

Diagnostic Radioisotopes

By

CHARLES A. OWEN, JR., M.D., Ph.D. (Med.)

Section of Clinical Pathology

Mayo Clinic

and

Associate Professor of Clinical Pathology

Mayo Foundation

Graduate School

University of Minnesota

Rochester, Minnesota

This book is copyright. It may not be reproduced by any means in whole or in part without permission. Application with regard to copyright should be addressed to the publishers.

Published and copyrighted 1959 in the United States of America by CHARLES C THOMAS • PUBLISHER, 301-327 East Lawrence Avenue, Springfield, Illinois.

Published simultaneously in Canada by THE RYERSON PRESS, Queen Street West, Toronto 2.

Printed in the United States of America

PREFACE

A number of excellent books on radioactive isotopes have been published. These tend to emphasize the basic principles of radiophysics and radiochemistry. The literature on medical applications of the radioactive isotopes is concerned primarily with treatment and only incidentally with the diagnostic tests.

This book is a review of the diagnostic aspects of radioactive elements and compounds. At first glance, the separation of diagnostic and therapeutic tests may appear to be artificial. Practically, however, their separation has advantages. The detecting equipment ideally suited to either one is poorly adapted to the other.

More important is the fact that the emphasis in radioisotopic therapy is on the biologic effect of radiation, a field in which the roentgenologist is thoroughly familiar. In the diagnostic application of radioisotopes, the emphasis is on precise measurement, which is the province of the clinical pathologist; the radiation is merely the agent used for quantitation, just as color, turbidity and pH are other agents available to the pathologist. At the Mayo Clinic, the diagnostic procedures are carried out in the Section of Clinical Pathology and treatment is given in the Section of Therapeutic Radiology; both rely on the Section of Biophysics for help and advice.

The purpose of this book is to review in detail the physiologic principles and technics of those radioisotopic methods already established as diagnostically useful, as well as those which appear likely to become so. Newer and incompletely tested procedures will be outlined in a more cursory fashion.

While it is not possible to acknowledge individually all those who have assisted me directly or indirectly in the preparation of this volume, I would like to express my particular appreciation to Dr. Marvin M. D. Williams, who patiently introduced me to the field of radioisotopes, Dr. Alan A. Orvis, whose advice in scintillation counting has been invaluable, Dr. William M. McConahey

for his help in metabolic problems, Dr. Donald S. Childs, Jr., for generous assistance from his Section of Therapeutic Radiology, and Dr. Lewis B. Woolner in the surgical pathologic applications of thyroidal disease. Great help also was received from Miss Elaine Graf and Miss Elizabeth Waldron, who supervise respectively the investigative and routine diagnostic radioisotope laboratories at the Mayo Clinic.

C.A.O.

CONTENTS

	<i>Page</i>
PREFACE	vii
 <i>Chapter</i>	
I. INTRODUCTION	3
 II. MEASURING RADIOACTIVITY IN THE DIAGNOSTIC LABORATORY	 6
Scintillation Crystal Counting	7
Standardization of a Scaler	10
High Voltage	11
Discriminator, or Selector	13
Attenuator, or Gain	13
Day-by-Day Standardization	14
Measurement of an Unknown Sample of Radioisotope	15
Background	16
Physical Decay	16
Counting Statistics	17
Counts Per Minute Vs. Counts Per Second	19
In Vitro Measurement of Radioactivity	19
Well-Crystal Counting	19
Volumetric Standardization	20
Counting Tubes	20
In Vitro Counting With a Solid Crystal	21
Method for Urine	21
Method for Feces	24
Other Types of Crystal Counters	25
In Vivo Measurement of Radioactivity	26
Distance and the Law of Inverse Squares	27
Measurement of Thyroidal I ¹³¹	29

CONTENTS

<i>Chapter</i>	<i>Page</i>
Compton Scatter: Corrections Needed	30
Pragmatic Standardization	32
Examples of Calculation After Single or	
Multiple Doses of I^{131}	34
Multiple Counting Units	36
Localization of Radioactivity	40
Scanning Technics	41
The Geiger-Mueller Tube	43
Measurement of Two Isotopes	45
Decay Method	45
Discrimination Methods	46
Errors in Measuring Radioactivity	49
Radiation Protection in the Diagnostic Laboratory	50
III. METABOLISM	56
Iodine Metabolism and Measurement of Thyroidal	
Function	56
The Iodine Cycle	57
Thyroidal Uptake	59
Rate of Uptake of I^{131} by the Thyroid	59
Thyroidal Clearance of Plasma I^{131}	62
Thyroidal Accumulation of I^{131} Reflected	
by Urinary Excretion	63
Measurement of Thyroidal Uptake of I^{131}	64
Assumption That Thyroidal Uptake of I^{131}	
Reflects Thyroidal Function	65
Conversion of Iodide to Thyroidal Hormone	66
Thyroglobulin; Thyroidal Colloid	69
Comparison With Other Glands	71
Thyroid-Stimulating Hormone	72
Inhibition of the Thyroid by Iodine	73

CONTENTS

Chapter

Page

Thyroidal Release of Hormone	75
Circulating Thyroidal Hormones	75
Butanol-Insoluble Iodine	78
Patterns in Thyroiditis	79
Appearance Rate of Labeled Hormone in Plasma	80
Metabolism of Hormonal Iodine	82
Role of the Liver	83
Salivary Iodide	84
Excretion of Hormonal Iodine	85
Diagnostic Tests Based on the Iodine Metabolic Cycle	85
Diagnostic Methods: Technical Details	95
Thyroidal Uptake of I^{131}	95
Source of I^{131}	95
Use of Glass Containers	96
Urinary Excretion of I^{131}	97
Renal Excretion Rate: Extrarenal Disposal Rate:	
Thyroidal Accumulation Rate	97
Thyroidal Clearance of Plasma I^{131} (Berson)	100
Urine	104
I^{131} in Blood: Protein-Bound I^{131} (PBI 131);	
Conversion Ratio; Butanol-Extractable I^{131} (BEI 131)	104
PBI 131	104
Trichloroacetic Acid (TCA) Method	104
Somogyi Zn(OH) $_2$ Method (Table 12)	105
Conversion Ratio	106
Butanol-Extractable I^{131} (BEI 131)	107
Alternative Methods for Measuring PBI 131	
Ion-Exchange Resin Technic	109
Silver Phosphate Technic	109
Radiochemical Assay of Thyroxine	109
Thyroid-Stimulating Hormone (TSH) Test:	
Adapted From Jefferies and Co-workers	109
Nonresponders: No Uptake Initially	110

CONTENTS

<i>Chapter</i>	<i>Page</i>
Responders: No Uptake Initially	110
Responders: Uptake Initially	110
Nonresponders: Uptake Initially	112
Triiodothyronine (T ₃) Inhibition Test	112
Results	113
Autoradiography	114
Scintiscanning	116
Pituitary Gland	148
Parathyroid Glands	148
Pancreas	149
Adrenal Glands	150
Vitamins	151
Vitamin B ₁₂	151
Vitamin D	151
IV. HEMATOLOGY	152
Determination of Blood Volume	152
Use of Radioiodinated Albumin	153
Plasma-Trapping Error in Hematocrit Values	154
Discrepancy Between Body Hematocrit and Venous Hematocrit	155
Labeling Erythrocytes With Radiochromium	157
Effect of Anticoagulant	158
Effect of Temperature	159
Effect of Hematocrit Value	160
Effect of Stable Chromium	160
Variation in Methods	161
Combined Measurement of Plasma and Erythrocytic Volumes	161
Methods for Determining Blood Volume	162
Plasma Volume With Radioiodinated Albumin	162

CONTENTS

<i>Chapter</i>	<i>Page</i>
Reagents	162
Equipment	163
Procedure	163
Calculation	164
Example	164
Alternative Method	164
Example	164
Erythrocytic Volume With Chromate-Cr ⁵¹	165
Reagents	165
Equipment	166
Procedure	166
Calculation	167
Example	167
Combined Measurement of Erythrocytic (Chromate-Cr ⁵¹) and Plasma (Chromic-Cr ⁵¹) Volumes (Kaplan)	168
Reagents	168
Equipment	168
Procedure	168
Hematocrit Standard	169
Whole-Blood Standard	169
Plasma Standard	169
Calculation	169
Example	170
Multiple Erythrocytic Volumes: Chromate-Cr ⁵¹	
Method	171
Example	171
Calculation	172
Multiple Erythrocytic (Cr ⁵¹) and Plasma (I ¹³¹ -Albumin) Volumes	172
Example	172
First Blood Volume	173
Second Blood Volume	173
Third Blood Volume	173
Standards and Doses	173

CONTENTS

Chapter	Page
Calculation	174
Evaluation of Survival of Circulating Erythrocytes	175
Advantages and Disadvantages of Cr^{51}	175
Labeling Erythrocytes for Survival Studies	180
Technic of Cr^{51} -Labeling Method for Measuring Erythrocytic Survival (Cooper and Owen)	181
Reagents	181
Equipment	181
Procedure	181
Calculation	182
Examples	184
Calculation for Patient A	184
Calculation for Patient B	185
Comment	185
Radioactive Iron	195
Disappearance Rate of Plasma Iron (Fig. 46)	196
Reagents	198
Equipment	198
Procedure	198
Calculation	199
Turnover of Plasma Iron	199
Example	200
In Vivo Localization of Radioiron	202
Procedure	203
Calculation	204
Example	208
Rate of Appearance of Fe^{59} -Labeled Erythrocytes in Circulation	211
Reagents and Equipment	211
Procedure	211
Calculation	213
Example	213
Other Uses of Radioiron	213

CONTENTS

<i>Chapter</i>	<i>Page</i>
Absorption of Fe ⁵⁹ From the Intestinal Tract	213
Iron-Binding Capacity of Serum	214
Vitamin B ₁₂ Labeled With Radiocobalt in Evaluation of Pernicious Anemia	218
The Schilling Test	222
Reagents and Equipment	223
Procedure	223
Interpretation of the Schilling Test	224
Assay of Intrinsic Factor	226
Isotopic Technics Applied to Leukocytes and Platelets . . .	230
Sequestration of Erythrocytes	230
 V. LOCALIZATION OF TUMORS	 232
Introduction	232
Tumors of the Alimentary Tract	236
Radiophosphorus	236
Radioiodinated Albumin	236
Radiogold	236
I ¹³¹ -Tetraiodophenolphthalein, I ¹³¹ -Rose Bengal . . .	236
Brain Tumors	238
Radiophosphorus	238
Radioarsenic	239
Radioiodine	240
Radioiodinated Albumin	243
Iodide-I ¹³¹	244
Radiopotassium	245
Boron	245
Tumors of the Breast	248
Radiophosphorus	248
Radiopotassium	248

CONTENTS

<i>Chapter</i>	<i>Page</i>
Tumors of the Bronchial Tree	249
Genital Tumors	250
Vagina and Cervix	250
Testis	250
Tumors of the Lymphatic System	251
Optic Tumors	251
Cutaneous Tumors	254
Thyroidal Tumors	255
Summary	258
 VI. GASTROINTESTINAL TRACT	 261
Liver	261
Radioiodinated Rose Bengal	261
Case 1 (Normal Pattern)	264
Case 2 (Pattern of Delayed Uptake)	265
Radiogold	265
Radiosilver	266
Copper Metabolism in Hepatolenticular Degeneration (Wilson's Disease)	266
Gallbladder	268
Pancreas	270
Digestion of Fats	270
Method	271
Digestion of Proteins	271
Zinc ⁶⁵ and Manganese ⁵²	273
Gastrointestinal Bleeding	274
Technic for Quantitating Gastrointestinal Bleeding	276
Reagents and Equipment	276
Procedure	276

CONTENTS

<i>Chapter</i>	<i>Page</i>
Example 1 (Normal Person)	277
Example 2 (Intestinal Hemorrhage)	278
Gastrointestinal Absorption of Electrolytes	280
Measurement of Fluid Volumes	281
Ascitic Fluid	281
Residual Fluid in Stomach	281
VII. CARDIOVASCULAR SYSTEM	282
Space Measurements	282
Plasma Proteins	282
Water Spaces of the Body	285
Extracellular Water: Sodium Space	285
Intracellular Water: Potassium Space	285
Total Body Water	286
Examples	286
K ⁴² Space	286
Na ²⁴ Space	287
Rate Measurements	288
Rates of Blood Flow	288
Arm to Leg	288
Arterial Circulation Times	290
Cardiac Output	290
Example of Measurement of Cardiac Output by	
Indirect RIHSA Method (Fig. 71)	292
Blood-Volume Data	293
Cardiac Output (Fig. 71)	293
Absorption of Injected Electrolytes	296
VIII. GENERAL APPLICATIONS OF RADIOISOTOPES	298
Bacteriology and Parasitology	298
Inorganic Chemistry	300

CONTENTS

<i>Chapter</i>	<i>Page</i>
Lungs	300
Neurology	301
Obstetrics	301
Ophthalmology	301
Orthopedics	302
Avascular Necrosis of the Femoral Head	302
Knee Joint	302
Plastic Surgery	303
Urology	304
The Radioisotopic "Renogram"	304
Other Urologic Uses	304
Radioiodinated Dyes	304
Renal Blood Flow	305
Absorption of Irrigating Fluid During	
Transurethral Prostatectomy	305
Zinc ⁶⁵	305
Electrolytes	306
Miscellaneous Uses of Radioisotopes	307
IX. RADIATION HAZARD: FEDERAL REGULATIONS	308
Requirements of the Atomic Energy Commission	311
Radioisotope Committee	311
"Permissible Doses" of Radiation	311
Training Requirements for Physicians	312
Handling of Radioactive Cadavers	314
X. APPENDICES	317
1. Tables of Physical Decay	317

CONTENTS

<i>Chapter</i>	<i>Page</i>
How to Use the Tables	317
Calculation of Residual Radioactivity of an Isotope Beyond That Shown in a Table	318
Example	318
Calculation of Physical Decay for an Unlisted Radioisotope	318
Procedure	318
Example	318
Physical-Decay Tables	319
2. Lists of Radioactive Isotopes	340
3. Four-Place Logarithm Tables	373
4. Nomogram for Determining Surface Area of the Body	381
AUTHOR INDEX	383
SUBJECT INDEX	401

Diagnostic Radioisotopes