

Con

Contributors	xix
Foreword	xxvii
Preface	xxxii

1 Getting Started

James C. Thompson

Text	1
------	---

2 Assessing Available Information

Edward E. Whang and Stanley W. Ashley

I. Introduction	3
II. Sources of Information	3
III. Assessing Published Studies: External Measures of Quality	5
IV. How to Read and Evaluate Published Studies	5
V. Suggestions for the Future	7
References	8

3 Organizing and Preliminary Planning for Surgical Research

Michael W. Mulholland

I. Research as the Foundation of an Academic Surgical Career	9
II. Research Training	10
III. Choosing a Research Mentor	10
IV. Choosing a Research Topic	10
V. General Preparation	11
VI. Experimental Preparation	11
VII. Grant Preparation	11
References	11

Contents

4 Writing a Protocol: Animals, Humans, and Use of Biologic, Chemical, and Radiologic Agents

Wayne R. Patterson

I. Introduction	13
II. Research Utilizing Laboratory Animals	14
III. Human Subject Research	17
IV. Institutional Safety Committees	19
V. Summary	22
References	22

5 Grantsmanship

B. Mark Evers

I. Introduction	23
II. Common Myths, Misconceptions, and Mistruths	23
III. Grant Preparation—General Comments	24
IV. Grant Preparation—Specific Comments	25
V. Other Considerations	27
VI. Conclusions	27
References	28

6 Informed Consent and the Protection of Human Research Subjects: Historical Perspectives and Guide to Current United States Regulations

Mary Jane Kagarise and George F. Sheldon

I. History of Informed Consent	29
II. United States Regulations Governing Informed Consent	36
III. Conclusion	43
References	44

7 Animal Care and Maintenance

David Lee-Parritz

I. Introduction	47
II. Ethical and Regulatory Overview	47
III. Available Resources	48
IV. Surgical Facility Design	50
V. Anesthesia	50
VI. Anesthetic Recommendations by Species	52
VII. Analgesia	58
VIII. Resources	60
References	60

8 Funding Strategies and Agencies: Academic-Industrial Relationships; Intellectual Property

Josef E. Fischer

I. Introduction	63
II. Academic Agencies	63
III. Industry	66
IV. State Incubators and Local University Incubators	67
V. Intellectual Property	68

9 Statistical Considerations

David T. Mauger and Gordon L. Kauffman, Jr.

I. Introduction	71
II. Hypothesis Testing	72
III. Sample Size Calculations	75
IV. Summary	80
References	80

10 Use of Nonexperimental Studies to Evaluate Surgical Procedures and Other Interventions: The Challenge of Risk Adjustment

Michael Schwartz, Arlene S. Ash, and Lisa I. Iezzoni

I. Introduction	81
II. Dimensions of Risk	82
III. Data Sources	86
IV. Multivariate Modeling Framework	87
V. Incorporating Risk in Multivariate Models	89
VI. Approaches for Improved Estimates of Treatment Effectiveness in Nonexperimental Studies: The Propensity Score and Instrumental Variables	90
VII. Conclusions	97
References	97

11 Measuring Surgical Outcomes

Jean Y. Liu and John D. Birkmeyer

I. Introduction	101
II. Generic Measures of Health Status	101
III. Specific Measures of Health Status	104
IV. Utilities	105
V. Patient Satisfaction	107
References	108
Appendix: The SF-36V ₂ Health Survey Questionnaire	111

12 Design of Clinical Trials

Kenneth K. Tanabe

I. Introduction	115
II. Hypotheses, Specific Aims, and Endpoints	116
III. Patient Eligibility	117
IV. Structure of Clinical Trials	117
V. Treatment Plan	119
VI. Data Collection and Quality Assurance	120
VII. Statistical Considerations in the Design of Clinical Trials	121
VIII. Informed Consent	123
IX. Summary	125
References	125

13 Using Administrative Data for Clinical Research

John D. Birkmeyer

I. Introduction	127
II. Overview of Administrative Databases Used for Clinical Research	127
III. Cautions about Using Administrative Databases for Research	132
IV. Conclusions	135
References	136

14 Research in the Intensive Care Unit: Ethical and Methodological Issues

Philip S. Barie, Matthew D. Bacchetta, Joseph J. Fins, and Soumitra R. Eachempati

I. Introduction	137
II. Spectrum of Research in the Intensive Care Unit	138
III. Site Selection and Investigator Responsibilities	146
IV. Ethical Issues	147
References	153

Contents

15 Research in the Operating Room

Liane Feldman, Jeffrey S. Barkun, and Jonathan L. Meakins	
I. Introduction and Overview	155
II. Randomized Controlled Trials in Surgery: Problems and Solutions	156
III. Randomized Controlled Trials in Surgery: What Works and Why	160
IV. The Operating Room as Laboratory	161
V. Technology Assessment	162
VI. Summary and Conclusions	164
References	165

16 Effects of Age and Gender

James M. Watters and Keith O'Rourke

I. Importance of Age and Gender	167
II. Age and Gender as Surrogates	168
III. Design Issues for Randomized Controlled Trials	168
IV. Design Issues for Observational Studies	169
V. Other Issues in Study Design	171
VI. Animal Models	172
VII. Summary	173
References	173

17 Strategies, Principles, and Techniques Using Transgenic and Knockout Mouse Models

Jeffrey M. Arbeit

I. Introduction	175
II. Design of Basic Experiments	175
III. Design of Advanced Experiments	181
IV. Pitfalls in Transgenic and Knockout Experiments	185
V. Stepwise Analysis of Genotype, Gene Expression, and Phenotypes in Transgenic and Knockout Mice	187
VI. Modification of Phenotype by Genetic Differences in Inbred Strains	188
VII. Combinatorial Genetic Manipulations in Mice	189
VIII. Conclusions	190
References	190

18 Tissue Culture, Cell Growth, and Analysis

Andrea L. Nestor, James Willey, and David C. Allison

I. Introduction and Environment	193
---------------------------------	-----

II. Sterilizing Techniques	193
III. Handling of Media and Cells	194
IV. Maintaining Frozen Stocks and Record Keeping	196
V. Basic Cell Culture	196
VI. Primary Cultures	198
VII. Contamination and Decontamination	200
VIII. Cell Growth Analysis	201
IX. Resources	203
References	205

19 Hematopoietic Stem Cells: Basic Concepts and Applications to Surgical Research

**Henry E. Rice, Robert W. Storms, Clay Smith,
and Alan W. Flake**

I. Introduction	207
II. Historical Review	208
III. Hematopoiesis	208
IV. Embryonic Stem Cells	208
V. Mesenchymal Stem Cells	210
VI. <i>In Utero</i> HSC Transplantation	210
VII. Stem Cell Transplantation to Induce Tolerance	211
VIII. <i>In Vitro</i> Techniques	211
IX. <i>In Vivo</i> Techniques	213
References	214

20 Basic Molecular Biological Methods in Surgical Research: Genetic Library Construction, Screening, and DNA Sequencing

Steve F. Abcouwer

I. Introduction	217
II. Genetic Library Construction, Screening, and DNA Sequencing	218
III. Conclusion	230
References	231

21 Transcription

George P. Yang and Ronald J. Weigel

I. Introduction	233
II. General Aspects of Eukaryotic Transcription	233
III. Methods to Identify Gene Expression	235
IV. Methods of Identifying Differentially Expressed Genes	237
V. Mapping a Eukaryotic Promoter	241

VI. Identifying and Cloning Transcription Factors	243
References	250

22 Signal Transduction and Apoptosis

Tanya K. Meyer and William G. Cance

I. Expression of Signal Transduction Proteins	253
II. Interactions between Signal Transduction Proteins	256
III. Protein Phosphorylation Plays a Key Role in Enzyme Activity Regulation	259
IV. Receptor Agonist and Antagonist with Blockade	261
V. Constitutively Active and Dominant Negative Proteins Elucidate the Importance of Signal Transduction Cascades	262
VI. Regulation of Signal Transduction Gene Expression	264
VII. Signal Transduction and Apoptosis	266
VIII. Key Resources	269
References	270

23 Mechanisms and Regulation of Eukaryotic Protein Synthesis

Theresa L. Eisenbraun, Patricia M. Scott, Gregory D. Kennedy, and John E. Niederhuber

I. Introduction	271
II. Overview of Protein Synthesis	271
III. Methods for Studying Protein Synthesis	279
References	282

24 Organelle Studies: Mitochondria, Golgi, and Endoplasmic Reticulum

Anirban Banerjee, Thomas N. Robinson, Fabia Gamboni-Robertson, Charles B. Cairns, and Rene J. P. Musters

I. The Mitochondria	285
II. Surgically Relevant Questions	286
III. Areas of Surgical Interest: How to Study	290
References	295

25 Membrane Biology and Biophysics

Raphael C. Lee and Jurgen Hannig

I. Medical Relevance	297
II. Methodology—General Considerations	298
III. Methodology—Assessing Membrane Integrity	298

IV. Cell Membrane Injury	302
V. Sealing of Permeabilized Membranes	304
References	304

26 Molecular Epidemiology: Beyond Gene Discovery to Clinical Diagnostic Tools

**Barbara A. Zehnbauer, Bradley D. Freeman,
and Timothy G. Buchman**

I. Introduction	307
II. Utility of Molecular Genetic Testing	308
III. State of the Science	310
IV. Recommendations to Surgical Investigators	314
References	316

27 Shock Models: Hemorrhage

Alfred Ayala, Ping Wang, and Irshad H. Chaudry

I. Introduction	317
II. Models of Hemorrhagic Shock	318
III. Anesthetized and Unanesthetized Fixed-Volume Bleed-Out Models of Hemorrhage	319
IV. Anesthetized and Unanesthetized Fixed-Pressure Models of Hemorrhage	319
V. Heparin as a Possible Confounding Variable	321
VI. Uncontrolled Hemorrhage Models	322
VII. Summary	322
VIII. Animal Models	322
References	327

28 Scoring Systems for Trauma Research

Walter L. Biffl and Ernest E. Moore

I. Introduction	331
II. The Abbreviated Injury Scale and Injury Severity Score	331
III. The New Injury Severity Score	332
IV. The Abdominal Trauma Index	332
V. Organ Injury Scaling	332
VI. Multiple Organ Failure Scoring	339
VII. Conclusions	339
References	345

29 Blunt Trauma Models: Fractures, Chest Trauma, Head Injury, Soft-Tissue Trauma, and Abdominal Trauma

R. Lawrence Reed II

I. Introduction	347
-----------------	-----

Contents

II. Blunt Head Injury Models	348
III. Blunt Chest Trauma Models	349
IV. Blunt Abdominal Trauma Models	350
V. Fracture Models	351
VI. Soft-Tissue Trauma Modeling	353
VII. Mathematical and Inanimate Modeling of Blunt Trauma	353
VIII. Conclusion	354
References	354

30 Trauma Models for Studying the Influence of Gender and Aging

Martin G. Schwacha, Ping Wang, and Irshad H. Chaudry

I. Introduction	357
II. Experimental Trauma Models	358
III. Methodology	358
IV. Conclusions	364
References	364

31 Animal Models of Burn Injury

Daniel L. Traber, Robert E. Barrow, and David N. Herndon

I. Introduction	367
II. Animal Rights Considerations	368
III. Methodology	368
IV. Large Animals	368
V. Small Animals	373
VI. Conclusion	374
References	374

32 Wound Care Models

David G. Greenhalgh and Glenn D. Warden

I. Introduction	379
II. <i>In Vitro</i> Models of Tissue Repair	380
III. Animal Models	381
IV. Impaired Healing Models	383
V. Transgenic Models	386
VI. Tissue Repair Models in Patients	386
VII. Conclusion	387
References	387

33 Models of Adult Respiratory Distress Syndrome—Aspiration

H. Hank Simms

I. Introduction	393
II. Intraabdominal Models	393

III. Ischemia-Reperfusion Models	394
IV. Models of Hemorrhage That Induce Acute Lung Injury	395
V. Models Using Intravenous Injections	396
VI. Aspiration-Induced Models	397
VII. Summary	398
References	398

34 Tumor Angiogenesis

Lee M. Ellis

I. Biology of Angiogenesis	401
II. Models of Angiogenesis	405
III. Antiangiogenic Therapy: Issues and Expectations	409
References	410

35 Approaches to Adoptive Immunotherapy

Harry D. Bear and Cynthia S. Chin

I. Introduction	415
II. Immunology Background	416
III. Tumor Evasion of the Immune System	418
IV. Developing Models for AIT	418
V. Methods for Evaluation of Lymphocytes for Adoptive Immunotherapy	423
VI. Conclusion	431
References	431

36 Metastasis: Biology and Experimental Models

Russell S. Berman, Jerald J. Killion, and Lee M. Ellis

I. Introduction	435
II. Biology of Metastasis	435
III. Experimental Models for Studying the Biology of Metastasis	440
References	442

37 Cancer Genetics

Douglas W. Green and Jeffrey A. Drebin

I. Introduction	445
II. Experimental Methods	447
III. Genetic Abnormalities in Human Cancer	452
IV. The Future	454
References	455

38 Cancer Gene Therapy

Kenneth K. Tanabe and James C. Cusack, Jr.

I. Introduction	457
II. Gene Transfer	457
III. Cancer Gene Therapy Techniques	484
IV. Summary	490
References	490

39 Active Immunotherapy for Cancer

Keith D. Amos, David C. Linehan, and Timothy J. Eberlein

I. Introduction	497
II. Methods of Antigen Identification	499
III. Assays of Cytotoxic T Lymphocyte Activation and Function	502
IV. Summary	505
References	505

40 Gastrointestinal Motility

Michael G. Sarr, Joseph J. Cullen, and Mary F. Otterson

I. Introduction	507
II. Physiology of Intestinal Contractions	507
III. Techniques of Measuring Contractile Activity	509
IV. Techniques of Measuring Gastric Emptying	514
V. Techniques of Measuring Intestinal Transit	517
VI. Techniques of Measuring Defecation	520
VII. Models for Studying Gastrointestinal Motility	521
References	529

41 Models of Intestinal Secretion and Absorption

Martin Riegler and Jeffrey B. Matthews

I. Introduction	533
II. <i>In Vitro</i> Studies	534
III. <i>In Vitro</i> Models of Intestinal Transport	538
IV. <i>In Vivo</i> Models	542
V. Conclusion	544
References	544

42 Surgical Models of Inflammatory Bowel Disease

Heidi Yeh and John L. Rombeau

I. Introduction	547
II. Spontaneous Models	548

III. Transgenic Rodent Models	550
IV. Other Models	552
V. Conclusions	554
References	554

43 Intestinal Regeneration and Adaptation Models

Sonia Y. Archer and Richard A. Hodin

I. Introduction	557
II. <i>In Vivo</i> Models	558
III. <i>In Vitro</i> Models	568
IV. Summary	570
References	570

44 Minimally Invasive Surgery

Daniel B. Jones and Robert V. Rege

I. Introduction	573
II. Models and Methodology	574
III. Setup and Equipment	579
IV. Funding	580
V. Conclusion	580
VI. Resources	580
References	581

45 Experimental Models and Endpoints for Studies of Intestinal Ischemia–Reperfusion Injury

Joseph Murphy and Richard H. Turnage

I. Overview	583
II. Clinical Relevance	584
III. Characteristics of Intestinal Ischemia–Reperfusion Injury	584
IV. <i>In Vivo</i> Models of Intestinal Ischemia–Reperfusion Injury	585
V. Considerations for Experimental Models of Intestinal Ischemia–Reperfusion Injury	590
VI. Endpoints for <i>In Vivo</i> Studies of Intestinal Ischemia–Reperfusion Injury	591
VII. <i>In Vitro</i> Models of Intestinal Ischemia–Reperfusion Injury	593
VIII. Endpoints for <i>In Vitro</i> Studies of Intestinal Ischemia–Reperfusion Injury	594
IX. Summary	595
References	595

Contents

46 Gut Barrier Failure

Justin T. Sambol, Raquel M. Forsythe, and Edwin A. Deitch	
I. Introduction	599
II. The Gut Barrier	600
III. Models for Studying Barrier Function	601
IV. Conclusion	609
References	610

47 Developmental Studies in the Gastrointestinal Tract

**George K. Gittes, Thomas S. Maldonado,
and Christopher A. Crisera**

I. Introduction	613
II. Working with Embryonic Tissues	613
III. Tissue and Organ Culture	616
IV. Transgenic Animals in Studies of Developmental Biology	620
References	621

48 Animal Models of Liver Failure

Jacek Rozga and Achilles A. Demetriou

I. Introduction	623
II. Models of Hereditary Liver Defects	623
III. Toxic Liver Injury	625
IV. Immune Liver Injury	627
V. Spontaneous Hepatitis	627
VI. Lethal Hepatocyte Apoptosis in Mice	627
VII. Surgical Models of Hepatic Failure	627
References	633

49 Portal Hypertension and Portacaval Shunt

Marshall J. Orloff

I. Portal Hypertension	637
II. Portal-Systemic Shunt	656
References	685

50 Animal Models of Liver Regeneration

Jacek Rozga

I. Introduction	703
II. Liver Regeneration	704
III. Regeneration Following Hepatic Injury	704
IV. Regeneration Following Partial Hepatectomy	705
V. Regeneration Following Portal Branch Ligation	706
VI. Direct Compensatory Hyperplasia	707

References	707
------------	-----

51 Animal Models for the Study of Hepatocyte Transplantation

Daniel Inderbitzin, Jacek Rozga, and Achilles A. Demetriou	
I. Introduction	709
II. Hepatocyte Isolation	710
III. Hepatocyte Cryopreservation	710
IV. Hepatocyte Transplantation Techniques	710
V. Human Hepatocyte Transplantation	716
References	717

52 Biliary Stone Formation

Matthew I. Goldblatt, Attila Nakeeb, and Henry A. Pitt	
I. Introduction	721
II. Gallstone Pathogenesis	721
III. Animal Models of Gallstones	724
IV. Models for Cholesterol Crystal Nucleation	726
V. Models for Studying Biliary Motility	729
VI. Gallbladder Mucosal Absorption	730
VII. Conclusion	731
References	731

53 Models for the Study of Pancreatitis

Michael L. Steer

I. Introduction	733
II. Acute Pancreatitis	734
III. Chronic Pancreatitis	741
IV. Preparation for <i>in Vitro</i> Study	742
V. Conclusions	743
References	744

54 Models of Endocrine Insufficiency

Thomas C. Vary

I. Introduction	747
II. General Approaches to Study of Endocrine Insufficiency	748
III. Methodology Considerations	749
IV. Hypothalamus	749
V. Pancreatic Insulin Insufficiency	750
VI. Adrenal Insufficiency	753
VII. Thyroid Insufficiency	754
VIII. Sex Hormones	755
IX. Conclusion	755
References	755

55 Animal Models in Transplantation

**I. L. Laskowski, J. B. Ames, M. Gasser, D. Whitley,
and N. L. Tilney**

I. Introduction	757
II. General Techniques	758
III. General Operative Procedures	762
IV. Organ Transplantation	764
V. Summary	769
References	770

56 Models to Study Surgical Nutrition and Metabolism

Wiley W. Souba and Douglas W. Wilmore

I. Introduction	773
II. Determining the Initial Metabolic/Nutritional State	744
III. Studying Altered Metabolic States	774
IV. Methodology—General Principles	775
V. Expressing Results	775
VI. Methods in Humans with Application in Animal Models	775
VII. Animal Models	781
VIII. Cultured Cells	784
IX. Organelle Studies	785
X. Conclusion	785
XI. Resources	786
References	787

57 Stable Isotopes

Robert R. Wolfe

I. Isotopes	789
II. Tracers	789
III. Analysis	791
IV. Calculation of Isotope Enrichment from Mass Spectrometer Data	792
V. Tracer Models	792
VI. Assumptions	794
VII. If Assumptions Are Not Satisfied	794
References	795

58 Body Composition

Lindsay D. Plank and Graham L. Hill

I. Introduction	797
II. Definition of Terms	797
III. Methodology	798
IV. Body Composition Models	806
V. Practical Problems in Measuring Body Composition in Intensive Care Patients	807

VI. Summary	807
VII. Resources	809
References	809

59 Energetics

Danny O. Jacobs and Takeaki Matsuda

I. Introduction	813
II. Whole Body Measurements	813
III. Regional Methods	817
IV. Cells	822
References	822

60 Models of Protein Metabolism

**Per-Olof Hasselgren, David R. Fischer,
and Timothy A. Pritts**

I. Introduction	825
II. Protein Synthesis	826
III. Protein Degradation	831
IV. Muscle	833
V. Intestine	838
VI. Conclusions	841
References	842

61 Membrane Transport of Nutrients

Bruce R. Stevens

I. Introduction	845
II. Survey of Methods	846
III. Experimental Conditions and Interpretations	846
IV. Practical Membrane Methods to Assess Solute Transport	852
V. Conclusions	856
References	856

62 Models of Wound Healing in Growth Factor Studies

Alexandrina Saulis and Thomas A. Mustoe

I. Introduction	857
II. Types of Wounds—Animal Models	858
III. Methods to Quantify Wound Healing	867
IV. Conclusion	869
References	870

63 Animal Models of Sepsis and the Multiple Organ Dysfunction Syndrome

Mitchell P. Fink

I. Rationale	875
--------------	-----

Contents

II. The Choice of Species	876
III. The Ideal Animal Model of Sepsis	878
IV. Specific Animal Models of Sepsis	878
References	885

64 The Immuno-Inflammatory Response

Eileen M. Bulger, Avery B. Nathens, and Ronald V. Maier

I. Introduction	893
II. Monocytes and Macrophages	893
III. Neutrophils	898
IV. T Helper Cells	905
References	905

65 Antibiotic Trials

E. Patchen Dellinger

I. Introduction	909
II. Preclinical Studies	909
III. Regulatory Considerations	910
IV. Surgical Trials	910
V. Current FDA Guidelines	915
VI. The Clinical Investigator	916
VII. Pitfalls and Publication Issues	916
References	917

66 Scoring Systems for Sepsis and the Multiple Organ Dysfunction Syndrome

John C. Marshall

I. Introduction	921
II. Composite Descriptors: Methodologic Principles	922
III. Scoring Systems for Sepsis	923
IV. Scoring Systems for Multiple Organ Dysfunction Syndrome	925
V. Limitations in the Use and Interpretation of Scores	930
VI. Conclusions	930
References	930

67 Cytokine Biology

Rebecca M. Minter, Frank J. Wessels, and Lyle L. Moldawer

I. Introduction	933
II. Cytokine Response to Inflammation	934
III. Exogenous Delivery of Cytokines	937
IV. Inhibition of Cytokine Production or Action	940
V. Measuring Cytokine Expression and Activities	942

VI. Conclusion	944
References	944

68 Biology of Nitric Oxide: Measurement, Modulation, and Models

Joy L. Collins, Yoram Vodovotz, and Timothy R. Billiar

I. Introduction	949
II. History	950
III. Biology of Nitric Oxide in Mammals	950
IV. Methods for Detection of NO and Measurement of NOS Activity	951
V. Methods of Manipulating NO in Experimental Models	957
VI. Conclusions	964
References	964

69 Endothelial Cell and Smooth Muscle Cell Biology in Vascular Disease

Richard D. Kenagy and Alexander W. Clowes

I. Introduction	971
II. General Areas of Vascular Cell Research	971
III. Experimental Models of Atherosclerosis, Aneurysm, and Restenosis	974
References	981

70 Coagulation Biology

**Daniel D. Myers, Jr., Shirley K. Wroblewski, Peter K. Henke,
and Thomas W. Wakefield**

I. Introduction	989
II. Hemodynamic Animal Model for Anticoagulant/Antagonist Evaluation	989
III. Venous Thrombosis Animal Models	990
IV. Biochemical/Molecular Biologic/Immunologic/ Evaluation Techniques	994
V. Summary	998
References	999

71 Endovascular Research: Stents

Darwin Eton, Kyung M. Ro, and Samuel S. Ahn

I. Introduction	1001
II. Protocols	1002
III. Experimental Design	1003
IV. Methods	1005
V. Clinical Evaluation	1008
VI. Conclusion	1008
References	1008

72 Noninvasive Vascular Measurements

Stephen R. Lauterbach, Nancy R. Macdonald,
and William M. Abbott

I. Introduction	1011
II. Patient Compliance, Safety, and Limitations	1012
III. Rationale for Acquiring Quantitative Hemodynamic Data	1012
IV. Hemodynamic Concepts and Principles	1012
V. Doppler Ultrasound	1014
VI. Measurements of Pressure	1016
VII. Measurements of Flow	1016
VIII. Pressure–Flow Relationships across Stenosis	1016
IX. Representative Studies	1019
X. New Technology	1024
References	1024

73 Techniques to Study Microcirculation

David A. Spain and R. Neal Garrison

I. Introduction	1027
II. <i>In Vivo</i> Videomicroscopy	1027
III. Isolated Microvessels	1030
IV. Laser Doppler Flowmetry	1031
V. Microspheres	1031
VI. Indirect Techniques	1032
VII. Summary	1032
VIII. Resources	1032
References	1033

74 Blood Substitutes in Surgery

Gus J. Vlahakes

I. Introduction	1037
II. General Principles	1037
III. Perfluorocarbon Emulsions	1038
IV. Hemoglobin-Based Oxygen-Carrying Solutions as Blood Substitutes	1039
References	1044

75 Research Models in Pediatric Surgery

Brad W. Warner

I. Introduction	1047
II. Biliary Atresia	1047
III. Hirschsprung's Disease	1049
IV. Necrotizing Enterocolitis	1051

V. Cryptorchidism	1053
VI. Intestinal Adaptation Following Massive Small Bowel Resection	1055
VII. Abdominal Wall Defects	1058
References	1060

76 Research in Fetal Surgery

Alexander Sasha Krupnick and N. Scott Adzick

I. Introduction	1065
II. Fetal Wound Healing	1065
III. Preterm Labor after Fetal Surgery	1068
IV. Disease-Based Models	1071
References	1079

77 Research in Plastic Surgery

**Gyu S. Chin, Jason A. Spector, Stephen M. Warren,
and Michael T. Longaker**

I. Introduction	1081
II. Gene Therapy	1081
III. Tissue Engineering	1082
IV. Craniofacial Surgery	1087
References	1091

78 Research Methods in Neurosurgery

Svetlana Ivanova and Kevin J. Tracey

I. Introduction	1095
II. Neuropathologic Techniques for Study of Cerebral Ischemia and Related Disorders of the CNS	1096
III. Neuroscience Techniques for Study of the Structure and Function of the CNS	1103
IV. Neural Cell Culture	1103
References	1104

79 Research in Urologic Surgery

Roger E. De Filippo and Anthony Atala

I. Introduction	1107
II. Cytogenetics	1107
III. Molecular Biology	1108
IV. Tissue Engineering	1113
V. Conclusion	1116
References	1116

80 Research in Cardiac Surgery

Robert M. Mentzer, Jr., Caren M. Mulford, and Robert D. Lasley

I. Introduction	1119
-----------------	------

Contents

II. Myocardial Stunning	1121
III. Hibernating Myocardium	1125
IV. Ischemic Preconditioning	1126
V. Apoptosis	1130
VI. Conclusion	1132
References	1133

81 Research in Orthopedic Surgery

A. Simon Turner

I. Introduction	1137
II. Long Bones	1139
III. Osteoporosis	1146
IV. Immobilization and the Effects of Exercise	
	1151
V. Spine	1154
VI. Implant Coatings	1159
VII. Joint Prostheses	1163
VIII. Articular Cartilage	1166
IX. Meniscus	1170
X. Tendons and Ligaments	1172
XI. Shoulder	1176
XII. Miscellaneous Conditions	1179
XIII. The Future Direction of Orthopedic Research	1182
References	1183

82 Statistical Analysis—Specific Statistical Tests: Indications for Use

David T. Mauger and Gordon L. Kauffman, Jr.

I. Introduction	1201
II. Continuous Data	1203
III. Categorical Data	1211
IV. Survival Data	1212
V. Correlation	1213
VI. Summary	1215
References	1215

83 Data Presentation: How to Write and Submit Abstracts and Papers

Nancy R. Ehrlich and Patricia A. Sheiner

I. Introduction	1217
II. What Makes a Good Abstract or a Good Paper	1217
III. Abstracts for Presentation at Meetings	1218
IV. Developing the Manuscript	1221
V. Formatting the Manuscript	1229

VI. The Ethics of Authorship	1230
VII. Choosing a Journal	1232
VIII. Responding to the Reviewers	1232
Exercise 1: The Health Club Dilemma	1233
References	1235

84 Audiovisual Communications as a Research Skill

Charles M. Balch

I. Introduction	1237
II. Preparation	1237
III. Timing and Speaking Style	1238
IV. Helpful Principles and Pointers	1238
V. Delivery	1239
VI. Summary	1240

85 Organizing and Managing Meetings and Conferences

Mary C. Schuerman and P. William Curreri

I. Introduction	1241
II. Choosing a Site	1242
III. Contracts	1243
IV. Establishing a Budget and Setting Appropriate Registration Fees	1243
V. Food and Beverage	1243
VI. Audiovisual	1244
VII. Entertainment	1244
VIII. Registration	1246
IX. Badges, Signage, and Printing	1246
X. Exhibits and Posters	1247
XI. Security Considerations	1247
XII. Accounting	1247
XIII. Professional Management	1248
References	1248

86 The Management and Organization of a Surgical Research Laboratory

David T. Efron, Daniel Most, and Adrian Barbul

I. Introduction	1249
II. Laboratory Personnel	1249
III. Collaboration	1251
IV. Utilization of Laboratory Space	1251
V. Laboratory Safety	1254
Suggested Reading	1259

87 History and Philosophy of Surgical Research

Clyde F. Barker

I. History and Philosophy of Surgical Research	1261
II. "Rules" for Successful Research by Surgeons	1264
III. Successful Surgeon-Scientists	1265
IV. Surgical Science History	1268
V. Surgical Science: Present and Future	1274
References	1275

88 The Surgical Research Program as a Business Enterprise

Jeffrey H. Lawson and Robert W. Anderson

I. Background	1279
II. A New Look at Surgical Research	1280
III. Environmental Assessment	1280
IV. Developing the Financial Plan	1281
V. Developing the Research Portfolio	1281
VI. Research as a Business	1284
VII. Summary	1286
References	1286

89 Nobel Laureates in Surgery

Moritz M. Ziegler

I. Introduction	1287
II. Surgical Award Winners	1288
III. Summary	1296
References	1297

90 Surgical Education Research

Andreas H. Meier, Paul J. Gorman, and Thomas M. Krummel

I. Introduction	1299
II. Historical Perspective	1299
III. Principles, Goals, Variables, Outcomes	1300
IV. Results of Research in Surgical Education	1302
V. Challenges for Surgical Education in the Future	1303
VI. Future Research Opportunities	1304
VII. Conclusion	1304
References	1304

91 Mathematical Modeling

Denise E. Kirschner and Timothy G. Buchman

I. Mathematical Modeling	1309
--------------------------	------

II. What Is (and What Is Not) a Mathematical Model?	1310
III. Summary	1315
Suggested Readings, References, and URLs	1317

92 Information Resource Discovery for Surgeons: Databases and the Internet

Suzy Conway, Anna Getselman, and Lucretia W. McClure

I. Review of Literature Formats	1319
II. Databases	1321
III. Internet Resources	1326
IV. Suggested Reading	1335
References	1335

93 How to Review a Manuscript

Ori D. Rotstein

I. Introduction	1337
II. Why Review Manuscripts?	1337
III. General Issues about Reviewing	1338
IV. Conclusions	1341
References	1341

94 Academic Surgical Mentoring

**Clay Cothren, Julie Heimbach, Thomas N. Robinson,
Casey Calkins, and Alden H. Harken**

I. Why Mentoring?	1343
II. The Surgical Mentor	1343
Recommended Reading	1347

95 Ethics and Surgical Research

Timothy M. Pawlik and Lisa Colletti

I. Introduction	1349
II. Guiding Principles of Ethical Surgical Research	1350
III. Character as an Ethical Guide in the Research Setting	1356
IV. Ethical Issues: Negotiating the Laboratory Experience	1356
V. Issues in Publication—Whose Paper Is It, Who Decides, and Who Controls Publication?	1358
VI. Conclusion	1359
References	1359

Contents

96 The National Institutes of Health: Procedures and Performance

Scott D. Somers

I. Introduction	1361
II. Structure of the NIH	1362
III. Key Terms and NIH Personnel	1362
IV. Funding Mechanisms	1363
V. Life Cycle of an NIH Application	1366
VI. Preparation of a Grant Proposal to the NIH	1370
VII. Summary	1373

97 Measuring the Performance of Surgical Research

Wiley W. Souba and Douglas W. Wilmore

I. Introduction	1375
II. Assessing the Performance of the Research Program	1376
III. A New Research Model in Surgical Research?	1379
References	1381

98 Virtual Reality and Surgery

Joseph M. Rosen, Marcus K. Simpson, and Charles Lucey

I. Introduction	1383
II. Definitions and Background	1384
III. Surgical Simulators	1384
IV. Augmented Reality	1389

V. Robotic Employment of Virtual Reality	1389
VI. Telesurgery	1390
VII. Conclusions and Future Research	1391
References	1391

99 Surgeons and Health Services Research

Robert S. Rhodes and Susan D. Horn

I. Introduction	1393
II. Methods	1394
III. Clinical Practice Improvement—A New Approach	1398
IV. Summary and Future Considerations	1401
References	1402

100 From Idea to Product: Financing and Regulatory Issues in Product Development

Jonathan Gertler and James Garvey

I. Introduction	1405
II. Development of an Idea into an Investment Proposition	1405
III. Regulatory Structure for New Device Products	1408
IV. Overview and Conclusion	1413
Recommended Reading	1414

Index	1415
-------	------