates, 201-203
 cherry products, 197t, 205-206, 255
 coffee/caffeine, 197t, 203-204
 dairy products, 204
 fasting or feasting, as gout trigger, 23t, 250t
 fiber, 206
 food pyramid, 208, 212
 foods to avoid, limit, and encourage, 351-352
 fructose, 195-198, 196t, 200, 207
 glycemic index, 201-203, 202
 gout and, 67, 71, 194-206, 196t-197t
 historical aspects, 194t
 risk factors, 254
 gout flares and, 254-255
 hyperuricemia and, 194, 196t-197t, 199t
 management strategy for gout patients, 207-208, 210t-211t
 advising gout patients on recommendations, 208, 210t-211t
 dinner plate size, 208, 211
 food pyramid, 208, 212
 nonpharmacologic approaches, 254-255
 recommendations, 209, 210t-211t
 moderation in, 254
 obesity and gout, 67, 68t, 70, 199-201, 206-207, 207t
 omega-3 fatty acids, 197t, 203, 255
 patient education on, 275-276, 276t, 277, 280t, 286-287
 purine content, 28, 193, 196t, 198, 207, 254
 recommendations for, 71, 209, 210t-211t, 220, 254, 286
 red meat, 193, 198
 seafood, 193, 198, 254
 soy, 203
 sugar, 195-201, 196t, 207
 take-away messages, 209
 Difficult gout and hyperuricemia, 297-329, 298t
 ACR 2012 recommendations on, 346t, 354-355, 356t
 aged/elderly, gout in, 297-300, 299t, 324
 CKD and, 203t, 300-304, 324. See also *Chronic kidney disease (CKD)*.
 defining stage of CKD, 300, 324
 NSAID and colchicine use in, 301-303
 ULT and XOI in, 300-301, 324
 ESRD and hemodialysis, 303-304, 304t, 325
 investigational oral agents, 311-313
 major-organ transplantation and, 317-333, 322t, 325

Difficult gout and hyperuricemia (*continued*)

- pegloticase
 - intravenous, 220, 313-317
 - for treatment-refractory chronic gout, 313-317, 325, 356t
 - refractory acute gout, 304-305
 - refractory hyperuricemia, 305, 306t-307t
 - treatment-refractory chronic gout, 313-317
 - uricase therapy, 313-317
 - uricosuric “add-on” therapy to XO1, 307-313, 308t, 325, 356t
 - take-away messages, 324-325
- Diltiazem, dose adjustment with colchicine, 267t
- Dinner plate size, 208, 211
- Diuretics
 - eliminating non-essential use, 71, 291t
 - gout and, 71, 81, 94, 100, 254
 - hyperuricemia and, 47
- Double contour sign, 105, 125-126, 128, 130-131, 132-133
 - reference standard, 153
- DRESS syndrome, 224, 228t
- Drug-drug interactions. See also *specific agents*.
 - with allopurinol or febuxostat, 224t
 - with colchicine, 180t, 182t, 262-268, 264, 265
 - with probenecid, 236, 237t
 - transplant-related gout and, 322, 322t, 325
- Dual-energy computed tomography. See *DECT*.

Ear

- crystal deposition in, 21
- tophus development in, 90, 91, 152

Early-onset gout, 94, 98, 218

Early treatment, benefits of, 57, 97

Education. See *Patient education*.

Elderly population

- colchicine use in, 182t-183t, 261-262
- gout in, 65, 81, 297-300, 324
- diagnosis difficulty in, 298-299
- incidence of, 65, 65, 297
- increase in, 81
- polyarticular gout, 94-95, 297-298
- prevalence of, 81, 297
- treatment strategy, 299, 299t

Heberden’s and Bouchard’s node involvement in, 92, 92, 93, 98

treatment of gout and hyperuricemia in, 299, 299t

- comorbid conditions, 299t
- women, gout in, 65, 65, 81, 86-87, 297

Elimination of uric acid. See *Renal elimination of uric acid*.

End-stage renal disease (ESRD), 303-304

- gout and, 72t
- hyperuricemia and, 72t
- treatment implications, 303-304, 304t

Epidemiology, 63-84

- heritability of gout, 63-64
- historical perspective (Hippocrates), 63, 64t
- incidence and prevalence of gout, xvii, 63-70, 65, 66, 80-81, 372-373
- increased gout prevalence and complexity, 64-70, 65
 - perfect storm of factors leading to, 66-67, 68t, 81
 - take-away messages, 80-81

Erythema, 107, 109, 152

Estrogen, urate-lowering properties of, 293t

Ethnicity. See *Race/ethnicity*.

Etoricoxib, 171

EULAR (European League Against Rheumatism)

- ACR/EULAR Classification of gout (2015), 105, 147-165
- ladder approach to gout diagnosis, 112-113, 113t

European League Against Rheumatism. See *EULAR*.

Exercise, 287

FACT trial, 258, 261

Family history of gout, 29, 63-64, 100

Famous men with gout, xviii

Fasting, as trigger for gout/gout flares, 23t

Feasting, as trigger for gout/gout flares, 23t, 250t

Febuxostat, 218, 224t, 231-235, 237, 243, 244, 255, 256, 280t, 288t, 292, 300, 306t, 307, 308t, 309, 322t, 322, 324, 331, 356t, 374t

- in ACR 2012 guidelines, 331, 337, 347
- action mechanism, 30, 48, 220, 221t, 222
- chemical structure of, 222, 231
- in CKD, 301, 303t
- in combined therapy, 291t
 - with lesinurad, 310-311

CONFIRMS trial, 231-232, 231, 233, 303t

contraindications/cautions for, 233

dosage, 221t, 231, 232-233

- in CKD, 301, 303t

efficacy, 232-233, 232

FACT trial, 258, 261

in renal disease/CKD, 301, 303t

safety, 232

tophus reduction with, 232-233, 232

vs allopurinol, 232-233

Fenofibrate, 237, 293t, 309, 337

Fiber, dietary, 206

Fibrates, 237

Flares. See *Gout flares*.

Food pyramid, 208, 212

Foot joints, 25

Franklin, Benjamin, xviii

Fructose, hyperuricemia and, 47, 195-198, 196t, 200, 207

Gastrointestinal effects of colchicine, 186

Gender. See *Men; Women*.

Genetic factors in gout, 29-35, 63-64
heritability of gout, 63-64, 80
heritability of serum urate levels, 29-35
inherited genetic variants, 29-41, 57
urate transporters and, 29, 36-38

GFR. See *Glomerular filtration rate*.

Glomerular filtration rate (GFR), 220, 244, 301, 302t
in CKD, 300
estimated (eGFR), 300, 302t, 324
reduced, 183t

Glucocorticoid crystals, 121, 125

Glucocorticoids, 304. See also *Corticosteroids*.
intra-articular injection of, 125

GLUT9, 29, 35t, 36

Glycemic index, 201-203, 202

Gout
in 21st century, xx
classification criteria, 105, 147-165, 154t-157t
clinical features and natural history, 85-101
comorbid conditions, 71-75, 72t-74t
costs of, 79-80, 80t, 81, 369
definition of, 22-24, 22t
diagnosis of, 103-145
diet and, 193-216, 194t
difficult/treatment-refractory, 297-329
heritability of, 63-64, 80
historical figures with, xviii
incidence and prevalence of, xvii, 63-70, 65, 66, 80, 372-373
inflammation in, 49-56, 52
as marker for cardiovascular disease, 24, 56, 75
new classification and, 42-43, 57
outdated caricature of, xix
progression of, 49, 51, 85-92, 97. See also *Natural course of gout*.
destructive tophaceous gout, 49, 52
early-onset age and, 218
stages in, 51, 85-92, 86
quality of care in primary care settings, 369-378
self-limiting aspects of, 54, 88
treatment of. See *Management of gout*.
vs rheumatoid arthritis, 92, 106t, 110
web sites on, 277-281
who gets gout, 63-84

Gout clinics, 370-371

Gout flares, 22, 249-274
in acute gout stage, 51, 87, 87t, 249
acute, leading to hospitalization, 370
in advanced gout stage, 91, 92t
alcohol and, 23, 23t, 73t, 195, 200t, 254
AMPK inhibition and, 255
cost of, 79-80, 80t, 81

Gout flares (*continued*)
diagnosis algorithm, 252-253
duration of, 366
early treatment of, 294
hemodialysis and, 325
joints commonly involved, 91
management of, 294
pain of, 22, 87, 91, 97
patient expectations and, 258, 260t, 271
precipitating factors, 250t-251t, 254-258, 270
patient education on, 270
prophylaxis of, 249-274, 366-367
ACR 2012 guidelines on, 366-367
algorithms for, 252-253, 366-367
approaches under investigation, 268-270
arhalofenate, 269-270
IL-1 inhibition, 269
best-practice guideline when initiating ULT, 258, 259t
cherry consumption and, 255
colchicine, 187, 200, 258-268, 271, 291, 366
clinical pharmacology, 262-268, 264, 265
dosing guidelines, 258, 259t, 261, 266t-267t, 271
dosing adjustments for use with other therapies, 265-268, 266t-267t
dosing for age and renal impairment, 261-262, 262t, 271
drug-drug interactions, avoiding, 262-268, 264, 265
evidence basis for, 259, 260
side effects, 261
diet and alcohol in, 254-255
in ERSD, 303-304, 304t
nonpharmacologic approaches, 254-255
NSAIDs, low-dose, 268, 269t, 271, 366
omega-3 fatty acids, 197t, 203, 255
patient expectations, addressing, 258, 260t, 271
prednisone, 366
advice to avoid use, 259, 268, 271
urate-lowering therapy, 248, 259t, 290-292, 294
best-practice guideline when initiating, 258, 259t
starting prophylaxis *prior* to, 271, 291t, 366
take-away messages, 270-271
rebound, after discontinuation of corticosteroids, 178, 188
recurrence rates, 88-89
seasonal, dehydration and, 23, 206, 250t
self-limiting aspects of, 54, 88, 168
time between occurrences, 89
triggers of, 23, 23t, 56, 254-258, 270
alcohol consumption, 23, 23t, 71, 73t, 195, 196t, 199t, 200t, 207, 254, 270
dehydration, 23, 23t, 206, 250t, 255, 270
diet, 67, 71, 194-206, 196t-197t, 254, 270
feasting or fasting, 23t, 250t

Gout flares, triggers of (*continued*)
hospitalization, 254-255
illness, trauma, or surgery, 23, 23t, 249, 250t
low-dose aspirin, 254, 258
low-dose NSAIDs, 258
urate-lowering therapy, 250t, 255-258, 256-257, 260t, 270-271

Gouty arthritis, 92, 92, 92t, 98, 167-192
acute gouty arthritis
case scenarios for defining, 357
recommendations for combination therapy, 261t
chronic tophaceous gouty arthropathy (CTGA), 340, 342-344
definition of, 22t
duration of attacks, 357
management of, 167-192, 287. See also *Management of gouty arthritis*.
pharmacologic monotherapy, 362-364
number of active joints, 357
risk model for, 78

Gouty nephropathy, 23-24, 95-96

Gram stain, 115

Hallux rigidus, 106t, 107, 108

Hands
arthritis in, 107, 108-109
with tophi, 91, 92, 93, 152, 297, 315
DECT imaging of, 138-139

Health care utilization, gout and, 79-80, 80t

Heberden's nodes, 92, 93, 98, 108, 109

Helix of ear, 21

Hemodialysis, 303-304, 304t, 325

Henry VIII (King of England), xviii

Heritability of gout, 63-64, 80. See also *Genetic factors in gout*.

High resolution ultrasound. See *Ultrasound, high-resolution*.

Hippocrates, 63, 64t, 66

Hispanics, metabolic syndrome in, 69, 70

Historical figures with gout, xviii

History of gout. See *Family history*.

HLA allele variants, 226-227, 226, 228t, 244
allopurinol and, 226, 226, 244, 353t
HLA-B*5801, 332, 353t

HPFS (Health Professionals Follow-up Study), 193

HPRT, X-linked deficiency of, 47-48

Human leukocyte antigen (HLA) alleles. See *HLA allele variants*.

Hydroxyapatite (HA) crystal deposition, 21

Hyperlipidemia, 73t

Hypertension, 74t. See also *Diuretics*.
antihypertensive medications and gout, 67t, 74t
gout associated with, 74t
in premenopausal women, 94
hyperuricemia associated with, 74t

Hyperuricemia, 24-28. See also *Urate-lowering therapy*.
asymptomatic, 22, 51, 65-66, 81, 85-86
importance of recognizing, 65
incidence of, 67
non-benign aspects of, 25, 65
pain and urate burden in, 86
cardiovascular (CV) disease/mortality associated with, 24, 56, 75, 81
causes of, need to identify, 28, 56, 71, 103
comorbid conditions, 72t-74t, 75-79, 77
definition of, 24-28, 26-27, 56
in ACR 2012 guidelines, 337
new classification, 42-43
serum urate levels in, 24-25, 26-27, 56
difficult (treatment-refractory), 297-329, 298t. See also *Difficult gout and hyperuricemia*.
disease progression to gout, 51, 65
factors contributing to, 34t-35t
alcohol, 47, 73t, 194, 199t
diet and alcohol, 195, 199t
fructose, 47, 195-198, 196t, 200, 207
inherited genetic variants, 29-35, 40t, 57
insulin resistance, 67
metabolic syndrome, 67, 70, 70t
obesity, 67
management of, 291-292, 291t. See also *Urate-lowering therapy*.
metabolic syndrome and, 67, 70, 70t, 75
pathogenesis of, 28-48
impaired renal elimination of uric acid, 34t-35t, 41-47, 46, 57
increased uric acid production, 34t, 47-48
inherited genetic variants, 29-41, 40t, 57
refractory, 305
investigational oral agents for, 311-313
organ transplantation and, 317-323
step-wise approach for, 306t-307t
as risk factor for gout, 65, 67
risk model for MI, 76-79, 78
serum urate levels, 24, 25. See also *Urate, serum levels of*.
tophus development and, 91

Hypoxanthine guanine phosphoribosyl transferase. See *HPRT*.

Ibuprofen, 171

Ice, topical, 167, 168, 170t, 186

IL-1 β . See *Interleukin-1 β* .

Illness, as trigger of gout flares, 23, 23t, 250t

Imaging of gout, 121-142, 149t-150t, 152
comparison of methods, 126-134, 128-129, 135-141
computed tomography (CT), 128-129, 141
DECT (dual-energy CT), 104-105, 129, 138-139, 140t
hyperechoic "double contour," 125-126, 128, 130-131, 132-133, 136
reference standard, 153

Imaging of gout (*continued*)

- magnetic resonance imaging (MRI), 129
- plain radiography, 123-124, 126-134, 127, 128
- polarized light microscopy, 117-121, 118, 119, 120-123, 134
- reference standards for, 153
- ultrasound, 104, 126, 132-133, 134t
 - high-resolution, 104, 124-135, 128
- Incidence of gout, 63, 64, 66, 80-81, 372-373
- Indomethacin, 171, 175t, 188
- Infectious arthritis. See *Septic arthritis*.
- Inflammation, 22, 49-56, 167
 - in acute gout, 49-56, 52, 53
 - acute inflammatory prophylaxis, prior to initiation of ULT, 271, 291t, 366
 - acute inflammatory response, 49-56, 52, 53
 - anti-inflammatory therapies, 167-169
 - ACR 2012 guidelines on, 366-367
 - agents for, 170t, 366
 - pain reduction by, 289
 - prior to urate-lowering therapy, 271, 291t
 - as prophylaxis, ACR 2012 guidelines on, 332
 - treatment strategy, 167-169, 168
 - chronic, in gout, 56, 57
 - IL-1 β and, 54, 55, 57
 - inflammatory cascades, 50, 52, 54, 55, 167, 289
 - inflammatory joint fluid, 114-117, 116
 - NLRP3 inflammasome, 54, 55, 167, 178
 - pathogenesis of, in gout, 21-22, 49-56, 52, 167
 - synovial/synovial fluid, 57, 114, 116
 - tophus formation and, 49, 50
 - urate crystals and, 49, 52, 54, 167
- Insulin resistance (metabolic syndrome), 67, 69, 70, 70t, 79, 79.
 - See also *Metabolic syndrome*.
 - hyperuricemia and, 70, 70t
- Interleukin-1 β (IL-1 β), 54, 55, 57, 187
 - urate crystal-induced release of, 187
- Interleukin-1 β (IL-1 β) inhibition, 187, 269
 - canakinumab (anti-IL-1 β), 178, 187, 269
 - for gout-flare prophylaxis, 269
 - for refractory arthritis, 304-305
 - rilonacept, 269
- Interstitial nephropathy, 23-24, 23t
- Intra-articular MSU crystals (microtophi), 86
- Japan, gout and hyperuricemia in, 39, 40t
- Jefferson, Thomas, xviii
- Joint aspiration, 104, 110, 111t, 134, 142
 - ultrasound-guided, 134-135
- Joint fluid, examination of, 111t, 117-121, 118, 119, 120-123. See also *Synovial fluid*.

- Joints. See also *Hands; Tophi; Urate crystals*.
 - in asymptomatic hyperuricemia, 25, 49
 - commonly involved in gout, 87, 91
 - crystal deposition in, 25, 48-49, 50, 89
 - gout diagnosis and, 104
 - distal, 21, 25, 109
 - erythema (redness) over, 107, 109
 - inflammation in, 56
 - intra-articular MSU crystals (microtophi) in, 86
 - less commonly involved in gout, 91
 - lower extremity, 91
 - MTP, 87, 88
 - number active in acute gouty arthritis, 357
 - pattern of involvement, 148t, 158
 - permanent damage, in lack of good gout management, 370
 - polyarticular gout, 92t, 94-95
 - synovitis, 56
 - upper extremity, 91, 91, 92t

Keratoconjunctivitis, 225

Ketoconazole, dose adjustment with colchicine, 266t

Kidney. See also *Renal entries*.

structures of, 31

uric acid elimination by, 31, 33

Kidney disease. See *Chronic kidney disease (CKD); Renal disease*.

Kidney stones. See *Urolithiasis*.

King, Martin Luther, xviii

Knee joint, 87, 91

Krystexxa. See *Pegloticase*.

Kubla Khan, xviii

Laboratory examinations in gout diagnosis, 114-121. See also

Diagnosis of gout, laboratory examinations.

Lesinurad, 57, 221t, 234-236, 308t, 309-311

action mechanism, 234, 309

chemical structure, 234

clinical trials, 309-310

in combination

with febuxostat, 310-311

with XO1, 309

indications for, 291t, 309-311

monotherapy, 309

Leukocyte count, 115

Lifestyle factors, 193-216, 286-289. See also *Diet*.

ACR 2012 guidelines, 351-352

Loop diuretics

associated with gout, 71, 81, 94, 100

elimination of use, if possible, 71, 291t

hyperuricemia and, 47

Losartan, 237, 337
 urate-lowering properties of, 293t, 309

Lumiracoxib, 171

Lyme disease, 106t, 110

Magnetic resonance imaging (MRI), 129, 141

Major organ transplantation. See *Organ transplantation*.

Management of gout, 167-192, 331-368

- ACR 2012 guidelines, 331-368
 - acute gout attack, management of, 358-360
 - acute gouty arthritis, 357
 - attack features, 357
 - combination therapy for, 361t
 - management in NPO patient, 365
 - pharmacologic monotherapy for, 362-364
 - assumptions in, 334, 339t
 - baseline recommendations and strategic plan, 345, 346-349
 - case scenarios, 336-337, 340-341
 - acute gouty arthritis, 357
 - CTGA, 340, 342-344
 - escalation of ULT, 354-355, 356t
 - gout, 340
 - refractory disease, 354-355, 356t
 - combination therapy, 361t
 - comorbidity checklist, 350t
 - health, diet, and lifestyle recommendations, 351-352
 - project design, 334-336
 - urate-lowering therapy (ULT) in, 285, 286, 287
 - escalation of, and refractory disease, 347, 354-355, 356t
 - algorithms for, 168, 252-253, 287, 346-349
 - long-term management, 348
 - management of acute gout attack, 358-360
 - anti-inflammatory treatment, 168
 - choice of treatment regimens, 169-171, 170t, 290t, 291t
 - frontline oral therapy choices, 170t, 175t, 290t
 - comprehensive management plan, 285-296
 - acute gout management, 288-289, 290t
 - comorbidity control in, 287-288, 298t
 - core elements of, 285-286, 288t
 - initiation of ULT and use of gout-flare prophylaxis, 290-292, 366
 - lifestyle adjustments in, 285
 - long-term goals, 286
 - patient education, 285-288, 286
 - reaching target serum urate level, 288t, 292, 293t
 - cost-effectiveness of, 369
 - diet and alcohol in, 193-216
 - difficult (treatment-refractory) gout, 297-329, 298t
 - in aged/elderly, 297-300, 299t
 - general approach, 298t
 - drug-drug interactions and, 169

Management of gout (*continued*)

- early intervention, need for, 57, 97, 218
- goals of treatment, 249
- gout flare prophylaxis, 249-274, 366-367
- long-term management, 348
- patient adherence. See *Patient adherence*.
- patient education, 275-283, 286, 289t
- patient expectations, 258, 260t, 271
- primary care-driven review of, 374t
- in primary care settings, 369-378
- rationale, from pathogenesis, 49-50
- specific agents. See also *Urate-lowering therapy*.
 - ACTH, 185-186
 - colchicine, 178-184, 290t
 - combinations of, 362t
 - corticosteroids, intra-articular, 170-171, 170t, 184-185
 - corticosteroids, systemic, 169-170, 176-178, 290t
 - emerging treatments, 187
 - ice, topical, 168, 170t, 186
 - NSAIDs and COX-2 inhibitors, 168, 171-176, 175t, 290t
 - opiates, 186
 - other agents with urate-lowering properties, 238
 - “treat to target” approach, 219, 287, 375
 - urate-lowering therapy, 217-248, 285, 286, 287
 - agents for, 220-242, 221t
 - indications for, 217-220, 218t, 294, 346
 - lifelong therapy, necessity for, 219, 291
 - timing of initiation of, 291, 294
 - treatment strategy, 242-244, 345, 346-347
 - take-away messages, 188-189, 294, 375

Management of gouty arthritis, 167-192

- algorithms for, 168, 287
- anti-inflammatory therapies, 167-169, 170t
- choice of treatment regimens, 169-171, 170t
- colchicine, 178-184
- corticosteroids, intra-articular, 184-185
- corticosteroids, systemic, 176-178, 177t, 290t
- emerging treatments, 187
- NSAIDs, 168, 171-176, 172-174, 175t, 290t
- other modalities, 186
- treatment goals, 167-169
- take-away messages, 188-189

Meat, 193, 198

Medications, hyperuricemia and, 72t-73t, 76t

Men

- age of onset of gout in, 98
- incidence and prevalence of gout in, 63, 64t, 65, 66, 80

Menopause, 24, 80

6-Mercaptopurine, 322

Metabolic syndrome, 67, 70, 70t, 74t
 diagnostic criteria for, 70t
 in Hispanics, 69, 70
 hyperuricemia and, 67, 70, 70t, 74t
 prevalence of, 70
 renal effects of, 67, 71
 as risk factor for gout, 67, 69, 71, 74t

Metatarsophalangeal (MTP) joint. See *MTP joint*.

Methylprednisolone, 177
 in ACR 2012 guidelines, 363

Microtophi, in synovium, 86

Monosodium urate crystals. See *MSU (monosodium urate) crystals*.

MRFIT study, 206-207

MSU (monosodium urate) crystals, 56. See also *Urate crystals; Urolithiasis*.
 in coronary arteries, 24
 deposition of, 21, 48-49, 95
 in gout definition, 22, 22t
 imaging of, 117-118, 120-121, 122, 123
 inflammation and, 49-50, 52, 53
 intra-articular (microtophi), 86
 in tophi, 22, 22t, 48-49, 50, 56

MTP (metatarsophalangeal) joint, 87, 88, 91
 acute gout in, 130-131
 osteoarthritis of (hallux rigidus), 106t, 107, 108
 podagra, 87, 88
 radiography of, 127
 ultrasound of, 133

Mutations, in renal urate transporters, 40t

Myocardial infarction (MI)
 hyperuricemia and, 75-79
 risk model for, 76-79, 78

Naproxen, 171, 175t

Natural course of gout, 51, 85-101, 86
 disease progression, 51, 85, 86, 97
 rate of, 85
 initial gout attack, classic description of, 87, 87t
 nonclassic presentations, 94-95
 stages of gout, 51, 85-92, 86
 acute intermittent gout, 86-90, 87t
 length of time in, 54, 89
 advanced gout, 51, 90-92, 92t
 asymptomatic hyperuricemia, 51, 65-66, 85-86, 86
 length of time in, 86
 intercritical gout, 51
 take-away messages, 97-100

Nephrolithiasis, prevalence of, 372-373

Nephron, 31, 44-45

Nephropathy
 chronic interstitial, 22t, 23-24
 gouty (chronic urate), 23-24, 95-96

Neutrophils, 49, 169

NHANES III study, 25

Niacin, hyperuricemia and, 71

NLRP3 inflammasome, 54, 55, 167, 178

Nonsteroidal anti-inflammatory drugs. See *NSAIDs*.

NPO patient, acute gout management in, 178, 189, 365

NSAIDs, 168, 171-176, 175t, 243
 ACR 2012 guidelines on, 332, 333, 358
 adverse effects, 176, 176t, 177
 in combination therapy, with colchicine, 186, 361t
 in comprehensive management plan, 290t
 contraindications and cautions, 170t, 175, 175t, 324-325
 cardiovascular safety, 175
 in CKD, 301, 302t
 with reduced GFR, 324
 dosage, 175t, 290t
 for gout flare prophylaxis, 268, 269t
 as frontline therapy for gout, 170t, 175t, 290t
 gout flares triggered by, 258
 indications for, 170t, 175t, 188, 243
 acute gout attack, 358
 acute gouty arthritis, 362
 gout flare prophylaxis, 268, 269t, 366
 pain reduction, 374t
 monotherapy with, 362
 pain reduction with, 171, 172-174

OAT4, 35, 36, 57

Obesity, 67, 74t, 199-201, 206-207, 207t
 metabolic syndrome and, 67
 as risk factor for gout, 67, 68t, 70, 74t, 199-201, 206-207, 207t
 BMI and, 68t, 207t
 weight loss reduces gout risk, 68t, 70, 289t

Olecranon bursa
 acute gout in, 89, 89, 91
 crystal deposition in, 21, 89
 effusion of, 89
 hyperechoic aggregates in, 132
 tophus in, 142

Omega-3 fatty acids, 197t, 203, 255

Opiates, 186

Organ transplantation, 74t, 94, 317-333
 cyclosporine use, 74t, 89, 94, 322t, 325
 drug-drug interactions and, 322, 322t, 325
 gout associated with, 74t, 89, 94, 317-333, 322t, 325
 gout treatment, 322-323

Organ transplantation (*continued*)

hyperuricemia associated with, 94, 317-322
prednisone for, 323, 325

Osteoarthritis

differential diagnosis of, 106t, 107-109, 108-109
of hands, tophi and, 92, 92, 108-109

Oxalate crystals, 21

Oxyprinol, 48, 222, 305

Pain. See also *Management of gout; Pain reduction.*

of acute gout attack, 22, 86, 87, 97, 289, 374t
cascade of events in, 50, 52, 54, 55, 167, 289
of stages of gout, 86

Pain reduction (analgesia), 374t

anti-inflammatory treatment and, 167, 170t, 171, 289
as goal of treatment, 167
with ice, 185
with NSAIDs, 171, 172-173
with opiates, 185
with reduction of gout flares, 169

Pathogenesis, 21-61

of acute gouty inflammation, 21-22, 23t, 49-56, 52
of hyperuricemia, 28-48
impaired renal elimination, 34t-35t, 41-47, 46
increased uric acid production, 34t, 47-48
of tophi, 48-49
take-away messages, 56-57

Patient adherence, 275, 370, 375

gout flares, information on, 258
to medications, 370
nonadherence, treatment failure rates and, 281, 281t

Patient education, 275-283, 286, 289t

ACR 2012 guidelines on, 359
on adherence to treatment plan, 279-281, 279t, 281t
barriers/obstacles for, 276-277, 277t, 281
cost savings with, 279
on diet and lifestyle, 275-276, 276t, 277, 280t, 286-287, 289t, 294
early communication with patient, value of, 285-288
EULAR Gout Task Force recommendations, 275
on expectations, 171, 282
on gout, 275-283, 370
explaining gout and its treatments, 279, 280t
five simple points, 276t
long-term management goals, 286
practical points and simplified information, 277-281, 280t
sources of information, 277, 278
web sites, 277, 279t
on gout flares, 270
on gout flares precipitated by ULT, 260t, 281t
improving, 369, 375

Patient education (*continued*)

lack of communication about, 275
patient expectations, about gout flares, 258, 260t, 271, 282
patient expectations, addressing, about ULT, 258, 271
patient vs physician perspective, 281t
simple points about gout, 276t
simplified informational materials for patients, 277-281
success in reaching target serum-urate values, 276
on urate-lowering therapy (ULT), 258, 260t, 271, 281t, 294
web sites on gout, 277, 279t
take-away messages, 282

Pavarotti, Luciano, xviii

Pegloticase, 32, 218, 220, 221t, 238-242, 245, 292, 294, 298t,

306t-307t, 315, 318-321, 369, 371
in ACR 2012 guidelines, 332, 354-355
action mechanism, 221t, 238-239, 238
adverse events, 241-242, 242, 243t
gout flares, 241-242
infusion-related reactions, 241-242, 242, 243t, 316
bone erosions healed with, 316
chemical structure, 239
dose, 221t
efficacy, 239-241, 240-241
organ transplant and, 323
FDA-approved for use in gout, 245
indications for, 220, 238, 239, 243-244
in ACR 2012 guidelines, 332, 354-355
for difficult (treatment-refractory) gout, 313-317, 325, 356t
hyperuricemia, 48
severe tophaceous gout, 48
intravenous, 313-317
limitations of, 316
safety, 316
tophus size reduction with, 242, 316, 318-319, 320-321, 325

PEGylated uricase. See *Pegloticase.*

Perfect storm of factors, 66-67, 68t, 81

Phosphoribosylpyrophosphate (PRPP) synthetase, 48

Physical exercise, 287

Podagra, 87, 88

Polarized light microscopy, 117-121, 134

birefringence in, 117, 118-121, 120-123, 142
microscope function, 117, 118, 119

Polyarticular gout, 92t, 94-95, 99, 324

in elderly patients, 94-95, 297-298

Posttraumatic arthritis, 106t, 107-109

Prednisolone, dosage, 188

Prednisone, 176, 188, 290t

in ACR 2012 guidelines, 366

dosage, 176, 177t, 363

increase in dose, 363

- Prednisone, dosage (*continued*)
 starting dose, 177t, 323, 363
 indications for
 acute gouty arthritis attack, 363
 as frontline therapy choice, 290t
 gout flare prophylaxis, 366
 rebound gout flares on discontinuation of, 188
 for transplant patients, 323, 325
- Premenopausal women, gout in, 25, 63, 66-67, 80, 94, 100
- Prevalence of gout, xvii, 63-70, 80-81, 372-373
 increased prevalence and complexity, 64-70, 65
 perfect storm of factors leading to, 66-67, 68t, 81
 race/ethnicity and, 63-64
- Primary care, 81, 369-378. See also *Patient education*.
 AHRQ reviews and conclusions, 371, 374t, 375
 gout clinics, 370-371
 patient education, 275-283, 369, 370, 375
 patient outcomes, worsening, 370
 acute gout flares, 370
 permanent joint damage, 370
 physician-patient perceptions, 281t
 prevalence and population estimate of gout, 372-373
 quality of care gaps, 369-375
 recognizing asymptomatic hyperuricemia in, 71
 rheumatologists and, 371
 serum urate monitoring, not regular, 369, 370, 375
 shortfalls in prescribing ULT and colchicine, 370, 375
 ULT
 benefits and harms of, evaluation of, 371
 lack of prescription of, 370
- Probenecid, 220, 234, 236-237
 in ACR 2012 guidelines, 347, 353t
 action mechanisms, 221t
 adverse reactions, 236-237, 237t
 chemical structure, 234
 clinical trials, 234-235, 235
 in comprehensive management plan, 347
 contraindications/cautions for, 353t
 GFR needed for, 291t
 not for use as primary ULT, 291t
 urolithiasis, 353t
 dosage/dosing, 220, 221t
 drug-drug interactions, 236, 237t
 efficacy, 234-235, 235
 glomerular filtration rate needed for, 291t
 indications for, 347, 356t
 contradicting advice, 353t, 356t
 as first choice among uricosurics for ULT monotherapy, 353t
 monitoring needed for, 353t
- Progression of gout, 49, 51, 85-92, 97. See also *Natural course of gout*.
 rate of progression, 85
- Prophylaxis of gout flares. See *Gout flares, prophylaxis of*.
- Proximal tubule transporters. See *Urate transporters*.
- PRPP synthetase, 48
- Pseudogout, 21, 106t, 107, 303-304
 treatment of, 187
- Psoriatic arthritis, 106t
- Puberty, serum urate levels and, 24
- PubMed, 336
- Purines
 dietary, 28, 193, 196t, 198, 207, 254
 in alcohol, 194, 254
 metabolism of, 24, 28, 30-32
 inherited (inborn) errors in, 28, 57, 63
- Quality of life (QOL), 92, 369, 375
 patient education and, 279
- Race/ethnicity
 gout and, 63-64
 heritable factors in hyperuricemia, 29, 40t
 HLA allele variants, 226-227, 226, 332, 353t
- Radiography, 123-124, 126-134, 127, 128
 compared with other imaging methods, 126-134, 128-129, 135
- RAND/UCLA Appropriateness Method, 334
- Rasburicase, 96, 238, 313. See also *Uricase*.
- Rash
 with allopurinol, 223-224, 229, 244
 with probenecid, 236
- RDEA3170, 311
- Recombinant uricase. See *Rasburicase*.
- Recurrence rates, 88-89
- Recurrent attacks, treatment of, 288t
- Refractory gout. See *Difficult gout and hyperuricemia*.
- Renal disease, 22t, 95-96, 97t, 98, 99. See also *Urolithiasis*.
 allopurinol dosing in, 324, 332-333
 chronic. See *Chronic kidney disease*.
 clinical presentation, with gout and hyperuricemia, 95-96, 97t, 98, 99
 colchicine dosing in, 182t-183t, 261-262, 262t, 325
 end stage (ESRD), 303-304, 304t
 febuxostat in, 231-232, 231
 gout and, 22t, 95-96, 97t, 98, 99
 interstitial nephropathy, 22t, 23-24
- Renal effects of metabolic syndrome, 67, 71
- Renal elimination of uric acid, 28-29, 33, 36-38, 41-47, 44-45
 factors affecting, 57
 impaired (underexcretion), 34t-35t, 41-47, 46, 57
 kinetics of, 33

Renal elimination of uric acid (*continued*)
 normal, 28-29, 36-38
 vs gout, 46

Renal stones. See *Urolithiasis*.

Rheumatoid arthritis (RA), 92
 differential diagnosis of, 106t, 110

Rheumatologist
 contacts with primary care providers, 371
 referral to, 80, 287, 294, 322

Rilonacept, 269

Risk factors
 for gout, 64t, 66-67, 68t, 71
 coffee/caffeine and, 203-204
 comorbidity-related, 71-75, 72t-74t
 insulin resistance, 67, 69
 metabolic syndrome, 67, 69
 obesity, 67, 68t, 70

Ritonavir, dose adjustment with colchicine, 266t

Roosevelt, Theodore, xviii

Salicylates. See *Aspirin*.

Seafood, 193, 198, 254

Seasonal factors in gout, 23

Self-limiting aspects of gout, 54, 88, 168

Septic arthritis, 104, 106t, 107

Serum urate. See *Urate, serum levels of*.

Sevelamer, 304t

Sirolimus (rapamycin), 322

Sites of gout (commonly involved joints), 87, 91. See also *Joints*.
 pattern of involvement, 148t, 158

SJS. See *Stevens-Johnson Syndrome*.

SLC2A9, 29-35, 63

SLC22A12, 29, 35, 35t, 36

Smoking, 204

Spondyloarthropathy, 109-110

Stages of gout, 51, 85, 85-92, 86. See also *Natural course of gout*.

Starch crystals, 121, 126

Steroids. See *Corticosteroids; Glucocorticoids*.

Stevens-Johnson Syndrome (SJS), 223-224, 225

Stones. See *Urolithiasis*.

Sugar, 195-201, 196t, 207

Sulfinpyrazone, 337

Sulindac, 171, 175t

Surgery, as trigger for gout, 23t

Synovial fluid
 crystal analysis of, 105, 114-117, 116, 116t, 142, 149t
 with polarized light microscopy, 117-121, 118, 119, 134
 Gram stain and culture, 115

Synovitis, 56

Synovium
 inflammation of, 56, 57
 MSU crystal deposition in, 21

Systemic symptoms of gout, 87

Tacrolimus, 317
 interactions with colchicine, 263

TEN. See *Toxic epidermal necrolysis*.

TGF- β , 56

Thiazide/loop diuretics, 47, 71, 81, 94, 100
 elimination if possible, 71, 291t

Tophaceous gout. See also *Acute gout*.
 imaging of, 132-133, 138-139
 “double contour,” 105, 125-126, 128, 130-131, 132-133

Tophi
 in advanced gout, 91-92, 92t
 bone destruction from, 52
 clinical evidence of, 149t, 151, 152, 159
 common sites of, 21, 93, 97-98
 definition of, 22t
 destructive tophaceous gout, 49, 52
 in diagnosis of gout, 105
 formation of, 48-49, 50, 89, 97
 cyclosporine and, 89, 317
 locations of, 89, 90, 91-92, 93, 97-98
 organ transplant and, 317-322
 in hands, 91, 92, 93, 108, 315
 in Heberden’s and Bouchard’s nodes, 92, 92, 93, 98, 108-109
 hyperuricemia, severity and duration and, 91
 microtophi, in synovium, 86
 MSU crystal deposition and, 22, 22t, 48-49, 50, 56
 factors promoting, 50
 pathogenesis of, 48-49
 reduced size, 245
 with febuxostat, 232-233, 232
 with low serum urate values, 292, 313
 with pegloticase, 242, 314-316, 315, 318-319, 320-321, 325
 with uricase, 313-314
 with XOIs, time for, 313
 remodeling, as factor in gout flares, 23t, 249

Toxic epidermal necrolysis (TEN), 223-224

Traditional Chinese Medicine, 374t

Transplantation. See *Organ transplantation*.

Transporters. See *Urate transporters*.

Trauma
 posttraumatic arthritis, 106t, 107-109
 as trigger for gout, 23t, 109, 249, 250t
 “Treat to target” approach, 219, 222, 245, 345

Treatment of gout. See *Management of gout*.

Treatment-refractory gout. See *Difficult gout and hyperuricemia*.

Triamcinolone
 IM, 170t, 178, 290t
 in ACR 2012 guidelines, 363
 intramuscular, 363

Triggers of gout flares, 23, 23t, 56, 254-258, 270
 identifying, 288

Tumor Lysis Syndrome (TLS), 95-96, 100t
 rasburicase approved for prevention of, 96, 238, 313

Tumor necrosis factor- α (TNF- α), 187

Uloric. See *Febuxostat*.

ULT. See *Urate-lowering therapy*.

Ultrasound, 104, 132-133, 134t
 high-resolution, 104, 124-135, 136-137
 compared with other methods, 126-134, 128, 135
 reference standard, 153

URAT1, 29, 36, 41, 57, 63

Urate. See also *Hyperuricemia*; *Urate-lowering therapy*.
 burden
 with disease progression, 86
 reducing, 217, 218. See also *Urate-lowering therapy*.
 total body, 86, 86

crystals, 21, 48-49, 56, 118, 120-121. See also *MSU crystals*.
 in acute gout, 89
 birefringence of, 117, 118, 123, 142
 gout diagnosis and, 104, 117-118, 120-121, 122, 123, 153
 gout progression and, 49, 51, 52
 imaging of, 117-118, 120-121, 122, 123
 inflammatory potential of, 49, 52, 167
 microscopic appearance of, 111-118, 120-121, 122, 123
 in tophi, 22, 22t, 48-49, 50, 56

miscible stores, daily turnover of, 29, 33, 56

reabsorption pathways, 36-38

serum levels of, 24, 26-27
 after puberty, 24
 in diagnosis, 114, 115, 142
 heritability of, 29-41, 40t
 for hyperuricemia, 24-25, 26-27, 56
 lowering, pharmacologic therapy for, 217-248
 monitoring frequency, 294, 305, 325, 369
 monitoring in primary care settings, 369
 normal levels, 25, 26-27
 solubility level, 217
 target levels, 219, 220, 222, 245, 292
 additional treatments to reach target level, 288t
 less than 4.0 mg/dL, 292, 294, 313
 less than 6.0 mg/dL, 287, 292, 294
 low, tophus resorption and, 245
 lower, improved outcomes with, 219t, 292, 308t, 311, 312-313

Urate, serum levels of, target levels (*continued*)
 reaching, 292
 “treat to target” approach, 219, 245, 287, 375
 solubility level, 217

Urate-lowering therapy (ULT), 217-248
 ACR 2012 guidelines on, 345, 346-347, 366
 core recommendations, 333t
 escalation of therapy and refractory disease, 347, 354-355, 356t
 management of acute gout attack, 358-360
 agents/drugs in, 220-242, 221t. See also *specific agents*.
 action mechanism, 220, 222
 allopurinol, 220-229, 347, 353t
 changes between, 243
 febuxostat, 231-233, 347
 first-line treatments, 331
 lesurinad, 234-236, 235
 other medications or supplements with urate-lowering properties,
 292, 293t
 other uricosurics, 237
 pegloticase, 238-242, 243-244
 probenecid, 236-237, 347, 353t
 selection of first-line agent, 347
 uricosurics, 353t
 xanthine oxidase inhibitor, uricosuric “add-on” therapy, 307-313,
 308t, 325

in CKD, 300-301
 combination therapy, 347
 in comprehensive management plan, 285, 286, 287
 duration of, 219, 245, 289, 291
 do not stop during acute gout flares, 289, 294
 lifelong, 219, 291
 factors needed for effectiveness of, 371
 follow-up with, 245
 glomerular filtration rate (GFR) and, 220
 goals of, 217-220, 219t, 244
 gout flare prophylaxis with, 248, 259t, 291-292, 347, 366
 gout flares precipitated by, 23t, 250t, 255-258, 256-257, 260t, 270-271
 patient adherence and, 258
 indications for, 217-220, 218t, 294, 346
 prevalence of adults with, 372-373
 initiation of, 290-292
 anti-inflammatory prophylaxis prior to, 271, 291t
 timing of initiation, 291, 294
 waiting until gout flare is over, 291
 lifelong therapy, necessity for, 219, 291
 outcomes with, 219t, 292, 308t
 patient education on, 258, 260t, 271, 281t
 primary care settings, lack of prescribing ULT and correct
 monitoring, 370

- Urate-lowering therapy (ULT) (*continued*)
 target levels for serum urate, 219-220, 219t
 less than 4.0 mg/dL, 292
 less than 6.0 mg/dL, 286, 287, 291, 292, 371
 reaching, improved outcomes with, 219t, 292, 308t
 total urate burden, reducing, 217, 218
 “treat to target” approach, 219, 222, 245, 294, 345, 371, 375
 treatment strategy, 242-244, 345, 346-347
 uricostatic agents, 220, 244
 uricosuric agents, 220, 234, 234, 244, 292
 take-away messages, 244-245
 “Urate sand,” 130-131
 Urate transporters, 29-41, 36-38, 40t, 63
 Uric acid
 body stores of, daily turnover of, 29, 33, 56
 crystallization of. See *MSU (monosodium urate) crystals*.
 distribution of, normal vs gout, 33
 excess of. See *Hyperuricemia*.
 excretion of, 28-29, 41, 44-45. See also *Renal elimination of uric acid*.
 in gouty vs nongouty patient, 46
 impaired, 34t-35t, 41-47, 46
 gut elimination of, 29, 33
 metabolism of, 28-48, 30-32
 in normal vs gouty patients, 33
 oxidation. See *Uric acid oxidase*.
 production (generation) of, 28, 33
 increased, 34t, 47-48
 overproduction, 34t, 47-48
 as target for therapy, 48
 renal elimination of. See *Renal elimination of uric acid*.
 sources and distribution, normal vs gout, 33
 24-hour excretion test, 104
 urolithiasis. See *Urolithiasis*.
 Uric acid oxidase. See *Uricase*.
 Uric acid urolithiasis. See *Urolithiasis*.
 Uricase (uric acid oxidase), 30, 238. See also *Pegloticase*.
 action mechanism, sites of action, 30-32
 in knockout mice, 28
 loss in human evolution, 28, 56
 PEGylated, 30, 238-242. See also *Pegloticase*.
 rasburicase (recombinant uricase), 96, 238, 313
 for treatment-refractory chronic gout, 313-314
 for tumor lysis syndrome, 96, 238, 313
 Uricostatic agents, 220, 244, 353t. See also *Allopurinol; Febuxostat*.
 definition of, 337
 Uricosuric agents, 220, 234, 234, 237, 244, 292. See also *Probenecid*.
 “add-on” therapy to XO1, 307-313, 308t, 325
 combined with allopurinol or febuxostat, 292
 contraindications for, 301
 Uricosuric agents (*continued*)
 drug-drug interactions, 292
 uricosuric properties of other agents, 237
 Urine, alkalization to prevent/reduce urolithiasis, 353t
 Urolithiasis, 23, 56, 95, 97t. See also *Crystals*.
 calcium oxalate, 56
 cautions on agents used, 220
 in early-onset gout, 94, 98
 imaging of, 98, 99
 urine alkalization for, 353t
 Vegetables, purine-rich, 198
 Verapamil, dose adjustment with colchicine, 267t
 Vertebrae, axial skeleton gout, 95, 96
 Vitamin C (ascorbate), 204-205, 237
 Water, consumption for hydration, 254-255
 Weight
 BMI and, 68t, 206, 207t, 289
 loss, 220, 286
 decreased risk of gout flares with, 70
 decreased risk of gout with, 68t
 patient discussion on, 286-287
 White blood cell (WBC) count, 87
 Women
 elderly
 gout prevalence in, 65, 66, 81, 100
 Heberden’s and Bouchard’s node involvement in, 92, 92, 93, 98
 family history of gout in, 100
 incidence and prevalence of gout in, 63, 65, 66
 menopause and, 24, 80
 postmenopausal, gout in, 24, 64t, 85, 87, 94, 100
 premenopausal, gout in, 25, 63, 66-67, 80, 94, 100
 X-linked deficiency of HPRT, 47-48
 X-rays. See *Radiography*.
 Xanthine, 30
 Xanthine oxidase, 30-32, 222
 Xanthine oxidase inhibitors, 48, 220-242, 221t, 222. See also
Allopurinol; Febuxostat; Urate-lowering therapy.
 ACR 2012 guidelines on, 332, 337, 347, 354-355
 action mechanisms, 222
 agents, 222
 caffeine as, 203-204
 cardiovascular (CV) disease and, 75, 77
 in CKD, 300-301
 combined therapy, 354
 monotherapy, 354
 for prevention of Tumor Lysis Syndrome, 96
 for refractory disease, 354-355

Xanthine oxidase inhibitors (*continued*)

targeting overproduction of uric acid, 48

tophus size and, 313

uricosuric “add-on” therapy, 307-313, 308t, 323, 325