Contents

Developmental Biology 15

Introduction 15
  The Mesonephros 17
  The Metanephros 17
  The Collecting System 20
  Ascent of Kidneys 20
  Urinary Bladder 20

Congenital Malformations of Urinary System 21
  Renal Agenesis 21
  Renal Hypoplasia 22
  Accessory Kidneys 22
  Renal Ectopia 22
  Horseshoe Kidney 22
  Renal Cystic Disease 23
  Anomalies of the Ureter 24
  Anomalies of the Urinary Bladder 24
  Anomalies of the Urethra 25

Urinary Tract Structure and Function 27

Introduction 27

Gross Anatomy 27

The Nephron 29
  Renal corpuscle 30
  Functional Aspects of the Glomerulus 34
  The Renal Tubule 35
  Juxtaglomerular Apparatus 40
  Distal Convoluted Tubule (DCT) 42

Collecting Tubule or Duct 42

Renal Vasculature 43
Body Fluid Composition 49

Introduction 49

Physicochemical Properties of Electrolytes and Definitions 50

Molarity 50
Equivalence 51
Osmolality 51
Osmolarity 52
Isoosmotic 52
Isotonic 52
Oncotic Pressure 53
Specific Gravity 53

Distribution and Composition of Body Fluids 53

Ionic Composition of the Extracellular Fluid 55
Ionic Composition of the Intracellular Fluid 56
Osmolality of the Body Fluids 56
Balance of Water and Electrolytes 56

Dynamics of Water and Ion Distribution 57

Simple Diffusion 58
Facilitated Diffusion 59
Coupled Transport 59
Solvent Drag 60
Active Transport of Solutes 60
Secondary Active Transport 61

Fluid Replacement Therapy 62

Principles of Renal Clearance 65

Introduction 65

Clearance Concepts and Creatinine Clearance 66
Quantititating GFR through Clearance Determinations 66
Relationship of the plasma creatinine to GFR 68
Clearance of Other Substances 69

Glucose 69
Paraaminohippurate 69
Phosphate clearance 70

Glomerular Ultrafiltration 71

Introduction 71

Glomerular Filtration Rate 72

Physical Determinants of Glomerular Filtration 73
Glomerular Ultrafiltration Dynamics 74

Regulation of Renal Blood Flow 77

Myogenic Stretch Reflex (Bayliss Mechanism) 79
Tubuloglomerular Feedback 79
Renin-Angiotensin System 81
Role of the Macula Densa in Regulating Renal Hemodynamics 82
Shift from Renal Compensation to Decompensation 84
Mediators of Altered Vascular Resistance 84

Transport in the Proximal Tubule 85

Introduction 85

Concept of Maximal Tubular Transport 86

Organization of the Proximal Tubule 87

Mechanisms of Solute Transport in the Proximal Tubule 88

Osmolarity Along the Proximal Tubule 94
Secretion of Organic Solutes in the Proximal Tubule 95

Net Fluid Reabsorption in the Proximal Tubule 96

Glomerulotubular Balance 98

Transport in the Loop 99

Introduction 99
Principles of Urinary Concentration and Dilution 101

Steps in the Development of Urine Dilution and Medullary Interstitial Concentration 102
Ion Transport in the mTAL 103
Water Permeability of the Collecting Duct 106
Antidiuretic Hormone 106
Role of Urea in Urinary Concentration 108
The Importance of Countercurrent Blood Flow 109

Transport in the Distal Nephron 113

Introduction 113

Cellular Mechanisms of Transport in the Distal Nephron 114
Transport in the Distal Convoluted Tubule 114
Transport in the Connecting Segment 116
Transport in the Cortical Collecting Duct 116
Transport in the Medullary Collecting Duct 119

Potassium Homeostasis 121

Introduction 121

Extrarenal Potassium Homeostasis 122
Renal Potassium Homeostasis 124
Transport of Potassium in the Proximal Tubule 125
Transport of Potassium in the Loop of Henle 125
Transport of Potassium in the Collecting Duct 126

Regulation of Potassium Secretion in the Collecting Duct 128
Effects of Diuretics on Potassium Excretion 129

Renal Endocrinology 131

Introduction 131

Mechanisms of Hormone Action 132
Non-Renal Hormones Acting on the Kidney 133
Systemically Acting Hormones Produced By the Kidney 138
Locally Acting Hormones Produced by the Kidney 143
Renal Catabolism of Hormones 145

Renal mechanisms for the disposal of hormones 145

**Water Disorders 147**

Introduction 147

Hyponatremia 148

Laboratory Evaluation of Hyponatremia 148
Cellular Adaptation to Hypoosmolality 149
Water Physiology 150

Pathophysiologic Approach to Hyponatremia 153

Conditions Associated with a Low Effective Volume 153
Conditions Associated with a Normal Effective Volume 155

Clinical Approach to the Hyponatremic Patient 156

Treatment of hyponatremia 157

Osmotic Cerebral Demyelinating Syndrome 158
Prudent Approach to Management of Hyponatremia 158

Hypernatremia 159

Pathophysiologic Approach to Hypernatremia 159
Pathophysiology of Polyuria 161
Principles of Management of Hypernatremia 162

Pathophysiology and Treatment of Edema 163

Introduction 163

Effective Circulating Volume Sensors 164

Pathophysiology of Edema Formation 165

Edematous Disorders Characterized By a Low Cardiac Output 167
Edematous Disorders Characterized By Arterial Vasodilatation 168

Pharmacology of Diuretics 169

Carbonic Anhydrase Inhibitors 170
Pathophysiology of Potassium Disorders 181

Introduction 181

Approach to Potassium Disorders 182

Hypokalemia 183
Hyperkalemia 187

Regulation of Acid-Base Homeostasis 191

Introduction 191

Daily Acid Production 192

The Defense of Blood pH 192

Temporal Response to Buffering 193
Chemical Buffers 194
Respiratory Control of pH 199
Renal Regulation of pH 200
Ammoniagenesis 207

Regulation of Renal Hydrogen Ion Excretion 209

Extracellular pH 210
Effective Circulating Volume 210
Aldosterone 211
Plasma Potassium Concentration 211

Pathophysiology of Acid-Base Disorders 213

Introduction 213

Defense Against Changes in the Systemic pH 214
Example of Respiratory Adaptation 214

**Simple Acid-Base Disturbances 215**

- Metabolic Acidosis 215
- Metabolic Alkalosis 215
- Respiratory Acidosis 216
- Respiratory Alkalosis 216
- Analysis of Acid-Base Disorders 216

**Metabolic Acidosis 217**

- The Serum Anion Gap 217

**Metabolic Alkalosis 222**

**Respiratory Acid-Base Disorders 225**

- Decreased Minute Ventilation 225
- Increased Minute Ventilation 226

**Anti-Hypertensive Drugs 227**

**Classification and Examples 227**

- Diuretics 227
- Sympatholytics 228
- Vasodilators 228
- Calcium Channel Blockers 228
- Angiotensin Converting Enzyme Inhibitors 229
- Angiotensin Receptor Antagonists 229

**Overview 229**

- Classification Of Antihypertensive Drugs By Their Primary Site Of Action 230

**Pharmacology of the Anti-Hypertensive Agents 235**

- Diuretics 236
- Sympatholytic Agents 239
- Ganglionic Blocking Agents 240
- Adrenergic Neuronal Blocking Agents 240
- Alpha-Adrenergic Antagonists 242
- Beta-Adrenergic Antagonists 242
- Mixed Acting Adrenergic Antagonist 244
- Vasodilators 244
- Angiotensin Converting Enzyme Inhibitors 249
Clinical Approach to Hypertension 253

Introduction 253
Classification, Epidemiology and Assessment 254
   Blood Pressure Assessment 255
Pathogenesis of Essential Hypertension 256
Diagnostic Workup of Hypertension 259
   Target Organ Assessment 260
Treatment of Hypertension 260
   Lifestyle Modifications 260
   Pharmacologic Therapies 261
Secondary Causes of Hypertension 266
   Renovascular Hypertension 266
   Primary Hyperaldosteronism 269
   Pheochromocytoma 271
Hypertensive Emergencies 272

Introduction to Renal Disease 275

Mechanisms of Renal Injury 275
   Immune Mechanisms of Renal Injury 275
   Nonimmune Mechanisms of Renal Injury 276
Approach to Renal Disease 279
   Measurement of Glomerular Filtration Rate 280
Urinalysis in the Evaluation of Suspected Renal Disease 282
   Dipstick Analysis of the Supernatant 282
   Evaluation of the Urine Sediment 283
   Radiologic Evaluation of the Genitourinary Tract 287
Diagnostic Approach to the Patient with Proteinuria 289
Diagnostic Approach to the Patient with Hematuria 291

**Introduction to Renal Pathology 293**

- Overview of Glomerular Anatomy 293
- Pathologic Alterations of Glomerular Compartments 295
- The Language of the Renal Pathologist 297
- Diagnostic Renal Pathology 300

**Pathology of Glomerular Disease 301**

- The Nephrotic Syndrome 301
  - Minimal Change Disease (Nil disease) 302
  - Focal Segmental Glomerulosclerosis (“FSGS”) 303
  - Membranous Nephropathy 305
  - Membranoproliferative Glomerulonephritis 307
  - Diabetes Mellitus 310
  - Amyloidosis 311

- The Nephritic Syndrome 311
  - Acute Proliferative Glomerulonephritis 313
  - Systemic Lupus Erythematosus (SLE) 315
  - IgA Nephropathy (Berger's Disease) 316
  - Anti-GBM Nephritis 317
  - Hereditary Nephritis 317
  - Rapidly Progressive Glomerulonephritis 318

**Pathology of Tubulointerstitial and Vascular Disease 323**

- Cystic Renal Diseases 323
  - Autosomal Dominant Polycystic Kidney Disease 323
  - Autosomal Recessive Polycystic Kidney Disease 325

- Acute Tubular Necrosis 326

- Acute Pyelonephritis 327
Chronic Pyelonephritis and Reflux Nephropathy 328
  Tubulointerstitial Nephritis 329

Diseases of Renal Blood Vessels 329
  Benign Nephrosclerosis (benign hypertension) 329
  Malignant Nephrosclerosis (malignant hypertension) 330
  Thrombotic Microangiopathy 330

Clinical Aspects of Glomerular Disease 333

Introduction 333
  Pathophysiology of the Nephrotic Syndrome 333
  History and Physical Examination 336
  Laboratory Studies and Radiologic Procedures 336

Differential Diagnosis of Glomerular Disease 339
  Glomerular Disease Associated with the Nephrotic Syndrome 339
  Glomerular Disease Associated with the Nephritic Syndrome 343

Clinical Aspects of Tubulointerstitial Disease 349

Introduction 349
  Acute interstitial nephritis 350
    Pathophysiology 350
    Clinical Features 351
    Diagnosis 352
    Treatment and Prognosis 352
  Chronic Interstitial Nephritis 352
    Analgesic nephropathy 354
    Reflux nephropathy and chronic pyelonephritis 354
  Cystic Renal Disease 355
    Polycystic kidney disease 355
  Urinary Tract Obstruction 357
Acute Renal Failure 361

Introduction 361

Prerenal Acute Renal Failure 364
  Management of Prerenal Acute Renal Failure 365

Acute Tubular Necrosis 365
  Mechanisms of Glomerular Filtration Failure 366
  Urine Electrolytes in the Differential Diagnosis of ARF 367
  Clinical Examples of Acute Tubular Necrosis 369

General Management of ARF 375

Chronic Kidney Disease 377

Introduction 377
  Differentiating Acute from Chronic Kidney Disease 379

Complications of Chronic Kidney Disease 379
  Renal Osteodystrophy 380
  Anemia of Chronic Renal Failure 382
  Bleeding in Uremia 383

Monitoring Progression of Renal Disease 384

Measures Employed to Slow Progression of Chronic Renal Failure 385
  Antihypertensive therapy 386
  Role of Intensive Insulin Therapy in Diabetic Renal Disease 387
  Protein Restricted Diets 388
  Role of Hyperlipidemia 388
  Role of Proteinuria 389

Pathology of the Urinary Bladder and Kidney 391

Urinary Bladder 391
  Congenital Anomalies 391
  Inflammations 392

Neoplasia 393
General Features 393
Clinical Features 394
Pathology 394
Bladder Carcinoma 395
Detection and Monitoring 397

**Ureter 397**

Obstructive Lesions 397
Tumors and Tumor-Like Lesions 398

**Tumors of the Kidney 399**

Renal Cell Carcinoma 399
Clinical Features 399
Classification 400
Prognostic Factors 402
Oncocytoma 402

**Urinary Tract Infections 403**

Introduction 403

**Epidemiology and Classification 404**

Incidence and Prevalence 405
Uropathogenic Bacteria 405

**Host Susceptibility and Bacterial Virulence Factors 407**

Normal Defense Mechanisms of the Urinary Tract 408

**Routes of Infection 408**

**Symptoms and Signs 409**

Physical Examination 410
Natural History 410

**Laboratory Studies and Diagnosis 411**

**Differential Diagnosis 412**

**Management 412**

Recurrent Urinary Tract Infections 414
Pathophysiology and Treatment of Stones 417

Introduction 417

Pathophysiology of Renal Calculi Formation 418
  Formation of Solid Phase Nuclei and Crystal Growth 419

Clinical Examples of Stones 421
  Calcium Containing Stones 421
  Magnesium Ammonium Phosphate Stones 425
  Uric Acid Stones 425
  Cystine Stones 425

Approach to the Patient With Acute Renal Colic 426

Principles of Management of Nephrolithiasis 428

Recurrent Stone Disease 428