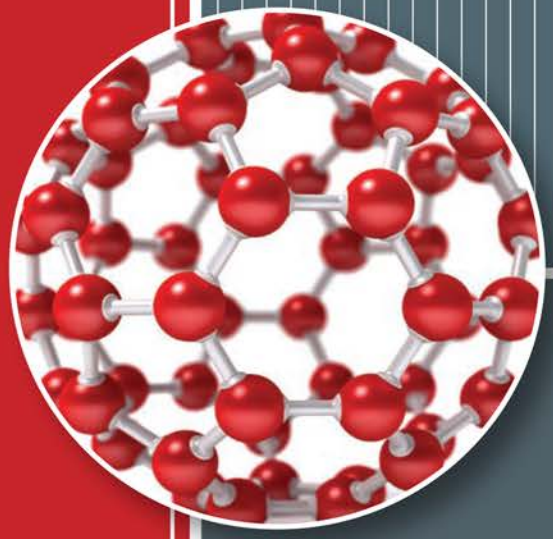

Advanced Nutrition and Human Metabolism

SEVENTH EDITION

Sareen S. Gropper | Jack L. Smith
Timothy P. Carr

Dietary Reference Intakes (DRI)

The Dietary Reference Intakes (DRI) include two sets of values that serve as goals for nutrient intake—Recommended Dietary Allowances (RDA) and Adequate Intakes (AI). The RDA reflect the average daily amount of a nutrient considered adequate to meet the needs of most healthy people. If there is insufficient evidence to determine an RDA, an AI is set. AI are more tentative than RDA, but both may be used as goals for nutrient intakes. (Chapter 9 provides more details.)

In addition to the values that serve as goals for nutrient intakes (presented in the tables on these two pages), the DRI include a set of values called Tolerable Upper Intake Levels (UL). The UL represent the maximum amount of a nutrient that appears safe for most healthy people to consume on a regular basis. Turn the page for a listing of the UL for selected vitamins and minerals.

Estimated Energy Requirements (EER), Recommended Dietary Allowances (RDA), and Adequate Intakes (AI) for Water, Energy, and the Energy Nutrients

Age (yr)	Reference BMI (kg/m^2)	Reference Height cm (in)	Reference Weight kg (lb)	Water[a] AI (L/day)	Energy EER[b] (kcal/day)	Carbohydrate RDA (g/day)	Total Fiber AI (g/day)	Total Fat AI (g/day)	Linoleic Acid AI (g/day)	Linolenic Acid[c] AI (g/day)	Protein RDA (g/day)[d]	Protein RDA (g/kg/day)
Males												
0–0.5	—	62 (24)	6 (13)	0.7[e]	570	60	—	31	4.4	0.5	9.1	1.52
0.5–1	—	71 (28)	9 (20)	0.8[f]	743	95	—	30	4.6	0.5	11	1.20
1–3[g]	—	86 (34)	12 (27)	1.3	1046	130	19	—	7	0.7	13	1.05
4–8[g]	15.3	115 (45)	20 (44)	1.7	1742	130	25	—	10	0.9	19	0.95
9–13	17.2	144 (57)	36 (79)	2.4	2279	130	31	—	12	1.2	34	0.95
14–18	20.5	174 (68)	61 (134)	3.3	3152	130	38	—	16	1.6	52	0.85
19–30	22.5	177 (70)	70 (154)	3.7	3067[h]	130	38	—	17	1.6	56	0.80
31–50	22.5[i]	177 (70)[i]	70 (154)[i]	3.7	3067[h]	130	38	—	17	1.6	56	0.80
>50	22.5[i]	177 (70)[i]	70 (154)[i]	3.7	3067[h]	130	30	—	14	1.6	56	0.80
Females												
0–0.5	—	62 (24)	6 (13)	0.7[e]	520	60	—	31	4.4	0.5	9.1	1.52
0.5–1	—	71 (28)	9 (20)	0.8[f]	676	95	—	30	4.6	0.5	11	1.20
1–3[g]	—	86 (34)	12 (27)	1.3	992	130	19	—	7	0.7	13	1.05
4–8[g]	15.3	115 (45)	20 (44)	1.7	1642	130	25	—	10	0.9	19	0.95
9–13	17.4	144 (57)	37 (81)	2.1	2071	130	26	—	10	1.0	34	0.95
14–18	20.4	163 (64)	54 (119)	2.3	2368	130	26	—	11	1.1	46	0.85
19–30	21.5	163 (64)	57 (126)	2.7	2403[j]	130	25	—	12	1.1	46	0.80
31–50	21.5[i]	163 (64)[i]	57 (126)[i]	2.7	2403[j]	130	25	—	12	1.1	46	0.80
>50	21.5[i]	163 (64)[i]	57 (126)[i]	2.7	2403[j]	130	21	—	11	1.1	46	0.80
Pregnancy												
1st trimester				3.0	+0	175	28	—	13	1.4	46	0.80
2nd trimester				3.0	+340	175	28	—	13	1.4	71	1.10
3rd trimester				3.0	+452	175	28	—	13	1.4	71	1.10
Lactation												
1st 6 months				3.8	+330	210	29	—	13	1.3	71	1.30
2nd 6 months				3.8	+400	210	29	—	13	1.3	71	1.30

NOTE: For all nutrients, values for infants are AI. Dashes indicate that values have not been determined.

[a]The water AI includes drinking water, water in beverages, and water in foods; in general, drinking water and other beverages contribute about 70 to 80 percent, and foods, the remainder. Conversion factors: 1 L = 33.8 fluid oz; 1 L = 1.06 qt; 1 cup = 8 fluid oz.

[b]The Estimated Energy Requirement (EER) represents the average dietary energy intake that will maintain energy balance in a healthy person of a given gender, age, weight, height, and physical activity level. The values listed are based on an "active" person at the reference height and weight and at the midpoint ages for each group until age 19. Chapter 8 provides equations and tables to determine estimated energy requirements.

[c]The linolenic acid referred to in this table and text is the omega-3 fatty acid known as alpha-linolenic acid.

[d]The values listed are based on reference body weights.

[e]Assumed to be from human milk.

[f]Assumed to be from human milk and complementary foods and beverages. This includes approximately 0.6 L (~2½ cups) as total fluid including formula, juices, and drinking water.

[g]For energy, the age groups for young children are 1–2 years and 3–8 years.

[h]For males, subtract 10 kcalories per day for each year of age above 19.

[i]Because weight need not change as adults age if activity is maintained, reference weights for adults 19 through 30 years are applied to all adult age groups.

[j]For females, subtract 7 kcalories per day for each year of age above 19.

SOURCE: Adapted from the *Dietary Reference Intakes* series, National Academies Press. Copyright 1997, 1998, 2000, 2001, 2002, 2004, 2005, 2011 by the National Academies of Sciences.

Recommended Dietary Allowances (RDA) and Adequate Intakes (AI) for Vitamins

Age (yr)	Thiamin RDA (mg/day)	Riboflavin RDA (mg/day)	Niacin RDA (mg/day)[a]	Biotin AI (µg/day)	Pantothenic acid AI (mg/day)	Vitamin B_6 RDA (mg/day)	Folate RDA (µg/day)[b]	Vitamin B_{12} RDA (µg/day)	Choline AI (mg/day)	Vitamin C RDA (mg/day)	Vitamin A RDA (µg/day)[c]	Vitamin D RDA (IU/day)[d]	Vitamin E RDA (mg/day)[e]	Vitamin K AI (µg/day)
Infants														
0–0.5	0.2	0.3	2	5	1.7	0.1	65	0.4	125	40	400	400 (10 µg)	4	2.0
0.5–1	0.3	0.4	4	6	1.8	0.3	80	0.5	150	50	500	400 (10 µg)	5	2.5
Children														
1–3	0.5	0.5	6	8	2	0.5	150	0.9	200	15	300	600 (15 µg)	6	30
4–8	0.6	0.6	8	12	3	0.6	200	1.2	250	25	400	600 (15 µg)	7	55
Males														
9–13	0.9	0.9	12	20	4	1.0	300	1.8	375	45	600	600 (15 µg)	11	60
14–18	1.2	1.3	16	25	5	1.3	400	2.4	550	75	900	600 (15 µg)	15	75
19–30	1.2	1.3	16	30	5	1.3	400	2.4	550	90	900	600 (15 µg)	15	120
31–50	1.2	1.3	16	30	5	1.3	400	2.4	550	90	900	600 (15 µg)	15	120
51–70	1.2	1.3	16	30	5	1.7	400	2.4	550	90	900	600 (15 µg)	15	120
>70	1.2	1.3	16	30	5	1.7	400	2.4	550	90	900	800 (20 µg)	15	120
Females														
9–13	0.9	0.9	12	20	4	1.0	300	1.8	375	45	600	600 (15 µg)	11	60
14–18	1.0	1.0	14	25	5	1.2	400	2.4	400	65	700	600 (15 µg)	15	75
19–30	1.1	1.1	14	30	5	1.3	400	2.4	425	75	700	600 (15 µg)	15	90
31–50	1.1	1.1	14	30	5	1.3	400	2.4	425	75	700	600 (15 µg)	15	90
51–70	1.1	1.1	14	30	5	1.5	400	2.4	425	75	700	600 (15 µg)	15	90
>70	1.1	1.1	14	30	5	1.5	400	2.4	425	75	700	800 (20 µg)	15	90
Pregnancy														
≤18	1.4	1.4	18	30	6	1.9	600	2.6	450	80	750	600 (15 µg)	15	75
19–30	1.4	1.4	18	30	6	1.9	600	2.6	450	85	770	600 (15 µg)	15	90
31–50	1.4	1.4	18	30	6	1.9	600	2.6	450	85	770	600 (15 µg)	15	90
Lactation														
≤18	1.4	1.6	17	35	7	2.0	500	2.8	550	115	1200	600 (15 µg)	19	75
19–30	1.4	1.6	17	35	7	2.0	500	2.8	550	120	1300	600 (15 µg)	19	90
31–50	1.4	1.6	17	35	7	2.0	500	2.8	550	120	1300	600 (15 µg)	19	90

NOTE: For all nutrients, values for infants are AI.

[a]Niacin recommendations are expressed as niacin equivalents (NE), except for recommendations for infants younger than 6 months, which are expressed as preformed niacin.

[b]Folate recommendations are expressed as dietary folate equivalents (DFE).

[c]Vitamin A recommendations are expressed as retinol activity equivalents (RAE).

[d]Vitamin D recommendations are expressed as cholecalciferol and assume an absence of adequate exposure to sunlight.

[e]Vitamin E recommendations are expressed as α-tocopherol.

Recommended Dietary Allowances (RDA) and Adequate Intakes (AI) for Minerals

Age (yr)	Sodium AI (mg/day)	Chloride AI (mg/day)	Potassium AI (mg/day)	Calcium RDA (mg/day)	Phosphorus RDA (mg/day)	Magnesium RDA (mg/day)	Iron RDA (mg/day)	Zinc RDA (mg/day)	Iodine RDA (µg/day)	Selenium RDA (µg/day)	Copper RDA (µg/day)	Manganese AI (mg/day)	Fluoride AI (mg/day)	Chromium AI (µg/day)	Molybdenum RDA (µg/day)
Infants															
0–0.5	120	180	400	200	100	30	0.27	2	110	15	200	0.003	0.01	0.2	2
0.5–1	370	570	700	260	275	75	11	3	130	20	220	0.6	0.5	5.5	3
Children															
1–3	1000	1500	3000	700	460	80	7	3	90	20	340	1.2	0.7	11	17
4–8	1200	1900	3800	1000	500	130	10	5	90	30	440	1.5	1.0	15	22
Males															
9–13	1500	2300	4500	1300	1250	240	8	8	120	40	700	1.9	2	25	34
14–18	1500	2300	4700	1300	1250	410	11	11	150	55	890	2.2	3	35	43
19–30	1500	2300	4700	1000	700	400	8	11	150	55	900	2.3	4	35	45
31–50	1500	2300	4700	1000	700	420	8	11	150	55	900	2.3	4	35	45
51–70	1300	2000	4700	1000	700	420	8	11	150	55	900	2.3	4	30	45
>70	1200	1800	4700	1200	700	420	8	11	150	55	900	2.3	4	30	45
Females															
9–13	1500	2300	4500	1300	1250	240	8	8	120	40	700	1.6	2	21	34
14–18	1500	2300	4700	1300	1250	360	15	9	150	55	890	1.6	3	24	43
19–30	1500	2300	4700	1000	700	310	18	8	150	55	900	1.8	3	25	45
31–50	1500	2300	4700	1000	700	320	18	8	150	55	900	1.8	3	25	45
51–70	1300	2000	4700	1200	700	320	8	8	150	55	900	1.8	3	20	45
>70	1200	1800	4700	1200	700	320	8	8	150	55	900	1.8	3	20	45
Pregnancy															
≤18	1500	2300	4700	1300	1250	400	27	12	220	60	1000	2.0	3	29	50
19–30	1500	2300	4700	1000	700	350	27	11	220	60	1000	2.0	3	30	50
31–50	1500	2300	4700	1000	700	360	27	11	220	60	1000	2.0	3	30	50
Lactation															
≤18	1500	2300	5100	1300	1250	360	10	13	290	70	1300	2.6	3	44	50
19–30	1500	2300	5100	1000	700	310	9	12	290	70	1300	2.6	3	45	50
31–50	1500	2300	5100	1000	700	320	9	12	290	70	1300	2.6	3	45	50

NOTE: For all nutrients, values for infants are AI.

Tolerable Upper Intake Levels (UL) for Vitamins

Age (yr)	Niacin (mg/day)[a]	Vitamin B_6 (mg/day)	Folate (µg/day)[a]	Choline (mg/day)	Vitamin C (mg/day)	Vitamin A (µg/day)[b]	Vitamin D (IU/day)	Vitamin E (mg/day)[c]	
Infants									
0–0.5	—	—	—	—	—	600	1000 (25 µg)	—	
0.5–1	—	—	—	—	—	600	1500 (38 µg)	—	
Children									
1–3	10	30	300	1000	400	600	2500 (63 µg)	200	
4–8	15	40	400	1000	650	900	3000 (75 µg)	300	
9–13	20	60	600	2000	1200	1700	4000 (100 µg)	600	
Adolescents									
14–18	30	80	800	3000	1800	2800	4000 (100 µg)	800	
Adults									
19–70	35	100	1000	3500	2000	3000	4000 (100 µg)	1000	
>70	35	100	1000	3500	2000	3000	4000 (100 µg)	1000	
Pregnancy									
≤18	30	80	800	3000	1800	2800	4000 (100 µg)	800	
19–50	35	100	1000	3500	2000	3000	4000 (100 µg)	1000	
Lactation									
≤18	30	80	800	3000	1800	2800	4000 (100 µg)	800	
19–50	35	100	1000	3500	2000	3000	4000 (100 µg)	1000	

[a]The UL for niacin and folate apply to synthetic forms obtained from supplements, fortified foods, or a combination of the two.
[b]The UL for vitamin A applies to the preformed vitamin only.
[c]The UL for vitamin E applies to any form of supplemental α-tocopherol, fortified foods, or a combination of the two.

Tolerable Upper Intake Levels (UL) for Minerals

Age (yr)	Sodium (mg/day)	Chloride (mg/day)	Calcium (mg/day)	Phosphorus (mg/day)	Magnesium (mg/day)[d]	Iron (mg/day)	Zinc (mg/day)	Iodine (µg/day)	Selenium (µg/day)	Copper (µg/day)	Manganese (mg/day)	Fluoride (mg/day)	Molybdenum (µg/day)	Boron (mg/day)	Nickel (mg/day)	Vanadium (mg/day)	
Infants																	
0–0.5	—	—	1000	—	—	40	4	—	45	—	—	0.7	—	—	—	—	
0.5–1	—	—	1500	—	—	40	5	—	60	—	—	0.9	—	—	—	—	
Children																	
1–3	1500	2300	2500	3000	65	40	7	200	90	1000	2	1.3	300	3	0.2	—	
4–8	1900	2900	2500	3000	110	40	12	300	150	3000	3	2.2	600	6	0.3	—	
9–13	2200	3400	3000	4000	350	40	23	600	280	5000	6	10	1100	11	0.6	—	
Adolescents																	
14–18	2300	3600	3000	4000	350	45	34	900	400	8000	9	10	1700	17	1.0	—	
Adults																	
19–50	2300	3600	2500	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8	
51–70	2300	3600	2000	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8	
>70	2300	3600	2000	3000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	1.8	
Pregnancy																	
≤18	2300	3600	3000	3500	350	45	34	900	400	8000	9	10	1700	17	1.0	—	
19–50	2300	3600	2500	3500	350	45	40	1100	400	10,000	11	10	2000	20	1.0	—	
Lactation																	
≤18	2300	3600	3000	4000	350	45	34	900	400	8000	9	10	1700	17	1.0	—	
19–50	2300	3600	2500	4000	350	45	40	1100	400	10,000	11	10	2000	20	1.0	—	

[d]The UL for magnesium applies to synthetic forms obtained from supplements or drugs only.
NOTE: An Upper Limit was not established for vitamins and minerals not listed and for those age groups listed with a dash (—) because of a lack of data, not because these nutrients are safe to consume at any level of intake. All nutrients can have adverse effects when intakes are excessive.

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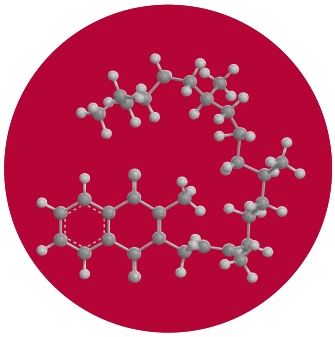
ADVANCED NUTRITION AND HUMAN METABOLISM

SEVENTH EDITION



ADVANCED NUTRITION AND HUMAN METABOLISM

SEVENTH EDITION

Sareen S. Gropper

FLORIDA ATLANTIC UNIVERSITY

AUBURN UNIVERSITY (PROFESSOR EMERITUS)

Jack L. Smith

UNIVERSITY OF DELAWARE

Timothy P. Carr

UNIVERSITY OF NEBRASKA-LINCOLN

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Sareen S. Gropper, Jack L. Smith, and Timothy P. Carr

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Content Developer: Kellie Petruzzelli
Marketing Manager: Ana Albinson
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To my children Michelle and Michael, and to my husband, Daniel, for their ongoing encouragement, support, faith, and love and to the students who continue to impress and inspire me.

Sareen Gropper

To my wife, Carol, for her continued support, constant inspiration, and assistance in the preparation of this book.

Jack Smith

To my family—Rebecca, Erin, and Marion—for their unwavering support and to the many students who have made my career so enjoyable.

Tim Carr

BRIEF CONTENTS

CONTENTS

PREFACE

Since the first edition was published in 1990, much has changed in the science of nutrition. But the purpose of the text—to provide thorough coverage of normal metabolism for upper-division nutrition students—remains the same. We continue to strive for a level of detail and scope of material that satisfy the needs of both instructors and students. With each succeeding edition, we have responded to suggestions from instructors, content reviewers, and students that have improved the text by enhancing the clarity of the material and by ensuring accuracy. In addition, we have included the latest and most pertinent nutrition science available to provide future nutrition professionals with the fundamental information vital to their careers and to provide the basis for assimilating new scientific discoveries.

Just as the body of information on nutrition science has increased, so has the team of authors working on this text. Dr. James Groff and Dr. Sara Hunt coauthored the first edition. In subsequent editions, Dr. Sareen Gropper became a coauthor as Dr. Hunt entered retirement. In the fourth edition, Dr. Jack L. Smith joined the author team now led by Dr. Gropper. In this seventh edition, Dr. Tim Carr has provided additional expertise and co-authorship on several chapters.

NEW TO THIS EDITION

All chapters of the seventh edition have been updated, and many feature new or enhanced tables and illustrations. The organization of the content among the chapters has remained similar to the sixth edition.

Chapter 1 The Cell: A Microcosm of Life

- expanded the discussion of the components of the cytoskeleton
- elaborated on the mechanisms of apoptosis
- condensed and focused chapter content

Chapter 2 The Digestive System: Mechanism for Nourishing the Body

- expanded coverage of saliva, the regulation of gastric secretions and motility, and the roles of colonic microflora
- added information on tight junctions
- incorporated discussion of disorders causing malfunction of the gastrointestinal tract from the Perspective into the Chapter
- included new figures to enhance presentation of hydrochloric acid secretion and hepatic physiology
- added a new Perspective addressing the nutritional impact of gastric bypass surgery

Chapter 3 Carbohydrates

- added a new Perspective on the trends in carbohydrate intake in the United States over the past several decades
- expanded coverage on dextrins in the food supply and their digestion and metabolism
- added information on glycolysis and updated the relevant figures
- expanded coverage on the role of insulin and added a new figure on insulin signaling

Chapter 4 Fiber

- added new fiber definitions
- refocused and condensed the discussion of the properties of fiber to reflect current trends
- added 2015 Dietary Guidelines recommendations related to dietary patterns

Chapter 5 Lipids

- provided more thorough coverage on lipid digestion and absorption
- added a new figure depicting the major fat sources in the American diet
- expanded coverage on cholesterol, phytosterols, phospholipids, and sphingolipids
- added a new section on dietary sources of lipids and recommended intake
- reorganized and expanded the section on lipid transport and metabolism
- added a new figure depicting ethanol oxidation in the liver

Chapter 6 Protein

- expanded the section on protein synthesis to include amino acid signaling, mTOR, and distribution of protein intake
- added information on new methodology used to evaluate protein quality
- provided a more detailed discussion of protein malnutrition and its diagnosis
- redirected the Perspective to address the impact of stress and inflammation on protein

Chapter 7 Integration and Regulation of Metabolism and the Impact of Exercise

- added a new Perspective on sports nutrition and supplementation
- expanded coverage on the distribution of fuel molecules and tissue-specific energy utilization
- added new section on muscle function and energy requirements during exercise, including new and updated figures
- expanded coverage on regulatory hormones
- expanded coverage on the fed-fast cycle, including new and updated figures

Chapter 8 Energy Expenditure, Body Composition, and Healthy Weight

- reorganized the chapter sections to improve flow and readability
- added a new figure depicting obesity prevalence in the United States
- added a new table describing the Institute of Medicine's Physical Activity Level (PAL) categories
- updated photographs illustrating methods of assessing body composition
- added new tables summarizing ideal body weight formulas and body mass index categories
- reorganized and updated the discussion on field and laboratory methods used to measure body composition
- provided more thorough coverage of factors regulating energy balance and body weight
- added a new section on the health implications of altered body weight

Chapter 9 Water-Soluble Vitamins

- provided new tables addressing the water-soluble vitamin contents of foods
- added information on the amounts and forms of the vitamins used in supplements
- included new tables addressing common manifestations of water-soluble vitamin deficiencies and an overview of water-soluble vitamin absorption and storage
- expanded coverage of the metabolic roles of thiamin, niacin, and pantothenic acid
- added sections on selected pharmacological uses of the vitamins
- updated and expanded coverage of water soluble vitamin deficiencies including those at risk for deficiency and the treatment of deficiencies

Chapter 10 Fat-Soluble Vitamins

- added tables to more thoroughly cover the fat-soluble vitamin content of foods
- included a new table addressing common manifestations of fat-soluble vitamin deficiencies
- expanded the coverage of fat-soluble vitamin deficiencies including those at risk of deficiencies and the treatment of deficiencies

Chapter 11 Major Minerals

- provided more thorough coverage of the major mineral contents of foods
- added information on the amounts and forms of the major minerals used in supplements
- expanded information on the manifestations associated with deficiencies of the major minerals and treatment of deficiencies
- added to the Perspective information on new tools used in assessing risk of osteoporosis

Chapter 12 Water and Electrolytes

- added new sections addressing water sources, absorption, and recommendations
- reorganized and expanded the discussion of water and sodium balance as well as acid base balance
- elaborated on the roles of the kidneys in maintaining fluid and sodium balance as well as acid base balance
- included several new figures depicting the role of the kidneys and hormones in maintaining fluid and sodium balance

Chapter 13 Essential Trace and Ultratrace Minerals

- provided more thorough coverage of the trace and ultratrace mineral contents of foods including the addition of new tables
- added information on the forms and amounts of trace minerals found in supplements
- added new sections on the pharmacological uses of minerals as appropriate
- expanded the discussion of the regulation of body and cellular iron along with a new figure showing controls on hepcidin
- included more information on manifestations of trace mineral deficiencies and their treatment

Chapter 14 Nonessential Trace and Ultratrace Minerals

- expanded the discussion of the roles of fluoride
- added information about the arsenic content of foods and arsenic toxicity

PRESENTATION

The presentation of the text is designed to make the book easy for the reader to use. The second color draws attention to important elements in the text, tables, and figures and helps generate reader interest. The Perspectives provide applications of the information in the chapter text.

Because this book focuses on normal human nutrition and physiological function, it is an effective resource for students majoring in either nutrition sciences or dietetics. Intended for a course in advanced nutrition, the text presumes a sound background in the biological sciences. At the same time, however, it provides a review of the basic sciences—particularly biochemistry and physiology, which are important to understanding the material. This text applies biochemistry to nutrient use from consumption through digestion, absorption, distribution, and cellular metabolism, making it a valuable reference for health care providers. Health practitioners may use it as a resource to refresh their memories with regard to metabolic and physiological interrelationships and to obtain a concise update on current concepts related to human nutrition.

We continue to present nutrition as the science that integrates life processes from the molecular to the cellular level and on through the multisystem operation of the whole organism. Our primary goal is to give a comprehensive picture of cell reactions at the tissue, organ, and system levels. Subject matter has been selected for its relevance to meeting this goal.

ORGANIZATION

Each of the 14 chapters begins with a topic outline, followed by a brief introduction to the chapter's subject matter. These features are followed in order by the chapter text, a brief summary that ties together the ideas presented in the chapter (in Chapters 1–8 and 12), a reference list, and a Perspective with its own reference list.

The text is divided into three sections. Section I (Chapters 1 and 2) focuses on cell structure, gastrointestinal tract anatomy, and function with respect to digestion and absorption.

Section II (Chapters 3–8) discusses metabolism of the macronutrients. This section reviews primary metabolic pathways for carbohydrates, lipids, and proteins, emphasizing those reactions particularly relevant to issues of health. Since most of the body's energy production is associated with glycolysis or the tricarboxylic acid cycle by the way of the electron transport chain and oxidative phosphorylation, the carbohydrates chapter (Chapter 3) covers these aspects of energy transformation. We include a separate chapter (Chapter 4) on fiber. The metabolism of alcohol, which contributes to the caloric intake of many people, is discussed within the lipids chapter (Chapter 5). Alcohol's chemical structure more closely resembles that of carbohydrates, but its metabolism is more similar to that of lipids. Chapter 7 discusses the interrelationships among the metabolic pathways that are common to the macronutrients. This chapter also includes a discussion of the regulation of the metabolic pathways and a description of the metabolic dynamics of the fed-fast cycle, along with a presentation of the effects of physical exertion on the body's metabolic pathways. Chapter 8 focuses on energy expenditure, energy balance, and healthy weight and also includes a brief discussion of measuring body composition and the health implications of altered body weight.

Section III (Chapters 9–14) concerns those nutrients considered regulatory in nature: the water- and fat-soluble vitamins and the minerals, including the major minerals, trace minerals, and ultratrace minerals. These chapters cover nutrient features such as digestion, absorption, transport, function, metabolism, excretion, deficiency, toxicity, and assessment of nutriture, as well as the latest Recommended Dietary Allowances or Adequate Intakes for each nutrient. Information about the major minerals has been split into two chapters: Chapter 11 addresses calcium, phosphorus, and magnesium, and Chapter 12 discusses sodium, potassium, and chloride. Chapter 12 integrates coverage of the maintenance of the body's homeostatic environment—including discussions of body fluids, electrolyte balance, and pH maintenance—with the presentation of the electrolytes.

SUPPLEMENTARY MATERIAL

New to this edition, MindTap is a digital learning platform that works alongside your campus LMS to deliver course curriculum across the range of electronic devices in your life. MindTap is built on an "app" model, allowing enhanced digital collaboration and delivery of engaging content across a spectrum of Cengage and non-Cengage resources. Additionally, to enhance teaching and learning from the textbook, the Instructor Companion Site provides instructors with book-specific lecture and class tools, such as PowerPoint® presentations, images, the instructor's manual, videos, and more, all available online via *www.cengage.com/login*. Lastly, Cengage Learning Testing Powered by Cognero is a flexible online system that allows the instructor to author, edit, and manage test bank content from multiple Cengage Learning solutions.

ACKNOWLEDGMENTS

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1 THE CELL: A MICROCOSM OF LIFE

CELLS ARE THE VERY ESSENCE OF LIFE. **Cells** may be defined as the basic living, structural, and functional units of the human body. They vary greatly in size, chemical composition, and function, but each one is a remarkable miniaturization of human life. Cells move, grow, ingest "food," excrete wastes, react to their environment, and reproduce. This chapter provides a brief review of the basics of a cell, including cellular components, biological energy, and an overview of a cell's natural life span.

Cells of multicellular organisms are called **eukaryotic cells** (from the Greek *eu* meaning "true," and *karyon* meaning "nucleus"). Eukaryotic cells evolved from simpler, more primitive cells called **prokaryotic cells** (from the Greek meaning "before nucleus"). One distinguishing feature between the two cell types is that eukaryotic cells possess a defined nucleus, whereas prokaryotic cells do not. Also, eukaryotic cells are larger and much more complex structurally and functionally than their ancestors. Because this text addresses human metabolism and nutrition, all descriptions of cellular structure and function in this and subsequent chapters pertain to eukaryotic cells.

While specialization among cells is necessary for life, cells, in general, have certain basic similarities. All human cells have a **plasma membrane** and a nucleus (or have had a nucleus), and most contain an endoplasmic reticulum, Golgi apparatus, and mitochondria. For convenience of discussion, a "typical cell" is presented (Figure 1.1) to enable the identification of the various organelles and their functions, which characterize cellular life. Our discussion begins with the plasma membrane which forms the outer boundary of the cell, and then moves inward to examine the organelles found within the cell.

COMPONENTS OF CELLS

Plasma Membrane

The plasma membrane is a sheet-like structure that encapsulates and surrounds the cell, allowing it to exist as a distinct unit. The plasma membrane, like other membranes within the cell, has distinct structural characteristics and functions.

- Plasma membranes are asymmetrical, with different inside and outside "faces."
- Plasma membranes are not static, but are fluid structures.

Plasma membranes are composed primarily of proteins, cholesterol, and phospholipids. Phospholipids, shown in Figure 1.2, provide both a **hydrophobic** and a hydrophilic moiety that allows them to spontaneously form bimolecular sheets, called lipid bilayers, in aqueous environments like the human body.

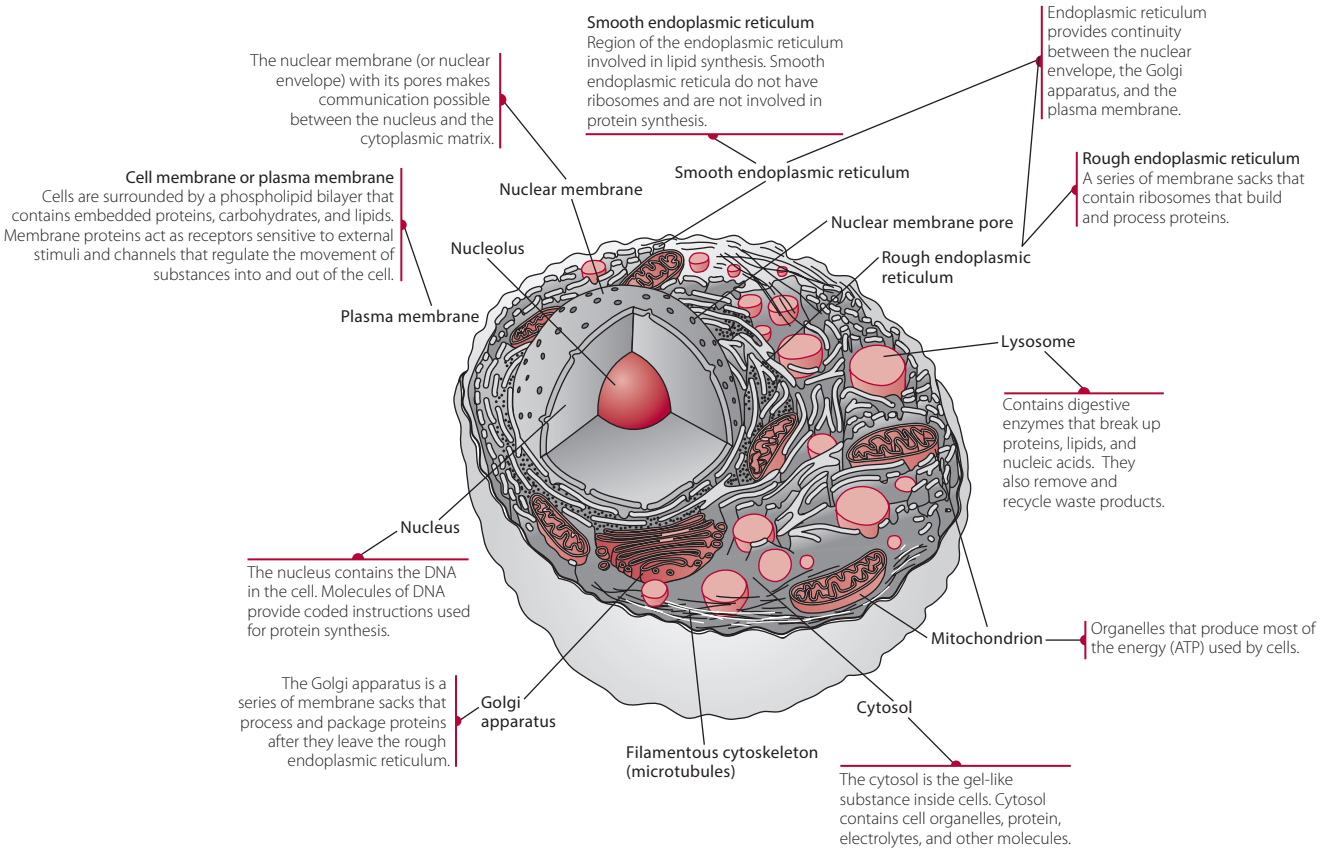

Figure 1.1 Three-dimensional depiction of a typical mammalian liver cell.
Source: Beerman/McGuire, *Nutritional Sciences*, 1/e. © Cengage Learning.

It is this lipid bilayer that determines the structure of the plasma membrane. The fatty acid portion (hydrocarbon chain) of the phospholipids forms the hydrophobic (water-fearing) core of the membrane bilayer; it also inhibits many water-soluble compounds from passing into the cell and helps to retain water-soluble substances within the cell. The glycerol and phosphate-containing portions (polar head) of the phospholipid are hydrophilic (i.e., polar, water loving) and thus are oriented toward the cell's aqueous environments found both outside the cell and in the cell cytosol.

Another important membrane lipid is cholesterol (Figure 1.3). Cholesterol influences the fluidity and thus permeability of membranes, affecting what may pass into and out of the cell; membranes with higher levels of cholesterol are less fluid. Within the membrane, cholesterol's hydrocarbon side chain associates with the fatty acid/hydrocarbon chain portion of the phospholipids and cholesterol's hydroxyl groups are positioned close to the polar head groups of the phospholipids. Cholesterol's rigid planar steroid rings are positioned so as to interact with and stabilize the regions of the hydrocarbon chains closest to the polar head groups of the phospholipids. The rest of the hydrocarbon chain remains flexible and fluid.

Both integral and peripheral proteins are found interspersed with the plasma membrane's lipid bilayer (Figure 1.3). These proteins are responsible for several membrane functions including mediating information transfer (as **receptors**), transporting ions and molecules (as channels, carriers, gates, and pumps), acting as cell adhesion molecules, and speeding up metabolic activities (as **enzymes**). Integral proteins are attached and embedded in the membrane through hydrophobic interactions; they are often transmembrane, spanning the entire structure. Peripheral proteins, in contrast, are associated with membranes through ionic interactions and are located on or near the membrane surface. Peripheral proteins may be attached to integral membrane proteins either directly or through intermediate proteins. Many of these membrane proteins have either lipid or carbohydrate attachments.

Carbohydrates are present in plasma membranes as glycolipids and glycoproteins. While some carbohydrate is found in all membranes, most of the glycolipids and glycoproteins of the cell are associated with the plasma membrane. The carbohydrate moiety of the membrane glycoproteins and glycolipids provides asymmetry to the membrane because the oligosaccharide side chains are located exclusively on the membrane layer facing the cell's

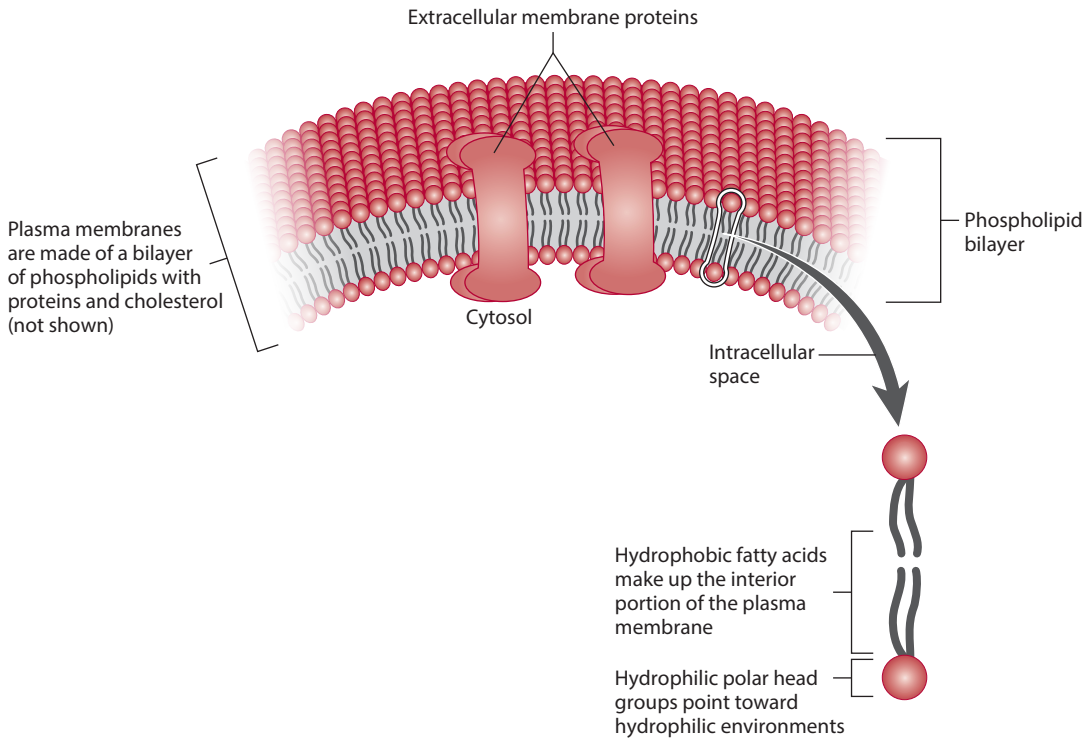

Figure 1.2 Lipid bilayer structure of biological membranes.

outer surface (and not toward the cytosol). In plasma membranes, these outer sugar residues form what is called the glycocalyx, the layer of carbohydrate on the cell's outer surface. On the membranes of the organelles within the cell, however, the oligosaccharides are directed inward. The plasma membrane glycoproteins may serve as the receptors for hormones, certain nutrients, and other substances that influence cellular function. Glycoproteins also may help regulate the intracellular communication necessary for cell growth and functions. Intracellular

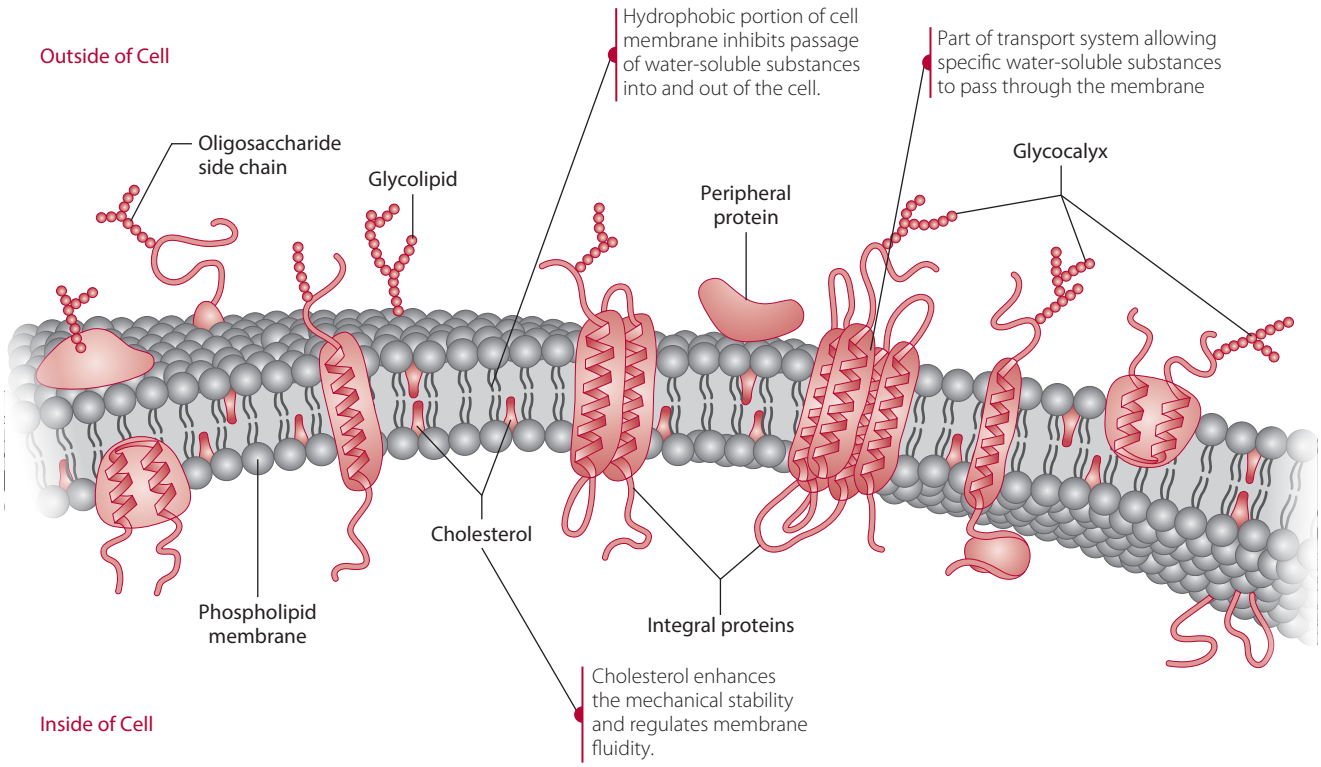

Figure 1.3 Fluid model of cell membrane. Lipids and proteins are mobile and can move laterally in the membrane.

communication occurs through pathways that convert information from one part of a cell to another in response to external stimuli. Generally, it involves the passage of chemical messengers from organelle to organelle or within the lipid bilayers of membranes. Intracellular communication is examined more closely in the "Receptors and Intracellular Signaling" section of this chapter.

Membranes are not structurally distinct from the aqueous compartments of the cell they surround. For example, the **cytosol** (or **cytoplasm**), which is the aqueous, gel-like, transparent substance, fills the cell and, together with a system of filaments, connects the various membranes of the cell. This interconnection creates a structure that makes it possible for a signal generated at one part of the cell to be transmitted quickly and efficiently to other regions of the cell.

Cytoplasmic Matrix

The cytoplasmic (or cytosolic) matrix consists of a system of filaments or fibers (referred to as the cytoskeleton) that is found within the cytosol (Figures 1.1 and 1.4). The cytoskeleton provides cells with:

- structural support, which defines the cell's shape and helps to maintain its function
- a framework for positioning the various organelles (such as microvilli, which are extensions of intestinal cells)
- a network to direct the movement of materials and organelles within the cells
- a means of independent locomotion for specialized cells (such as sperm, white blood cells, and fibroblasts)
- a pathway for intercellular communication among cellular components (vital for cell activation and survival)
- possible transfer of RNA and DNA [1].

The cytoskeleton is made up of three groups of fibers: **microtubules**, **intermediate filaments**, and **microfilaments**.

Microtubules, Intermediate Filaments and Microfilaments

Microtubules are hollow (with about a 24 nm outer diameter), relatively rigid tubular structures (Figure 1.4). They consist of primarily two proteins—α-tubulin and β-tubulin—which form heterodimers that polymerize end-to-end. Microtubules, once formed, can be further lengthened at one end by the addition of more dimers; the other end, however, may undergo disassembly. Microtubules interact with a number of intracellular components, including proteins. They provide mechanical support, like a platform or scaffold, to influence cell shape. They also provide a structure for the intracellular movement of organelles and the assembly of cellular components (such as spindle fibers for mitosis). Flagella and cilia also rely on microtubules for movement.

Intermediate filaments, about 10 nm in diameter, are a heterogeneous group of fibers that are dynamic, undergoing constant assembly and disassembly, controlled in part by phosphorylation and dephosphorylation. Intermediate filaments (Figure 1.4) provide mechanical strength to cells that are subjected to physical stress, such as neurons, muscle cells, and epithelial cells lining body cavities.

Microfilaments, the thinnest (about 4–6 nm in diameter) of the fibers making up the cytoskeleton, are long, linear, solid fibers made up of actin. Microfilaments, like the other fibers, polymerize and unpolymerize according to the needs of the cells. Microfilaments provide scaffolding or tracks for various cell functions. Microfilaments interact with microtubules to facilitate the movement of cellular organelles and vesicles, and their interactions with intermediate filaments are thought to enable communication from extracellular stimuli to organelles within the cytosol.

Structural Arrangement

The structural arrangement within the cell influences metabolic pathways. The fluid portion of the matrix contains small molecules such as glucose, amino acids, oxygen, and carbon dioxide. This aqueous part of the cell is in contact with the cytoskeleton over a very broad surface area, and enables enzymes that are associated with the polymeric lattice to be in close proximity to their substrate molecules in the aqueous portion. Furthermore, the enzymes that catalyze the reactions of many metabolic pathways are oriented sequentially so that the product of one reaction is released in close proximity to the next enzyme for which it is a substrate; this enhances the velocity of the overall metabolic pathway. Such an arrangement exists among the enzymes that participate in glycolysis. Some other metabolic pathways that occur in the cytoplasmic matrix and that might be similarly affected include the **hexose monophosphate shunt** (pentose phosphate pathway), glycogenesis, glycogenolysis, and fatty acid synthesis. The cytoplasmic matrix of eukaryotic cells contains a number of organelles, enclosed in bilayer membranes and described briefly in the following sections.

Mitochondrion

The **mitochondria** are the primary sites of oxygen use in cells and are responsible for most of the metabolic energy (ATP) produced in cells. All cells in the body, with the exception of the erythrocyte, possess mitochondria. The erythrocyte disposes of its mitochondria and nucleus during the maturation process and then must depend solely on energy produced through anaerobic mechanisms,

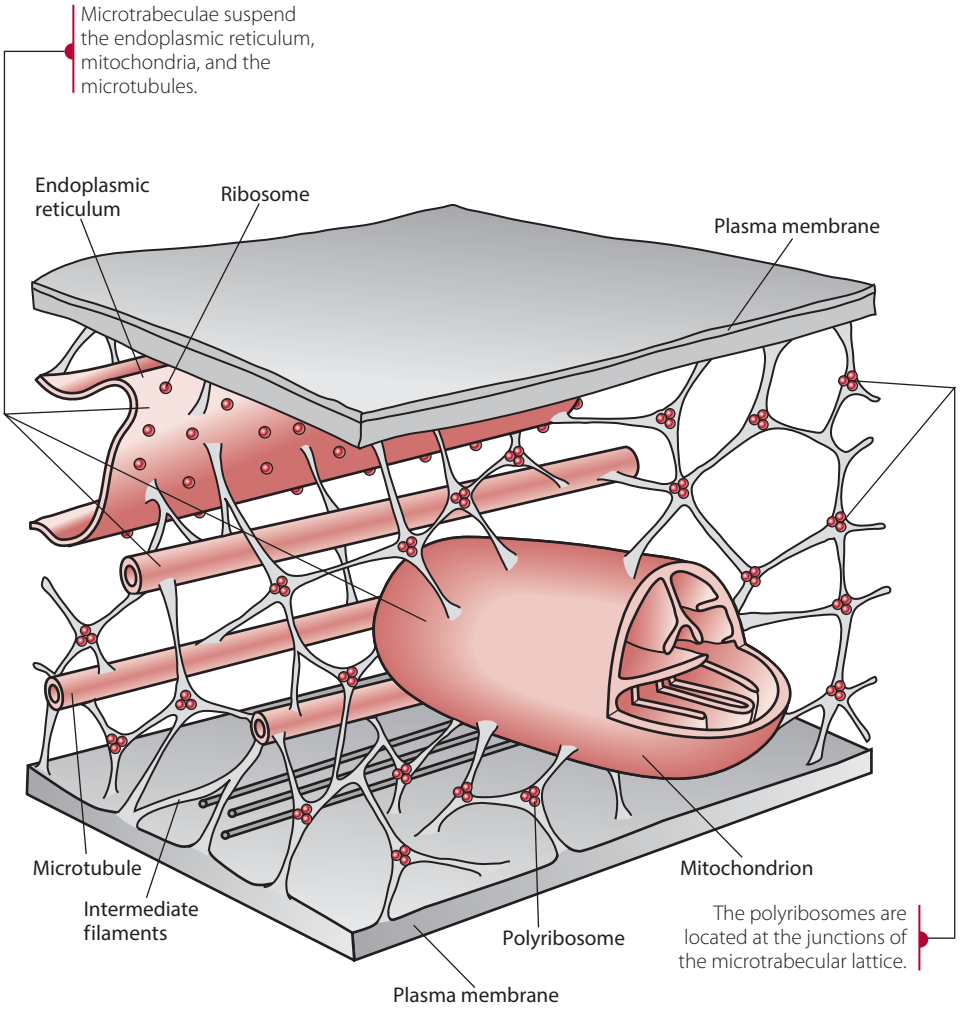

Figure 1.4 The cytoskeleton (microtrabecular lattice) provides a structure for cell organelles, microvilli (as found in intestinal mucosa cells), and large molecules. The cytosol is shown at about 300,000 times its actual size and was derived from hundreds of images of cultured cells viewed in a high-voltage electron microscope.
Source: Adapted from Porter and Tucker, "The Ground Substance of the Cell," 1981, *Scientific American*. Used by permission of Nelson Prentiss.

primarily glycolysis. The mitochondria in different tissues vary according to the function of the tissue. In muscle, for example, the mitochondria are held tightly among the fibers of the contractile system. In the liver, however, the mitochondria have fewer restraints and move freely through the cytoplasmic matrix.

Mitochondrial Membrane

The mitochondrion consists of a matrix or interior space surrounded by a double membrane (Figures 1.5 and 1.6). The mitochondrial outer membrane is relatively porous, whereas the inner membrane is selectively permeable, serving as a barrier between the cytoplasmic matrix and the mitochondrial matrix. The inner membrane has many invaginations, called the cristae, which increase its surface area, and has all the components of the electron transport chain embedded within it.

The electron transport (respiratory) chain is central to the process of **oxidative phosphorylation**, the mechanism by which most cellular ATP is produced. The components of the electron transport chain carry electrons and hydrogens during the catalytic oxidation of nutrients by

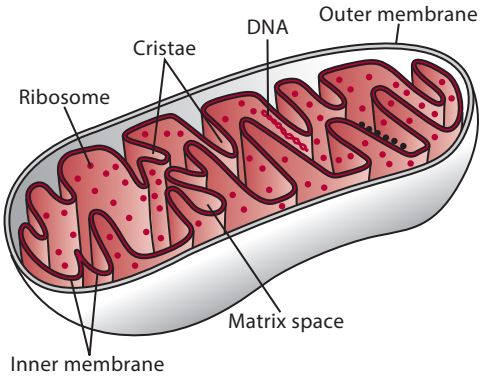

Figure 1.5 The mitochondrion.

enzymes in the mitochondrial matrix. The details of this process are described more fully in Chapter 3. Briefly, the mitochondria carry out the flow of electrons through the electron transport chain. This electron flow is strongly exothermic, and the energy released is used in part for ATP synthesis, an endothermic process. Molecular oxygen is ultimately, but indirectly, the oxidizing agent in these

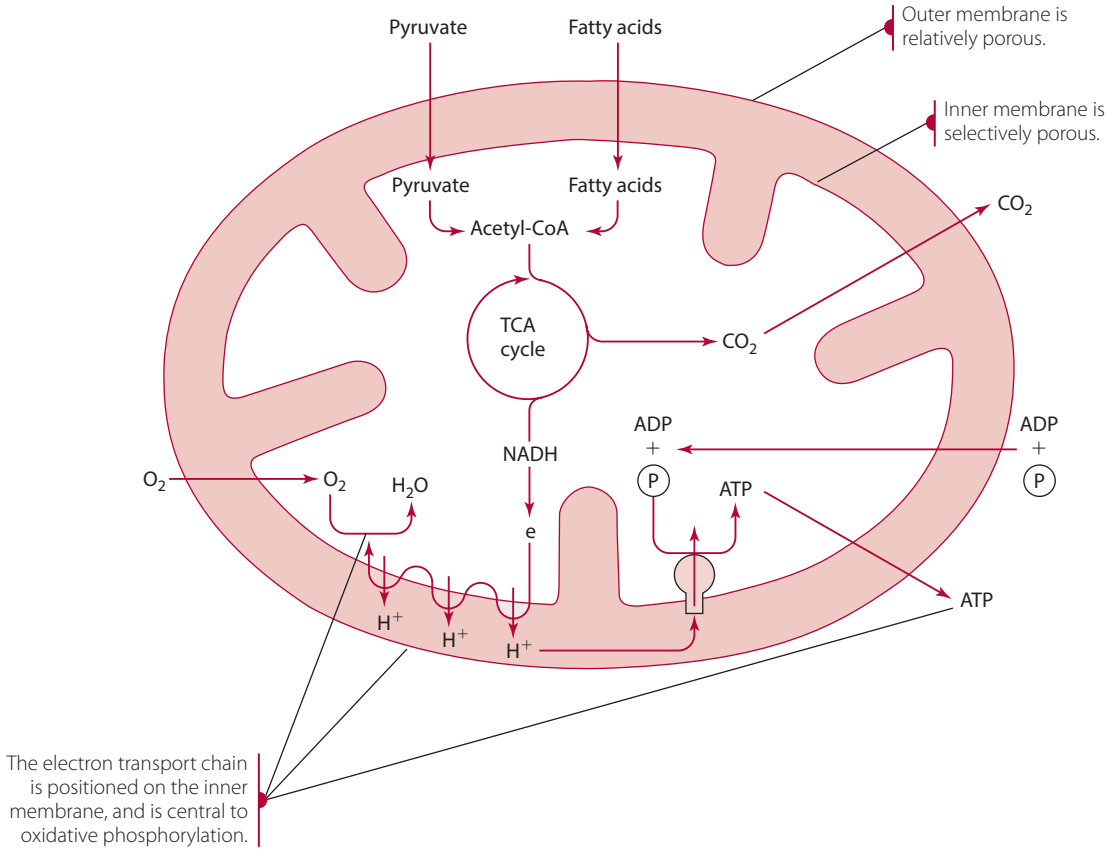

Figure 1.6 Overview of a cross section of the mitochondria.

reactions. The function of the **electron transport chain** is to couple the energy released by nutrient oxidation to the formation of ATP. The chain components are precisely positioned within the inner mitochondrial membrane, an important feature of the mitochondria, because it brings the products released in the matrix into close proximity with molecular oxygen. Figure 1.6 shows the flow of major reactants into and out of the mitochondrion.

Mitochondrial Matrix

Among the metabolic enzyme systems functioning in the mitochondrial matrix are those that catalyze the reactions of the tricarboxylic cycle (TCA cycle; Chapter 3) and fatty acid oxidation (Chapter 5). Other enzymes are involved in the oxidative decarboxylation and carboxylation of pyruvate (Chapter 3) and in certain reactions of amino acid metabolism (Chapter 6).

Mitochondria are capable of both fission and fusion, depending on the needs of the cell. They reproduce by dividing in two. Although the nucleus contains most of the cell's deoxyribonucleic acid (DNA), the mitochondrial matrix contains a small amount of DNA and a few ribosomes, enabling limited synthesis of protein within the mitochondrion. Most mitochondrial enzymes are coded by nuclear DNA, synthesized on the rough endoplasmic reticulum (RER) in the cytosol, and then incorporated into existing mitochondria. The genes contained in mitochondrial DNA, unlike those in the nucleus, are inherited only from the mother and code primarily for proteins needed for normal mitochondrial function and for ATP production. Several diseases—such as cytochrome c oxidase deficiency (also called complex IV deficiency), Leigh syndrome, and Kearns-Sayre syndrome—result from mutations in mitochondrial genes.

Nucleus

The nucleus (see Figure 1.1) is the largest of the organelles within the cell. Because of its DNA content, the nucleus initiates and regulates most cellular activities. Surrounding the nucleus is the **nuclear envelope**, a dynamic structure composed of an inner and an outer membrane. The dynamic nature of these membranes makes communication possible between the nucleus and the cytoplasmic matrix and allows a continuous channel between the nucleus and the endoplasmic reticulum. At various intervals the two membranes of the nuclear envelope fuse, creating pores in the envelope. Clusters of proteins on the outer nuclear membrane serve as microtubule organization centers (MTOCs); these centers function to begin polymerizing and organizing the microtubules during mitosis. Within the nucleus, a matrix exists to facilitate nuclear functions.

The nucleus (or nuclear matrix) contains substances such as minerals needed for nuclear function and molecules of DNA. DNA encodes the cell's genetic information plus all the enzymes needed for its duplication. DNA is found wrapped around proteins called histones, and organized into structures called chromatin. Long strands of DNA and histones are known as chromosomes. Also within the nucleus is the **nucleolus**, a nonmembranebound structure, containing ribosomal RNA (rRNA), proteins, and DNA; it is the site of rRNA transcription and processing, and of ribosome assembly/synthesis.

Encoded within the nuclear DNA are thousands of **genes** that direct the synthesis of proteins. Each gene codes for a single specific protein. The cell **genome** is the entire set of genetic information, that is, all of the DNA within the cell. Barring mutations that may arise in the DNA, daughter cells, produced from a parent cell by mitosis, possess the identical genomic makeup of the parent cell. The process of DNA replication enables the DNA to be precisely copied at the time of mitosis.

After the cell receives a signal that protein synthesis is needed, protein biosynthesis occurs in phases referred to as transcription, translation, and elongation (Figure 1.7). Each phase requires DNA activity, RNA activity, or both. These phases, together with replication, are reviewed briefly in this chapter, but the scope of this subject is large; interested readers should consult a current cell biology text or comprehensive biochemistry text for a more thorough description of protein biosynthesis.

Nucleic Acids

Nucleic acids (DNA and RNA) are macromolecules formed from repeating units called **nucleotides**, sometimes referred to as nucleotide bases or just bases. Structurally, they consist of a nitrogenous core (either purine or pyrimidine), a pentose sugar (ribose in RNA, deoxyribose in DNA), and phosphate. Five different nucleotides are contained in the structures of nucleic acids: adenylic acid and guanylic acid are purines, and cytidylic acid, uridylic acid, and thymidylic acid are pyrimidines. The nucleotides are more commonly referred to by their nitrogenous base core only—namely, adenine, guanine, cytosine, uracil, and thymine, respectively. For convenience, particularly in describing the sequence of the polymeric nucleotides in a nucleic acid, the single-letter abbreviations are most often used. Adenine (A), guanine (G), and cytosine (C) are common to both DNA and RNA, whereas uracil (U) is unique to RNA and thymine (T) is found only in DNA. When two

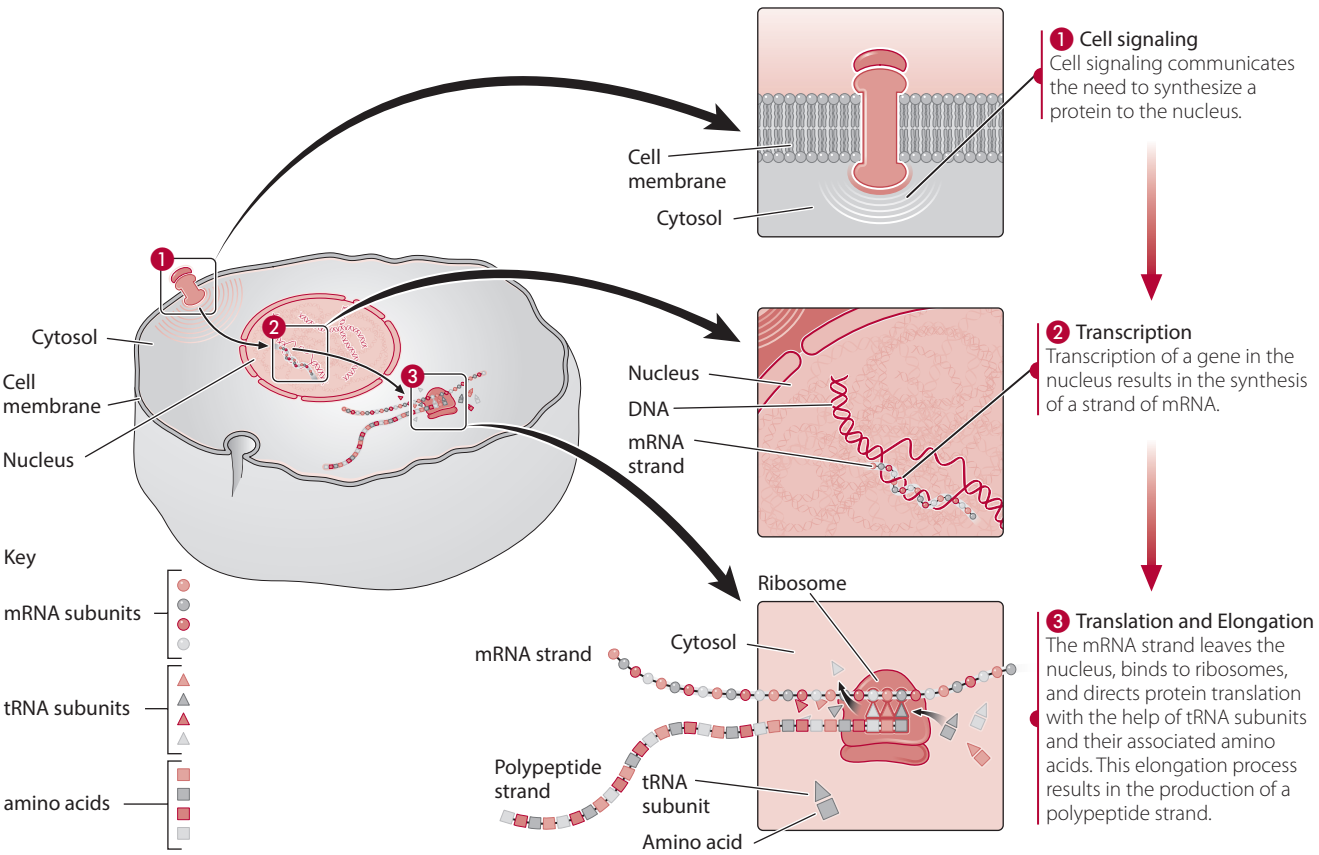

Figure 1.7 Steps of protein synthesis. (1) Signals that protein synthesis needs to occur. (2) Transcription: The DNA molecule (gene) synthesizes the corresponding mRNA. (3) Translation: The corresponding mRNA molecule binds to a ribosome and directs protein synthesis based on the codon for each amino acid and the appropriate tRNA.
Source: Beerman/McGuire, *Nutritional Sciences*, 1/e. © Cengage Learning.

strands of nucleic acids interact with each other—as occurs in replication, transcription, and translation—bases in one strand pair specifically with bases in the second strand: A always pairs with T or U, and G pairs with C, in what is called **complementary base pairing**.

The nucleotides are connected by phosphates esterified to hydroxyl groups on the pentose—that is, deoxyribose or ribose—component of the nucleotide. The carbon atoms of the pentoses are assigned prime (′) numbers for identification. The phosphate group connects the 3′ carbon of one nucleotide with the 5′ carbon of the next nucleotide in the sequence. The 3′ carbon of the latter nucleotide in turn is connected to the 5′ carbon of the next nucleotide in the sequence, and so on. Therefore, nucleotides are attached to each other by 3′, 5′ diester bonds. The ends of a nucleic acid chain are called either the free 3′ end or the free 5′ end, meaning that the hydroxyl groups at those positions are not attached by phosphate to another nucleotide.

Cell Replication

Cell replication involves the synthesis of daughter DNA molecules that are identical to the parental DNA. At cell division, the cell must copy its genome with a high degree of fidelity. Each strand of the DNA molecule acts as a template for synthesizing a new strand (Figure 1.8). The DNA molecule consists of two large strands of nucleic acid that are intertwined to form a double helix. During cell division the two unravel, with each forming a template for synthesizing a new strand through complementary base pairing. Incoming nucleotide bases first pair with their complementary bases in the template and then are connected through phosphate diester bonds by the enzyme DNA polymerase. The end result of the **replication** process is two new DNA chains that join with the two chains from the parent molecule to produce two new DNA molecules. Each new DNA molecule is therefore identical in base sequence to the parent, and each new cell of a tissue consequently carries within its nucleus identical information to direct its functioning. The two strands in the DNA double helix are antiparallel, which means that the free 5′ end of one strand is connected to the free 3′ end of the other. With this process, a cell is able to copy or replicate its genes before it passes them on to the daughter cell. Although errors sometimes occur during replication, mechanisms exist that correct or repair mismatched or damaged DNA.

Transcription

Transcription is the process by which the genetic information (through the sequence of base pairs) in a single strand of DNA makes a specific sequence of bases in a messenger RNA (mRNA) chain (see Figure 1.7). A single strand of DNA can make many copies of the corresponding mRNA,

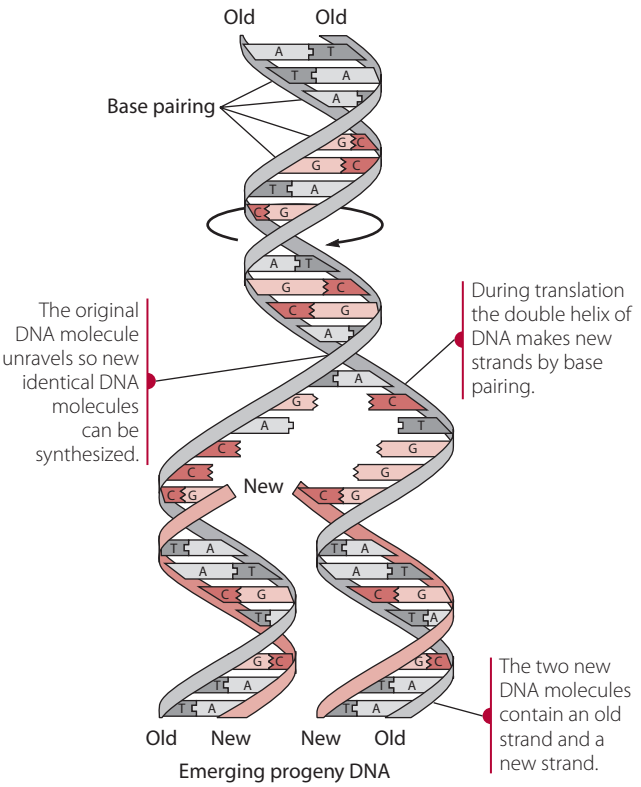

Figure 1.8 DNA replication.

which become multiple templates for the assembly of a specific protein. This process multiplies the information contained in the DNA to produce many corresponding protein molecules. Transcription may require **transcription factors**, discussed under the subsection "Control of Gene Expression."

Transcription proceeds continuously throughout the entire life cycle of the cell. In the process, various sections of the DNA molecule unravel, and one strand—called the **sense strand**—serves as the template for synthesizing mRNA. Sequences of DNA known as promoters allow genes to be turned "off" or "on" and can initiate transcription; this promoter is usually found near (upstream) of the gene. The genetic code (gene) of the DNA is transcribed into mRNA through complementary base pairing, as in DNA replication, except that the purine adenine (A) pairs with the pyrimidine uracil (U) instead of with thymine (T). Genes are composed of critically sequenced base pairs along the entire length of the DNA strand that is being transcribed. A gene, on average, is just over 1,000 base pairs in length, compared with the nearly 5 million (5×10^6) base pair length of typical chromosomal DNA chains. Although these figures provide a rough estimate of the number of genes per transcribed DNA chain, not all the base pairs of a gene are transcribed into functional mRNA.

Many genes for specific proteins are located on regions of the DNA nucleotide sequences that are not adjacent

to each other. Those regions that are part of the gene but do not code for a protein product are called **introns** (intervening sequences), and have to be removed from the mRNA before it is translated into protein (see the "Translation" section of this chapter). Enzymes excise the introns from the newly formed mRNA, and the ends of the functional, active mRNA segments are spliced together in a process called post-transcriptional processing. The gene segments that get both transcribed and translated into the protein product are called **exons** (expressed sequences).

Translation

Translation is the process by which genetic information in an mRNA molecule is turned into the sequence of amino acids in the protein. After the mRNA is synthesized in the nucleus (see Figure 1.7), the mRNA is exported into the cytoplasmic matrix, where it is attached to ribosomal RNA (rRNA) of the ribosomes of the rough endoplasmic reticulum (RER) or to the free-standing polyribosomes (also called polysomes). On the ribosomes, the transcribed genetic code in the mRNA is used to bring amino acids into a specific sequence that produces the specified protein.

The genetic code for specifying the amino acid sequence of a protein resides in the mRNA in the form of three-base sequences called **codons**. Each codon codes for a single amino acid. Although a given amino acid may have several codons (e.g., the codons CUU, CUC, CUA, and CUG all code for the amino acid leucine), codons can code for only one amino acid. Each amino acid has one or more transfer RNAs (tRNAs), which deliver the amino acid to the mRNA for peptide synthesis. The three-base sequences of the tRNA attach to the codons by complementary base pairing.

Amino acids are first activated by ATP at their carboxyl end and then transferred to their specific tRNAs that bear the **anticodon** complementary to each amino acid's codon. For example, because codons that code for leucine are sequenced CUU, CUC, CUA, or CUG, the only tRNAs to which an activated leucine can be attached would need to have the anticodon sequence GAA, GAG, GAU, or GAC. The tRNAs then bring the amino acids to the mRNA situated at the protein synthesis site on the ribosomes. After the amino acids are positioned according to codon–anticodon association, peptide bonds are formed between the aligned amino acids in a process called **elongation** (see Figure 1.7). Elongation extends the polypeptide chain of the protein product by translation. Each incoming amino acid is connected to the end of the growing peptide chain with a free carboxyl group (C-terminal end) by formation of further peptide bonds. New amino acids are incorporated until all the codons (corresponding to one completed protein or polypeptide chain) of the mRNA have been translated. At this point, the process stops, signaled by a "nonsense" codon that does not code for any amino acid. The completed protein dissociates from the mRNA. After translation, the newly synthesized protein may require some chemical, structural, or spatial (three-dimensional) modification to attain its active form.

Post-translational modifications of proteins may involve, for example, the covalent addition of functional groups or the cleavage of a portion of the protein. Common modifications include phosphorylation as well as glycosylation, ubiquitination, methylation, and acetylation, among others. An example of protein modifications involving proteolytic cleavage is that needed to convert zymogens, such as those involved in protein digestion, to active enzymes.

Control of Gene Expression

Each cell in the body contains a complete set of genes. Only a portion of the genes are expressed in specialized cells of a given organ. The regulation of gene expression occurs primarily at three different levels. (1) Transcription-level control mechanisms determine if a particular gene can be transcribed. Transcriptional control is accomplished by large numbers of proteins (called transcriptional factors) that bind to the DNA at a site other than the one involved in serving as a template for the mRNA. These transcriptional factors can enhance, inhibit, or, in some cases, alter the frequency (number of times transcription occurs within a specified time span) of the gene's transcription. Several hormones, such as insulin, thyroid hormone, glucagon, and glucocorticoids, as well as nutrients, such as vitamins A and D, can alter the transcription of DNA by binding along with transcription-factor proteins to DNA. (2) Processing-level control mechanisms determine the path by which mRNA can be translated into a polypeptide. This mechanism of regulating gene expression is based on the splicing of RNA molecules, thus making it possible for one gene to code for two associated proteins. (3) Translation-level control mechanisms determine whether a particular mRNA is actually translated and, if so, how often and for how long. The translation-level control mechanism can involve the localization of the mRNA in a particular part of the cell or organ. It can also operate through interactions between specific mRNAs and various small RNA strands present within the cytosol. **MicroRNAs** (abbreviated miRNA) are small non-coding RNAs that silence gene expression by binding to mRNA to inhibit its translation and/or promote its degradation. For more detailed information on the control of gene expression and its relationship to disease, which is vastly more complex than has been presented here, the reader is referred to a recent textbook on molecular biology and biochemistry or cell biology.