
THE LIPIDS

Their Chemistry and Biochemistry

HARRY J. DEUEL, Jr.

*Dean, Graduate School, and Professor of Biochemistry,
University of Southern California, Los Angeles*

Volume II: BIOCHEMISTRY

Digestion, Absorption, Transport and Storage

1955

PREFACE

The present volume encompasses the available information on the digestion, absorption, transport (in the blood and lymph), and storage of fats and other lipids in the animal body. Although it was the original plan to include all the biochemical data in a single volume, the recent great increase of new findings reported in these fields has forced a revision of these plans. Rather than limit the topics to be discussed or curtail the extent of discussion of such topics, it was decided to expand the scope of the biochemical section of *The Lipids* to make up two volumes. Volume III will include Biosynthesis, Metabolism, Oxidation, and the Nutritional Value of the lipids.

Although Volumes II and III are concerned chiefly with the biochemical phases of lipids, it was necessary to include some topics of a more chemical nature. The description of the properties, composition, and behavior of the lipases and lipoxidases belongs essentially in this category. The description of the chemistry, structure, and composition of the bile acids is included in Volume II; these products are not lipids, but their chemistry must be understood to ensure the proper comprehension of fat absorption.

An attempt has been made to list all the investigators who have contributed to any study, irrespective of whether they were the first to report these findings or among the numerous workers who have confirmed and extended the data. The author realizes that he has been only partially successful in recognizing all workers; he will be most grateful for any suggestions calling to his attention mistakes of omission or commission.

Acknowledgment should again be made to Mrs. Margaret Ritter, who has continued with redoubled energy as an editorial assistant throughout the preparation of the volume. Recognition should also be given Mrs. Lilla Aftergood, who abstracted much of the recent information on lipids, and so made it possible to render this volume fairly current. Above all, the author is truly grateful to his wife, who willingly accepted the verdict that the manuscript on *Lipids* should be the most important task during the past eight years. Again, mention should be made of the skill and accuracy of Mrs. Marie Visser in furnishing a satisfactory typescript for the publisher.

HARRY J. DEUEL, JR.

Pasadena, California
November, 1954

CONTENTS

Preface.....	v
I. Introduction.....	1
II. The Digestion and Absorption of Fats in the Gastrointestinal Tract.....	3
1. Introduction.....	3
2. Enzymes Concerned with the Digestion of Lipids.....	3
(1) Lipases.....	5
a. Gastric Lipase.....	5
b. Pancreatic Lipase (Steapsin).....	6
(a) Activation of Pancreatic Lipase by Bile Salts.....	6
(b) Activators and Inhibitors of Pancreatic Lipase.....	7
(c) Synthetic Action of Pancreatic Lipase.....	9
(d) Properties of Pancreatic Lipase.....	9
(e) Specificity of Pancreatic Lipase.....	9
c. Intestinal Lipase.....	10
d. Serum Lipase.....	10
e. Ricinus Lipase (Castor-Bean Lipase).....	11
f. Lipases in Molds and Bacteria.....	13
(2) Esterases.....	14
a. Origin of Esterases.....	14
b. Distribution of Esterases.....	14
(a) The Presence of Several Esterases in Liver and Pancreas....	15
(b) Serum Esterase.....	15
c. Properties of Esterases.....	16
d. Factors Altering the Action of Esterases.....	17
e. Preparation of Esterases.....	18
f. Esterases <i>vs.</i> Lipases.....	19
(3) Other Lipid-Hydrolyzing Enzymes.....	19
a. Cholesterol Esterase.....	20
(a) Hydrolytic Action of Cholesterol Esterases.....	20
(b) Synthetic Action of Cholesterol Esterases.....	22
b. Lecithinases.....	23
(a) Lecithinase A.....	23
(b) Lecithinase B.....	24
(c) Lecithinase C.....	24
(d) Lecithinase D.....	25
c. Cholinesterases.....	26
(a) Introduction.....	26
(b) Discovery of Acetylcholine and Cholinesterases.....	26
(c) Types of Cholinesterases.....	28
(d) Properties of Cholinesterases.....	31
a'. General Properties of Cholinesterases.....	31
b'. Specificity of Cholinesterases.....	33
c' Inhibition of Cholinesterases.....	34

II. The Digestion and Absorption of Fats in the Gastrointestinal Tract (continued)

(e) Cell Permeability in Relation to Cholinesterases.....	44
(f) Physiological and Pathological Factors Altering the Amount of Cholinesterases.....	46
(g) Distribution of Cholinesterases.....	52
a'. Cholinesterases in Blood.....	52
b'. Cholinesterases in Brain and Nervous Tissue.....	53
c'. Cholinesterases in Glandular Tissues.....	55
d'. Cholinesterases in Miscellaneous Tissues.....	56
e'. Cholinesterases in Snake Venom.....	57
f'. Acetylcholinesterase in Citrus.....	59
(h) Preparation of Cholinesterases.....	59
(i) Acetylcholine in Tissues.....	60
d. Choline Acetylase.....	61
(a) Introduction.....	61
(b) Mechanism of Action.....	61
(c) Distribution of Choline Acetylase.....	63
(d) Factors Altering the Activity of Choline Acetylase.....	64
e. Chlorophyllase.....	65
f. Phytase.....	67
3. The Role of Bile in Lipid Absorption.....	69
(1) The Nature, Distribution, and Properties of the Bile Acids.....	70
a. Distribution of the Bile Acids.....	70
b. Conjugation of the Bile Acids.....	79
c. Properties of the Bile Acids.....	85
d. Synthesis of the Bile Acids.....	88
e. Interrelations of the Bile Acids.....	88
(a) Reduction of Ketocholanic Acids.....	89
(b) Removal of Hydroxyl Groups.....	90
(c) Oxidation of Hydroxy- to Keto-Acids.....	90
(d) Change in Isomeric Form.....	91
(2) The Action of Bile in Lipid Absorption.....	91
a. Choleic Acids and Related Coordination Compounds.....	92
(a) Discovery.....	93
(b) General Properties.....	94
(c) Occurrence and Types of Choleic Acids.....	94
(d) Coordination Number.....	95
(e) Apocholic Acid Complexes.....	104
(f) Physical Properties of Choleic Acids.....	105
(g) Factors Involved in the Formation of Choleic Acid.....	108
(h) Types of Coordination Compounds of Bile Acids Other Than Choleic Acids.....	108
(i) Physiological Importance of Choleic Acid Formation.....	108
b. Circulation of the Bile Acids.....	111
(a) Absorption of the Bile Acids.....	111
(b) Reexcretion of the Bile Acids.....	113

II. The Digestion and Absorption of Fats in the Gastrointestinal Tract (continued)

4. The Pathways for Lipid Absorption.....	115
(1) The Sites of Absorption in the Gastrointestinal Tract.....	115
a. Mouth.....	115
b. Stomach.....	115
c. Small Intestine.....	117
d. Large Intestine.....	117
(2) Anatomical Features of the Small Intestine of Importance in Absorption.....	117
a. The Surface Structure of the Small Intestine.....	117
b. The Histological Structure of the Intestinal Mucosa.....	120
5. Methods for the Study of Fat Absorption and Lipid Absorption in General.....	123
(1) Thiry-Vella Fistulas.....	123
(2) Cori Technic.....	126
a. Method of Irwin, Steenbock, and Templin.....	127
b. Method of Deuel, Hallman, and Quon.....	127
(3) Other Methods for the Study of Fat Absorption.....	129
a. Cannulation of the Thoracic Duct.....	129
b. Chylomicron Method.....	130
c. Hemolipokrit Method.....	132
d. Studies on the Portal Blood.....	133
e. Roentgenologic Method for the Study of Fat Absorption.....	133
f. The Use of Radioactive Iodinated Fat.....	133
g. Elaeostearic Acid as a Tracer for the Study of Fat Absorption...	134
6. The Digestion of Fats.....	134
(1) Digestion in the Stomach.....	135
(2) Digestion in the Small Intestine.....	136
a. The Action of Lipases.....	136
b. The Extent of Hydrolysis of Fats.....	137
c. The Bile Requirement.....	141
7. The Absorption and Transport of Fats.....	142
(1) The Absorption of Fats from the Gastrointestinal Tract.....	142
a. Introduction.....	142
b. Theories of Fat Absorption.....	144
(a) Early Theories on Fat Absorption.....	144
(b) Lipolytic Theory (Verzár).....	146
a'. The Hydrotropic Action of Bile Salts.....	147
b'. Phosphorylation and Absorption.....	148
(c) Partition Theory (Frazer).....	151
a'. Emulsification.....	151
b'. Hydrolysis.....	153
c'. The Passage of Fat through the Outer Border of the Intestinal Cell.....	154
d'. Adrenalectomy and Fat Absorption.....	156

II. The Digestion and Absorption of Fats in the Gastrointestinal Tract

(continued)

(2) Changes in Fat in the Intestinal Cells.....	157
a. The Breakdown of the Fatty Acid + Bile Salt Complex in the Intestinal Cells.....	158
b. The Synthesis of Phospholipids in the Intestinal Mucosa.....	158
(a) Phospholipids as Obligatory Components in Fat Synthesis....	160
(b) Functions of Phospholipids Other Than in Fat Synthesis....	161
c. The Synthesis of Fats.....	162
(3) The Transfer of Fat to the Interior of the Villi.....	164
a. Introduction.....	164
b. Theories for the Mechanism of Transfer.....	164
(a) Theory of Schäfer.....	164
(b) Theory of Heidenhain.....	164
(c) Hydrolysis-Resynthesis Theory of Loevenhart.....	165
(4) The Transport of Fat to the Liver and Tissues.....	165
a. The Transport of Fat in the Lymph.....	165
(a) The Comparative Composition of Ingested and Lymph Fat.....	167
b. The Transport of Fat in the Portal Circulation.....	168
c. The Route of Distribution of Fats <i>vs.</i> Fatty Acids.....	170
(5) Current Status of Theories of Fat Absorption.....	172
8. The Rate of Absorption of Common Fats.....	172
9. Factors Affecting the Rate of Absorption of Fats.....	178
(1) Age and Sex.....	178
(2) The Nature of the Fat.....	180
a. The Rate of Absorption of Synthetic Simple Triglycerides.....	180
b. The Rate of Absorption of Fatty Acids.....	181
c. The Absorption of Short-Chain Acids.....	181
d. The Effect of the Melting Point of the Fat.....	184
(3) The Presence of Emulsifying Agents.....	185
a. The Effect of Lecithin on the Absorption of Fat.....	185
b. The Effect of Diglycerides and Monoglycerides on the Absorption of Fat.....	188
c. The Effect of Isopropyl and Stearyl Citrates on the Absorption of Fat.....	188
d. The Effect of Polyoxyethylene Sorbitan Monooleate (PSM) on the Absorption of Fat.....	188
(4) The Role of Adrenocortical Hormones.....	189
(5) The Effect of Inhibitors on Fat Absorption.....	191
a. Monoiodoacetic Acid.....	191
b. Phlorhizin.....	192
(6) Miscellaneous Factors Affecting Fat Absorption.....	193
III. The Digestibility of Fats.....	195
1. Introduction.....	195
2. Methods for the Study of Digestibility of Lipids.....	196
(1) Procedure of Atwater Used in U.S.D.A. Studies.....	196
a. Correction for Metabolic Fat or Metabolic Lipid.....	197

III. The Digestibility of Fats (*continued*)

(2) Procedure of Deuel, Johnson <i>et al.</i>	197
(3) Methods for the Study of Digestibility of Lipids in Rats	199
a. General Procedures	199
b. Determination of Metabolic Lipid	201
(4) Methods for the Study of the Digestibility of Lipids in Dogs	202
(5) The Use of Inert Chemical Substances as Indices of Digestibility	203
a. Ferric Oxide as an Inert Material in the Determination of Digestibility	203
b. Lignin as an Inert Material in the Determination of Digestibility	204
c. Silica as an Inert Material in the Determination of Digestibility	204
d. Chromic Oxide as an Inert Material in the Determination of Digestibility	205
e. Indigestible Chromogenic Substances as Inert Materials in the Determination of Digestibility	206
f. Comparison of Different Technics for the Determination of Digestibility	207
(6) Determination of Fecal Lipids	207
a. Methods Employing Dried Feces	207
b. Methods Employing Wet Feces	210
(7) Methods for the Determination of Inert Chemical Substances	211
a. Lignin	211
b. Chromic Oxide	212
(8) Special Methods for the Calculation of Digestibility of Lipids	212
a. General Formulas for the Calculation of Digestibility of Higher Alcohols, Hydrocarbons, or Waxes	213
3 Digestibility Studies on Fats, Oils, and Fatty Acids	215
(1) Studies on Human Subjects	215
a. Digestibility of Vegetable and Animal Fats Melting Under 50°C	215
b. Digestibility of High-Melting Fats	218
c. Digestibility of Oleomargarines	220
(2) Studies on Animals Other Than Man	221
a. Digestibility of Natural Fats	221
b. Digestibility of Simple Triglycerides and Fatty Acids	225
4. Normal Factors Altering the Digestibility of Fats	227
(1) The Effect of Age	227
(2) The Effect of Sex	228
(3) The Effect of Species	228
(4) The Effect of Melting Point	229
(5) The Effect of Structural Configuration	230
(6) The Effect of Polymerization	232
(7) The Effect of Emulsifying Agents	235
(8) The Effect of Foodstuffs Concomitantly Present with Ingested Fat	235
a. The Effect of Calcium and Magnesium Salts	235
b. The Effect of Protein	239
c. The Effect of Crude Fiber	239
(9) Miscellaneous Factors	240

III. The Digestibility of Fats (*continued*)

5. Pathologic Factors Altering the Digestibility of Fats.....	240
(1) Methods for the Recognition of Defective Fat Absorption.....	240
a. By Chemical Estimation of Fecal Fat.....	240
b. By the Use of the Fat Balance.....	241
c. By the Use of Labeled Fats.....	241
(2) General Changes Occurring in Defective Fat Absorption.....	242
(3) Steatorrhea Related to Deficiency of Pancreatic Juice.....	243
(4) Steatorrhea Related to Deficiency of Bile.....	244
(5) Non-tropical Sprue.....	245
(6) Congenital Steatorrhea.....	246

IV. The Digestion, Absorption, and Digestibility of Lipids Other than Fats.....

1. Introduction.....	247
2. The Digestion and Absorption of Phospholipids.....	247
3. The Absorption and Digestibility of Waxes.....	250
(1) Waxes Containing Aliphatic Alcohols.....	250
a. Jojoba Oil.....	251
b. Cetyl Palmitate.....	251
c. Distearyl Citrate.....	253
(2) Waxes Containing Cyclic Alcohols.....	254
4. The Absorption and Digestibility of Higher Aliphatic Alcohols.....	255
(1) Cetyl Alcohol.....	255
(2) Stearyl Alcohol.....	257
(3) Oleyl Alcohol.....	258
(4) Other Alcohols.....	258
5. The Digestion, Absorption, and Transformations of Sterols in the Gastrointestinal Tract.....	259
(1) The Digestion and Absorption of Cholesterol.....	259
a. Absorption Experiments with Cholesterol.....	259
(a) The Effect of Fat on Cholesterol Absorption.....	260
(b) The Effect of Bile on Cholesterol Absorption.....	260
(c) The Esterification of Cholesterol in Relation to Its Absorption.....	261
(d) Other Factors Concerned with the Absorption of Cholesterol.....	264
b. The Effect of Cholesterol on the Absorption of Fatty Acids.....	264
c. Balance Experiments with Cholesterol.....	265
(a) Balance Experiments in Man.....	266
(b) Balance Experiments on Animals.....	267
(2) The Digestion and Absorption of Sterols Other Than Cholesterol....	268
(3) The Effect of Plant Sterols on the Absorption of Cholesterol.....	270
(4) Changes in Sterols in the Gastrointestinal Tract.....	271
(5) The Transport of Cholesterol from the Gut.....	274
6. The Digestion and Absorption of Hydrocarbons.....	275
(1) Paraffins.....	275
(2) Unsaturated Hydrocarbons.....	278
(3) Carcinogenic and Related Non-carcinogenic Hydrocarbons.....	279

IV. The Digestion, Absorption, and Digestibility of Lipids Other than Fats (*continued*)

7. The Digestion, Absorption, and Transformation of the Carotenoids in the Gastrointestinal Tract.....	282
(1) The Absorption of Carotenoids from the Intestine.....	283
a. The Absorption of β -Carotene.....	283
(a) Factors that Affect the Absorption of β -Carotene.....	285
a'. Surface Area and the Absorption of β -Carotene.....	285
b'. The Effect of Bile on the Absorption of β -Carotene.....	286
c'. The Effect of Simultaneous Fat Feeding on the Absorption of β -Carotene.....	286
d'. The Effect of Emulsifying Agents on the Absorption of β -Carotene.....	288
e'. The Effect of Thyroxine and Thiouracil on the Absorption of β -Carotene.....	289
f'. The Effect of Substances Fed Concomitantly with β -Carotene on Its Absorption.....	290
g'. The Effect of Pteroylglutamic Acid.....	293
b. The Absorption of α - and γ -Carotenes.....	293
c. The Absorption of Lycopene.....	294
d. The Absorption of Oxycarotenoids.....	294
(a) Cryptoxanthin.....	294
(b) Lutein.....	295
(c) Zeaxanthin.....	296
(d) Other Oxycarotenoids.....	296
e. Stereoisomeric Forms of Carotenoids.....	296
(2) The Stability of β -Carotene in the Intestine.....	297
(3) The Digestibility of Carotenoids.....	300
a. Factors Affecting the Digestibility of Carotenes.....	300
(a) The Amount of Carotene Administered.....	300
(b) The Effect of the Food Given Simultaneously with Carotene.....	301
(c) The Effect of Thyroxine and Thiouracil.....	302
(4) Changes in the Carotenoids in the Intestinal Wall.....	303
a. The Transformation of Carotenoids into Vitamin A.....	304
b. Sites for the Conversion of Carotene to Vitamin A Other Than the Small Intestine.....	306
c. The Effect of the Thyroid Gland on the Transformation of Carotene to Vitamin A.....	307
8. The Digestion and Absorption of Phytofluene in the Gastrointestinal Tract.....	310
9. The Digestion, Absorption, and Transformations of the Fat-Soluble Vitamins.....	310
(1) Vitamin A.....	310
a. The Absorption of Vitamin A from the Intestine.....	310
(a) Hydrolysis of Vitamin A Esters as a Preliminary to Absorption.....	311
(b) Factors Altering the Rate of Absorption of Vitamin A.....	317
a'. The Effect of Age.....	317

IV. The Digestion, Absorption, and Digestibility of Lipids Other than Fats (*continued*)

b'. The Effect of Concentration of Administered Vitamin A.	312
c'. The Effect of Bile.	312
d'. The Effect of Fat Feeding.	313
e'. The Effect of Mineral Oil.	313
f'. A Comparison of the Utilization of Vitamin A Alcohol and Vitamin A Esters.	313
g'. The Effect of Emulsifying Agents.	317
h'. The Utilization of Vitamin A in Aqueous Dispersion.	317
i'. The Effect of Thyroxine.	319
j'. Miscellaneous Factors Affecting Absorption.	319
(c) The Stability of Vitamin A in the Intestine.	320
b. The Esterification of Vitamin A in the Intestinal Wall.	322
c. The Transformation of Retinene into Vitamin A.	322
(2) Vitamins D.	323
a. The Absorption of the Vitamins D from the Intestine.	323
(3) Vitamins E (Tocopherols).	326
(4) Vitamins K.	328
a. The Absorption of the Vitamins K from the Gastrointestinal Tract.	328
b. The Synthesis of Vitamin K ₂ in the Gastrointestinal Tract.	330
10. The Transport of Carotenoids and of Fat-Soluble Vitamins in Lymph and Blood.	332
(1) The Transport of Carotenoids in the Lymph and Blood.	332
(2) The Transport of Vitamin A in the Lymph and Blood.	333
(3) The Transport of the Vitamins D in the Lymph and Blood.	335
(4) The Transport of the Vitamins E in the Lymph and Blood.	335
(5) The Transport of the Vitamins K in the Lymph and Blood.	336
11. The Excretion of Lipids by Way of the Large Intestine.	336
(1) The Excretion of Lipids in the Bile.	330
a. Factors Altering the Lipid Content of Bile.	337
b. Bile as a Source of Intestinal Lipids.	348
(2) The Excretion of Lipids by the Intestinal Wall.	340
(3) The Effect of the Food Ingested.	342
12. The Composition of Fecal Lipids.	344
V. Blood Lipids	349
1. Introduction.	349
2. The Nature of Blood Lipids.	350
(1) Fatty Acids.	351
a. Fatty Acids in Phospholipids.	352
b. Fatty Acids in Cholesterol Esters.	353
c. Fatty Acids Combined with Protein.	354
(2) Neutral Fats.	357
(3) Phospholipids.	358
a. C.A. Preparation.	360
b. Other Lipoprotein Preparations.	360

V. Blood Lipids (continued)

(4) Cerebrosides.....	361
(5) Free Fatty Acids.....	362
(6) Unsaponifiable Components.....	362
a. Cholesterol and Cholesterol Esters.....	363
(a) Fatty Acids Combined with Cholesterol.....	363
(b) Cholesterol Combined with Protein.....	363
b. Hydrocarbons.....	365
c. Carotenoids.....	365
(a) The Nature of the Carotenoid and Vitamin A Combinations in the Blood.....	366
d. Fat-soluble Vitamins.....	368
(a) Vitamins A.....	368
(b) Vitamins D.....	369
(c) Vitamins E (Tocopherols).....	369
(d) Vitamins K.....	370
(7) Lipoproteins in the Blood.....	370
a. Types of Lipoprotein.....	372
(a) β -Lipoproteins in Plasma.....	373
(b) α -Lipoproteins in Plasma.....	373
(c) Elinin.....	374
(d) Lipovitellin.....	374
b. The Nature of the Lipid-Protein Combinations in Lipoproteins.....	374
c. Factors Altering the Level of Lipoproteins in Blood.....	375
3. Quantitative Relations of Blood Lipids.....	378
(1) Normal Values of Blood Lipids in Man.....	378
a. Unsaturated Fatty Acids in Blood.....	378
b. Free Choline in Blood.....	379
(2) Normal Values of Blood Lipids in Various Animal Species.....	381
(3) The Lipid Components in Blood Cells.....	381
a. Lipids in Erythrocytes.....	381
b. Lipids in Leucocytes.....	386
(4) Interrelations between Blood Lipids.....	386
a. Lipemic Constant.....	387
b. Lipemic Index.....	387
c. Cholesterol:Lipid Phosphorus Ratio.....	387
d. Cholesterol Ester:Total Cholesterol Ratio.....	389
4. The Constancy in the Level of Blood Lipids.....	390
(1) Normal Variations in the Blood Lipids in Animals of the Same Species.....	390
a. Total Lipids.....	391
b. Phospholipids.....	391
c. Cholesterol.....	392
(2) Normal Variations in the Blood Lipids of the Same Individual.....	392
5. The Site of Synthesis of Plasma Lipids.....	393
6. The Turnover Rate of Plasma Lipids.....	394
7. Factors Altering the Concentration of Blood Lipids.....	395

V. Blood Lipids (*continued*)

(1) Factors Altering the Concentration of Neutral Fat, Phospholipids, and Cholesterol.....	396
a. The Effect of Age.....	396
(a) Total Blood Lipids in the Newborn and in Young Children..	396
(b) Blood Phospholipids in the Newborn and in Young Children	396
(c) Blood Cholesterol in the Newborn and in Young Children...	397
(d) Blood Lipids in the Young and in the Aged.....	399
(e) Chylomicrons and Lipemia.....	400
b. The Effect of Sex.....	400
c. The Effect of Race.....	401
d. Diurnal Variations in Blood Lipids.....	401
e. The Effect of Menstruation.....	402
f. The Effect of Ovulation.....	403
g. The Effect of Pregnancy.....	406
h. The Maternal-Fetal Transfer of Lipids.....	407
i. The Effect of Lactation.....	409
j. The Effect of Immunization.....	410
(2) The Effect of Diet on the Level of Blood Lipids.....	410
a. The Effect of the Ingestion of Fats.....	410
(a) Immediate Effects of the Ingestion of Fat.....	411
a'. The Effect of the Ingestion of Fat on Blood Fats and Fatty Acids.....	411
b'. The Effect of the Ingestion of Fat on Blood Phospholipids	412
c'. The Effect of the Ingestion of Fat on Blood Cholesterol..	414
(b) Postabsorptive Effects of the Ingestion of Fat.....	416
b. The Effect of the Ingestion of Phospholipid on the Level of the Blood Lipids.....	417
c. The Effect of the Ingestion of Cholesterol on the Level of Blood Lipids.....	418
(a) Hypercholesterolemia in Man.....	418
(b) Hypercholesterolemia in Animals Other Than Man.....	419
(c) The Effect of Ingested Cholesterol on Other Blood Lipids...	419
(d) The Effect of Cholesterol Injected Intravenously.....	420
(3) The Effect of Inanition on the Level of Blood Lipids.....	420
a. The Effect of Complete Starvation.....	420
b. The Effect of Carbohydrate Deficiency.....	424
(4) The Effect of Overnutrition on the Level of Blood Lipids.....	424
(5) The Effect of Work on the Level of Blood Lipids.....	425
(6) Specific Compounds that Affect Alimentary Lipemia.....	426
a. The Effect of Heparin.....	426
(a) Heparin as an Anticoagulant.....	426
(b) Heparin as a Clearing Agent.....	426
b. The Effect of Protamine.....	430
c. The Effect of Bile Acids.....	431
d. The Effect of Miscellaneous Substances.....	431
(7) The Effect of Abnormal Conditions on the Level of Blood Lipids....	432
a. Idiopathic Familial Hyperlipemia.....	432

V. Blood Lipids (continued)

b. The Blood Lipids Following Tissue Injury	433
c. The Blood Lipids Following the Administration of Various Anesthetics	433
d. The Blood Lipids as Affected by Vitamin Deficiencies	434
e. The Blood Lipids as Affected by Essential Fatty Acid Deficiency	435
f. The Blood Lipids as Affected by Disturbances of the Endocrine Glands	436
(a) Variations Primarily Related to the Thyroid Gland	436
a'. Serum Cholesterol and Thyroid Secretion	437
b'. Serum Cholesterol and Basal Metabolism	438
c'. Blood Phospholipids and Fats, and Thyroid Secretion	439
(b) Variations Primarily Related to the Anterior Lobe of the Pituitary Gland	440
(c) Variations Primarily Related to the Adrenal Glands	441
(d) Variations Primarily Related to the Pancreas	444
a'. Hyperlipemia in Experimental Pancreatectomy	444
b'. The Blood Lipids in Diabetes Mellitus	447
c'. The Blood Lipids in Pancreatitis	454
d'. The Blood Lipids in Alloxan Diabetes	454
(e) Variations in the Blood Lipids Primarily Related to the Sex Hormones	454
a'. The Effect of Natural Estrogenic Hormones and of Stilbestrol on Chicks	455
g. The Blood Lipids in Anemia	456
(a) The Blood Lipids in Experimental Anemias	456
(b) The Blood Lipids in Anemias of Man	457
h. The Blood Lipids in Diseases of the Gastrointestinal Tract	458
i. The Blood Lipids in Hepatic Disease	459
(a) In Cholelithiasis	459
(b) In Obstruction of the Common Bile Duct	459
(c) In Acute Hepatitis	461
(d) In Cirrhosis of the Liver	462
(e) Following Partial or Functional Hepatectomy	462
j. The Blood Lipids in Diseases of the Kidney	463
(a) In Nephroses	463
(b) In Nephritides	464
(c) In Experimental Nephrectomy	465
k. The Blood Lipids in Arteriosclerosis	466
(a) Experimental Studies on Atherosclerosis	466
a'. The Relationship of Cholesterol to the Formation of the Atheromatous Lesions	466
b'. Dietary and Other Factors Related to the Formation of Atheromas	468
(b) Arteriosclerosis in Man	472
a'. Comparison of Atherosclerosis in Rabbits and Arteriosclerosis in Man	472
b'. Gross Blood Lipid Changes in Arteriosclerosis	473

V. Blood Lipids (*continued*)

c'. The Relationship of the S_1 10-20 Fraction to Atherosclerosis.....	473
d'. The Relationship of Fractions Higher Than S_1 10-20 to Atherosclerosis.....	476
e'. The Relationship of Total Serum Cholesterol to the Concentration of the S_1 10-20 Fraction.....	478
f'. The Effect of Lipotropic Factors on Atherosclerosis.....	480
l. The Blood Lipids in Diseases of the Central Nervous System.....	481
m. The Blood Lipids in Infectious Diseases.....	483
n. The Blood Lipids in Cancer.....	484
o. The Effect of Drugs on Blood Lipids.....	485
(a) Phlorhizin.....	485
(b) Phosphorus.....	486
(c) Chloroform and Carbon Tetrachloride.....	486
8. Factors Altering the Concentration of the Carotenoids and of the Fat-Soluble Vitamins in Blood.....	486
(1) Carotenoids and Vitamins A.....	486
a. Normal Values for Serum Carotene and Vitamin A.....	486
b. General Physiological Factors Related to the Level of Serum Carotene and Vitamin A.....	488
(a) Maternal-Fetal Transfer of Carotene and Vitamin A.....	489
(b) Plasma Carotene and Vitamin A in Children.....	490
(c) Plasma Carotene and Vitamin A in the Aged.....	491
(d) Plasma Carotene and Vitamin A as Influenced by Sex.....	492
(e) Seasonal Changes in Plasma Carotene and Vitamin A.....	493
(f) Plasma Carotene and Vitamin A as Influenced by Parturition.....	494
(g) The Effect of Hormones on Plasma Carotene and Vitamin A.....	494
c. The Effect of Diet on the Level of Carotene and Vitamin A in the Blood.....	495
(a) The Effect of Ingested Carotene on the Level of Plasma Carotene and Vitamin A.....	495
(b) The Effect of Ingested Vitamin A on the Level of Plasma Vitamin A.....	497
a'. Vitamin A Tolerance Curves.....	498
b'. The Relationship between Plasma and Liver Levels of Vitamin A Alcohol.....	501
(c) The Effect of Massive Doses of Carotene on Plasma Carotene and Vitamin A Levels.....	502
(d) The Effect of Massive Doses of Vitamin A on Plasma Carotene and Vitamin A Levels.....	502
(e) The Effect of Carotene-free and Vitamin A-free Diets on Plasma Carotene and Vitamin A.....	505
(f) The Effect of Miscellaneous Substances on Plasma Carotene and Vitamin A.....	505
d. Plasma Carotene and Vitamin A as Indices of Nutritional Status.....	506
e. Plasma Carotene and Vitamin A Levels in Abnormal Conditions.....	507
(a) Plasma Carotene and Vitamin A Levels in Diabetes.....	507

V. Blood Lipids (continued)

(b) The Relationship of Acetonemia to Plasma Vitamin A.....	508
(c) The Effect of Liver Disease on Plasma Carotene and Vitamin A.....	508
(d) The Effect of Miscellaneous Diseases on Plasma Carotene and Vitamin A.....	508
(2) Tocopherols (Vitamins E).....	509
a. Normal Values for Plasma Tocopherols.....	509
b. General Physiologic Factors Related to the Level of Plasma Tocopherols.....	511
(a) Relation to Ingested Tocopherol.....	511
(b) Maternal-Fetal Transfer of Tocopherols.....	511
(c) Plasma Tocopherols in the Newborn and Young Animal.....	513
(d) Plasma Tocopherols in Pregnancy.....	517
c. The Plasma Tocopherol Levels in Abnormal Conditions.....	518
(a) Plasma Tocopherols in Sprue.....	518
(b) Plasma Tocopherols in Diabetes.....	518
(c) Plasma Tocopherols in Muscular Dystrophies.....	519
(d) Plasma Tocopherols in Miscellaneous Abnormalities.....	519

VI. The Occurrence of Lipids in the Animal as a Whole..... 521

1. Introduction.....	521
2. Theoretical Considerations in the Deposition of Lipids in Different Species.....	522
3. Sources of Fat in the Animal Body.....	524
(1) Dietary Fat as a Source of Lipids.....	524
a. The Effect of Dietary Fats Containing Short-Chain Acids on the Composition of Storage Fat.....	526
b. The Effect of Fats Containing Fatty Acids with an Odd Number of Carbon Atoms on the Composition of Storage Fat.....	527
c. The Effect of Unsaturated Fats in the Diet on the Composition of Storage Fat.....	528
(a) Oleic Acid.....	528
(b) Elaidic Acid.....	529
(c) Linoleic Acid.....	530
(d) Linolenic Acid.....	530
(e) Elaeostearic Acid.....	532
(f) Arachidonic Acid.....	532
(g) Miscellaneous Fatty Acids.....	534
d. The "Soft Pork Problem" in Relation to the Ingestion of Unsaturated Fats.....	534
(a) The Relationship of the Linoleate Content to the Type of Fat Ingested.....	535
(b) The Hardening Effect of Cottonseed Oil.....	536
(c) Factors Affecting the Ratio of Palmitic to Stearic Acid.....	536
(d) The Hardening Effect of Carbohydrates.....	537
(2) Carbohydrates as a Source of Body Fat.....	538
a. Experimental Proof of the Conversion of Carbohydrate to Fat....	538

VI. The Occurrence of Lipids in the Animal as a Whole (continued)

b. The Site of Conversion of Carbohydrate to Fat.....	540
c. The Mechanism of the Transformation of Carbohydrate to Fat..	541
d. The Nature of the Fat Synthesized from Carbohydrate.....	545
(3) Protein as a Source of Body Fat.....	546
a. Balance Experiments as Proof of the Conversion of Protein to Fat	546
b. Respiration Experiments as Proof of the Conversion of Protein to	
Fat.....	548
c. Proof of the Conversion of Proteins and Amino Acids to Fat,	
Based upon the Formation of Carbohydrate.....	549
(a) The Formation of Glycogen or Glucose.....	550
a'. Experiments with Protein.....	550
b'. Experiments with Amino Acids.....	551
(b) Respiration Experiments as Proof of the Conversion of Pro-	
tein to Carbohydrate.....	551
4. The Lipid Content and Composition of the Animal as a Whole.....	553
(1) Methods for Determining the Lipid Content of Animals, Including	
Man.....	553
a. Direct Analyses.....	553
b. Indirect Methods for the Estimation of Body Fat.....	553
(a) The Use of "Standard" Weight Tables.....	553
(b) The Use of Subcutaneous Fat Estimates.....	554
a'. Skinfold Measurements.....	555
b'. Fat-Skeleton-Muscle Analyses.....	556
c'. Roentgenograms.....	556
d'. Direct Measurement of the Thickness of the Subcutaneous	
Layer.....	557
(c) The Use of Density Measurements.....	557
(d) The Use of Body Water for the Determination of Body Fat.	559
a'. Test Solutes for the Determination of Water.....	559
b'. Formula for the Calculation of Fat Content from Body	
Water Data.....	563
(e) The Use of Fat-Soluble Indicators.....	565
(2) The Normal Fat Content of Man and Animals.....	565
(3) The Normal Composition of Animal Fats.....	567
(4) The Distribution and Composition of the Lipids in the Storage De-	
pots and in the Several Organs.....	568
a. The Normal Distribution of Lipids.....	568
b. The Comparative Lipid Composition of Different Tissues.....	568
(5) Factors Altering the Distribution, Content, and Composition of Tis-	
sue Lipids.....	573
a. The Effect of Age.....	573
(a) The Distribution of Tissue Lipids as Affected by Age.....	573
(b) The Content of Tissue Lipids as Affected by Age.....	573
(c) The Composition of Tissue Lipids as Affected by Age.....	575
b. The Effect of Embryonic Development.....	579
c. The Effect of Sex.....	579
(a) The Effect on Total Fat.....	579

VI. The Occurrence of Lipids in the Animal as a Whole (continued)

(b) The Effect on Subcutaneous Fat.....	580
(c) The Effect on the Fat Content of Specific Tissues.....	582
(d) The Effect of Ovariectomy on the Distribution of Storage Fat.....	584
(e) Sex Differences in Fat Metabolism.....	585
d. The Effect of Environmental Temperature.....	586
(a) The Effect on Animal Fats.....	586
(b) The Effect on Vegetable Fats.....	588
e. The Effect of Exercise on the Distribution of Storage Fat.....	591
f. The Effect of Diet on the Distribution of Storage Fat.....	591
g. The Effect of Inanition on the Content and Composition of Body Fat.....	593
h. The Effect of Thyroxine on the Distribution of Storage Fat.....	596
5. Variable and Constant Components of Lipids.....	597
(1) The Nature of the Constant Component.....	598
(2) The Nature of the Variable Component.....	602
6. The Lipid Distribution in the Cell.....	603
7. The Physiology of Adipose Tissue.....	607
(1) The Specific Nature of Adipose Tissue.....	607
(2) The Specific Innervation and Blood Supply of Adipose Tissue.....	608
(3) Changes in Fat Composition Occurring in Fat Depots.....	609
a. The Mobile Nature of Fat in Fat Depots.....	610
b. Fat Synthesis in Adipose Tissue.....	611
c. The Control of Fat Mobilization and Deposition.....	612
(a) The Metabolism of Adipose Tissue as a Controlling Factor..	612
(b) Hormone Control of Fat Mobilization and Deposition in Adipose Tissue.....	612
a'. The Regulation by the Anterior Pituitary Gland.....	612
b'. The Regulation by the Adrenal Cortex and Medulla.....	614
c'. The Regulation by Insulin.....	615
d'. The Regulation by Thyroid Hormones.....	616
(c) Nervous Control of Fat Mobilization and Deposition in Adipose Tissue.....	616
(4) Glycogen Deposition in Adipose Tissue.....	618
(5) Normal Metabolism in Adipose Tissue.....	619
(6) Enzyme Activity in Adipose Tissue.....	620
(7) Brown <i>vs.</i> White Adipose Tissue.....	622
8. Lipid Storage under Abnormal Conditions.....	623
(1) Abnormal Deposition of Triglyceride Fats in General.....	623
a. Obesity Resulting from Overconsumption of Foodstuffs.....	624
(a) Obesity Due to Hyperinsulinism.....	625
(b) Obesity Due to Lesions of the Hypothalamus.....	625
a'. Metabolic Aspects of Hypothalamic Obesity.....	628
(c) Obesity Resulting from the Injection of Gold-Thioglucose...	630
b. Obesity Resulting from Reduced Basal Metabolism.....	630
c. Obesity Resulting from Reduced Activity.....	630
d. Hereditary Obesity in Mice.....	631