

Index

A

- ABCG2. *See* ATP-binding cassette subfamily G member 2 (ABCG2)
- Accelerated ATP degradation
- acetaldehyde, 78
 - acetyl-AMP, 78
 - acetyl-CoA synthetase, 78
 - alcohol dehydrogenase, 78
 - β -hydroxybutyrate, 78
 - carnitine palmityltransferase deficiency, 78
 - ethyl alcohol, 78
 - glucose-6-phosphatase deficiency, 75
 - glycogen storage diseases, 78
 - hypoxemia, 80
 - inosine, 79
 - lactate, 78
 - muscle metabolism, 78
 - NADH, 78
 - nicotinamide adenine dinucleotide (NAD), 78
 - phosphofructokinase deficiency, 78
 - phosphoglycerate mutase deficiency, 78
 - secondary gout, 75
 - Von Gierke's disease, 75
 - xanthine oxidase, 79
- Accelerated nucleotide degradation
- AMP deaminase, 84
 - myoadenylate deaminase, 83
- Acute attack, 93, 97, 207–278, 295, 296, 315, 316, 320, 323, 339, 354, 355
- Acute attack gout mechanisms
- acute gouty arthritis, 207–208, 211, 212, 218, 219, 228, 229, 237, 238, 240, 243, 252, 253, 255, 259, 262
 - acute inflammatory response, 207, 208, 218, 231, 232, 234, 235, 259, 261–263, 270, 276, 278
 - apoptosis, 208, 216, 230, 233, 234, 256, 257, 260, 262, 269–272
 - cell migratron, 208, 243, 247
 - phagocytosis, 207–209, 230, 233, 234, 242, 247–252, 256, 258–260, 263, 265, 269, 270, 273
- Acute attacks
- prophylaxis against, 355
 - treatment, 354
 - urate-lowering treatment, 354
- Acute gouty arthritis, 92, 95, 96, 99, 101, 116, 124, 136, 137, 140, 141, 191, 199, 200, 207–209, 211, 212, 218, 219, 228, 229, 237, 238, 240, 243, 252, 253, 255, 259, 262, 294–297, 301, 304, 313–315, 322, 323, 327, 331, 348, 353
- Acute inflammatory response, 187, 207, 208, 218, 231, 232, 234, 253, 259, 261–263, 270, 276, 278, 316, 319, 320
- Acute uric acid nephropathy
- medullary cystic disease, 117
 - polycystic kidney disease, 117
- Acute uric acid nephropathy management
- alkylating agents, 340
 - allopurinol, 340
 - hematopoietic system, 340
 - hemodialysis/peritoneal dialysis, 340
 - malignant neoplasms, 340
 - tubular interstitial nephritis, 340
 - ultrasonography, 340
 - urine alkalinization, 340
- Adenine, 4, 25, 77, 107, 249, 330
- Adenine phosphoribosyltransferase (APRTase), 35, 42, 47–54, 131–133
- ACG, 51
 - adenosine monophosphate (AMP), 47
 - APRT enzyme forms, 51
 - ATG, 51
 - deficiency, 47
 - de novo, 54
 - 2,8-dihydroxyadenine stones, 51
 - 2,8-dihydroxyadenine urolithiasis, 52
 - familial juvenile hyperuricemic nephropathy (FJHN), 53
 - gene, 49
 - hereditary orotic aciduria, 54
 - inhibition of APRTase activity, 47
 - Morquio syndrome, 52
 - mutant forms of APRTase, 49
 - TGA, 51
 - TGG, 51
 - type I APRTase deficiency, 49
- Adenosine deaminase, 34, 79, 108, 140
- Adenosine kinase, 34, 35
- Adenosine monophosphate (AMP), 11, 28, 30, 31, 33–36, 38, 40–43, 47, 54, 76, 79–84, 101, 107, 108, 140, 235, 263, 269, 276, 310

- Adenylic, 27, 55
 Adenylosuccinase, 33, 34, 40
 Adenylosuccinate, 33, 34, 40
 Adhesion molecules, 210, 211, 216, 217, 219, 221, 228, 237–245, 255, 261, 272, 277
 E-selectin, 242–243
 integrins, 238, 243
 integrins ligand, 245–247
 integrin structure, 243–245
 L-selectin, 239–240
 P-selectin glycoprotein ligand-1, 239
 selectins (structures), 238–239
 unique L-selectin properties, 240–242
 ADPKD. *See* Autosomal dominant polycystic kidney disease (ADPKD)
 AIC. *See* 5-amino-4-imidazolecarboxamide (AIC)
 Albrecht Wallenstein, 6
 Alcohol, 11, 12, 78, 80, 93, 100, 101, 105, 116, 135, 136, 141, 142, 148–150, 188, 191, 194, 199, 202, 222, 266, 291, 293, 313, 324, 339, 348, 349, 352, 354
 Alexander Gutman, 5
 Alexander Hamilton, 6
 Alexander of tralles, 2
 Alexander the great, 6
 Alfred Garrod, 5
 Allopurinol
 acute gouty arthritis, 331
 alloxanthine (oxypurinol), 329
 azathioprine, 330
 cyclophosphamide, 330
 de novo, 330
 feedback inhibition, 330
 histocompatibility locus antigen (HLA), 334
 hypersensitivity reactions, 332
 induced gout, 136–137
 6-mercaptopurine, 330
 orotidine-5-monophosphate decarboxylase, 330
 oxypurinol, 331
 prophylactic colchicine, 331
 standard treatment regimens, 330
 Stevens-Johnson syndrome (STS), 333
 T cell-mediated delayed hypersensitivity, 334
 toxic epidermal necrolysis (TEN), 332, 333
 toxic reactions, 331
 treatment stones, 348
 vasculitis, 332
 in vitro, 330, 332
 in vivo, 330
 xanthine oxidase, 330
 Amino acid structure of CSA, 235
 5-amino-4-imidazolecarboxamide (AIC), 48
 AMP. *See* Adenosine monophosphate (AMP)
 Ancient greek and roman civilization, 1
 Annexins, 278
 Anti-inflammation, 265, 270–271
 Anti-inflammatory eicosanoid, 232, 262–263
 Anti-inflammatory lipoxins effects
 in vivo, 265
 Antimetabolites, 35, 48, 106, 291, 295, 330, 337
 Antituberculous drugs, 137, 326
 Anton de Storck, 4
 Anton van Leeuwenhoek, 2
 Apoptosis, 208, 216, 230, 233, 234, 256, 257, 260, 262, 269–272, 312, 329
 APRTase. *See* Adenine phosphoribosyltransferase (APRTase)
 Archibald E. Garrod, 5
 Arthrocentesis techniques, 188–189
 Associated disorders
 DNA Polymorphisms, 151–152
 familial apolipoprotein c-II deficiency, 149
 familial combined hyperlipidemia, 149
 familial lipoprotein lipase deficiency, 149
 familial lipoprotein lipase inhibitor, 149
 fish-eye disease, 151
 high density lipoprotein (HDL), 148
 lecithin/cholesterol acyltransferase (LCAT) deficiency, 151
 low density lipoproteins (LDL), 148
 monogenic hypertriglyceridemia, 149–150
 nonsteroidal anti-inflammatory drugs (NSAIDs), 148
 type III hyperlipoproteinemia, 150–151
 very low density lipoproteins (VLDL), 148
 Asymptomatic hyperuricemia
 chlorthalodine, 293
 chronic renal disease, 292
 diuretics, 293
 drug-induced hyperuricemia, 293
 ethambutol, 294
 hypertension, 293
 nicotinic acid, 294
 pyrazinamide-induced hyperuricemia, 294
 renal calculi, 292
 salicylates, 293
 Atherosclerosis, 11, 147, 148, 150, 151, 153, 154, 352
 ATP-binding cassette subfamily G member 2 (ABCG2), 16, 17
 ATP degradation, 75–81, 83, 107, 108, 113, 125
 Aulus Cornelius Celsus, 1
 Autosomal dominant polycystic kidney disease (ADPKD)
 cerebral aneurysms, 119
 hypertension, 119
 renal failure, 119
 urinary tract infections, 118
 Avascular necrosis, 95, 199, 202 *See also* Osteonecrosis
- B**
 Bacterial arthritis, 96, 97, 194
 Beer, 11, 12, 136, 339, 348, 349, 352
 Benjamin Franklin, 4, 6
 Ben Johnson, 6
 Benzbromarone, 14–16, 96, 133, 138, 139, 325–326, 328–329
 severe hepatotoxicity, 329
 Biological functions of PAF, 227–228
 Blunt ends, 192

- Body mass index, 11, 349
Bony erosions, 199–201
 tophi, 200
Bursa, 92, 94, 95, 199, 200, 203, 208
Byzantine empire, 2
- C**
C5a, 210, 218–222, 227, 229, 235, 240,
 241, 243, 244
C5a des Arg, 220–221
Calcium pyrophosphate dihydrate (CPPD) crystals, 98,
 188, 191–193, 202, 209, 215,
 257, 297, 298
Cardinal Wolsey (the last medieval prince of the
 church), 6
Cardiovascular disease, 10, 15, 147, 153, 232, 303, 306,
 311, 320, 339, 351
C5a receptor, 220–222, 227
Carl Linnaeus, 6
Carl Scheele, 3
Carpal tunnel syndrome, 94, 105, 353
Cell membrane, 14, 43, 209, 241, 249, 250, 257,
 259–260, 275, 297, 301, 302
Cell migration, 208, 243, 247
Charles Darwin, 6
Chemoattractants, 207, 209, 210, 218–220, 222,
 227–229, 235–237, 240, 241, 244–246, 253,
 263, 320
Chemotactic peptide generation, 297
Cholesterol, 10, 12, 109, 110, 139, 148–153, 329, 345,
 351, 352
Chondrocalcinosis, 98, 199, 202–203
 pseudogout, 202
Chondrocytes, 15, 266
Chronic gouty arthritis, 2, 94–96, 348
Chronic renal failure, 10, 53, 87, 105, 118,
 127, 142, 352
Chronic tophaceous gout, 2, 5, 92–96, 98, 99, 109, 137,
 200, 324, 342
Clinical aspects of gout and associated
 disease states
 decreased renal clearance of urate, 91
 increased purine biosynthesis, 91
 microcrystals, 91
 primary gout, 91
 pseudogout, 91
 Secondary gout, 91
 synovium, 91
 uric acid overproduction and underexcretion, 91
Colchicine
 acute gout, 296
 gastrointestinal toxicity, 296
 mechanism action, 297
 myopathy, 96, 300
 pharmacokinetics, 298–299
 toxicity
 colchicine-induced myopathy, 299
 colchicine myoneuropathy, 299
 intravenous colchicine, 300
Colchicum autumnale, 6
Co-morbidities
 alcohol, 348
 beer, 349
 dietary factors, 348
 wine, 349
Compensated polarized microscopy, 191, 192, 194
Complement fragments, 220–221
Cotton Mather, 6
Count Nikolaus Ludwig von Zinzendorff (German
 theologian), 6
Crystal identification, 99, 191, 192, 296
Cyclooxygenase inhibitors classification
 cardiovascular events, 312
 renal hemodynamics, 311
Cyclosporine, 91, 93, 95, 96, 118, 128, 135, 137–139,
 145, 294, 300, 301, 328, 329, 346
 Arthrobacter protoformiae, 138
 Aspergillus flavus, 138
 Candida utilis, 138
Cytokines, 15, 194, 210, 211, 214–218, 220, 236–238,
 240–242, 244, 245, 253, 255–262, 264, 269,
 271, 273, 275, 277, 315, 319, 334
Cytotoxic agents, 135, 136, 294
- D**
DAMPs. *See* Inflammasome
DAP. *See* 2,6-diaminopurine (DAP)
Decreased hypoxanthine reutilization, de novo, 74, 75
DECT. *See* Dual energy computed tomography (DECT)
Denis, W., 4
De novo, 5, 13, 25, 30–34, 37, 39–44, 46, 47, 53–55,
 69–76, 81, 82, 103, 104, 106–108, 111, 127,
 140, 141, 223, 226, 227, 330, 352
De novo purine nucleotide synthesis
 adenosine monophosphate, 30
 adenosine triphosphate (ATP), 30
 adenylosuccinase, 30
 aspartic acid, 30
 carbon dioxide, 30
 de novo, 30
 energy phosphate compounds, 30
 formate, 30
 10-formyl-tetrahydrofolate, 30
 fumarate, 30
 glutamine, 30
 glycine, 30
 guanosine monophosphate, 30
 inosine-5'-phosphate (IMP), 30
 5, 10-methenyltetrahydrofolate, 30
 5-phospho- α -D-ribosyl pyrophosphate (PRPP), 30
 (COMP: Please insert correct symbol.)
 phosphoribosylamine, 30
 5'-phosphoribosyl-5-aminoimidazole
 (AIR), 30
 5'-phosphoribosyl-5-aminoimidazole-4-carboxamide
 (AICAR), 30
 phosphoribosylaminoimidazolecarboxamide formyl
 transferase, 30

- De novo purine nucleotide synthesis (*cont.*)
 phosphoribosylaminoimidazole
 carboxylase, 30
 5'-phosphoribosyl-5-aminoimidazole-4-carboxylate
 (CAIR), 30
 5'-phosphoribosyl-5-aminoimidazole-4-(*N*-succino)
 carboxamide (Succino-AICAR), 30
 phosphoribosylaminoimidazole-succinocarboxamide
 synthetase, 30
 phosphoribosylaminoimidazole synthetase, 30
 5'-phosphoribosyl-5-formamidoimidazole-4-
 carboxamide (formyl-AICAR), 30
 phosphoribosyl-formylglycineamidine synthetase, 30
 5'-phosphoribosyl-glycineamide (GAR), 30
 phosphoribosylglycineamide formyl transferase, 30
 phosphoribosylglycineamide synthetase, 30
 5'-phosphoribosyl-*N*-formylglycinamidine
 (FGAM), 30
 5'-phospho-ribosyl-*N*-formylglycine (FGAR), 30
 phosphoribosylpyrophosphate amidotransferase, 30
 purine salvage pathways, 30
 ribosylamine, 30
- Deoxyribo nucleic acid (DNA), 25, 26, 28, 39, 44, 46,
 47, 49, 53, 119, 148, 245, 251, 260, 261, 271,
 273, 275–278, 317, 343
- Deoxyribose phosphate, 26
- Desquamation, 93
- Destructive arthropathy, 94
- DeWitt Stetten, 5
- Diabetes mellitus, 10, 11, 96, 98, 100, 139, 147, 149,
 150, 152, 189, 294, 295, 309, 349, 351, 352
- 2,6-diaminopurine (DAP), 33, 38, 48, 50, 51
- Dicarboxylates, 16, 17
- Diet
 alcohol, 348
 beer, 349
 dietary factors, 348
 wine, 349
- Dietary restrictions, 11, 12, 339, 342, 352
- Differential diagnosis
 acute neuropathic joints, 98
 aspiration, 97
 bacterial arthritis (septic arthritis), 96
 calcification, 98
 calcium pyrophosphate
 crystal deposition disease, 96
 dihydrate, 97
 charcot joints, 98
 chondrocalcinosis, 98
 chronic neuropathic joints, 98
 chronic tophaceous gout, 98
 E. coli, 97
 gram-negative infections, 97
 gram-positive organisms, 97
 gram stain, 97
 hemochromatosis, 98
 hemodialysis, 97
 HIV disease, 97
 hyperparathyroidism, 98
 hypomagnesemia, 98
 hypophosphatemia, 98
 immunocompromised host, 96
 infected prosthetic joints, 97
 joint infections, 97
 N. gonorrhoeae, 97
 positive birefringence, 98
 pseudogout, 96, 97
 Pseudomonas aeruginosa, 97
 psoriatic arthritis, 98
 Reiter's syndrome, 98
 S. aureus, 97
 septic arthritis, 96
 Serratia marcescens, 97
 severe degenerative arthritis, 96
 synovial fluid
 culture, 97
 glucose, 97
 white blood cell count, 97
 syphilis, 97
 traumatic arthritis, 96, 98
- 2,8-dihydroxyadenine lithiasis
 adenine phosphoribosyltransferase, 132
 adenine phosphoribosyltransferase
 deficiency, 133
- 2,8-dihydroxyadenine stones, 36, 124, 127, 129, 132
- Diuretic(s), 11, 86, 87, 91, 93, 95, 100, 105, 115, 117,
 127, 135–137, 145–147, 148, 150, 152, 194,
 293, 306, 307, 309, 311, 314, 324, 326, 328,
 332, 345, 346, 349, 353, 354
- amiloride, 135
 benzothiadiazines, 135
 diuretic-induced gout, 135
 ethacrynic acid, 135
 furosemide, 135
 induced hyperuricemia, 115
 spironolactone, 135
 triamterene, 135
- Drug-induced hyperuricemia and gout, 135
- Dual energy computed tomography
 (DECT), 203–204
- Dyslipidemia, 10, 11, 152, 154, 349, 351–353
- E**
- Egyptian archeology, 1–2
- Elimination of uric acid
 acetoacetate, 85
 β -hydroxybutyrate, 85
 lactate, 85
 urate reabsorption mechanisms, 85
 uric acid renal elimination, 84
 urinary uric acid excretion, 85
- Emil Fischer, 4, 25
- Empress Maria Theresa of Austria, 4
- Endonucleases, 26
- E-selectin, 210, 237–239, 241–243, 261
- Ethanol, 77, 78, 80, 100, 101, 103, 105, 107, 135–137,
 307, 348

Excessive purine intake, 84, 105, 128
 Exonucleases, 26
 Extra-articular tophi, 94, 199, 201

F

Familial juvenile gouty nephropathy (FJGN), 120–121, 144, 145
 Familial juvenile hyperuricemic nephropathy (FJHN), 13, 53–55, 120, 145, 353
 Famous sufferers, 6
 Fatty acid oxidation deficiencies
 carnitine palmitoyltransferase II, 113
 heritable palmitoyltransferase deficiency, 113
 myoglobinuria, 113
 Febuxostat
 adverse reactions, 337
 hepatic metabolism, 337
 xanthine oxidase, 337
 Females gout
 hyperuricemia and gout in pregnancy, 146
 juvenile hyperuricemia and gout, 144–145
 postmenopausal hyperuricemia and gout, 146–147
 premenopausal hyperuricemia and gout, 145–146
 Fenofibrate
 Fenofibrate, hyperlipidemia, 345
 Fever and chills, 92
 FJGN. *See* Familial juvenile gouty nephropathy (FJGN)
 FJHN. *See* Familial juvenile hyperuricemic nephropathy (FJHN)
 Folin, O., 4
 Fructose, 11–16, 76–78, 107, 111, 127, 133, 135, 139–140, 338, 341–342, 349, 352
 Fructose-1,6-bisphosphatase deficiency, 78, 107
 Fructose-induced hyperuricemia, 11, 12, 107, 139–140
 de novo, 140
 Fructose-1-phosphate, 11, 140

G

Galen, 1
 Gemfibrozil, 12
 Generation of reactive oxygen radicals, 247
 Genetic abnormalities, 13–17
 Genetic polymorphisms of SLC2A9/GLUT9, 14
 Genome-wide association studies (GWAS), 13, 14, 16
 George Hitchings, 5
 George Mason (American statesman and drafter of the constitution), 6
 Gertrude Elion, 5
 Glucocorticoids, 278
 annexin, 318
 chemotaxis, 319
 cyclooxygenase synthesis, 318
 dexamethasone, 316
 glucocorticoid-induced inhibition, 318
 glucocorticoid-inducible protein, 318
 glucocorticoid response elements (GRE), 317
 hydrocortisone, 316

intercellular adhesion molecule-1 (ICAM-1), 320
 lipocortin-1, 318
 mechanism, 316
 methylprednisolone, 322
 neutrophilia, 319
 neutrophil migration, 320
 phospholipase, 319
 prednisone, 316
 transcortin, 316
 in vitro, 317
 in vivo, 317
 Glucose/fructose transporter, 13
 GLUT9, 14–16
 Glutamine hypothesis, 72
 GLUT9ΔN, 14
 GLUT9L, 14
 GLUT9S, 14
 Glycogen storage diseases (GSD)
 β2-microglobulinuria, 341
 calcium oxalate, 109
 creatine phosphokinase, 110
 debranching enzyme
 deficiency, 109
 de novo, 111
 generalized aminoaciduria, 341
 glucose-6-phosphatase deficiency, 108
 glycogen storage disease type XI, 113
 hemolytic anemia, 112
 inosine monophosphate, 111
 lactate dehydrogenase-A deficiency, 113
 metabolic myopathies, 111
 muscle phosphoglycerate mutase
 deficiency, 112
 myoadenylate deaminase deficiency, 111
 myoglobinuria, 110
 myopathy, 110
 nephrocalcinosis, 109
 phosphofructokinase activity deficiency, 111
 phosphofructokinase deficiency, 110
 phosphoglycerate kinase deficiency, 112
 phosphoglycerate mutase deficiency, 111
 phosphorylase kinase deficiency, 112
 Tarui's disease, 110
 type III, 110
 type V, 110
 type VII, 110
 GMP. *See* Guanosine-5'-monophosphate (GMP)
 GRE. *See* Glucocorticoids
 GTP, 33, 34, 36, 82, 83, 140, 216, 221
 Guanine, 4, 25, 27, 28, 30, 34, 42–44, 46, 72, 81, 130, 249, 330, 336, 337
 Guanosine-5'-monophosphate (GMP), 31, 33–35, 40–43, 46, 55, 82, 272
 Guanosinic acid, 72
 Guanylic, 26
 Guanylic acid, 27, 28, 55
 GWAS. *See* Genome-wide association studies (GWAS)

H

- HapMap, 14
- Hematological malignancies, 108, 128
- Henry Fielding, 6
- Hereditary fructose intolerance (HFI), 77, 78, 107, 127, 133, 139, 140, 341–342
- Hereditary xanthinuria, migratory polyarthritis, 131
- Heterozygote carriers of HGPRTase deficiencies, 72
- HFI. *See* Hereditary fructose intolerance (HFI)
- HGPRTase. *See* Hypoxanthine-guanine phosphoribosyltransferase (HGPRTase)
- High-energy phosphates, 30, 31, 34, 101, 140
- Hippocrates, 1
- Histone acetylation and glucocorticoids, 277–278
- HLA. *See* Allopurinol
- HPRTase. *See* Hypoxanthine-guanine phosphoribosyltransferase (HGPRTase)
- Hydrogen peroxide, 11, 248, 250–252, 260
- Hyperglycemia, 10, 152, 217, 351, 352
- Hyperlipidemia, 11, 12, 108, 109, 147–154, 291, 294, 312, 345, 352, 354
- Hypertension
 - alcohol, 352
 - de novo, 352
 - dyslipidemia, 351
 - meat, 351
 - metabolic syndrome, 351
 - obesity, 351
 - seafood, 351
 - vascular disease, 351
- Hypertriglyceridemia, 9–12, 33, 148–152, 345, 350–352
- Hyperuricemia
 - chemical properties of the uric acid, 187
 - uric acid has a solubility, 187
- Hyperuricemia and gout
 - diagnostic criteria for
 - acetate, 101
 - acetoacetate, 101
 - acetylcoenzyme A, 101
 - acute renal failure, 101
 - adenosine monophosphate, 101
 - adenosine triphosphate, 101
 - asymptomatic hyperuricemia, 100
 - β -hydroxybutyrate, 101
 - chemotherapy, 102
 - compensated polarized light microscopy, 99
 - ethanol, 101
 - hypercatabolic states, 101
 - hyperlacticacidemia, 101
 - hyperuricemia, 100
 - inosine, 101
 - lactate, 101
 - needle-like uric acid crystals, 99
 - nitroglycerin, 101
 - normal serum uric acid levels, 99
 - nucleoproteins, 101
 - 5'-nucleotidase, 101
 - radiation, 102
 - rhabdomyolysis, 101
 - seizures, 102
 - solubility uric acid, 99
 - toxemia pregnancy, 100
 - urate nephropathy, 100
 - urolithiasis, 100
 - management
 - colchicine, 291
 - corticosteroids, 291
 - NSAIDs, 291
 - overview, 291–292
 - proper, 291
 - uric acid lowering therapy, 291
 - uricosuric agents, 291
- Hyperuricemia mechanisms
 - 1-¹⁴C-glycine, 72
 - de novo, 72
- Hyperuricemia renal mechanisms
 - decreased tubular secretion, 85
 - postsecretory reabsorption, 85
 - pyrazinamide suppression test, 85
 - urate excretion, 85
 - urate underexcretion, 86
- Hyperuricosuric calcium oxalate nephrolithiasis, calcium oxalate, 134
- Hypoxanthine, 5, 13, 25, 71, 101, 291
- Hypoxanthine-guanine phosphoribosyltransferase (HGPRTase)
 - adenine phosphoribosyltransferase (APRTase), 42
 - deficiency, 41, 72, 73, 106, 121, 123, 124, 144, 145
 - de novo, 42–44, 46
 - dimagnesium PRPP, 43
 - DNA methylation, 46
 - hypoxanthine-guanine phosphoribosyltransferase
 - deficiency, 44
 - enzyme, 44
 - gene, 44
 - pseudogenes, 43
 - inosine monophosphate (IMP) dehydrogenase, 45
 - Kelley-Seegmiller syndrome, 45
 - Lesch-Nyhan syndrome, 45
 - NAD synthetase, 45
 - nicotinamide adenine dinucleotide (NAD), 45
 - nicotinic acid phosphoribosyltransferase, 45
 - X-chromosome activation, 46
 - X-chromosome inactivation, 46
- I**
- ICAM-1. *See* Glucocorticoids
- ICAMs. *See* Intercellular adhesion molecules (ICAMs)
- I κ B, 261, 262, 273, 274
- IL-8 gene, in vitro, 237
- Immunoglobulin, 192, 213, 230, 233, 245, 319, 335
- IMP. *See* Inosine monophosphate (IMP)
- Increased cells deficient, 33
- Increased nucleic acid turnover
 - adenine phosphoribosyltransferase, 81
 - ATP degradation, 83
 - de novo, 81
 - epidermal turnover, 81
 - hemoglobinopathies, 81

- hemolytic anemias, 81
- hyperlacticacidemia, 83
- hyperuricosuria, 83
- ineffective erythropoiesis, 81
- multiple myeloma, 81
- muscle contractions, 83
- muscular exercise, 83
- myeloproliferative disorders, 81
- neoplasms, 81
- nucleotide degradation, 81
- pentose phosphate pathway, 81
- pernicious anemia, 81
- phosphoribosylpyrophosphate (PRPP), 81
- polycythemia, 81
- psoriasis, 81
- Indomethacin**
 - toxicity, 314
 - in vivo, 314
- Inflammasome**
 - autoinflammatory, 213, 322
 - caspase-1, 214, 216–218
 - cryopyrin, 213, 216
 - danger-associated molecular patterns (DAMPs), 214–215
 - IL-1b, 15, 213–215, 218
 - IL-1 β , 216
 - innate immune system, 213–216
 - NLRP3, 213–217
 - Nod (nucleotide oligomerization domain)-like receptors (NLRs), 215, 216
 - pathogen-associated molecular patterns (PAMPs), 214–215
 - periodic fever syndrome, 213, 214
 - periodic fever syndromes, 213, 214
 - pro-IL-1 β , 216, 217
 - RIG-I-like receptors (RLRs), 215
- Inflammatory cell chemotaxis**, 297
- Inflammatory response**, 53, 92, 127, 187, 188, 194, 207, 208, 210, 212, 215, 216, 218, 221, 223, 227, 230–232, 234, 237, 238, 243, 246, 247, 252–256, 258–267, 270–274, 276–278, 294, 297, 298, 301, 302, 310, 316, 317, 319, 320
- Inhibitory concentration**, 297
- Inosine monophosphate (IMP)**, 30, 31, 33–35, 40, 43, 45, 46, 55, 74, 79, 80, 82, 83
- Inosine 5'-phosphate dehydrogenase**, 34
- Inosinic acid**, 27, 28, 33, 34, 40, 72–74, 79, 80, 82, 83, 108
- Insulin resistance**, 10, 12, 139, 149, 152, 349, 351, 353
- Insulin resistance syndrome**, 10, 152, 351
- Integrins**, 210, 211, 237, 238
- Integrins**, 210, 211, 227–229, 237, 238, 240, 241, 243–247, 258
- Integrin structure**, 243–245
- Intercellular adhesion molecules (ICAMs)**, 210, 245
- Intercritical gout**, 92–94, 193
 - asymptomatic gout, 94
 - familial juvenile gouty nephropathy, 94
 - glomerulonephritis, 94
 - polycystic kidney disease, 94
 - sarcoidosis, 94
- Interleukin-8 (IL-8)**, 209, 210, 218–221, 227–229, 235–238, 240, 241, 244–246, 253, 255, 256, 258, 259, 261, 267, 274, 319, 320
 - amino acid structure, 235–236
 - Amino Acid Structure of CSa, 235
 - Amino Acid Structure of IL-8, 235
- Interleukin-18**, 216–217
- Interleukin-1 β** , 216–217
- Interleukin-1 β and interleukin-18**, 216–217
- Interleukin 1 inhibitors**
 - anakinra, 322
 - canakinumab, 323
 - decoy receptor, 323
 - rilonacept, 323
- In vitro**, 35, 54, 131, 210, 212, 213, 237, 249, 255, 264, 297, 303, 310, 317, 330, 332
- In vivo**, 54, 234, 235, 237, 241, 249, 264, 265, 273, 297, 314, 317, 330
- Isaac Newton**, 6
- Ischemic heart disease**, 10, 115, 152, 351, 352
- Isotopes**
 - accelerated production of uric acid, 54
 - de novo, 54, 55
 - estimation, 54
 - glycine alpha-N¹⁵, 54
 - glycine-1-C¹⁴, 54
 - rate of purine synthesis, 54
 - in vitro, 54
 - in vivo, 54
- J**
- James Wyngaarden**, 5
- Jay Seegmiller**, 5
- Johann Wolfgang von Goethe**, 6
- John Buchanan**, 5
- John Calvin**, 6
- John Dryden**, 6
- John Hunter**, 6
- John Milton**, 6
- John Wesley (English evangelist and theologian)**, 6
- Joint effusions, magnetic resonance image**, 200
- Joint involvement**, 92, 94, 147
- K**
- Kelley-Seegmiller syndrome**
 - hypoxanthine-guanine phosphoribosyltransferase, partial deficiency, 104
 - nephrolithiasis, 105
 - neurological dysfunction, 105
- Kidney stones**, 11, 12, 15, 47, 48, 104–106, 122–125, 128, 132, 134, 187, 201, 352
- Kossel**, 25

L

- Leonardo da Vinci, 6
 Lesch-Nyhan, 5, 35, 44, 45, 103–105, 115, 120, 123, 124, 127–129, 131, 141, 145, 341, 353
 Lesch-Nyhan syndrome
 central nervous system dysfunction, 103
 choreoathetosis, 104
 de novo, 104
 hypoxanthine-guanine phosphoribosyltransferase, 103
 nephrolithiasis, 103
 neurological disorder, 103
 Leukotriene B₄ (LTB₄), 218, 219, 229–231, 233, 235, 253, 315, 319
 biosynthesis
 lipoxygenase, 230–231
 phospholipase A₂, 230–231
 Lifestyle, 354
 Ligands for integrins, VEGF, 246
 Lipoxin biosynthesis
 in vitro, 264
 in vivo, 264
 Lord Beaverbrook, 6
 Lord Howe, 6
 Losartan
 angiotensin II (AII) receptor antagonist (ARB), 345
 uricosuric effect, 346
 Low-purine diet, 49, 339
 purine-free diets, 339
 L-selectin, 210, 238–243
 LTA4 Hydrolase, 230–232

M

- MAP kinase, 230, 249, 256, 259, 278
 Marshal Saxe, 6
 Martin Luther, 6
 Mechanisms of NLRP3 activation
 asbestos, 217
 MSU crystals, 217
 reactive oxygen species (ROS), 217
 silica, 217
 Medullary cystic disease (MCD), 119–120
 Megaloblastic anemia, 104, 106, 117, 140–141
 de novo, 141
 Mercaptopurine, 5, 25, 27, 31, 35, 37, 42, 96, 137, 138, 295, 330, 332, 337
 6-mercaptopurine, 5, 25, 27, 31, 35, 37, 42, 96, 137, 138, 295, 330, 332, 337
 Metabolic myopathies, 77–79, 107, 111, 113
 Metabolic syndrome, 10–12, 15, 16, 152, 338, 349, 351–353
 Michael Lesch, 5
 Miscible pool of urate
 de novo, 70
 ¹⁵N-labeled uric acid, 71
 Mode of action
 glucocorticoid receptors, 275
 glucocorticoids, 277–278

- Monoarticular or oligoarticular arthritis, 92, 95, 96, 99, 354
 Monocarboxylates, 16, 17
 Monogenic mutations, 15
 Monosodium urate (MSU)
 crystal-induced neutrophil activation, 256
 crystallization
 acute gout, 211
 diagnosis of acute gout, 211
 hyperuricemia, 211
 immunoglobulins, 213
 intra-articular temperatures, 212
 serum, 211, 212
 in vitro, 212, 213
 crystals, 93, 94, 191–193, 199, 204, 207, 213, 215, 217, 218, 237, 253–260, 273, 298, 353
 monohydrate crystals, 91, 116
 Monosodium urate crystal
 in vitro, 210, 255
 Musculoskeletal ultrasound
 hyperechoic enhancement, 203
 radiological examinations, 199
 urate deposits, 203
 Myeloperoxidase (MOP), 230, 250–252, 260
 Myelosuppression, 96
 Myoadenylate deaminase deficiency, 83, 108, 111, 112

N

- NAD⁺, 34
 NADPH oxidase assembly
 in vitro, 249
 in vivo, 249
 Naproxen
 cardiovascular toxicity, 315
 treatment regimens, 315
 Neoplastic disease
 acute uric acid nephropathy, 295
 antineoplastic treatment, 295
 Nephrogenic diabetes insipidus (NDI), 121–122
 Nephrolithiasis, uric acid calculi, 348
 Neurological deficits, 44, 95, 104–106, 353
 Neutrophil and macrophage apoptosis, 260
 Neutrophil chemoattractants
 chemoattractants, 207, 218–219, 227, 229, 235, 237, 253, 263
 chemotactic cytokines, 218, 219
 neutrophil chemotaxis, 218–220, 227
 Neutrophil migration, 207, 219–220, 235, 237, 240, 241, 247, 320
 NF-κB, 215, 256, 261, 262, 271–275, 277
 NHANES III, 9
 Nicotinic acid, 45, 87, 135, 139, 294
 Nitric oxide, 9, 216, 217, 242, 248, 251–252, 264, 265, 270–274, 349, 351
 Nitric oxide and bacterial killing, 251–252
 NLRP3 activation mechanisms
 asbestos, 217
 MSU crystals, 217

reactive oxygen species (ROS), 217
 silica, 217
 NLRs. *See* Inflammasome
 Nonsteroidal anti-inflammatory drugs
 (NSAIDs)
 arachidonic acid, 301
 cyclooxygenase-1 [COX-1], 301
 cyclooxygenase-2 [COX-2]), 301
 eicosanoids, 301
 inhibition of cyclooxygenase, 301
 nonselective NSAIDs, 302
 prostaglandin endoperoxides, 301
 selective COX-2 inhibitors, 303
 toxicity
 acute renal papillary
 necrosis, 308
 gastrointestinal bleeding, 307
 hyperkalemia, 309
 hypertension, 309
 hyponatremia, 309
 hyporeninemic hypoaldosteronism, 309
 nephrotoxic disorders, 307
 NSAID-induced interstitial nephritis, 308
 NSAID-induced nephrotoxicity, 309
 sodium retention, 309
 upper GI toxicity, 305
 in vitro, 303
 NPT1, 16, 17
 Nucleases, 26, 261
 Nucleic acids, 4, 26, 28, 30, 31, 33, 55, 69, 70,
 75, 78, 81–83, 91, 100, 103, 105, 107,
 108, 111, 115–117, 124, 128, 129,
 136, 145, 261, 262
 Nucleoside, 27, 28, 34, 54, 70, 75, 79, 80, 140,
 218, 328, 330, 336, 337
 Nucleoside phosphorylase(s), 27, 28, 34, 54, 79,
 80, 140, 336, 337
 5'-nucleotidases, 28, 34, 35, 79, 80, 101, 140
 Nucleotide, 11, 14, 15, 17, 25, 30–43, 47, 52, 54, 70, 71,
 73–77, 81–84, 100, 106, 108, 110, 127, 214,
 215, 227, 232, 249, 251, 258

O

Obesity, 9, 10, 12, 33, 100, 147–150, 152–154, 291, 293,
 294, 313, 324, 332, 339, 348–354
 Oded Sperling, 5
 Olecranon bursa, 92, 94, 95, 200, 203
 Oligoarticular, 92
 Organ transplantation, 95, 137, 145, 202, 328, 329
 Orotic acid, 33, 38, 54, 330
 Osteonecrosis, 202
 Oxidants and oxidant-mediated destructive
 responses
 fenton reaction, 250
 haber-weiss reaction, 250
 Oxidants and uric acid destruction, 252
 Oxipurinol calculi, 133
 Oxygen free radicals, 11, 255, 259
 Oxygen radical generation, 227, 247–249

P

PAF. *See* Platelet-activating factor (PAF)
 PAMPs. *See* Inflammasome
 Pegloticase
 adverse events, 344
 antibodies, 344
 glucose-6-phosphate deficiency, 345
 infusion reactions, 344
 Krystexxa, 344
 mammalian recombinant uricase, 344
 Phagocytosis, 207–209, 230, 233, 234, 242, 247–252,
 256, 258–260, 263, 265, 269, 270, 273, 297,
 319, 320
 Phosphatases, 33, 34, 75, 249, 265, 298, 299
 Phosphoenol pyruvate carboxykinase deficiency, 107
 Phospholipase classification, in vivo, 234
 Phospholipase D, 257–258, 298
 Phospholipids metabolizing enzymes, 258
 Phosphoribosylamine (PRA), 33, 72, 81
 5-phosphoribosyl-1-pyrophosphate, 33, 37
 Phosphoribosyl pyrophosphate (PRPP), 5, 13, 30–47, 50,
 51, 54, 55, 71–76, 81, 82, 103, 105–107, 111,
 117, 120, 123, 124, 127, 128, 132, 133,
 139–141, 145, 291, 292, 330, 337, 348, 353
 amidotransferase
 adenosine monophosphate (AMP), 40–42
 de novo, 40–42
 feedback inhibitors, 40
 feedback regulation, 40
 gene, 41
 glutamine phosphoribosylpyrophosphate
 amidotransferase, 40
 guanosine monophosphate (GMP), 40–42
 inosine monophosphate (IMP), 40
 5-phosphoribosylamine, 40
 phosphoribosylpyrophosphate (PRPP), 40–42
 ribonucleotides, 40
 Phosphoribosyl pyrophosphate synthetase (PRPP
 synthetase), 5, 13, 32, 33, 36–40, 71, 73, 82,
 103, 106, 117, 120, 123, 124, 128, 132, 133,
 348, 353
 allosteric regulation, 36
 amidotransferase, 36
 de novo, 37, 39
 hypoxanthine-guanine phosphoribosyltransferase, 36
 overactivity
 de novo, 106
 neurological deficits, 106
 phosphoribosylpyrophosphate
 amidotransferase, 106
 pretranslational regulation, 39
 Platelet-activating factor (PAF), 210, 218–230, 232, 235,
 238, 241, 244, 255, 259, 263, 264, 270, 271
 acetylhydrolase, 228–229, 270–271
 biological functions, 227–228
 de novo, 223, 230
 receptor, 222, 223, 227, 241
 Podagra, 1, 92, 99, 212, 353
 Polyarticular, 92, 95–98, 320, 321
 Polyarticular gout, 92, 98, 320, 321

- Polymerase chain reactions, 194
 Prepatellar bursae, 94, 200
 Prevalence, 9–17, 100, 122, 123, 148, 309, 349, 351, 352
 Primary underexcretor gout, 114
 Probenecid
 acute gouty arthritis, 327
 benemid treatment regimens, 327
 methotrexate toxicity, 327
 uric acid nephrolithiasis, 327
 Proinflammatory mediators
 bradykinin, 254
 non-chemotactic, proinflammatory cell mediators, 253
 tumor necrosis factor, 254–255
 vasoactive arachidonic acid metabolites, 253
 Prophylactic colchicine, 93, 331
 Proteinases, 219–220,
 237, 252
 P-selectin glycoprotein ligand-1, 220, 239, 242, 243
 Purine(s), 4, 11, 25–55, 69, 91, 187, 201, 260, 291
 kinase, 34
 nucleotides, 25, 28, 30–34, 37–43, 52, 54, 70, 71,
 73–76, 78–82, 100, 106–108, 127, 136, 141,
 336, 337
 Purine biosynthesis
 decreased renal function, 70
 de novo, 69, 70
 glycine, 70
 hereditary renal hypouricemia, 70
 overproducers of uric acid, 70
 secondary gout, 70
 urate excretion, 70
 urate overexcretors, 70
 uric acid excretion, 69
 uric acid overexcretion, 70
 urinary uric acid excretion, 70
 Pyruvate carboxylase deficiency, 107
 Pyruvate dehydrogenase deficiency, 107
- Q**
 Queen Anne (queen of England, Scotland), 6
- R**
 Reactive oxygen species (ROS), 9, 214, 217, 229, 241,
 242, 248, 250, 274, 320, 329, 350, 351
 Refractory gout
 allantoin, 343
 allergic reactions, 343
 Aspergillus flavus, 343
 hydroxyisourate, 343
 pegloticase, 343
 rasburicase, 343
 tumor lysis syndrome, 343
 uricase, 343
 Renal function determination
 cockcroft formula, 334
 gault formula, 334
 Renal tubular transport, 13–17
 Resolvin biosynthesis, resolution, 266
 Resolvin receptors, 266–270
 Rheumatoid nodules, 95
 Rhomboid, 192, 193
 Ribo nucleic acid (RNA), 404, 442, 449, 450, 579, 583,
 585, 587
 Ribonucleotides, 31, 33, 35, 40
 Ribose phosphate, 26, 33
 Ribose-5-phosphate, 32, 33, 36–39, 73, 75, 111, 140
 Ribose phosphate pyrophosphokinase, 31, 33, 34, 37,
 39–42, 46, 55, 72, 105, 123, 124, 140, 141,
 145, 291, 292, 324. *See also* Phosphoribosyl
 pyrophosphate synthetase (PRPP synthetase)
 RLRs. *See* Inflammasome
 Roentgenographic findings, 199–204
 radiological examinations, 199
- S**
 Salicylates, 102, 115, 126, 133, 135, 136, 138, 294,
 325–328, 348
 Salvage pathways, 13, 30, 33–38, 40, 43, 54, 352
 Samuel Johnson, 6
 Secondary gout renal mechanisms
 acetoacetate, 87
 β -adrenergic blockers, 87
 β -hydroxybutyrate, 87
 branched chain keto acids, 87
 catecholamines, 87
 chronic renal disease, 86
 cyclosporin A, 87
 decreased glomerular filtration rate, 86
 dehydration, 87
 diabetes insipidus, 87
 diuretic-induced hyperuricemia, 87
 furosemide, 87
 hyperuricemia of renal failure, 87
 lactate, 87
 lacticacidemia, 87
 lead, 87
 lead intoxication, 86
 levodopa, 87
 nicotinic acid, 87
 nonsteroidal anti-inflammatory drugs, 87
 pyrazinamide, 87
 salicylate, 87
 saturnine gout, 87
 secondary hyperuricemia, 86
 tubular reabsorption of urate, 86
 tubular secretion of urate, 86
 Secondary hyperuricemia, 81, 86, 87, 103, 105, 107–108
 Selectins (structures), 210, 211, 237–241,
 243–245, 247, 258
 Septic joints, 92, 97, 98, 191
 Single nucleotide polymorphisms (SNPs), 14–17
 Sir Alfred B. Garrod, 4
 Sir Thomas Sydenham, 2
 SLC2A9, 13–17

- SLC5A8, 16, 17
 SLC 5A12, 16, 17
 SLC17A1, 16
 SNPs. *See* Single nucleotide polymorphisms (SNPs)
 Soft tissue swelling, 98, 199–200
 magnetic resonance image, 200
 STS. *See* Allopurinol
 Sugar-sweetened soft drink, 11, 12, 15, 349, 352
 Superoxide, 11, 221, 227, 230, 232, 248, 250–252, 257, 258, 265, 272
 Symptomatic drug-induced hyperuricemia
 drug-induced, 294
 symptomatic hyperuricemia, 294
 Synovial fibroblast-like cells, 237, 255, 256
 Synovial fluid
 analysis, 93, 97, 188, 189, 193
 culture, 97, 99, 188–190
 differential cell, 191
 gram stain, 190, 191
 white blood cell counts, 97, 189–191, 194
 Synovial membrane, 207–211, 218, 219, 223, 231, 239, 241, 255, 259, 264
 chemoattractants, 207, 209, 210, 218–223, 227–229, 235–237, 240, 241, 244–246, 253, 263
 cytokines, 210, 211, 214–218, 220, 236, 238, 241, 242, 244, 253, 255, 256, 259–262, 264, 269, 271, 273, 275, 277, 315
 integrins, 210, 211, 241
 inter cellular adhesion molecules (ICAMs), 209, 210, 237, 240, 242, 244, 245, 256, 261
 selectins, 210, 211, 239, 241, 243
 type A synovial membrane lining cells, 209, 218
 type B synovial membrane cell, 209
 in vitro, 210, 212, 213, 237, 249, 255, 264
- T**
 TEN. *See* Allopurinol
 Therapeutic regimens
 ACTH dosage, 322
 adrenocorticotrophic hormone (ACTH), 321
 estrogens, 321
 hyperthyroidism, 321
 intra-articular injection steroids, 320
 intravenous methylprednisolone, 321
 mini-pulse methylprednisolone, 321
 polyarticular gout, 320
 toxicities, 321
 6-thioguanine, 35, 37
 Thomas Gray, 6
 Tissue hypoxia, 77, 80, 81, 103, 105, 107, 154
 Tophaceous deposits management
 Lesch-Nyhan disease, 341
 lithotripsy, 341
 oxypurinol stones, 341
 surgery, 340
 xanthine stones, 341
 Tophaceous gout, 2, 5, 92–96, 98, 99, 106, 109, 137, 142, 152, 200, 292, 324, 328, 330, 332, 342, 353, 355
 Tophi, 1, 3, 70–72, 78, 91, 94–96, 99, 100, 105, 112, 137, 147, 199–204, 211, 213, 218, 294, 340, 342, 353, 354
 Transplant gout, 95, 96
 Tsai F.Yu, 5
 Type A synovial membrane lining cells (macrophage-like synoviocytes), 209, 218
 Type B synovial membrane cell (fibroblast-like synoviocyte), 209
- U**
 URAT1, 14–17
 Urate-lowering therapy, uricosuric drugs, 324
 Urate nephropathy
 microbial uricase, 115
 microtophi, 115
 urate nephropathy, 115, 116
 Urate reabsorption, 14–16, 85, 86, 114, 115, 125–127, 135
 Urate transport, 13–16, 121, 126, 133
 Urate turnover, 72
 Uric acid
 calculus
 ultrasonography, 201
 uric acid nephrolithiasis, 201
 excretion, decrease, 114–121
 metabolism
 de novo, 69
 gout, 69
 hyperuricemia, 69
 mechanisms, 69
 nucleic acids, 69
 uric acid, 69
 nephrolithiasis, 122–135
 cystine stones, 125
 cystinuria, 125
 de novo, 127
 hemoglobinopathies, 125
 hereditary renal hypouricemia, 125
 hypercalciuria, 126
 hypouricemia, 125
 Kelley-Seegmiller syndrome, 124
 Lesch-Nyhan syndrome, 124
 malignancies, 127
 Prader-Willi syndrome, 129
 xanthinuria, 127
 overproduction
 de novo, 103
 hyperuricemia and gout, secondary forms, 103
 Kelley-Seegmiller syndrome, 103
 Lesch-Nyhan syndrome, 103
 phosphoribosylpyrophosphate (PRPP), 103
 phosphoribosylpyrophosphate synthetase superactivity, 103
 secondary hyperuricemia and gout, 103

Urinary uric acid measurements
 24-h urinary uric acid, 102
 24-h urine collection, 102
 overproducer, 102
 radiocontrast materials, 102
 underexcretor, 102
 uricase method, 102

V

Vascular disease, 10, 150, 151, 153, 312, 351
Visceral tissues, 95

W

Wayne Rundles, 5
William Congreve, 6

William Heberden, 3
William Kelley, 5
William Nyhan, 5
William Pitt the Elder and the Younger, 6

X

Xanthine

 dehydrogenase, 11, 124, 127, 130, 131
 lithiasis, 123, 129–130
 oxidase, 5, 11, 25, 27, 28, 48, 49, 52, 53, 73, 79,
 80, 130, 131, 133, 137, 140, 154, 217, 291,
 294, 295, 324, 325, 329–337, 340, 343,
 349, 350, 354

Xanthinuria, 123, 127, 129–133

Xanthosine monophosphate (XMP), 31, 34, 45

XMP. *See* Xanthosine monophosphate (XMP)