INDEX

Note: PH stands for pulmonary hypertension;
PAH for pulmonary arterial hypertension.
Page numbers in *italics* indicate figures.
Page numbers followed by a "t" indicate tables.
Clinical trials are indexed under the acronym of the name.

```
6MWD (6-minute walk distance)
 effect of exercise on, 213
 effect of riociguat on, 193-194, 195, 195t, 196, 197, 198t
 effect of sildenafil and tadalafil on, 181-183, 182, 185
 in evaluation of treatment efficacy, 101-107, 116, 283, 285t, 286-287
 goal level, 114, 119, 284t, 287
 PAH risk and, 36, 112t
 predictive value of, 286-287
Activin A receptor type II-like 1 (ACVRL1), 34, 81
Acute pulmonary hypertension, 239-242, 240
 right heart failure in, 241, 244-245, 246t
Acute respiratory distress syndrome (ARDS), 239, 241, 249
Acute respiratory failure, 251-253, 252
 extracorporeal life support, 253, 255-256
Acute vasodilator testing (AVT), 270, 271
Acute vasoreactivity test, 102, 110-111
Adempas. See Riociguat.
Adenosine, 62, 110
Adjunctive therapy and supportive care for PAH, 203-216
 anticoagulants, 206-209
 cardiopulmonary rehabilitation, 211-212
 digoxin, 211
 diuretics, 203-206
 in pediatric patients, 276-277
 supplemental oxygen, 209-210, 213
Advanced care practitioner, 295-296, 296t, 297
Age, PAH and, 31-32, 35, 44
Air travel, 292-293
Altitude, hypoxia and, 268, 292, 293
AMBITION trial, 116-118, 117
Ambrisentan, 160-165, 166t, 275. See also Endothelin receptor antagonists
  (ERAs).
 action mechanism, 160
 adverse reactions, 163-164, 166t
 AMBITION trial, 116-118, 117
 CYP interactions, 156t
 dosing information, 156t, 166t
 drug interactions, 169, 170t, 171t, 172
 efficacy and safety, 160-166, 163
   ARIES-1 trial, 160-163, 163
   ARIES-2 trial, 163-164, 164
   ARIES-3 study, 164-165, 165
   ARIES-E (extension study), 164, 165
   as initial treatment for PAH, 116-118, 117
   with PAH of various etiologies, 164-165, 165
```

indications for, 104t, 160, 172 in combination with sildenafil, 108t

| Ambrisentan, indications for (continued) | Bosentan, indications for (continued) |
|---|--|
| in combination with tadalafil, 106t, 116-118, 117 | FDA approved uses, 172 |
| FDA approved uses, 172 | in pediatric patients, 275 |
| monitoring information, 166t | liver aminotransferase, 159, 162t, 169 |
| pharmacokinetic characteristics, 156t | monitoring information, 162t |
| receptor binding, 154, 156t, 160, 275 | pharmacokinetic characteristics, 156t |
| when to discontinue, 166t | receptor binding, 154, 156t, 157, 274 |
| Aminorex, 18, 35, 37t | when to discontinue, 162t |
| Aminotransferase. See <i>Liver aminotransferase</i> . | Brain natriuretic peptide (BNP), 61-62, 177, 178, 274 |
| Ammodanistetase. See Elver ammoransjerase. Amlodipine, 274 | monitoring and follow-up, 284t, 285t, 287-288 |
| | |
| Amphetamines, 18, 31, 37, 37t | BREATHE-1 trial, 157-159 |
| Angiography, 58-60, 222-225, 270 | BREATHE-5 trial, 159 |
| Anticoagulants, 25, 206-209, 214. See also <i>Platelet aggregation</i> . | Bronchodilators, 100 |
| agents | C |
| other than warfarin, 208-209 | C-type natriuretic peptide (CNP), 178 |
| warfarin, 207-209, 208 | Calcification |
| for CTEPH, 100, 217, 228 | of aortic valve, 93 |
| ERA interactions with, 171t | of pulmonary arteries, 73, 75, 76 |
| hypercoagulable state in PAH, 206 | Calcium-channel blockers (CCBs), 62, 102, 271-274 |
| in IPAH, 207, 208, 209 | indications and efficacy, 104t, 110, 271-274 |
| treatment recommendations, 100, 209 | in pediatric patients, 271-274 |
| Antifungals, 171t | CAMPHOR Quality of Life questionnaire, 231 |
| Antihypertensives, 100 | Capillary hemangiomatosis, 16t, 17, 19, 92 |
| Anxiety, 291 | causes and findings, 59t, 80t, 92, 96-97 |
| Aortic valve calcification, 93 | Carbon monoxide, diffusing capacity of the lung (DLCO), 57 |
| APAH-CHD, 40-41 | in CTEPH, 221 |
| Appetite suppressants, 18, 31, 35, 37t | Cardiac index, 289 |
| ARIES-1 trial, 160-163, 163 | Cardiac magnetic resonance (CMR), 60-61 |
| ARIES-2 trial, 163-164, 164 | Cardiac output, 30, 239 |
| ARIES-3 study, 164-165, 165 | atrial septostomy and, 255 |
| | diuretics and, 204-205 |
| ARIES-E (extension study), 164, 165 Arterial blood gas, 270 | iloprost effect on, 143 |
| e · | |
| Aspirin, 209 | increased, 25, 30, 64 |
| Atrial natriuretic peptide (ANP), 177, 178 | liver disease and, 39 |
| Atrial septostomy, 255 | measurement of, 64 |
| for pediatric patients, 277 | mPAP and, 14 |
| Autoimmune thyroiditis, 26 | in PH/PAH, 25, 30, 30, 39, 64, 111, 241 |
| | outcomes and, 32, 35 |
| Beraprost, 104t, 147-148 | PVR and, 19 |
| Biomarkers, 61-62 | Cardiopulmonary exercise testing, 112t, 284t, 285t, 287 |
| BMPR2. See Bone morphogenic protein receptor-2. | Cardiopulmonary rehabilitation, 211-212, 291 |
| BNP. See Brain natriuretic peptide. | Cardiopulmonary resuscitation (CRP), 256, 292 |
| Bone morphogenic protein receptor-2 (BMPR2), 18, 33, 34, 44, 81, 267-268 | "do not resuscitate" order, 292 |
| Borg Dyspnea Scale, 194-196, 195t, 198t | Catheterization. See Right heart catheterization. |
| Bosentan, 157-160, 162t. See also Endothelin receptor antagonists (ERAs). | Central venous pressure (CVP), 243, 257 |
| adverse events, 159-160, 162t, 169 | CHEST-1 trial, 193-196, 194, 195t, 229 |
| CYP interactions, 156t | CHEST-2 trial, 196 |
| dosing information, 156t, 162t | Chest radiography, 53, 69-70, 70, 270. See also <i>Radiography</i> . |
| drug interactions, 169, 170t, 171t, 172 | congenital shunts, 80-81 |
| with sildenafil/tadalafil, 170t | for CTEPH, 221 |
| efficacy and safety, 119, 121, 157-160, <i>158</i> | Children, PH in, 266-277. See also <i>Pediatric patient</i> . |
| | |
| BREATHE 1 trial, 157-159 | causes of, 263, 266-269 |
| BREATHE-5 trial, 159 | diagnostic studies, 270, 272-273 |
| EARLY study, 159-160, 161 | mPAP for definition of, 263 |
| indications for, 104t, 157, 172 | symptoms, 269, 269t |
| in combination therapy, 106t, 108t | treatment, 271-277 |
| for CTEPH, 230-231 | Chronic hemoglobinopathies, 39-40 |

| hronic obstructive pulmonary disease. See <i>COPD</i> . hronic thromboembolic pulmonary hypertension (CTEPH), 24-25, 217-238 | Chronic thromboembolic pulmonary hypertension (CTEPH), treatment (continued) |
|--|--|
| causes of, 24, 269 | riociguat, 100, 119, 191, 201, 229, 233 |
| characteristics of, 217 | CHEST-1 trial, 193-196, 194, 195t, 229 |
| abnormal V/Q scan, 217, 218, 222, 223 | sGC stimulators (riociguat), 100, 191-202, 229, 233 |
| single or recurrent PE, 217 | sildenafil, 231-232 |
| classification with PEA, 226, 227t | surgery (PEA), 225-228 |
| clinical presentation, 41-42, 219-220, 220t | eligibility for, 226, 226t, 232 |
| exercise intolerance, 219-220 | treprostinil, subcutaneous, 230 |
| exertional dyspnea, 219-220 | as WHO Group 4, 16t, 24-25, 100, 217, 232 |
| findings on physical exam, 220 | Cigarette smoking, 120 |
| heart sounds, 220 | Cirrhosis, 39, 89 |
| prior history, 219, 221 | Classification of pulmonary hypertension (PH), 15-25, 16t-17t, 26 |
| diagnosis and evaluation, 221-225, 232 | Dana Point classification, 15, 16t-17t |
| distinguishing from other forms of PH, 217, 220t | GROUP 1: PAH (pulmonary arterial hypertension), 16t, 17-21, 26, 44, 99 |
| excluding from PH diagnosis, 58 | functional capacity, classification by, 19-21, 22t, 44 |
| physical examination, 220 | medications for, 27, 44, 100 |
| workup, 221-225, 232 | treatment approach, 99-119, 100 |
| chest X-ray, 221 | GROUP 1[7]: pulmonary veno-occlusive disease (PVOD) and/or |
| CT pulmonary angiography (CTPA), 222-224, 224 | pulmonary capillary hemangiomatosis (PCH), 16t, 17, 19 |
| MRI of pulmonary vessels, 224-225 | GROUP 1['']: persistent PH of the newborn (PPHN), 16t, 263-266 |
| pulmonary angiography, conventional, 225 | GROUP 2: PH due to left heart disease, 16t, 21-23 |
| pulmonary function testing, 221 | congenital cardiomyopathies, 263 |
| right heart catheterization, 225, 270 | GROUP 3: PH due to lung diseases and/or hypoxia, 16t, 23-24 |
| transthoracic echocardiography (TTE), 222 | GROUP 4: chronic thromboembolic PH (CTEPH), 16t, 24-25, 217, 232 |
| V/Q scanning, 58, 75, 218, 220t, 222, 223, 270 | GROUP 5: PH with unclear multifactorial mechanisms, 17t, 25-26 |
| imaging of, 74-77, 76, 77t, 221-225 | treatment/medication decisions and, 27, 29, 44, 99, 123 |
| contrast CT angiography, 58-59, 60 | general schematic, 100 |
| ground glass attenuation, 76 | WHO classification groups, 14-26, 16t-17t, 47 |
| mosaic attentuation, 74, 77, 79 | treatment/medication decisions and, 27, 29, 44, 99 |
| parenchymal findings, 74, 77, 77t | Clinical presentation of PAH, 42-44, 43t |
| pulmonary webs, 75, 79 | multifactorial PH and, 29 |
| vascular findings, 74-77, 76, 77t | "textbook" presentations, 29 |
| incidence of, 26, 217-218 | Cocaine, 18, 37 |
| morbidity and mortality, 217 | Collagen vascular diseases, 84 |
| mPAP >25 mm Hg, 217, 232 | Computerized tomography (CT), 58-60, 59t |
| pathogenesis and risk factors, 218 | angiography, 71, 72-73 |
| perfusion defects on V/Q scan, 218 | causes of PH and findings, 59t, 93 |
| platelets and coagulation, 218 | chronic pulmonary emboli on, 93, 222-224, 224 |
| pulmonary embolism, disturbed resolution of, 217-218, 219, 220t | congenital shunts, 81 |
| pulmonary embolism or thrombosis, 218, 221, 232 | CT pulmonary angiography (CTPA), 222-224, 224 |
| pulmonary embolism (PE) and, 217-218, 219, 220t | for CTEPH, 222-224, 224 |
| confirming presence of, 221, 222-224 | findings in IPAH, 74t |
| screening for, 42, 218, 221-225 | Congenital heart defects, 266-267 |
| shunts in, 76-77 | Congenital heart diseases, 19, 20t, 21t |
| treatment, 100, 225-232 | PAH associated with (APAH-CHD), 40-41 |
| anticoagulants, 25, 100, 228 | PAH risk and, 40-41 |
| bosentan, 230-231 | as subgroup of WHO Group 2, 263 |
| endothelin receptor antagonists (ERAs), 230-231 | Congenital systemic-to-pulmonary shunts, 19, 20t, 21t, 77-83, 82-83. |
| epoprostenol, intravenous, 229-230 | See also Shunts. |
| iloprost, inhaled, 230 | causes of, 77-80 |
| lung transplantation, 228 | imaging of, 77-83, 82-83 |
| medical therapy (medications), 228-232 | chest radiography, 80-81 |
| outcomes of, 217 | CT findings, 59t |
| phosphodiesterase-5 inhibitors, 231-232 | progression to PH, 80 |
| prostacyclin analogues 220 230 | pulmonary arteriovenous malformations (PAVMs) 81 83 |

pulmonary artery endarterectomy (PEA), 225-228, 232

| Connective tissue disease, 18 | Diagnosis (continued) |
|--|--|
| collagen vascular diseases, 84 | in pediatric patient, 270, 272-273 |
| PAH risk and, 32, 38 | physical exam, 49 |
| serologic testing for, 61 | screening for PH, 48, 57 |
| Continuous positive airway pressure (CPAP), 100 | signs and symptoms, 48-49 |
| COPD (chronic obstructive pulmonary disease), 23-24, 87 | in infants and children, 269t |
| causes and findings, 80t, 87 | timing of, and clinical outcomes, 47-48, 65 |
| CT findings, 59t | Diet control, amphetamine use, and PAH, 18, 31, 35 |
| digoxin and, 211 | Diffusing capacity. See <i>Carbon monoxide</i> . |
| NOTT trial, 209-210 | Digoxin, 211 |
| sildenafil cautions in, 121 | ERA interactions with, 171t |
| | |
| supplemental oxygen in, 209-210 | in pediatric patients, 276 |
| Cor pulmonale, 120, 251 | Diltiazem, 274 |
| CPAP (continuous positive airway pressure), 100 | Direct thrombin, 208 |
| CREST variant, 38 | Diuresis, 248, 257 |
| Critically ill patients. See ICU, pulmonary hypertension in. | Diuretics, 203-206, 213 |
| CTEPH. See Chronic thromboembolic pulmonary hypertension. | indications for, 100, 203-204 |
| Cutaneous scleroderma, 38 | individual titration of therapy, 205-206 |
| Cyclic AMP (cAMP), 179, 188 | in pediatric patients, 276 |
| prostacyclin and, 129 | potassium supplements and, 205-206 |
| Cyclic GMP (cGMP), 177, 178, 179, 275 | RV function and, 204, 205 |
| NO/cGMP signaling pathway, 191, 192 | treatment goals for, 204 |
| Cytochrome P450 pathway, 169 | "Do not resuscitate" order, 292 |
| | Dobutamine, 248-249, 257 |
| Daily living, activities of, 291 | Dopamine, for PPHN, 265 |
| Dana Point classification system, 15, 16t-17t | Drug- and toxin-related PAH, 16t, 18, 35-37, 37t |
| Dasatinib, 37t | Dyspnea, 29, 42, 48 |
| Dead space ventilation, 220 | exertional dyspnea, 219-220, 269 |
| Definitions and classification, 13-28. See also <i>Classification of pulmonary</i> | Dysrhythmias, 253-254 |
| hypertension. | Dysiny tillings, 255-25 1 |
| classification system, 15-25, 16t-17t, 26 | EARLY study, 159-160, 161 |
| Dana Point classification, 15, 16t-17t | Echocardiography, 53-57, 54, 270, 285t, 288 |
| pulmonary hypertension as mPAP >25 mm Hg, 13, 14, 26 | assessment of geometric relationship between ventricles, 247 |
| Depression, 291 | assessment of right ventricular function, 56-57, 56 |
| Dexfenfluramine, 35, 37t | causes of PH, identification with, 57 |
| Diagnosis, 47-68 | contrast echocardiography, 54-55 |
| algorithm for, 50-51 | follow-up, 285t, 288 |
| diagnostics, 49-64, 65. See also <i>Radiography</i> . | goal-directed (GDE), 243-247, 257 |
| 0 1 1 | |
| arterial blood gas, 270 | information from, 53, 57, 288 |
| biomarkers, 61-62 | negative results, meanings of, 55 |
| cardiac catheterization, 62-64, 270 | transthoracic echocardiography (TTE), 53-57, 65, 65, 69 |
| cardiac magnetic resonance (CMR), 60-61 | in screening for PH, 48, 57 |
| chest radiography, 53, 270 | sPAP calculation and measurement, 53-54 |
| computerized tomography (CT), 58-60, 59t | tricuspid annular plane systolic excursion (TAPSE) and, 47 |
| echocardiography, 53-57, 54, 270 | ECMO (extracorporeal membrane oxygenation), 255-256, 266 |
| sPAP calculation and measurement, 53-54 | Edema, 32 |
| transthoracic echocardiography (TTE), 48, 53-57, 65, 65 | peripheral, 269 |
| electrocardiography (EKG), 49-53, 52, 270 | diuretics for, 203-206 |
| pulmonary angiography, 58-60, 225, 270 | with ERAs, 168-169 |
| pulmonary function tests (PFTs), 57, 270 | pulmonary, 92 |
| right heart catheterization, 62-64, 65, 270 | PAH-specific medications and, 92 |
| sleep study, 66 | Education for patient, 296t |
| vasodilator testing, 62-64, 65 | Eisenmenger syndrome, 19, 21t, 40, 77, 267 |
| ventilation-perfusion (V/Q) scan, 58, 222, 270 | causes and findings, 80t, 82-83 |
| early diagnosis, 65 | Electrocardiography (EKG), 49-53, 52, 270 |
| history, 49 | Emphysema, 120, 121 |
| late diagnosis, 47, 48 | |
| | |

| End of life care, 292 | Epidemiology of PH/PAH; heritability, genetics, and environmental factors |
|--|---|
| Endoglin, gene mutations, 34, 81 | (continued) |
| Endothelin (ET-1), 153, 172 | congenital heart disease, 40-41 |
| action mechanism, 153-154, 155 | connective tissue disease, 38 |
| actions of, 153-154, 155 | СТЕРН, 41-42 |
| vasoconstriction, 153, 155, 172 | drug- and toxin-related PAH, 35-37, 37t |
| vasodilation, 154, 155, 160 | hemolytic anemias, 39-40 |
| PAH and, 154, 155 | heritability and mutations, 33-35, 44 |
| receptors, 153-154, 155, 156t, 275 | HIV, 38-39 |
| ET-A receptors, 153-154, 155, 275 | portal hypertension (PPH), 39 |
| ET-B receptors, 153, 154, 155, 275 | pulmonary veno-occlusive disease, 41 |
| synthesis, factors regulating, 154 | sickle cell disease, 39-40 |
| synthesis, inhibitors of, 154 | incidence of PAH, 31 |
| Endothelin receptor antagonists (ERAs), 153-175. See also specific agents. | natural history of PH, 29, 30, 30 |
| action mechanism, 153-154, 155 | risk assessment, 32-33, 33 |
| adverse effects, 168-172 | factors associated with poor outcome, 32 |
| drug interactions, 169, 170t, 171t, 172 | REVEAL risk calculator, 32-33, 36-37, 290 |
| agents | survival rates, 31, 32, 33, 45 |
| ambrisentan, 160-165, 166t | Epoprostenol. See also <i>Prostacyclin therapy</i> . |
| bosentan, 157-160, 162t | action mechanism, 128-129, 274 |
| macitentan, 165-168, 168t | commercial products (generic, Flolan, Veltri), 130t |
| cautions and contraindications, 169-172, 250 | delivery devices, 130t |
| CYP interactions, 156t, 170t | dosage, 134-136 |
| cytochrome P450 pathway and, 169 | effects of, 128 |
| dosing information, 162t, 166t, 169t | efficacy of, 127, 131-133, 133, 149 |
| drug interactions, 169, 170t, 171t | FDA approval for PAH, 127 |
| efficacy, study of, 107 | formulations, 134 |
| indications for, 104t, 114, 154, 172 | half-life, 129 |
| in combination therapy, 106t, 108t, 114, 116 | indications for, 102-103, 104t, 149 |
| as initial therapy for PAH, 118, 123, 154 | in combination therapy, 106t, 108t, 116 |
| for critically ill patients with PH, 250 | for critically ill patients with PH, 250 |
| for CTEPH, 230-231 | for CTEPH, 229-230 |
| in pediatric patients, 275 | as initial therapy, 131 |
| WHO Group 1 (PAH), 100 | in pediatric patients, 274 |
| liver aminotransferase, 159, 162t | infusion pumps, 134, 135 |
| monitoring information, 162t, 166t, 168t, 172 | inhaled, 250, 257 |
| in overall approach to patient, 100 | intravenous, 130t, 132-138 |
| PAH and, 154, 155 | indications for, 104t, 115, 229-230 |
| in pediatric patients, 275 | for critically ill patients with PH, 250 |
| pharmacokinetic characteristics, 156t | infusion pump for, 134, 135 |
| pregnancy cautions, 169-172 | in pediatric patients, 274 |
| receptor binding, 154, 155, 156t, 275 | stability, 130t, 134 |
| dual receptor binding (bosentan), 154, 156t, 275 | heat-stable form, 129, 134 |
| ET-A selective (ambrisentan, macitentan), 154, 156t, 160 | synthesis of, 128 |
| when to discontinue, 162t, 166t, 169t | vs prostaglandin E ₁ , 128 |
| Environmental factors, 35-42. See also Epidemiology of PH/PAH. | ERA. See Endothelin receptor antagonists (ERAs). |
| Epidemiology of PH/PAH, 29-42 | ESC/ERS treatment recommendations, 101, 102-103, 104t-106t, 108t-109t |
| age and, 31-32, 44 | Exercise capacity |
| anorectic amphetamine use and, 31 | exercise program for PAH, 212, 213 |
| case registries/databases and, 31 | phosphodiesterase-5 inhibitors and, 181-183 |
| clinical presentation, 29, 42-44, 43t | sildenafil/tadalafil and, 181-183 |
| associated features, 31 | Exercise intolerance, 29, 219-220 |
| characteristics of PAH, 31, 42-44 | Exercise recommendations, 212, 213, 291 |
| family history of PAH, 31 | Exercise testing, 284t, 285t, 287 |
| gender and, 31, 32, 45 | risk level and, 112t |
| heritability, genetics, and environmental factors, 33-42, 44 | Exertional dyspnea, 219-220, 269 |
| chronic hemoglobinopathies, 39-40 | 71 |

Extracorporeal life support, 253, 255-256 GROUP 2: PH due to left heart disease, 16t, 21-23 Extracorporeal membrane oxygenation (ECMO), 255-256 congenital cardiomyopathies, 263 treatment approach, 100, 119-121 Factor Xa inhibitors, 208 GROUP 3: PH due to lung diseases and/or hypoxia, 16t, 23-24 Fatigue, 29, 42, 48 treatment approach, 100, 119, 120-121 Fenfluramine, 18, 35, 37t GROUP 4: chronic thromboembolic PH (CTEPH), 16t, 24-25, 217, 232 Fenfluramine/phentermine phentolamine (fen-phen), 18 treatment approach, 100 Fetal circulation, 264 GROUP 5: PH with unclear multifactorial mechanisms, 17t, 25-26 FEV₁, 57 treatment approach, 100, 119, 122-123 FEV, to FVC ratio, 57 Guanylate cyclase stimulators, 191-202. See also Soluble guanylate cyclase Fibrosis. See Mediastinal fibrosis; Pulmonary fibrosis. stimulators Flolan, 130t, See also Epoprostenol. Flu vaccine, 289-291 Heart sounds, in CTEPH, 220 Fluid responsiveness, 243-247 Hemodynamics, 116 Follow-up of PAH patient, 123, 283-299. See also Monitoring risk level and, 113t recommendations. treatment goals, 284t advanced care practitioner, 295-296, 296t, 297 Hemoglobinopathies, chronic, 39-40 air travel, 292-293 Hemolytic anemias, 25, 39-40 cardiopulmonary exercise testing, 284t, 285t, 287 Heparins, 208, 209 echocardiography, 285t, 288 Hepatitis, testing for, 61 exercise, 291 Hepatopulmonary syndrome, 89-90 frequency and type of monitoring, 284, 285t, 297 causes and findings, 59t, 80t, 89-90 lung transplantation, 294-295 Hereditary hemorrhagic telangiectasias (HHT), 81 NT-proBNP, 285t, 287-288 Heritability of PAH, 33-35, 44 obtaining medication, 294 family history of PH, 33 palliative/end of life care, 292, 297 mutations, 33-35, 44, 81, 267-268 psychosocial issues, 291, 297 Heritable PAH (HPAH), 16t, 18, 35, 44 right heart catheterization, 285t, 289 mutations in, 268 treatment goals, 284, 284t pediatric patients and, 263, 268 treatment success, evaluation of, 283-284, 284t High altitude, hypoxia and, 268, 292, 293 vaccinations and, 289-291 HIV (human immunodeficiency virus), 38-39, 88-89 WHO functional class, 286 causes and findings, 59t, 80t Forced expiratory volume in one second (FEV₁), 57 and PH/PAH, 38-39, 88-89 Functional assessment of PAH, 286-287 diagnosis, 88-89 Functional classes (WHO), 19-21, 22t, 44, 286 prognosis, 38-39 follow-up and, 286 testing for, 61 goal level, 114, 284t Honeycombing, 83-84, 86-87 risk level and, 111-115, 112t-113t HPAH. See Heritable PAH. treatment recommendations based on, 104t-105t, 106t Hypercoagulable state, 206 Hypokalemia, 205-206 Hypothyroidism, 26 G-proteins, 128-129, 153 Gastroesophageal reflux disease (GERD), 269 Hypoxemia, 213, 265 Gaucher's disease, 26 nocturnal, 276 Gender, PAH and, 31, 32, 45 Hypoxia Genetics, 16t, 18, 33-35 alveolar, 251 mutations, 18, 33-35, 44, 81 chronic, 268 GERD (gastroesophageal reflux disease), 269 high altitudes and, 268, 292, 293 Glycogen storage disorders, 26 PH due to, 16t, 23-24, 120-121, 209 Goal-directed echocardiography (GDE), 243-247 vasoconstriction and, 251 Ground glass attenuation, 76 Ground glass nodules, 92, 96-97 ICU, pulmonary hypertension in, 239-262 Ground glass opacities, 92 acute pulmonary hypertension, 239-242 GROUP 1: PAH (pulmonary arterial hypertension), 16t, 17-21, 26, 44, 99 acute respiratory failure, 251-253, 252 medications for, 27, 44, 100 extracorporeal life support, 253, 255-256 treatment approach, 99-119, 100, 123 cardiopulmonary resuscitation (CRP), 256, 292 treatment recommendations, 101, 102-103, 104t-106t, 108t-109t "do not resuscitate" order, 292

316

dysrhythmias, 253-254

| Left heart disease, PH due to, 21-23, 26, 41, 93, 267 |
|---|
| treatment approach, 100, 119-121, 124 |
| as WHO Group 2, 16t, 24-25 |
| Left ventricle |
| ventricular interdependence in PH, 205, 241, 242 |
| ventricular volume, relationships of right and left ventricles, 242 |
| ventricular volume changes, pressures and, 240-241, 240 |
| Left ventricular diastolic dysfunction, 31-32, 41 |
| Left ventricular end-diastolic area, 247 |
| Left ventricular end-diastolic pressure (LVEDP), 13, 32, 204, 205 |
| Left ventricular failure, 267 |
| Left ventricular function, 205, 241, 242, 254 |
| Life support, extracorporeal, 253, 255-256. See also <i>Ventilation</i> . |
| Liver aminotransferase |
| increase with ERAs, 159, 169 |
| monitoring recommendations |
| ambrisentan, 166t |
| bosentan, 162t, 169 |
| macitentan, 168t |
| Liver disease, 39, 89. See also Hepatopulmonary syndrome; Portal |
| |
| hypertension. |
| Liver function tests (LFTs), monitoring recommendations |
| ambrisentan, 166t |
| bosentan, 162t, 169 |
| ERAs, 162t, 166t, 168t, 172 |
| macitentan, 168t |
| Liver toxicity, ERAs and, 172 |
| Lung diseases, PH due to, 23-24, 26 |
| treatment approach, 100, 119, 120-121, 124 |
| as WHO Group 3, 16t, 23-24 |
| Lung transplant. See Transplantation, lung. |
| Lymphangioleiomyomatosis (LAM), 88 |
| Lymphangiomyomatosis, 26 |
| |
| Macitentan, 165-168, 168t, 275. See also Endothelin receptor antagonists |
| (ERAs). |
| action mechanism, 165 |
| adverse reactions, 167-168, 168t |
| CYP interactions, 156t |
| dosing information, 156t, 168t |
| drug interactions, 169, 170t, 171t, 172 |
| efficacy and safety, 107, 165-168 |
| SERAPHIN study, 165-167, 167 |
| indications for, 104t, 165, 172 |
| in combination therapy, 108t |
| FDA approved uses, 172 |
| monitoring information, 168t |
| pharmacokinetic characteristics, 156t |
| receptor binding, 154, 156t, 275 |
| when to discontinue, 168t |
| Mean PAP (mPAP) |
| calculation from sPAP, 54 |
| changes during exercise, 14 |
| elevated, 17-18, 30, 64 |
| in PH (>25 mm Hg), 13, 14, 26, 217 |
| in infants and children, 263 |
| In mano and emident, 200 |
| |

| Mechanical ventilation, 251. See also <i>Ventilation</i> . for PPHN, 266 | Oxygen (O_3) , 121, 209-210 air travel and, 292-293 |
|--|--|
| pulse pressure variation (PPV) and, 247 Mediastinal fibrosis, 90 | high concentrations of, to lower PVR, 265 hypoxia, effects in PH, 209 |
| causes and findings, 59t, 80t, 90, 91 | monitoring, in critically ill patients, 251 |
| Medications, obtaining, 294 | in overall approach to patient, 100 |
| Milrinone, 249 | oxygen index, 266 |
| Mitral stenosis, 267 | partial pressure of oxygen, goal for, 210 |
| Monitoring recommendations, 283-299 | saturation recommendations, 292-293 |
| ambrisentan, 166t | supplemental oxygen, 209-210, 213 |
| bosentan, 162t | for air travel, 293 |
| ERAs, 162t, 166t, 168t, 172 | in pediatric patients, 276 |
| frequency and type of monitoring, 284, 285t, 297 | portable oxygen concentrators, 293 |
| liver aminotransferase, 162t, 166t, 168t | for WHO Group 3 (lung diseases), 100 |
| macitentan, 168t | Oxygen-poor environment. See <i>Hypoxia</i> . |
| riociguat, 199t | , 8 F, F |
| sGC stimulators, 199t | PA diastolic pressure (dPAP), 41 |
| Monoamine oxidase (MAO) inhibitors, 37 | Palliative/end of life care, 292, 297 |
| Mosaic attentuation, 73-74, 75, 93 | PAP. See Pulmonary arterial pressure. |
| in CTEPH, 74, 77, 79 | PATENT-1 trial, 196-197, 197, 198t |
| MRI | PATENT-2 trial, 197 |
| phase contrast, 81 | Patient education, 296t |
| of pulmonary vessels, 224-225 | PDE5Is. See Phosphodiesterase type-5 inhibitors. |
| Multifactorial PH, 17t, 25-26, 29 | PE. See Pulmonary emboli. |
| Murmurs, in CTEPH, 220 | PEA. See Pulmonary artery endarterectomy. |
| Mutations, in PAH, 18, 33-35, 44, 81, 267-268 | Pediatric patient, pulmonary hypertension in, 263-281 |
| MVR/AVR, 100 | causes of PH in, 263, 266-269 |
| Myocardial volume, 60 | early diagnosis and treatment, 277 |
| • | infants and children, 266-277 |
| NAION (nonarteritic ischemic optic neuropathy), 185-187 | causes of PH in, 263 |
| Natriuretic peptides, 177-179, 178 | clinical manifestation, 269, 269t |
| Natural history of pulmonary hypertension (PH), 29, 30, 30 | diagnostic studies, 270, 272-273 |
| Newborns. See Persistent pulmonary hypertension of the newborn (PPHN). | cardiac catheterization, 270, 277 |
| Nifedipine, 274 | epidemiology and etiology, 266, 277 |
| Nitric oxide (NO), 25, 40, 178, 249 | congenital heart defects, 266-267 |
| inhaled (iNO), 249, 250, 257 | Eisenmenger syndrome, 267 |
| for PPHN, 265-266 | heritable PAH (HPAH), 263, 268 |
| inhibition of endothelin synthesis, 154 | idiopathic PAH (IPAH), 263, 264, 267-268 |
| NO/cGMP signaling pathway, 191, 192 | incidence rates, 266 |
| vasodilation via, 154, 177, 179, 188, 191, 240-250 | registries, 266, 271 |
| vasodilator testing with, 62 | respiratory disorders, 268-269 |
| Nitric oxide synthetase (NOS), 177, 179 | thromboembolic disease, 269 |
| Nonarteritic ischemic optic neuropathy (NAION), 185-187 | mPAP for definition of PH in, 263 |
| Nonspecific idiopathic pneumonia (NSIP), 83-84 | presentation, 269-270 |
| Norepinephrine, 248, 257 | prognosis, 263, 271, 277 |
| NOTT trial, 209-210 | symptoms, 264, 269, 269t |
| NSAIDs, ERA interactions with, 171t | treatment, 271-277 |
| NT-proBNP, 112t, 285t, 287-288 | adjuvant therapies, 276-277 |
| | algorithm for treatment, 278 |
| O ₂ . See Oxygen. | atrial septostomy, 277 |
| Obstructive sleep apnea, 24, 120-121, 268 | calcium-channel blockers (CCBs), 271-274 |
| Older patients, 31-32, 44 | combination therapy, 276 |
| comorbid conditions in, 31 | endothelin receptor antagonists (ERAs), 275 |
| delayed diagnosis in, 31 | goal of, 271 |
| PAH in, 31-32 | lung transplantation, 277 |
| Orenitram, 130t. See also Treprostinil. | phosphodiesterase inhibitors, 275-276 |
| Osler-Weber-Rendu syndrome, 81 | |

| Pediatric patient, pulmonary hypertension in; infants and children; treatment (continued) | Phosphodiesterase-5 inhibitors (PDE5Is), indications for (continued) for PAH, 100, 180-181, 187-188 |
|---|---|
| prostacyclin analogues, 274-275 | in pediatric patients, 275-276 |
| sildenafil, 275-276 | long-term effect of, 184-185 |
| warning for ages 1-17 years, 276 | in overall approach to patient, 100 |
| persistent pulmonary hypertension of the newborn (PPHN), 263-266, 277 | in pediatric patients, 275-276 |
| Perfusion pressure, 248, 257 | Phosphodiesterases (PDEs), 178, 179 |
| Pericardial effusion, 288 | Physical activity. See Exercise. |
| Pericardium, 241, 242 | Platelet aggregation, 206 |
| Peripheral edema, 168-169, 269 | anticoagulants and, 206-209 |
| diuretics for, 203-206 | CTEPH and, 218 |
| Peripheral vessels, small tortuous, 72, 72-73 | epoprostenol effect on, 128 |
| Persistent pulmonary hypertension of the newborn (PPHN), 263-266, 277. | prostacyclin and, 206, 266 |
| See also Pediatric patient. | serotonin and, 206 |
| clinical manifestations, 264 | Pneumococcal vaccine, 289-291 |
| diagnosis, 265 | Portal hypertension (PPH), 18-19, 39 |
| epidemiology and etiology, 263-264 | Positive end-expiratory pressure (PEEP), 253 |
| oxygen index in, 266 | Positive pressure ventilation, 241, 251, 252 |
| pathophysiology, 264 | Potassium supplements, 205-206 |
| as subgroup of WHO Group 1, 16t, 263 | PPHN. See Persistent pulmonary hypertension of the newborn. |
| treatment, 265-266 | Pregnancy |
| ECMO, 266 | ERA cautions in, 169-172 |
| mechanical ventilation, 266 | riociguat cautions in, 200 |
| medications, 265-266 | Risk Evaluation and Mitigation Strategies (REMS), 169-172 |
| surfactant, 266 | Primary PH. See Idiopathic PAH (IPAH). |
| PGI ₂ . See <i>Prostacyclin</i> . | Prostacyclin therapy, 127-152. See also <i>specific agents</i> . |
| Phase contrast MRI, 81 | acronym: PGI ₂ , 127 |
| Phenylephrine, 248 | action mechanism, 128-129, 206, 266 |
| PHIRST trial, 181, 182, 183-185, 186t | agent (prostacyclin receptor agonist): selexipeg, 131 |
| Phosphodiesterase-5 inhibitors (PDE5Is), 177-190. See also specific agents. | agents (prostacyclin analogues), 130t |
| action mechanism, 177-179, 178, 275 | epoprostenol, 127, 129, 130t |
| adverse effects, 185-187, 186t | iloprost, 129, 130t, 131 |
| acute PE, 185 | treprostinil, 129, 130t |
| nonarteritic ischemic optic neuropathy (NAION), 185-187 | cautions and contraindications, 132 |
| agents | delivery devices, 130t, 134, 135, 144, 145 |
| sildenafil, 179-188 | development of, 127-132 |
| tadalafil, 179-188 | dosage, 131, 134-136, 148 |
| vardenafil, 180 | efficacy, 101, 115, 131-132, 148-149 |
| cautions and contraindications, 187, 250 | inhaled prostacyclin, 141-144, 143t |
| drug interactions, 170t | intravenous, 127, 131-132 |
| with riociguat, 200-201 | non-equivalence of agents, 132, 149 |
| effects and metabolism, 179, 180, 187, 275 | oral and inhaled formulations, 115-116, 131 |
| efficacy in PAH, 179, 180-181, 182, 187-188 | ESC/ERS recommendations, 101, 104t-105t |
| 6MWD, increase in, 181-183, 182, 185 | extravasation of prostacyclin, 136, 137 |
| changes in PVR and, 180, 183 | indications for, 104t-105t, 115, 123, 148 |
| exercise capacity, 181-183 | for critically ill patients with PH, 250 |
| functional class, 184 | for CTEPH, 229-230 |
| hemodynamic effects, 183 | as initial therapy, 131 |
| long-term effect, 184-185 | for PPHN, 266 |
| PHIRST trial, 181, 182, 183-185, 186t | WHO Group 1 (PAH), 100 |
| SUPER trial, 181, 182, 183-185, 186t | infections and, 138 |
| time to clinical worsening, 184 | infusion pumps, 134, 135 |
| indications for, 104t, 114, 179-181, 187-188 | interruptions of therapy, results of, 136 |
| in combination with ERA, 106t, 108t, 109t, 114, 116, 118 | intravenous, 101, 115, 123, 132-138 |
| as initial therapy for PAH, 118, 123 | central venous access, 136, 138 |
| for critically ill patients with PH, 250 | efficacy of, 131 |
| for CTEPH, 231-232 | |

| Prostacyclin therapy, intravenous (continued) | Pulmonary arterial hypertension (PAH) (continued) |
|---|--|
| infusion pumps for, 134, 135 | progression of, 30, 31 |
| risks of, 115, 138 | as progressive disease, 17, 23, 99, 256, 297 |
| monotherapy with, 104t-105t | pulmonary vascular thrombosis in, 206 |
| in overall approach to patient, 100 | pulmonary vasodilator response, testing for, 107-110 |
| patient characteristics and knowledge for therapy, 136-138 | risk assessment, 111-115, 112t-113t |
| in pediatric patients, 274-275 | subtypes, 16t, 17, 31 |
| platelet aggregation and, 206 | associated with other conditions, 16t, 17 |
| routes of administration, 130t, 148 | drug- and toxin-induced PAH, 16t, 18, 35-37, 37t |
| inhalation (treprostinil, iloprost), 129, 130t, 131, 141-146 | heritable PAH, 16t, 18 |
| efficacy, 141-146, 143t | idiopathic PAH, 16t, 17, 18, 72-74 |
| nebulizers for, 141, 144, 145 | survival rates, 31, 32, 33, 45 |
| intravenous (epoprostenol), 130t, 132-138 | treatment, 99-119. See also Treatment; and specific treatments. |
| intravenous infusion (treprostinil, iloprost), 129, 130t, 131 | adjunctive therapy and supportive care, 203-216 |
| oral (beraprost), 147-148 | calcium-channel blockers in, 62, 101 |
| oral (treprostinil), 129, 130t, 146-148 | combination therapy recommendations, 102-103, 106t |
| subcutaneous infusion (treprostinil), 129, 130t, 138-140 | sequential combination therapy, 108t-109t |
| stability of agents, 130t, 134 | efficacy, evaluation of, 101-107 |
| synthesis of prostacyclin, 127-128 | ERAs (endothelin receptor antagonists), 153-174 |
| tachyphylaxis and, 131, 136 | ESC/ERS recommendations, 101, 102-103, 104t-106t, 108t-109t |
| thromboxane/prostacyclin ratio, 206 | exercise and, 212, 213 |
| Prostaglandins, 127 | functional assessment of, 286-287 |
| Protease inhibitors, ERA interactions with, 171t | monotherapy recommendations, 102, 104t-105t |
| Psychosocial issues, 291, 297 | obtaining medications, 294 |
| Pulmonary angiography, 58-60, 225, 270 | overall treatment approach, 99-119, 100, 123 |
| CT pulmonary angiography (CTPA), 222-224, 224 | phosphodiesterase-5 inhibitors, 177-190 |
| Pulmonary arterial hypertension (PAH), 17-21 | prostacyclin therapy, 127-152 |
| air travel and, 292-293 | pulmonary vasodilator response, testing prior to treatment, 107-11 |
| characteristics of, 31 | soluble guanylate cyclase stimulator (riociguat), 100, 191-202 |
| classification of, 16t, 17-21, 26. See also Classification of pulmonary | as WHO GROUP 1, 16t, 17-21, 26, 44, 99 |
| hypertension. | Pulmonary arterial pressure (PAP) |
| clinical presentation of, 30, 42-44, 43t | causes of elevation, 110, 258 |
| PVR in, 30 | mean PAP (mPAP) |
| diagnosis, 47 | in PAH (elevated), 17-18, 30 |
| epidemiology, 29-42 | clinical detection of, 42 |
| age and, 31-32, 35, 44 | in PH (>25 mm Hg), 13, 14, 26, 47, 64, 217 |
| anorectic amphetamine use and, 31, 35, 37t | in infants and children, 263 |
| APAH-CHD, 40-41 | obstructive sleep apnea and, 268 |
| family history of PAH, 31 | pulmonary artery diastolic pressure (dPAP), 41 |
| gender and, 31, 32, 45 | WHO groups and, 100 |
| heritability, genetics, and environmental factors, 33-42 | Pulmonary arteries |
| HIV, 38-39 | calcification of, 73, 75, 76 |
| subtypes based on age, 31 | dilatation of, 69 |
| follow-up for, 283-299. See also Follow-up of PAH patient. | with congenital shunts, 81 |
| heritable PAH, 16t, 18, 35, 44, 263 | with pulmonary fibrosis, 86-87 |
| in pediatric patients, 263 | enlarged, 70, 70, 72-73 |
| hypercoagulable state in, 206 | in CTEPH, 76 |
| idiopathic (IPAH), 16t, 17, 18 | diameter >29 mm, 71, 93 |
| anticoagulants and, 207, 208, 209 | in HIV, 88-89 |
| formerly known as primary PH, 267 | evaluation with radiology, 69-70, 70 |
| imaging features of, 72-74, 72-73, 74t | Qp:Qs ratio, 81 |
| in pediatric patients, 263, 267-268 | sclerosis of, 14-15, 30 |
| vasodilator testing for, 62-63, 65 | Pulmonary arteriovenous malformations (PAVMs), 81-83 |
| incidence of, 31 | Pulmonary artery |
| medications for, 27, 29 | contrast CT angiography of, 58-60 |
| mPAP elevation in, 17-18, 30 | diameter of (dPA), 71 |
| natural history, 30 | enlarged, 70, 70, 72-73, 86-87, 88 |

| Pulmonary artery catheter (PAC), 243 | Pulmonary hypertension (PH) (continued) |
|--|--|
| Pulmonary artery endarterectomy (PEA), 225-228 | diagnosis, 47-68 |
| classification of CTEPH with, 226, 227t | epidemiology, 29-42 |
| eligibility criteria for, 226, 226t, 232 | in ICU, 239-262 |
| operative mortality rates, 227 | natural history, 29, 30, 30 |
| PH after, riociguat for, 233 | obstructive sleep apnea and, 24, 120-121 |
| postoperative complications, 227-228 | outcomes |
| treatment goals of, 225-226 | factors in, 47 |
| for WHO Group 4 (CTEPH), 100, 225-228 | survival rates, 31, 32, 33, 45 |
| Pulmonary artery systolic pressure (sPAP), 53-54 | timing of diagnosis and, 47-48 |
| Pulmonary capillary hemangiomatosis (PCH), 16t, 17, 19, 59t | in pediatric patient, 263-281 |
| Pulmonary capillary wedge pressure (PCWP), 13, 32 | PH syndrome, 14-15 |
| Pulmonary circulation, 239-240 | primary PH (now IPAH), 14-15, 31 |
| Pulmonary emboli (PE), 42 | progression of, 30, 48 |
| acute PE | radiography, 69-98 |
| CTEPH after, 217-218 | general findings, 69-71, 70, 93 |
| disturbed resolution of, 218, 219, 220t | screening for, 48, 57 |
| on chest X-ray, 221 | secondary PH, 14-15 |
| management strategies, 241 | signs and symptoms, 48-49 |
| right heart failure and, 241 | survival rates, 31, 32, 33, 45 |
| Pulmonary fibrosis, 24, 25, 26, 83, 93 | treatment. See also <i>Treatment</i> . |
| | approach to patient, 99-126, 100 |
| causes and findings, 59t, 80t, 83-86, 93 | |
| idiopathic fibrosis, 83-84, 86-87 | goal-oriented approach, 114 |
| imaging of, 83-86, 84-85, 86-87 | in ICU, 239-262 |
| honeycombing, 83-84, 86-87 | Non-Group 1 PH, 119-123 |
| sarcoidosis, 84-85, 88-89 | WHO Group 1 (PAH), 99-119, 100 |
| treatment of PH in, 121 | Pulmonary Hypertension Association, 291 |
| Pulmonary function tests (PFTs), 57, 270 | Pulmonary Langerhans cell histiocytosis (PLCH), 87-88, 122 |
| in CTEPH, 221 | Pulmonary rehabilitation, 211-212, 291 |
| Pulmonary histiocytosis, 26 | Pulmonary sclerosis, 14-15, 30 |
| Pulmonary hypertension (PH) | Pulmonary vascular remodeling, 25, 80, 268 |
| acute, 239-242. See also Acute pulmonary hypertension. | Pulmonary vascular resistance (PVR), 14, 22, 26 |
| approach to patient with, 99-126 | chronic hypoxia and, 268 |
| causes of, 77t, 80t, 93 | estimation from, TRV/VTI [RVOT] ratio, 56 |
| findings in, 59t, 71, 72-73, 80t | medications used in lowering, 257, 265 |
| identification with echocardiography, 57 | in newborn, 264 |
| clinical presentation, 29, 42-44, 43t | oxygen, high concentrations of, to lower, 265 |
| characteristics, 47, 69 | progression in PH, 30 |
| morphologic findings, 69 | rise of, in PH/PAH, 30, 30 |
| as mPAP of >25 mm Hg, 13, 14, 26, 47, 64 | Pulmonary vascular thrombosis, anticoagulant therapy for, 206-20 |
| presenting symptoms, 48 | Pulmonary vascular tone, 41, 62 |
| rise in PVR, 30, 30 | Pulmonary vasodilation, 249-251, 257. See also Vasodilation. |
| as complication to other conditions, xi | Pulmonary vasodilator response. See Vasodilator testing. |
| in critically ill patients, 239-262 | Pulmonary vasodilator therapies, 119-120 |
| definitions and classification, 13-28, 16t-17t. See also Classification of PH. | Pulmonary veno-occlusive disease (PVOD), 16t, 17, 19, 41, 92 |
| chronic thromboembolic PH (CTEPH), 16t, 24-25, 217 | causes and findings, 59t, 80t, 92, 94-95 |
| functional capacity, classification by, 19-21, 22t | diagnosis, vs PAH, 92, 94-95 |
| in infants and children, 263 | mosaic attentuation in, 74 |
| as mPAP of >25 mm Hg, 13, 14, 26, 47, 217, 263 | Pulmonary venous pressures, 31-32, 41 |
| PAH (pulmonary arterial hypertension), 16t, 17-21 | Pulmonary vessels, MRI of, 224-225 |
| persistent PH of the newborn (PPHN), 16t, 263-266 | Pulmonary webs, in CTEPH, 75, 79 |
| PH due to left heart disease, 16t, 21-23 | Pulse pressure variation (PPV), 247 |
| PH due to lung diseases and/or hypoxia, 16t, 23-24 | PVOD. See <i>Pulmonary veno-occlusive disease</i> . |
| PH with unclear multifactorial mechanisms, 17t, 25-26 | PVR. See Pulmonary vascular resistance. |
| pulmonary capillary hemangiomatosis (PCH), 16t, 17, 19 | 1 VA. See I unionally vascular resistance. |
| pulmonary veno-occlusive disease (PVOD), 16t, 17, 19 | Qp:Qs ratio, 81 |
| | Qp.Q5 1α110, 01 |
| WHO groups, 14-26, 16t-17t, 47 | |

| Radiography, 69-98, 270 | Right heart failure (continued) |
|--|---|
| capillary hemangiomatosis, 92, 96-97 | diuretics for, 203-204, 213 |
| chest radiographs, 53, 69-70, 70, 81, 270 | positive pressure ventilation and, 241 |
| chronic thromboembolic disease/CTEPH, 74-77, 76, 77t | Right ventricle |
| computerized tomography pulmonary angiography (CTPA), 222-224, 224 | afterload, 204, 239-241, 240, 251 |
| congenital shunts, 77-83, 82-83 | cardiac output, 204, 239 |
| COPD, 87 | dilation of, 56, 247 |
| CT angiography, 71, 72-73, 81, 93 | overload, 205, 205, 212, 213, 247, 255 |
| general findings for PH, 69-71, 70, 93 | perfusion/perfusion pressure, 248, 257 |
| hepatopulmonary syndrome, 89-90 | preload, 203-204, 239-240 |
| HIV, 88-89 | central venous pressure (CVP) as surrogate for, 243 |
| idiopathic pulmonary arterial hypertension (IPAH), 72-74, 72-73, 74t | pressure overload, 47, 220 |
| mosaic attentuation, 73-74, 75 | primary function of, 239 |
| left-sided cardiac disease, 93 | stroke volume, 239-240, 240, 241 |
| mediastinal fibrosis, 90, 91 | ventricular interdependence in PH, 205, 241, 242 |
| mosaic attentuation, 73-74, 75, 93 | ventricular volume, relationships of right and left ventricles, 242 |
| in CTEPH, 74, 77, 79 | ventricular volume changes, pressures in, 240-241, 240 |
| MRI of pulmonary vessels, 224-225 | volume overload, 44, 203, 247, 255 |
| phase contrast MRI, 81 | Right ventricle failure, 14, 30, 30, 120 |
| pulmonary angiography, 58-60, 225, 270 | cardiopulmonary rehabilitation, 211-212 |
| CTPA, 222-224, 224 | causes of, 241, 246t |
| pulmonary fibrosis, 83-86, 84-85, 86-87 | hospitalization for, 206 |
| pulmonary Langerhans cell histiocytosis, 87-88 | pathophysiology of, in acute PH, 241, 244-245 |
| pulmonary veno-occlusive disease (PVOD), 92, 94-95 | riociguat and, 194 |
| risk assessment and, 113t | triggers of, 241, 246t |
| RAP, risk level and, 113t | Right ventricular assist devices (RVADs), 255 |
| Rate control, 100 | Right ventricular dysfunction, 40, 247, 269 |
| Raynaud's syndrome, 43, 47 | risk in older patients, 31 |
| Registries and databases, 31, 44, 266 | supraventricular tachyarrhythmias, 253-254 |
| REVEAL, 31, 271, 289 | Right ventricular end-diastolic area, 247 |
| Remodeling, pulmonary vascular, 25, 80, 268 | Right ventricular end-diastolic pressure (RVEDP), 204, 205 |
| Remodulin, 130t. See also <i>Treprostinil</i> . | Right ventricular function |
| REMS (Risk Evaluation and Mitigation Strategies), 169-172 | assessment of, 56-57, 56, 288 |
| Rescue therapies, 255-256 | coronary blood flow and, 241 |
| atrial septostomy, 255 | digoxin and, 211 |
| devices to bypass right heart, 255 | digoxiii and, 211 diuretics and, 204, 205, 213 |
| right ventricular assist devices (RVADs), 255 | evaluation with cardiac magnetic resonance (CMR), 60-61 |
| veno-arterial extracorporeal membrane oxygenation (V-AECMO), 255-256 | sepsis and, 254 |
| | |
| Respiratory bronchiolitis interstitial lung disease (RB-ILD), 88 | stroke volume and, 239-240, 240, 241 |
| Resuscitation, 247-249 | Tei-index, 56-57 |
| target CVP for, 243 | ventricular interdependence in PH, 205, 241, 242 |
| REVEAL Registry, 31, 271, 289 REVEAL rich calculator, 22, 22, 26, 27, 200 | ventricular volume changes, 240-241, 240 |
| REVEAL risk calculator, 32-33, 36-37, 290 Phaymatoid authritia, 18, 28 | Right ventricular hypertrophy, 69, 83 |
| Rheumatoid arthritis, 18, 38 | CT angiography of, 71, 72-73 |
| Right atrial enlargement, 70 | electrocardiographic results in, 49-53, 52 |
| Right atrial pressure (RAP), 54, 288, 289 | Riociguat (Adempas), 191-202 |
| Right end-diastolic ventricular mass, 60 | action mechanism, 191, 201 |
| Right heart catheterization, 62-64, 65, 270, 289 | adverse events, 194, 196-197, 199t, 200, 201 |
| cost of, 69 | cautions and contraindications, 200-201, 250 |
| for diagnosis of CTEPH, 225 | as direct sGC stimulator, 191 |
| for diagnosis of PH, 48, 62-64 | dosing and monitoring information, 199t |
| in follow-up, 285t, 289 | drug interactions, 200-201 |
| PAH risk and, 36 | FDA approval of, 191 |
| Right heart failure, 30, 30. See also Right ventricle failure. | history of, 191-193 |
| acute right heart failure, 241, 246t | indications for, 104t, 119, 191, 201 |
| causes of, 241, 246t | in combination therapy, 108t, 109t |
| in chronic PH, 241, 246t | for CTEPH. 100, 119, 191, 201, 229, 233 |

| Riociguat (Adempas), indications for (continued) | Sildenafil (continued) |
|--|---|
| WHO Group 1 (PAH), 100, 191, 201 | efficacy, 180-181, 182, 187-188 |
| WHO Group 4 (CTEPH), 100, 119, 191, 201, 229, 233 | 6MWD, increase in, 181-183, 182, 185 |
| phase 2 trials, 193 | exercise capacity, 181-183 |
| phase 3 trials, 193-197 | functional class, 184 |
| 6MWD, 193-194, 195, 195t, 196, 197, 198t | hemodynamic effects, 183 |
| Borg Dyspnea Scale, 194-196, 195t, 198t | long-term effect, 184-185 |
| CHEST-1, 193-196, 194, 195t, 229 | for PAH, 180-181, 182 |
| CHEST-2, 196 | PHIRST trial, 181, 182, 183-185, 186t |
| PATENT-1, 196-197, 197, 198t | SUPER trial, 181, 182, 183-185, 186t |
| PATENT-2, 197 | time to clinical worsening, 184 |
| WHO functional class, 194, 195t, 197 | generic form, 188 |
| pregnancy and, 200 | indications for, 104t, 179-181, 187-188 |
| when to discontinue, 199t | in combination therapy, 106t, 108t, 109t, 116 |
| Risk assessment, 32-33, 33, 111-115, 112t-113t | for critically ill patients with PH, 250 |
| in pregnancy, 169-172 | for CTEPH, 231-232 |
| REVEAL risk calculator, 32-33, 36-37, 290 | for PAH, 180-181 |
| Risk Evaluation and Mitigation Strategies (REMS), 169-172 | in pediatric patients, 275-276 |
| Kisk Evaluation and Wittigation Strategies (KEWIS), 109-172 | long-term effect of, 184-185 |
| Sarcoidosis, PH associated with, 25, 84-85, 88-89 | |
| | metabolism of, 179, 180, 187 |
| treatment, 122 | in pediatric patients, 275-276 |
| Schistosomiasis, PAH associated with, 19 | STARTS-1 and -2 studies, 275-276 |
| Scleroderma, 18, 38, 84, 207 | Sinus venosus ASD, 80 |
| Sclerosis 14.15.20 | Sjögren's syndrome, 38 |
| of pulmonary arteries, 14-15, 30 | Sleep apnea, 24, 120-121, 268 |
| systemic, 18, 32 | Smooth muscle, cyclic GMP and, 177, 178 |
| Selective serotonin reuptake inhibitors (SSRIs), 37 | Soluble guanylate cyclase stimulators (sGC stimulators), 191-202. |
| Selexipeg, 104t, 108t, 131. See also <i>Prostacyclin therapy</i> . | See also Riociguat. |
| Sepsis, 254-255 | action mechanism, 191, 201 |
| ICU mortality in PH patients, 254 | adverse events, 194, 196-197, 199t, 200, 201 |
| mechanical ventilation for, 247 | cautions and contraindications, 200-201 |
| resuscitation in, target CVP, 243 | dosing and monitoring information, 199t |
| Septic shock, resuscitation in, target CVP, 243 | indications for, 100, 191, 201 |
| SERAPHIN study, 165-167, 167 | WHO Group 1 (PAH), 100, 191, 201 |
| sGC stimulators. See Soluble guanylate cyclase stimulators (sGCS). | WHO Group 4 (CTEPH), 100, 191, 201, 229, 233 |
| Shock, 247-249 | nitric oxide/cGMP signaling pathway, 191, 192 |
| septic, resuscitation in, 243 | in overall approach to patient, 100 |
| Shunts | phase 2 trials, 193 |
| congenital heart defects, 266-267 | phase 3 trials, 193-197 |
| congenital systemic-to-pulmonary shunts, 19, 20t, 21t | riociguat, 191-202 |
| causes of, 77-80 | SPAP. See Pulmonary artery systolic pressure. |
| imaging of, 59t, 77-83, 82-83 | SSRIs, PAH risk and, 37 |
| in CTEPH, 76-77 | St. John's wort, 37 |
| fetal circulation, 264 | STARTS-1 and -2 studies, 275-276 |
| left-to right, 266-267 | Statins, ERA interactions with, 171t |
| right-to-left, 269 | Stroke volume, 239-240, 240, 241 |
| Sickle cell disease, 25, 39-40, 122 | SUPER trial, 181, 182, 183-185, 186t |
| Signs and symptoms, 48-49. See also Symptoms of PH. | Supportive care for PAH. See <i>Adjunctive therapy</i> . |
| Sildenafil, 179-188 | Supraventricular tachyarrhythmias (SVT), 253-254 |
| action mechanism, 275 | Surfactant, 266 |
| adverse effects, 185-187, 186t | Survival rates, 31, 32, 33, 45 |
| acute PE, 185 | Symptoms of PH, 29, 42, 48-49 |
| nonarteritic ischemic optic neuropathy (NAION), 185-187 | dyspnea, 29, 42, 48, 219-220, 269 |
| cautions and contraindications, 121, 122, 187 | exercise intolerance, 29, 219-220 |
| warning for pediatric patients and children, 276 | fatigue, 29, 42, 48 |
| drug interactions, 170t, 200-201 | in infants and children, 269t |
| drug interactions, 170t, 200-201 | minimum and children, 2091 |

| Syncope, 32, 48, 269 | Transthoracic echocardiography (TTE), 53-57, 65, 69 |
|---|---|
| bosentan and, 159 | in CTEPH, 222 |
| riociguat and, 194 | in screening for PH, 48, 57 |
| risk level and, 112t | sPAP calculation and measurement, 53-54 |
| Systemic lupus erythematosus (SLE), 18, 38 | Trauma patients, PH and, 254 |
| Systemic sclerosis, 18, 32 | Treatment |
| , | adjunctive therapy and supportive care, 203-216 |
| Tachyphylaxis, 131, 136 | anticoagulants, 206-209 |
| Tadalafil, 179-188, 275 | cardiopulmonary rehabilitation, 211-212 |
| adverse effects, 185-187, 186t | digoxin, 211 |
| acute PE, 185 | digram, 211 diuretics, 203-206 |
| | |
| nonarteritic ischemic optic neuropathy (NAION), 185-187 | supplemental oxygen, 209-210 |
| AMBITION trial, 116-118, 117 | approach to PH patient, 99-126 |
| cautions and contraindications, 187 | classification of PH and, 99, 100, 123 |
| drug interactions, 170t, 200-201 | combination therapy recommendations, 102-103, 106t, 123 |
| efficacy, 180-181, 182, 187-188 | sequential drug combination therapy, 108t-109t |
| 6MWD, increase in, 181-183, 182, 185 | efficacy |
| exercise capacity, 181-183 | adequate clinical response, definition of, 111-115 |
| functional class, 184 | evaluation of, 101-107, 116 |
| hemodynamic effects, 183 | real-world evaluations, 283-284 |
| as initial treatment for PAH, 116-118, 117 | follow-up recommendations, 283-299 |
| long-term effect, 184-185 | therapeutic success, evaluation of, 283-284 |
| PHIRST trial, 181, 182, 183-185, 186t | treatment goals, 284, 284t |
| SUPER trial, 181, 182, 183-185, 186t | follow up, 123, 283-299 |
| time to clinical worsening, 184 | general approach, 99-126 |
| indications for, 104t, 179-181, 187-188 | goal-oriented approach, 114 |
| in combination therapy, 106t, 108t | goals of, 284, 284t |
| with ambrisentan, 106t, 116-118, 117 | functional class improvement, 44, 114, 284t, 286 |
| for PAH, 179-181 | for pediatric patients, 271 |
| long-term effect of, 184-185 | insurance plans and, 294 |
| metabolism of, 179, 180, 187 | monotherapy recommendations, 102, 104t-105t, 116 |
| TAPSE. See Tricuspid annular plane systolic excursion. | natural history and, 29 |
| Team, interdisciplinary, 295-296, 297 | non-improvement with, adding new therapies for, 118, 123 |
| Tei-index, 56-57, 288 | obtaining medications for PAH, 294 |
| Terbogrel, 250 | PAH, 99-119, 100 |
| Thrombin, direct, 208 | adjunctive therapy and supportive care, 203-216 |
| Thromboembolism | calcium-channel blockers, 62, 101 |
| in CTEPH, 222-224, 224, 269 | ERAs (endothelin receptor antagonists), 153-174 |
| in pediatric patients, 269 | ESC/ERS recommendations, 101, 102-103, 104t-106t, 108t-109t |
| prior history of, 221 | general treatment approach, 99-119, 100 |
| Thrombosis. See also <i>Pulmonary emboli</i> . | medication recommendations, 104t-106t, 108t-109t |
| anticoagulant therapy for, 206-209 | obtaining medications for, 294 |
| classification (perioperative) with PEA, 226, 227t | phosphodiesterase-5 inhibitors, 177-190 |
| CTEPH and, 218, 219, 221, 222-224, 224 | prostacyclin therapy, 127-152 |
| Thromboxane, 206 | soluble guanylate cyclase stimulators (sGCs), 191-202 |
| thromboxane/prostacyclin ratio, 206 | palliative/end of life care, 292, 297 |
| | |
| Thromboxane synthase inhibitor (terbogrel), 250 | pediatric patients, 271-277 |
| Thyroid disease, 26 | specific treatments |
| Tidal volumes, 251 | algorithm for approach, 100 |
| Toxin-related PAH, 16t, 18, 35-37, 37t | calcium-channel blockers, 62 |
| Transplantation, lung, 294-295 | ERAs (endothelin receptor antagonists), 153-174 |
| for CTEPH, 228 | ESC/ERS recommendations, 101, 102-103, 104t-106t, 108t-109t |
| indications for, 100, 102-103, 114 | phosphodiesterase-5 inhibitors, 177-190 |
| mechanical/ventilatory support while waiting for, 255-256 | prostacyclin therapy, 104t-105t, 127-152 |
| patient selection for, 294-295 | soluble guanylate cyclase stimulators (sGCs), 191-202 |
| for pediatric patients, 277 | of underlying conditions, 123 |
| Transpulmonary gradient (TPG) 22-23 25 | WHO functional class and 104t-105t 106t |

| Treatment (continued) | Vasoconstriction |
|---|---|
| WHO Groups and, 99-126, 100 | endothelins/ERAs and, 153, 155, 172 |
| Non-Group 1 PH, 119-123 | hypoxia and, 251 |
| WHO Group 1 (PAH), 99-119, 100 | thromboxane and, 206 |
| medications for Group 1 PAH only, 27, 29, 44 | Vasodilation, 249-251, 257 |
| treatment recommendations, 101, 102-103, 104t-106t, 108t-109t | epoprostenol and, 128, 274 |
| Treprostinil, 129, 130t, 138-140, 146-148. See also <i>Prostacyclin therapy</i> . | ERAs and, 154, 155, 160 |
| commercial product names (Remodulin, Tyvaso, Orenitram), 130t | nitric oxide (NO) and, 154, 177, 179, 191, 249-250 |
| dosage, 134-136 | oxygen and, 210 |
| efficacy, 132, 133-134 | phosphodiesterase-5 inhibitors and, 177, 178, 188, 275 |
| inhaled treprostinil, 144-146 | prostacyclin and, 206, 266 |
| oral treprostinil, 146-147 | pulmonary vasodilators, 249-251 |
| subcutaneous infusion, 139, 140 | Vasodilator response, 102 |
| indications for, 104t | anorectic drug use and, 110 |
| in combination therapy, 106t, 108t, 116 | Vasodilator testing, 62-64, 65, 107-111, 270 |
| for CTEPH, 230 | indications for, 63, 110-111, 271 |
| oral treprostinil, 147 | prior to treatment, 107-110 |
| in pediatric patients, 274 | risks of, 63 |
| infusion pumps, 134, <i>135</i> , 138 | Vasodilator therapies, 119-120 |
| in pediatric patients, 274 | Vasopressin, 248, 257 |
| routes of administration, 129, 130t | Vasoreactivity, testing for, 102, 107-110 |
| inhalation, 129, 130t, 141-146 | Veltri, 130t. See also <i>Epoprostenol</i> . |
| efficacy of, 144-146 | Veno-arterial extracorporeal membrane oxygenation (V-AECMO), 255-256 |
| half-life, 141, <i>142</i> | Ventavis, 130t. See also <i>Iloprost</i> . |
| nebulizers for, 141, 144, <i>145</i> | Ventilation |
| intravenous infusion, 129, 130t, 133-134 | dead space ventilation, 220 |
| infusion pump for, 134, <i>135</i> , 138 | lung protective ventilation, 251 |
| oral, 129, 130t, 146-148 | mechanical ventilation, 247, 251 |
| subcutaneous infusion, 129, 130t, 138-140 | avoiding if possible in critically-ill PH patients, 251 |
| adverse effects of, 140 | for PPHN, 266 |
| for CTEPH, 230 | strategies in PH patient, 253 |
| disadvantages of, 139-140 | positive end-expiratory pressure (PEEP), 253 |
| efficacy of, 139, 140 | positive pressure ventilation, 251 |
| infusion pumps for, 134, 135 | right heart failure and, 241 |
| infusion site discomfort, 139-140 | and V/Q relationships, Zone I and Zone II lung, 251, 252 |
| vs intravenous infusion, 138-139 | Ventilation-perfusion (V/Q) scan, 58, 207, 270 |
| stability, 130t | in CTEPH, 57, 75, 217, 218, 222, 223 |
| heat-stable form, 134 | in PAH, 222 |
| Tricuspid annular plane systolic excursion (TAPSE), 47, 288 | Ventricular hypertrophy, in CTEPH, 76 |
| Tricuspid regurgitation, 44 | Ventricular interdependence in PH, 205, 241, 242 |
| Tricuspid regurgitation murmur, 220 | Ventricular mass index (VMI), 60-61 |
| Tricuspid regurgitation pressure gradient, 53, 54 | Ventricular septal defects, 77, 82, 267 |
| Tricuspid regurgitation velocity (TRV), 56 | Ventricular volume, 242 |
| TRV/VTI [RVOT] ratio, 56 | Vitamin K, 209 |
| L-tryptophan, 37t | Volume responsiveness, 246, 255. See also <i>Stroke volume</i> . |
| Tyvaso, 130t. See also <i>Treprostinil</i> . | Volume status, 243-247, 255, 257 |
| V | von Willebrand factor, 206 |
| Vaccinations, 289-291 | Wf 207 200 |
| Valvular gradients, 55 | Warfarin, 207-209 |
| Vane, John , 127, 128 | in pediatric patients, 276 |
| Vardenafil, 275 | WHO functional places 10.21, 104t 105t 106t 286 |
| changes in PVR and, 180 drug interactions, with riociguat, 200-201 | WHO functional classes, 19-21, 104t-105t, 106t, 286 risk level and, 112t |
| indications for, 104t, 179 | |
| Vascular tone. See <i>Pulmonary vascular tone</i> . | WHO (World Health Organization), classification groups, 14-26, 16t-17t, 44. |
| Vascular tone. See Pulmonary vascular tone. Vasculitis, 26 | See also Classification of pulmonary hypertension. Women, PAH prevalence in, 31, 45 |
| *#3Cullu3, 20 | women, 17111 prevaience in, 51, 45 |

Young patients, 32

Zone I and Zone II lung, 251, 252