

Alluru S. Reddi

Fluid, Electrolyte and Acid-Base Disorders

Clinical Evaluation
and Management

Second Edition

 Springer

Fluid, Electrolyte and Acid-Base Disorders

Alluru S. Reddi

Fluid, Electrolyte and Acid-Base Disorders

Clinical Evaluation and Management

Second Edition

 Springer

Alluru S. Reddi, MD, PhD
Professor of Medicine
Chief, Division of Nephrology and Hypertension
Rutgers New Jersey Medical
Newark, NJ
USA

ISBN 978-3-319-60166-3 ISBN 978-3-319-60167-0 (eBook)
DOI 10.1007/978-3-319-60167-0

Library of Congress Control Number: 2017954276

© Springer Science+Business Media LLC 2018

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

Like the previous edition, the second edition of *Fluid, Electrolyte and Acid–Base Disorders* provides a clear and concise understanding of the fundamentals of these clinical problems that are encountered daily in our practice. Most of the chapters have been updated and expanded. Six pertinent new chapters have been added. Also, some new study questions have been discussed.

Similar to the first edition, each chapter begins with pertinent basic physiology followed by its clinical disorders. Cases for each fluid, electrolyte, and acid–base disorder are discussed with answers. In addition, board-type questions with explanations are provided for each clinical disorder to increase the knowledge of the physician.

The revision of the book would not have been possible without the help of many students, house staff, and colleagues, who made me understand nephrology and manage patients appropriately. I am grateful to all of them. I am extremely thankful and grateful to my family for their immense support and patience. I extend my thanks to Gregory Sutorius of Springer New York for his continued support, help, and advice. Finally, I am thankful to many readers for their constructive critique of the previous edition and also expect such a positive criticism from readers of the current edition of the book.

Newark, NJ, USA

Alluru S. Reddi

Contents

Part I Physiologic Basis and Management of Fluid, Electrolyte and Acid-Base Disorders

1	Body Fluid Compartments	3
	Terminology	3
	Units of Solute Measurement	3
	Conversions and Electrolyte Composition	4
	Osmolarity Versus Osmolality	5
	Total Osmolality Versus Effective Osmolality	6
	Isosmotic Versus Isotonic	7
	Body Fluid Compartments	7
	Water Movement Between ECF and ICF Compartments	8
	Study Questions	10
	Suggested Reading	13
2	Interpretation of Urine Electrolytes and Osmolality	15
	Certain Pertinent Calculations	16
	Fractional Excretion of Na^+ (FE_{Na}) and Urea Nitrogen (FE_{Urea})	16
	Fractional Excretion of Uric Acid (FE_{UA}) and Phosphate (FE_{PO_4})	16
	Urine Potassium (U_{K}) and Urine Creatinine (U_{Cr}) Ratio	17
	Urine Anion Gap	17
	Electrolyte-Free Water Clearance	18
	Urine Specific Gravity Versus Urine Osmolality	19
	Study Questions	20
	Suggested Reading	21
3	Renal Handling of NaCl and Water	23
	Proximal Tubule	23
	Na^+ Reabsorption	23
	Cl^- Reabsorption	25
	Thin Limbs of Henle's Loop	26
	Thick ascending limb of Henle's loop	26
	Distal Tubule	27
	Collecting Duct	29

Water Reabsorption	30
Proximal Tubule	30
Loop of Henle	30
Distal Nephron	31
Effect of Various Hormones on NaCl and Water	
Reabsorption (Transport)	31
Disorders of NaCl Transport Mechanisms	32
Study Questions	32
Suggested Reading	33
4 Intravenous Fluids: Composition and Indications	35
Crystalloids	36
Dextrose in Water	36
Sodium Chloride (NaCl) Solutions	36
Dextrose in Saline	38
Balanced Electrolyte Solutions	38
Colloids	38
Albumin	38
Goals of Fluid Therapy	39
How Much Fluid Is Retained in the Intravascular Compartment?	39
Maintenance Fluid and Electrolyte Therapy	42
Fluid Therapy in Special Conditions	43
Volume Contraction	43
Septic Shock	43
Hemorrhagic Shock Due to Gastrointestinal Bleeding	44
Hemorrhagic Shock Due to Trauma	44
Cardiogenic Shock	44
Adult Respiratory Distress Syndrome (ARDS)	44
Phases of Fluid Therapy in Critically Ill Patients	45
Study Questions	45
Suggested Reading	49
5 Diuretics	51
Classification of Diuretics	51
Physiologic Effects of Diuretics	53
Clinical Uses of Diuretics	53
Complications of Diuretics	54
Study Questions	55
Suggested Reading	56
6 Disorders of Extracellular Fluid Volume: Basic Concepts	57
Mechanisms of Volume Recognition	57
Conditions of Volume Expansion	59
Concept of Effective Arterial Blood Volume (EABV)	59
Formation of Edema	60
Suggested Reading	61

7 Disorders of ECF Volume: Congestive Heart Failure	63
Clinical Evaluation	64
Treatment of CHF	65
Management of Edema	65
Ambulatory Patient	65
In-Hospital Patient with Acute Decompensated Heart Failure (ADHF)	66
Inhibition of Renin–AII–Aldosterone, Sympathetic Nervous System, and ADH	67
Cardiorenal Syndrome	67
Study Questions	68
Suggested Reading	71
8 Disorders of ECF Volume: Cirrhosis of the Liver	73
Clinical Evaluation	75
Treatment of Edema	75
Formation of Ascites	76
Treatment of Ascites	77
Salt Restriction	78
Diuretics	78
Large-Volume Paracentesis	78
Refractory Ascites	79
Hepatorenal Syndrome	79
Treatment	80
Other Treatment Modalities	81
Study Questions	81
Suggested Reading	83
9 Disorders of ECF Volume: Nephrotic Syndrome	85
Clinical Evaluation	86
Treatment	87
Study Questions	88
Suggested Reading	90
10 Disorders of ECF Volume: Volume Contraction	91
Causes of Volume Contraction	91
Dehydration vs Volume Depletion	92
Types of Fluid Loss	92
Clinical Evaluation	93
Treatment	94
Dehydration	94
Volume Depletion	94
Study Questions	94
Suggested Reading	96

11 Disorders of Water Balance: Physiology	97
Control of Thirst	97
Structure and Synthesis of ADH	98
Control of ADH Release	98
Copeptin	99
Distribution of Aquaporins in the Kidney	100
Mechanism and Actions of ADH	100
Mechanism	100
Actions	101
Urinary Concentration and Dilution	102
Measurement of Urinary Concentration and Dilution	102
Calculation of Electrolyte-Free Water Clearance	104
Disorders of Water Balance	105
Study Questions	105
Suggested Reading	106
12 Disorders of Water Balance: Hyponatremia	107
Development of Hyponatremia	107
Approach to the Patient with Hyponatremia	107
Step 1. Measure Serum Osmolality	107
Step 2. Measure Urine Osmolality and Na ⁺ Concentration	108
Step 3. Estimate Volume Status	108
Step 4. Obtain Pertinent Laboratory Tests	109
Step 5. Know More About Pseudo or Factitious Hyponatremia	109
Step 6. Know More About Hypertonic (Translocational) Hyponatremia	110
Step 7. Rule Out Causes Other than Glucose That Increase Plasma Osmolality	111
Pathophysiology of Hyponatremia	111
Specific Causes of Hyponatremia	111
Syndrome of Inappropriate Antidiuretic Hormone Secretion	111
Cerebral Salt Wasting or Renal Salt Wasting Syndrome	113
Nephrogenic Syndrome of Inappropriate Antidiuresis	114
Reset Osmostat	115
Thiazide Diuretics	116
Ecstasy	116
Selective Serotonin Reuptake Inhibitors	116
Exercise-Induced Hyponatremia	117
Beer Potomania	117
Poor Oral Intake	117
Postoperative Hyponatremia	118
Hypokalemia and Hyponatremia	118
Diagnosis of Hypotonic Hyponatremia	118
Signs and Symptoms of Hyponatremia	119
Brain Adaptation to Hyponatremia	119

Complications of Untreated Chronic Hyponatremia	120
Treatment of Hyponatremia	120
Treatment of Acute Symptomatic Hyponatremia	120
Treatment of Chronic Symptomatic Hyponatremia	122
Complication of Rapid Correction of Hyponatremia	122
Risk Factors	123
Clinical Manifestations	123
Diagnostic Test	124
Management and Prognosis	124
Treatment of Asymptomatic Hyponatremia in Hospitalized Patients.	124
Treatment of Asymptomatic Chronic Hyponatremia Due to Syndrome of Inappropriate Antidiuretic Hormone Secretion in Ambulatory Patients	125
Treatment of General Causes of Hyponatremia	126
Study Questions	127
Suggested Reading	144
13 Disorders of Water Balance: Hypernatremia.	147
Mechanisms of Hypernatremia	147
Patients at Risk for Hypernatremia	147
Approach to the Patient with Hypernatremia	148
Step 1: Estimate Volume Status	148
Step 2: History and Physical Examination	148
Step 3: Diagnosis of Hypernatremia	149
Brain Adaptation to Hypernatremia	149
Signs and Symptoms of Hypernatremia	150
Specific Causes of Hypernatremia	150
Polyuria	150
Diagnosis of Polyuria	152
Solute Diuresis	152
Hypernatremia in the Elderly	153
Hypodipsic (Adipsic) Hypernatremia	154
Treatment of Hypernatremia	155
Correction of the Underlying Cause	155
Calculation of Water Deficit	155
Selection and Route of Fluid Administration	156
Volume Status	156
Treatment of Acute Hypernatremia	156
Treatment of Chronic Hypernatremia	157
Treatment of Specific Causes	157
Hypovolemic Hypernatremia	157
Hypervolemic Hypernatremia	157
Normovolemic (Euvolemic) Hypernatremia	157
Study Questions	158
References	164
Suggested Reading	164

14 Disorders of Potassium: Physiology	165
General Features	165
Renal Handling of K^+ Transport	165
Proximal Tubule	166
Loop of Henle	166
Distal Nephron	167
Distal Tubule	167
Connecting Tubule	168
Cortical Collecting Duct	168
Outer Medullary Collecting Duct	169
Inner Medullary Collecting Duct	169
Factors Affecting K^+ Excretion	170
Dietary Intake and Plasma $[K^+]$	170
Urine Flow Rate and Na^+ Delivery	170
Hormones	171
Aldosterone	171
Antidiuretic Hormone	171
Angiotensin II	171
Tissue Kallikrein	171
Acid-Base Balance	172
Anions	172
Diuretics	172
Suggested Reading	173
15 Disorders of Potassium: Hypokalemia	175
Some Specific Causes of Hypokalemia	176
Hypokalemic Periodic Paralysis (HypoPP)	176
Hypokalemic-Hypertensive Disorders	177
Activating Mutations of the Mineralocorticoid Receptor	178
Hypokalemic-Normotensive Disorders	179
Gitelman Syndrome	179
Hypokalemia Due to Aminoglycosides	180
Diagnosis	180
Step 1	180
Step 2	180
Step 3	180
Step 4	182
Step 5	182
Clinical Manifestations	182
Treatment	182
Severity	183
Underlying Cause	183
Degree of K^+ Depletion	184
Study Questions	184
References	191
Suggested Reading	191

16 Disorders of Potassium: Hyperkalemia	193
Some Specific Causes of Hyperkalemia	195
Hyperkalemic Periodic Paralysis (HyperPP)	195
Chronic Kidney Disease Stage 5 (CKD5)	195
Decreased Effective Arterial Blood Volume	195
Addison Disease	195
Adrenal Hyperplasia	196
Syndrome of Hyporeninemic Hypoaldosteronism (SHH)	196
Pseudohypoaldosteronism Type I (PHA I)	196
Pseudohypoaldosteronism Type II (PHA II)	197
Posttransplant Hyperkalemia	197
Diagnosis	197
Step 1	197
Step 2	198
Step 3	199
Clinical Manifestations	200
Treatment	201
Acute Treatment	201
Chronic Treatment	203
Study Questions	203
Suggested Reading	209
17 Disorders of Calcium: Physiology	211
General Features	211
Ca ²⁺ Homeostasis	212
Ca ²⁺ -Sensing Receptor (CaSR)	213
PTH	213
Active Vitamin D ₃ (1,25-Dihydroxycholecalciferol or 1,25(OH) ₂ D ₃ or Calcitriol)	214
Calcitonin	214
Defense Against Low and High Plasma [Ca ²⁺]	214
Renal Handling of Ca ²⁺	215
Proximal Tubule	215
Thick Ascending Limb	215
Distal and Connecting Tubule	215
Collecting Duct	216
Factors Influencing Ca ²⁺ Transport	216
Factors Influencing Ca ²⁺ Channel (TRPV5)	217
Suggested Reading	218
18 Disorders of Calcium: Hypocalcemia	219
Some Specific Causes of Hypocalcemia	221
Hypoparathyroidism	221
Pseudohypoparathyroidism (PsHPT)	221
Vitamin D Deficiency	222
Diagnosis	222

Clinical Manifestations	225
Treatment	225
Acute Hypocalcemia	225
Chronic Hypocalcemia	226
Study Questions	227
Suggested Reading	231
19 Disorders of Calcium: Hypercalcemia	233
Some Specific Causes of Hypercalcemia	234
Primary Hyperparathyroidism	234
Multiple Endocrine Neoplasia Type 1 and Type 2a	235
Jansen's Disease	236
Familial Hypocalciuric Hypercalcemia	236
Neonatal Severe Hyperparathyroidism	236
Renal Failure	236
Milk (Calcium)-Alkali Syndrome	237
Malignancy	238
Granulomatous Diseases	239
Vitamin D Overdose	239
Clinical Manifestations	240
Diagnosis	240
Treatment	242
Acute Treatment	242
Chronic Treatment	243
Study Questions	244
Reference	250
Suggested Reading	250
20 Disorders of Phosphate: Physiology	251
General Features	251
Phosphate Homeostasis	252
Renal Handling of Phosphate	253
Proximal Tubule	253
Regulation of Renal Phosphate Handling	254
Suggested Reading	257
21 Disorders of Phosphate: Hypophosphatemia	259
Some Specific Causes of Hypophosphatemia	261
X-Linked Hypophosphatemia	261
Autosomal Dominant Hypophosphatemic Rickets (ADHR)	262
Autosomal Recessive Hypophosphatemic Rickets (ARHR)	262
Tumor-Induced Osteomalacia (TIO)	262
Hereditary Hypophosphatemic Rickets with Hypercalciuria (HHRH) Due to Type Iic Mutation	262
Hereditary Hypophosphatemic Rickets with Hypercalciuria (HHRH) Due to Type Iia Mutation	263
Refeeding Syndrome (RFS)	263

Hypophosphatemia in Critical Care Units	263
Clinical Manifestations	263
Diagnosis	265
Treatment	266
Acute Severe Symptomatic Hypophosphatemia	266
Chronic Hypophosphatemia	267
Study Questions	268
Reference	272
Suggested Reading	272
22 Disorders of Phosphate: Hyperphosphatemia	273
Some Specific Causes of Hyperphosphatemia	274
Acute Kidney Injury (AKI)	274
Chronic Kidney Disease (CKD)	274
Sodium Phosphate Use and Hyperphosphatemia	276
Familial Tumor Calcinosis (FTC)	276
Clinical Manifestations	276
Diagnosis	277
Treatment	277
Diet	277
Phosphate Binders	277
Acute Hyperphosphatemia	279
Chronic Hyperphosphatemia	279
Study Questions	280
References	284
Suggested Reading	285
23 Disorders of Magnesium: Physiology	287
General Features	287
Mg ²⁺ Homeostasis	287
Renal Handling of Mg ²⁺	288
Factors that Alter Renal Handling of Mg ²⁺ in TALH and DCT	290
Suggested Reading	291
24 Disorders of Magnesium: Hypomagnesemia	293
Some Specific Causes of Hypomagnesemia	295
Familial Hypomagnesemia with Hypercalciuria and Nephrocalcinosis (FHHNC)	295
Familial Hypomagnesemia with Hypercalciuria and Nephrocalcinosis with Ocular Manifestation	295
Familial Hypomagnesemia with Secondary Hypocalcemia	295
Isolated Dominant Hypomagnesemia with Hypocalciuria	296
Isolated Recessive Hypomagnesemia (IRH) with Normocalciuria	296
Bartter and Gitelman Syndromes	296
Hypomagnesemia-Induced Hypocalcemia	296
Hypomagnesemia-Induced Hypokalemia	298
Clinical Manifestations	298
Diagnosis	299

Treatment 300

 Acute Treatment 300

 Chronic Treatment 301

Study Questions 301

Suggested Reading 305

25 Disorders of Magnesium: Hypermagnesemia 307

Clinical Manifestations 307

Treatment 308

 Asymptomatic Patient 308

 Symptomatic Patient 308

Study Questions 309

Suggested Reading 310

26 Acid–Base Physiology 311

Production of Endogenous Acids and Bases 311

 Endogenous Acids 312

 Endogenous Bases 312

Maintenance of Normal pH 312

 Buffers 312

 Lungs 314

 Kidneys 314

Reabsorption of Filtered HCO₃⁻ 314

 Proximal Tubule 315

 Loop of Henle 316

 Distal Tubule 316

 Collecting Duct 317

Regulation of HCO₃⁻ Reabsorption 317

Generation of New HCO₃⁻ by Titratable Acid Excretion 317

Generation of HCO₃⁻ from NH₄⁺ 319

Net Acid Excretion (Urinary Acidification) 320

Suggested Reading 320

27 Evaluation of an Acid–Base Disorder 321

Arterial vs. Venous Blood Sample for ABG 321

Evaluation of an ABG 322

Henderson Equation 322

Anion Gap 323

 Normal AG Values 324

 Hyperglycemia and AG 324

 Clinical Use of AG 324

 Mnemonic for High AG Metabolic Acidosis 325

 Normal AG Metabolic Acidosis 325

 Low AG Metabolic Acidosis and Correction for Low Serum Albumin 326

 Use of ΔAG/ΔHCO₃⁻ 326

Secondary Physiologic Response (or Compensatory Response) 327

Pathogenesis of Acid-Base Disorders	328
How to Evaluate an Acid-Base Disorder	329
How to Evaluate a Mixed Acid-Base Disorder	330
Hydration and Acid-Base Disorder-Induced Changes in Serum $[Na^+]$ and $[Cl^-]$	332
Study Questions	333
Suggested Reading	337
28 High Anion Gap Metabolic Acidosis	339
Clinical Manifestations of Metabolic Acidosis	340
Acidosis Due to Kidney Injury	340
Acute Kidney Injury (AKI)	340
Chronic Kidney Disease Stages 4-5	341
Acidosis Due to Accumulation of Organic Acids	341
Acidosis Due to Toxins	349
General Considerations	349
Study Questions	359
Reference	365
Suggested Reading	365
29 Hyperchloremic Metabolic Acidosis: Renal Tubular Acidosis	367
Urine pH	367
Urine Anion Gap (U_{AG})	368
Urine Osmolal Gap (U_{OG})	368
Proximal RTA	368
Characteristics	368
Pathophysiology	369
Hypokalemia	369
Causes	370
Clinical Manifestations	370
Specific Causes of Isolated Proximal RTA	371
Autosomal Recessive Proximal RTA	371
Autosomal Dominant Proximal RTA	371
Sporadic Form	371
Carbonic Anhydrase (CA) Deficiency	371
Fanconi Syndrome	372
Definition	372
Laboratory and Clinical Manifestations	372
Causes	372
Diagnosis	372
Treatment	372
Hypokalemic Distal (Classic) or Type I RTA	373
Characteristics	373
Pathophysiology	374
Causes	374
Diagnosis	375
Complications	376

Hypokalemia 376

 Nephrocalcinosis and Nephrolithiasis 376

Treatment 376

Toluene Ingestion and Distal RTA 377

Incomplete (Type III) RTA 377

Distal RTA with Hyperkalemia 377

 Hyperkalemic Distal RTA (Type IV) with Urine pH <5.5 378

 Hyperkalemic Distal RTA with Urine pH >5.5
 (Voltage-Dependent RTA) 378

Causes of Both Types of Hyperkalemic Distal RTAs 378

Diagnosis of Hyperkalemic Distal RTAs 379

Treatment of Hyperkalemic Distal RTAs 381

Distinguishing Features of Various RTAs 381

Dilutional Acidosis 382

Acidosis Due to Chronic Kidney Disease 382

Hyperchloremic Metabolic Acidosis During Treatment of Diabetic
Ketoacidosis 382

Study Questions 383

Suggested Reading 390

30 Hyperchloremic Metabolic Acidosis: Nonrenal Causes 391

 Water Handling 391

 Intestinal Electrolyte Transport 392

 Na⁺ and Cl⁻ Transport (Jejunum) 392

 Na⁺ and Cl⁻ Transport (Ileum) 392

 Na⁺ and K⁺ Transport (Colon) 393

 Intestinal Secretion of Cl⁻ 393

 HCO₃⁻ Handling in the Colon 393

 Volume and Electrolyte Concentrations of GI Fluids 393

 Diarrhea 394

 Water and Electrolyte Loss 394

 Types of Diarrhea 394

 Diagnosis 395

 Types of Acid–Base Disorders in Diarrhea 396

 Treatment 397

 Biliary and Pancreatic Fistulas 397

 Villous Adenoma 397

 Urinary Intestinal Diversions 397

 Laxative Abuse 398

 Cholestyramine 398

 Study Questions 398

 Suggested Reading 401

31 Metabolic Alkalosis 403

 Course of Metabolic Alkalosis 403

 Generation Phase 403

Maintenance Phase	404
Recovery Phase	405
Respiratory Response to Metabolic Alkalosis	405
Classification.	406
Causes	406
Pathophysiology	406
Renal Mechanisms	406
Renal Transport Mechanisms	406
Genetic Mechanisms	407
Acquired Causes	408
GI Mechanisms	410
Vomiting and Nasogastric Suction	410
Congenital Chloride Diarrhea	411
Villous Adenoma	411
Laxative Abuse	412
Clinical Manifestations	412
Diagnosis.	413
Treatment	414
Study Questions	415
Suggested Reading	427
32 Respiratory Acidosis	429
Physiology.	429
CO ₂ Production	429
CO ₂ Transport	430
CO ₂ Excretion	430
CNS Control of Ventilation.	430
Respiratory Acidosis	431
Secondary Physiologic Response to Hypercapnia	431
Acute Respiratory Acidosis.	432
Chronic Respiratory Acidosis	435
Study Questions	437
Suggesting Reading	440
33 Respiratory Alkalosis	441
Secondary Physiologic Response to Respiratory Alkalosis (Hypocapnia).	441
Causes of Acute and Chronic Respiratory Alkalosis	442
Clinical Manifestations	442
Acute Respiratory Alkalosis	442
Chronic Respiratory Alkalosis	444
Diagnosis.	444
Arterial Blood Gas (ABG)	445
Serum Chemistry	445
Other Tests	446
Treatment	446

Study Questions	446
Suggested Reading	448
34 Mixed Acid–Base Disorders	449
Analysis of Mixed Acid–Base Disorders	450
Metabolic Acidosis and Metabolic Alkalosis	452
Metabolic Acidosis and Respiratory Alkalosis	452
Metabolic Acidosis and Respiratory Acidosis	453
Metabolic Alkalosis and Respiratory Alkalosis	453
Metabolic Alkalosis and Respiratory Acidosis	454
Triple Acid–Base Disorders	455
Treatment	456
Metabolic Acidosis and Metabolic Alkalosis	456
Metabolic Acidosis and Respiratory Alkalosis	456
Metabolic Acidosis and Respiratory Acidosis	456
Metabolic Alkalosis and Respiratory Alkalosis	456
Metabolic Alkalosis and Respiratory Acidosis	457
Study Questions	457
Suggested Reading	462
35 Drug-Induced Acid–Base Disorders	463
Metabolic Acidosis	463
Metabolic Alkalosis	465
Respiratory Acidosis	465
Respiratory Alkalosis	465
Suggested Reading	466
 Part II Fluid, Electrolyte and Acid-Base Disorders in Special Conditions	
36 Acute Kidney Injury	469
Definition	469
Fluid and Sodium (Na) Imbalances	469
Potassium (K) Imbalance	470
Calcium (Ca) Imbalance	471
Phosphate Imbalance	471
Magnesium (Mg) Imbalance	471
Acid–Base Changes	471
Suggested Reading	472
37 Chronic Kidney Disease	473
Definition	473
Sodium (Na) Imbalance	474
Water Imbalance	474
Potassium (K) Imbalance	475
Calcium (Ca) Imbalance	476

Phosphate Imbalance	476
Magnesium (Mg) Imbalance.	477
Acid–Base Changes	477
Suggested Reading	478
38 Kidney Transplantation	479
Volume Changes	479
Electrolyte Abnormalities	479
Acid–Base Changes	481
Suggested Reading	481
39 Liver Disease	483
Fluid Imbalance	483
Water Imbalance	484
Potassium (K) Imbalance	485
Calcium Imbalance	485
Phosphate Imbalance	486
Magnesium (Mg) Imbalance.	486
Acid–Base Changes	486
Suggested Reading	487
40 Pregnancy	489
Hemodynamic Changes	489
Volume Changes	489
Electrolyte Abnormalities	490
Acid–Base Changes	491
Others	491
Suggested Reading	492
Index	493

Part I

**Physiologic Basis and Management of Fluid,
Electrolyte and Acid-Base Disorders**

Water is the most abundant component of the body. It is essential for life in all human beings and animals. Water is the only solvent of the body in which electrolytes and other nonelectrolyte solutes are dissolved. An electrolyte is a substance that dissociates in water into charged particles called *ions*. Positively charged ions are called *cations*. Negatively charged ions are called *anions*. Glucose and urea do not dissociate in water because they have no electric charge. Therefore, these substances are called *nonelectrolytes*.

Terminology

The reader should be familiar with certain terminology to understand fluids not only in this chapter but the entire text as well.

Units of Solute Measurement

It is customary to express the concentration of electrolytes in terms of the number of ions, either milliequivalents/liter (mEq/L) or millimoles/L (mmol/L). This terminology is especially useful when describing major alterations in electrolytes that occur in response to a physiologic disturbance. It is easier to express these changes in terms of the number of ions rather than the weight of the ions (milligrams/dL or mg/dL).

Electrolytes do not react with each other milligram for milligram or gram for gram; rather, they react in proportion to their chemical equivalents. Equivalent weight of a substance is calculated by dividing its *atomic weight* by its *valence*. For example, the atomic weight of Na^+ is 23 and its valence is 1. Therefore, the equivalent weight of Na^+ is 23. Similarly, Cl^- has an atomic weight of 35.5 and valence of 1. Twenty-three grams of Na^+ will react with 35.5 g of Cl^- to yield 58.5 g of NaCl. In other words, one Eq of Na^+ reacts with one Eq of Cl^- to form one Eq of NaCl. Because the

electrolyte concentrations of biologic fluids are small, it is more convenient to use *milliequivalents* (mEq). One mEq is 1/1,000 of an Eq. One mEq of Na^+ is 23 mg.

So far, we have calculated equivalent weights of the monovalent ions (valence = 1). What about divalent ions? Ca^{2+} is a divalent ion because its valence is 2. Since the atomic weight of Ca^{2+} is 40, its equivalent weight is 20 (atomic weight divided by valence or $40/2 = 20$). In a chemical reaction, 2 mEq of Ca^{2+} (40 g) will combine with 2 mEq of monovalent Cl^- (71 g) to yield one molecule of CaCl_2 (111 g).

Nonelectrolytes, such as urea and glucose, are expressed as mg/dL. To simplify the expression of electrolyte and nonelectrolyte solute concentrations, *Système International* (SI) units have been developed. In SI units, concentrations are expressed in terms of *moles* per liter (mol/L), where a molar solution contains 1 g molecular or atomic weight of solute in 1 L of solution. On the other hand, a *molal* solution is defined as 1 g molecular weight of solute in a kilogram of solvent. A *millimole* (mmol) is 1/1000 of a mole. For example, the molecular weight of glucose is 180. One mole of glucose is 180 g, whereas 1 mmol is 180 mg ($180,000 \text{ mg}/1000 = 180 \text{ mg}$) dissolved in 1 kg of solvent. In body fluids, as stated earlier, the solvent is water.

Conversions and Electrolyte Composition

Table 1.1 shows important cations and anions in plasma and intracellular compartments. The table illustrates expression of electrolyte concentrations in mEq/L (conventional expression in the United States) to other expressions because ions react

Table 1.1 Normal (mean) plasma and intracellular (skeletal muscle) electrolyte concentrations

Electrolyte	Mol wt	Valence	Eq wt	Concentrations			Intracellular concentration
				mg/dL	mEq/dL	mmol/L	mEq/L
<i>Cations</i>							
Na^+	23	1	23	326	142	142	14
K^+	39	1	39	16	4	4	140
Ca^{2+a}	40	2	20	10	5	2.5	4
Mg^{2+}	24	2	12	2.5	2	1.0	35
Total cations	—	—	—	354.5	153	149.5	193
<i>Anions</i>							
Cl^-	35.5	1	35.5	362	104	104	2
HCO_3^{-b}	61	—	22	55	25	25	8
$\text{H}_2\text{PO}_4^- - \text{HPO}_4^{2-}$	31	1.8	17	4	2.3	1.3	40
SO_4^{2-}	32	2	16	1.5	0.94	0.47	20
Proteins	—	—	—	7,000	15	0.9	55
Organic acids ^c	—	—	—	15	5.76	5.5	68
Total anions	—	—	—	7,437.5	153	137.17	193

^aIncludes ionized and bound Ca^{2+}

^bMeasured as total CO_2

^cIncludes lactate, citrate, etc.

Table 1.2 Conversion between conventional and SI units for important cations and anions using a conversion factor

Analyte	Expression of conventional units	Conventional to SI units (multiplication factor)	SI to conventional units (multiplication factor)	Expression of SI units
Na ⁺	mEq/L	1	1	mmol/L
K ⁺	mEq/L	1	1	mmol/L
Cl ⁻	mEq/L	1	1	mmol/L
HCO ₃ ⁻	mEq/L	1	1	mmol/L
Creatinine ^a	mg/dL	88.4	0.01113	μmol/L
Urea nitrogen	mg/dL	0.356	2.81	mmol/L
Glucose	mg/dL	0.055	18	mmol/L
Ca ²⁺	mg/dL	0.25	4	mmol/L
Mg ²⁺	mg/dL	0.41	2.43	mmol/L
Phosphorus	mg/dL	0.323	3.1	mmol/L
Albumin	g/dL	10	0.1	g/L

^a1 mg creatinine = 0.0884 mmol/L

mEq for mEq, and not mmol for mmol or mg for mg. Furthermore, expressing cations in mEq demonstrates that an equal number of anions in mEq are necessary to maintain electroneutrality, which is an important determinant for ion transport in the kidney. It is clear from the table that Na⁺ is the most abundant cation, and Cl⁻ and HCO₃⁻ are the most abundant anions in the plasma or extracellular compartment. The intracellular composition varies from one tissue to another. Compared to the plasma, K⁺ is the most abundant cation, and organic phosphate and proteins are the most abundant anions inside the cells or the intracellular compartment. Na⁺ concentration is low. This asymmetric distribution of Na⁺ and K⁺ across the cell membrane is maintained by the enzyme, Na/K-ATPase.

Some readers are familiar with the conventional units, whereas others prefer SI units. Table 1.2 summarizes the conversion of conventional units to SI units and vice versa. One needs to multiply the reported value by the conversion factor in order to obtain the required unit.

Osmolarity Versus Osmolality

When two different solutions are separated by a membrane that is permeable to water and not to solutes, water moves through the membrane from a lower to a higher concentrated solution until the two solutions reach equal concentration. This movement is called *osmosis*. Osmosis does not continue indefinitely but stops when the solutes on both sides of the membrane exert an equal *osmotic force*. This force is called *osmotic pressure*.

The osmotic pressure is the colligative property of a solution. It depends on the number of particles dissolved in a unit volume of solvent and not on the valence, weight, or shape of the particle. For example, an atom of Na⁺ exerts the same

osmotic pressure as an atom of Ca^{2+} with a valence of 2. Osmotic pressure is expressed as *osmoles* (Osm). One *milliosmole* (mOsm) is 1/1000 of an osmole, which can be calculated for each electrolyte using the following formula:

$$\text{mOsm} / \text{L} = \frac{\text{mg} / \text{dL} \times 10}{\text{Mol wt.}}$$

Osmolarity refers to the number of mOsm in 1 L of solution, whereas *osmolality* is the number of mOsm in 1 kg of water. However, osmolality is the preferred physiological term because the colligative property depends on the number of particles in a given weight (kg) of water.

The osmolality of plasma is largely a function of Na^+ concentration and its anions (mainly Cl^- and HCO_3^-) with contributions from glucose and urea nitrogen. Since each Na^+ is paired with a univalent anion, the contribution from other cations such as K^+ , Ca^{2+} , and Mg^{2+} to the osmolality of plasma is generally not considered. Therefore, the plasma osmolality is calculated by doubling Na^+ and including the contribution from glucose and urea nitrogen (generally expressed as blood urea nitrogen or BUN), as follows:

$$\text{Osmolality (mOsm / kg H}_2\text{O)} = 2[\text{Na}^+] + \frac{\text{Glucose} + \text{BUN}}{18 \quad 2.8}$$

where 18 and 2.8 are derived from the molecular weights of glucose and urea, respectively. Because serum glucose and urea concentrations are expressed as mg/dL, it is necessary to convert these concentrations to mOsm/L by dividing the molecular weights of glucose (180) or urea nitrogen (28) by 10. Normal serum values are $\text{Na}^+ = 142 \text{ mEq/L}$, glucose = 90 mg/dL, and urea nitrogen = 12 mg/dL. The serum osmolality, therefore, is:

$$\text{mOsm} / \text{kg H}_2\text{O} = 2[142] + \frac{90}{18} + \frac{12}{2.8} = 284 + 5 + 4 = 293$$

The normal range is between 280 and 295 mOsm/kg H_2O (some use the value $285 \pm 5 \text{ mOsm/kg H}_2\text{O}$). Inside the cell, the major electrolyte that contributes to the osmolality is K^+ .

Total Osmolality Versus Effective Osmolality

The term *total serum* or *plasma osmolality* should be distinguished from the term *effective* osmolality or *tonicity*. Tonicity is determined by the concentration of those solutes that remain outside the cell membrane and cause osmosis. Na^+ and glucose remain in the extracellular fluid compartment (see the following text) and cause water movement. These solutes are, therefore, called *effective osmolytes* and thus contribute to plasma tonicity. Mannitol, sorbitol, and glycerol also behave as effective osmolytes. On the other hand, substances that can enter the cell freely do not maintain an osmotic gradient for water movement. Urea can penetrate the

membrane easily and therefore does not exert an osmotic force that causes water movement. For this reason, urea is referred to as an *ineffective osmolyte*. Urea, therefore, does not contribute to tonicity. Ethanol and methanol also behave like urea. The contribution of urea is thus not included in the calculation of effective osmolality. Effective osmolality is calculated using the following equation:

$$\text{Effective osmolality (mOsm / kg H}_2\text{O)} = 2[\text{Na}] + \frac{\text{glucose}}{18}$$

The normal range for effective osmolality is between 275 and 290 mOsm/kg H₂O.

Isosmotic Versus Isotonic

The term *isosmotic* refers to identical osmolalities of various body fluids, e.g., plasma versus cerebrospinal fluid. However, when discussing osmolalities of solutions used clinically to replace body fluid losses, the terms *isotonic*, *hypotonic*, or *hypertonic* are used. A solution is considered isotonic if it has the same osmolality as body fluids. When an isotonic solution is given intravenously, it will not cause red blood cells to change in size. However, a hypotonic solution will cause red blood cells to swell, and a hypertonic solution will cause red blood cells to shrink. Isotonic solution that is commonly used to replace loss of body fluids is 0.9% NaCl (normal saline).

Body Fluid Compartments

As stated, the major body fluid is water. In a lean individual, it comprises about 60% of the total body weight. Fat contains less water. Therefore, in obese individuals the water content is 55% of the total body weight. For example, a 70 kg lean person contains 42 L of water ($70 \times 0.6 = 42$ L). This total body water is distributed between two major compartments: the *extracellular fluid* (ECF) and *intracellular fluid* (ICF) compartments. About one-third (20%) of the total amount of water is confined to the ECF and two-thirds (40%) to the ICF compartment (Fig. 1.1). The ECF compartment, in turn, is divided into the following subdivisions:

1. Plasma
2. Interstitial fluid and lymph
3. Bone and dense connective tissue water
4. Transcellular (cerebrospinal, pleural, peritoneal, synovial, and digestive secretions)

Of these subdivisions, the plasma and interstitial fluids are the two most important because of constant exchange of fluid and electrolytes between them. Plasma and interstitial fluid are separated by the capillary endothelium. Plasma circulates in the blood vessels, whereas the interstitial fluid bathes all tissue cells except for the formed elements of blood. For this reason, Claude Bernard, the French physiologist, called

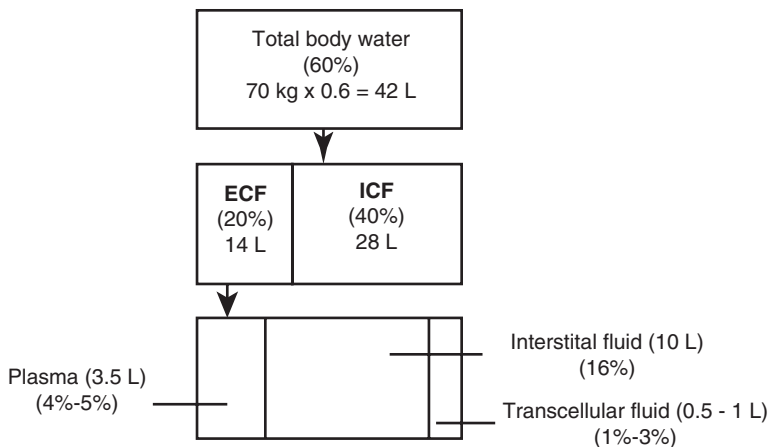


Fig. 1.1 Approximate distribution of water in various body fluid compartments: *ECF* extracellular fluid, *ICF* intracellular fluid. A 70 kg lean man has 42 L of water, assuming the total body water content is 60% of the body weight ($70 \times 0.6 = 42$ L)

the interstitium “the true environment of the body” (*milieu interieur*). Figure 1.1 summarizes the distribution of water in various body fluid compartments.

Water Movement Between ECF and ICF Compartments

In a healthy individual, the ECF and ICF fluids are in osmotic equilibrium. If this equilibrium is disturbed, water moves from the area of lower solute concentration to the area of greater solute concentration in order to reestablish the osmotic equilibrium. The following *Darrow–Yannet* diagram illustrates this point (Fig. 1.2). Let us assume that a lean male weighs 70 kg and the osmolality in both ECF and ICF compartments is 280 mOsm/kg H_2O . His total body water is 60% of the body weight; therefore, the total body water is 42 L. Of this amount, 28 L are in the ICF and 14 L are in the ECF compartment. What happens to osmolality and water distribution in each compartment if we add 1 L of water to the ECF? Initially, this additional 1 L of H_2O would not only increase the ECF volume but it would also decrease its osmolality from 280 to 261 mOsm/kg H_2O (total ECF mOsm ($280 \times 14 = 3,920$ mOsm)/new ECF water content (15 L) = $3,920/15 = 261$ mOsm). Since the ICF osmolality is higher than this new ECF osmolality, water will move into the ICF until a new osmotic equilibrium is reached. As a result, the ICF volume also increases. The net result is an increase in volume and a decrease in osmolality in both compartments. These changes are shown in Fig. 1.2.

Thus, addition of 1 L of water to ECF decreases the final osmolality to 273 mOsm/kg H_2O (total body mOsm ($280 \times 42 = 11,760$)/new total body water (43 L) = $11,760/43 = 273$ mOsm) and increases water content in the ICF by 0.72 L and ECF by 0.28 L (ICF mOsm ($280 \times 28 = 7,840$)/new osmolality (273) = $7,840/273 = 28.72$ L). It should be noted that these changes are minimal in

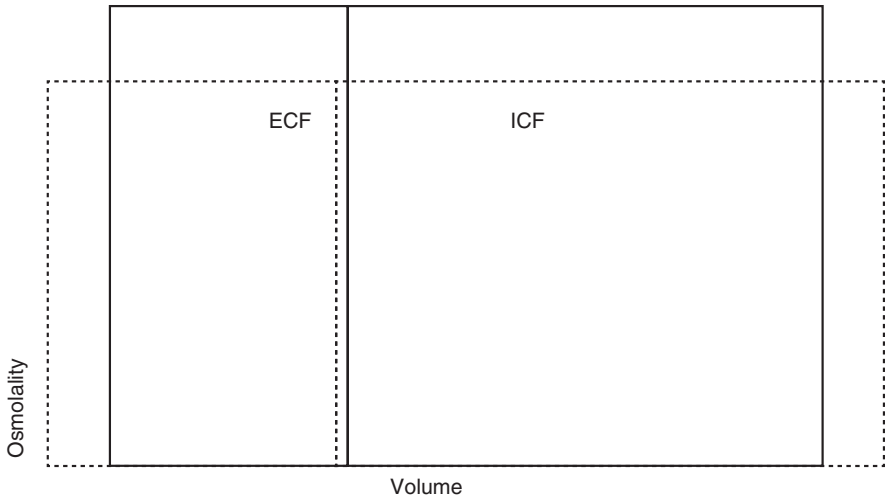


Fig. 1.2 Darrow–Yannet diagram showing fluid and osmolality changes in the ECF and ICF compartments following addition of 1 L of water to the ECF. Initial state is shown by a *solid line* and final state by a *dashed line*. Width represents the volume of the compartments, and height represents osmolality

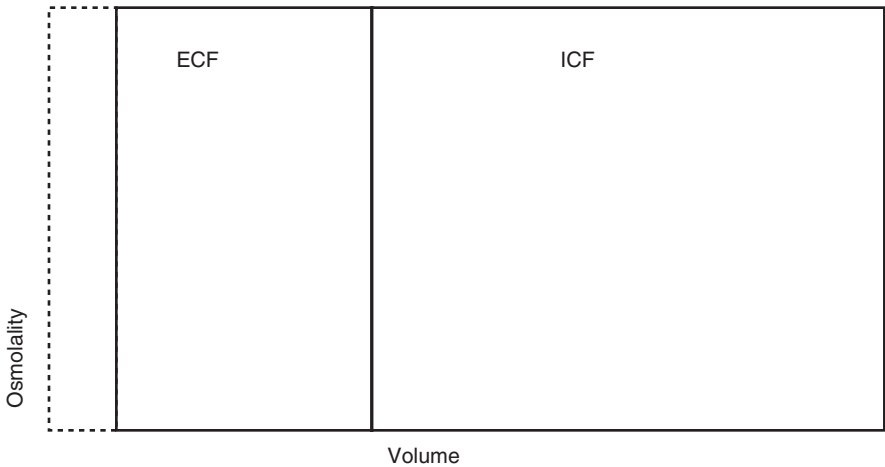


Fig. 1.3 Darrow–Yannet diagram showing volume change following addition of 1 L of isotonic NaCl

an individual with normal renal function, since the kidneys compensate for these changes by excreting excess water in order to maintain fluid balance.

Let us use another example. What would happen if 1 L of isotonic (0.9%) saline is added instead of pure water to ECF? Since 0.9% saline is isotonic, it does not cause water movement. Therefore, body osmolality does not change. However, this isotonic saline will remain in the ECF compartment and cause its expansion, as shown in Fig. 1.3. Healthy individuals excrete saline to maintain normal ECF volume.

Study Questions

Case 1 A 28-year-old type 1 diabetic male patient is admitted to the hospital for nausea, vomiting, and abdominal pain. His weight is 60 kg and the initial laboratory values are:

$$\text{Na}^+ = 146 \text{ mEq/L}$$

$$\text{K}^+ = 5 \text{ mEq/L}$$

$$\text{HCO}_3^- = 10 \text{ mEq/L}$$

$$\text{BUN} = 70 \text{ mg/dL}$$

$$\text{Glucose} = 540 \text{ mg/dL}$$

Question 1 Calculate this patient's plasma osmolality and explain his fluid shift.

Answer Plasma osmolality is calculated by using the following formula:

$$\begin{aligned} \text{Plasma osmolality} &= 2[\text{Plasma Na}^+] + \frac{\text{Glucose}}{18} + \frac{\text{BUN}}{2.8} \\ &= 2[146] + \frac{540}{18} + \frac{70}{2.8} = 347 \text{ mOsm / kg H}_2\text{O} \end{aligned}$$

Because plasma osmolality is elevated, water initially moves out of cells, i.e., from the ICF to the ECF compartment, and causes expansion of the latter until a new steady state is reached. The patient receives insulin and normal saline. Repeat blood chemistry shows:

$$\text{Na}^+ = 140 \text{ mEq/L}$$

$$\text{K}^+ = 4.2 \text{ mEq/L}$$

$$\text{HCO}_3^- = 20 \text{ mEq/L}$$

$$\text{BUN} = 40 \text{ mg/dL}$$

$$\text{Glucose} = 180 \text{ mg/dL}$$

Question 2 Does increase in BUN contribute to fluid shift?

Answer No. Although BUN contributes 14 mOsm to plasma osmolality, no fluid shift will occur on its account. The lack of fluid shift is due to its ineffectiveness as an osmole, i.e., urea crosses the cell membrane easily and does not establish a concentration gradient.

Question 3 Calculate this patient's plasma tonicity (effective plasma osmolality).

Answer Tonicity is a measure of the osmotically active particles from Na^+ and glucose. Therefore, the serum concentration of BUN is not included in the calculation. The plasma tonicity is:

$$\frac{2[140] + 180}{18} = 290 \text{ mOsm / kg H}_2\text{O}$$

Case 2 A 30-year-old patient with AIDS (acquired immunodeficiency syndrome) is admitted for weakness, weight loss, fever, nausea, vomiting, and mental irritability. His blood pressure is low. The diagnosis of Addison’s disease (a disease caused by deficiency of glucocorticoid and mineralocorticoid hormones produced by the adrenal cortex) is made. Admitting laboratory values are as follows:

- Na⁺ = 120 mEq/L
- K⁺ = 6.2 mEq/L
- Cl⁻ = 112 mEq/L
- HCO₃⁻ = 14 mEq/L
- BUN = 70 mg/dL
- Glucose = 60 mg/dL

Question 1 Explain the fluid shift in this patient.

Answer This patient lost Na⁺ than water from the ECF compartment due to mineralocorticoid (aldosterone) deficiency. As a result of low serum Na⁺, his plasma osmolality is low. Decreased plasma osmolality causes water to move from the ECF to the ICF compartment. The net result is the contraction of ECF volume and a transient increase in ICF volume and reduction in osmolality in both compartments, as shown in Fig. 1.4.

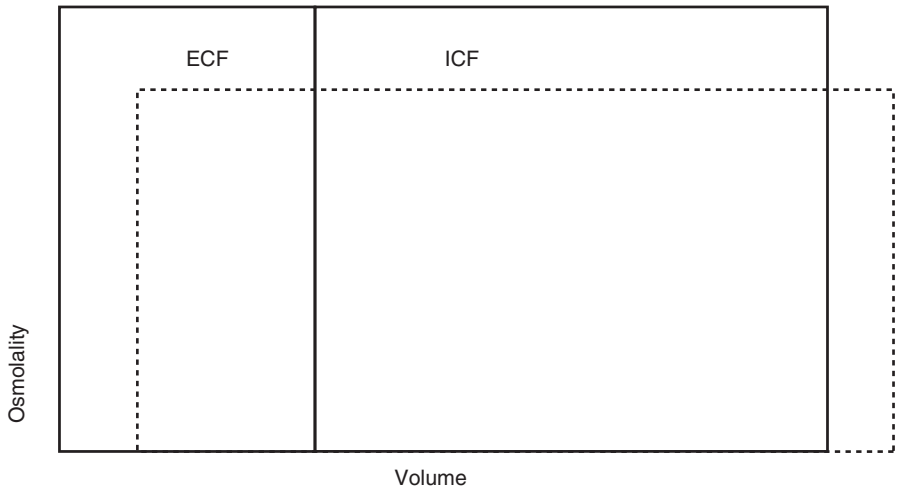


Fig. 1.4 The net result in this patient is the contraction of ECF volume and a transient increase in ICF volume and reduction in osmolality in both compartments. Initial state is represented by *solid line* and final state by *dashed line*