# CHEMICAL DIAGNOSIS OF DISEASE

Edited by:

STANLEY S. BROWN

FREDERICK L. MITCHELL

and '

DONALD S. YOUNG

# **CHEMICAL DIAGNOSIS OF DISEASE**

Edited by:

STANLEY S. BROWN

Head, Research and Development Subdivision and Deputy Head, Division of Clinical Chemistry, Medical Research Council Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England

#### FREDERICK L. MITCHELL

Head, Division of Clinical Chemistry, Medical Research Council Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England

and

#### DONALD S. YOUNG

Professor of Laboratory Medicine, Mayo Medical School and Head, Section of Clinical Chemistry, Mayo Clinic, Rochester, MN 55901, U.S.A.



1979

ELSEVIER/NORTH-HOLLAND BIOMEDICAL PRESS AMSTERDAM - NEW YORK - OXFORD

# **Preface**

Some four years ago, the Editors canvassed opinion in several countries as to the need for an authoritative book on the interpretative aspects of clinical chemistry tests. It was felt that several detailed volumes on methodology were available, but similar depth of coverage of interpretation was incomplete or somewhat dated. All the individuals who were approached agreed on the value of an endeavour to gather together comprehensive surveys by authorities in all branches of the subject.

In seeking potential authors, we asked both physicians who were often faced with the problem of differential diagnosis of diseases and laboratory scientists who were commonly presented with isolated abnormal test values, to discuss the choice of tests and the interpretation of results from their different perspectives. Inevitably, this led to a certain measure of overlap, yet we felt that a dual approach was essential to provide adequate coverage of many different topics. We are grateful to the authors for minimizing duplication, but yet at the same time achieving thorough coverage of their own subjects. Strong efforts have been made not to overlook topics of actual or potential importance, but we would be grateful if readers could draw our attention to areas which they feel have been inadequately covered.

So far as possible, the material of each chapter has been organized in a uniformly systematic way, but the authors have been encouraged to adopt their own individual styles within this framework. Many of the chapters, and in some instances subsections of chapters, have been the subject of listinct monographs; and it has been essential to be highly selective. Undoubtedly on occasion the selection has been biased by the particular interests of the editors or the author concerned. However, a general attempt has been made to concentrate on the areas of major clinical importance; details of methodology have only been incorporated when they have an immediate bearing on the clinical interpretation of results. On matters over which there is still room for debate, authors have been aware in many instances of a need to cut corners by the use of dogmatic statements. This has been necessary to avoid a review format which attempts to mention all points of view and decide nothing.

Since the chapters have been written over a period during which moves towards the Système Internationale d'Unités have taken place, or are being considered in many countries, we have felt compelled to use both SI and traditional units throughout the book. An attempt has been made to implement many of the latest recommendations on nomenclature, and it is perhaps not surprising that problems have been encountered which may not have been appreciated by those making the recommendations.

In the past, it has sometimes been necessary to make clinical interpretations of results which were obtained by very dubious methodologies. Modern technology has rendered many of these interpretations obsolete and attention has been drawn to certain instances where the lack of specificity of an assay is likely to render the clinical interpretation of a result difficult or confusing.

It may be said by some that the title of the book should have incorporated the term "clinical chemistry", and indeed the book does concern a major aspect of this subject. Various definitions of clinical chemistry — or chemical pathology — have been proposed (IFCC Newsletters, Nos. 6–10, 1971–1974) which indicate three main divisions: analytical, fundamental research into the biochemistry of health and disease (in some countries termed clinical biochemistry), and the interpretation of results. It is this last — neglected — facet which is dealt with here. However, we hope that our readership will include both clinicians and laboratory scientists; the title of the book was chosen to emphasize that the interpretative role of clinical chemistry covers an area where clinicians and biochemists meet on common ground.

July 1979

Stanley S. Brown Frederick L. Mitchell Donald S. Young

# List of affiliations

)

#### PAUL D. BERK, M.D., F.A.C.P.

Head, Division of Hematology, Department of Medicine, Mount Sinai School of Medicine, New York, NY 10029, U.S.A.

### DOUGLAS A.K. BLACK, Kt., M.D., F.R.C.P.

Emeritus Professor of Medicine, University of Manchester and President, Royal College of Physicians of London, 11 St. Andrew's Place, Regent Park, London NW1 4LE, England

#### WILLIAM Z. BORER, M.S., M.D.

Clinical Chemistry Service, Clinical Pathology Department, National Institutes of Health, Bethesda, MD 20014, U.S.A.

# STANLEY S. BROWN, Ph.D., F.R.I.C., M.R.C.Path.

Head, Research and Development Subdivision and Deputy Head, Division of Clinical Chemistry, M.R.C. Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England

#### J. STEWART CAMERON, M.D., F.R.C.P.

Professor of Renal Medicine, Guy's Hospital Medical School, London Bridge, London SE1 9RT, England

#### ROBIN W. CARRELL, M.B., Ph.D., F.R.A.C.P., M.R.C.Path.

Professor of Clinical Biochemistry, Department of Pathology, Christchurch Hospital, Christchurch, New Zealand

#### ISRAEL CHANARIN, M.D., F.R.C.Path.

Head, Section of Haematology and Consultant Haematologist, M.R.C. Clinical Research Centre, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England

#### KAY W. COLSTON, B.Sc., Ph.D.

Senior Research Officer, Endocrine Unit, Royal Postgraduate Medical School, Du Cane Road, London W12 OHS, England

#### JAMES B. ELDER, M.D., F.R.C.S.(Ed.), F.R.C.S.(Eng.)

Reader in Surgery, University of Manchester and Consultant Surgeon, The Royal Infirmary, Manchester M13 9WL, England

#### IMOGEN M.A. EVANS, M.D., Ph.D., F.R.C.P.(C.)

Honorary Consultant, Endocrine Unit, Royal Postgraduate Medical School, Du Cane Road, London W12 0HS, England

#### PROVASH C. GANGULI, M.B., F.R.C.P.

Senior Lecturer in Gastroenterology, University of Manchester and Consultant Physician, The Royal Infirmary, Manchester M13 9WL, England

#### PETER B. GREENBERG, M.D., Ph.D., F.R.A.C.P.

Physician, Royal Melbourne Hospital, Melbourne, Victoria, Australia

#### C. NICHOLAS HALES, M.A., M.D., Ph.D., M.R.C.Path, F.R.C.P.

Professor and Head of Department of Clinical Biochemistry, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QR, England

# R. ANGUS HARKNESS, M.B., Ph.D., F.R.C.P.E., F.R.C.Path.

Deputy Head, Division of Perinatal Medicine, M.R.C. Clinical Research Centre and Honorary Consultant Chemical Pathologist, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England

#### RAYMOND HOFFENBERG, M.D., Ph.D., F.R.C.P.

William Withering Professor of Medicine and Head of Department of Medicine, University of Birmingham, Birmingham B15 2TH, England

#### C. DEREK HOLDSWORTH, M.D., F.R.C.P.

Consultant Physician, Gastrointestinals Unit, Hallamshire Hospital, Sheffield S10 2JF, England

# MOGENS HØRDER, Fr.Med.Sc., M.D.

Associate Professor in Clinical Chemistry at the University of Odense and Head, Department of Clinical Chemistry, Odense University Hospital, DK-5000 Odense, Denmark

#### VIVIAN H.T. JAMES, D.Sc., Ph.D., F.R.I.C., F.R.C.Path.

Professor of Chemical Pathology, Department of Chemical Pathology, St. Mary's Hospital Medical School, Paddington, London W2 1PG, England

#### E. ANTHONY JONES, M.D., M.R.C.P.

Head, Section of Diseases of the Liver, Digestive Diseases Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, MD 20205, U.S.A.

# RICHARD G. LARKINS, M.D., Ph.D., F.R.A.C.P.

First Assistant, Department of Medicine, University of Melbourne, Repatriation General Hospital, Heidelberg, Victoria 3077, Australia

#### ALEXANDER A.H. LAWSON, M.D., F.R.C.P.E.

Consultant Physician, Milesmark Hospital, Dunfermline, and to the West Fife Group of Hospitals; Honorary Consultant Tutor, Department of Medicine, University of Edinburgh and Postgraduate Tutor for West Fife, Scotland

#### HERMANN LEHMANN, M.D., Sc.D., F.R.C.P., F.R.S., F.R.I.C., F.R.C.Path.

Emeritus Professor of Clinical Biochemistry, University of Cambridge, University Department of Biochemistry, Tennis Court Road, Cambridge CB2 1QW, England

#### BARRY LEWIS, M.D., Ph.D., F.R.C.P., M.R.C.Path.

Professor, Department of Chemical Pathology and Metabolic Disorders, St. Thomas' Hospital Medical School, London SE1 7EH, England

#### IAIN MacINTYRE, M.B., Ch.B., Ph.D., D.Sc., F.R.C.P., F.R.C.Path.

Professor of Endocrine Chemistry and Director, Endocrine Unit, Royal Postgraduate Medical School, Du Cane Road, London W12 0HS, England

#### ROBERT D.G. MILNER, M.A., M.D., Ph.D., F.R.C.P.

Professor and Head of Department of Paediatrics, University of Sheffield, Children's Hospital, Sheffield S10 2TH, England

#### FREDERICK L. MITCHELL, D.Sc., Ph.D., F.R.I.C., F.R.C.Path.

Head, Division of Clinical Chemistry, M.R.C. Clinical Research Centre, Harrow, Middlesex HA1 3UJ, England

#### HIPOLITO V. NIÑO, Ph.D.

Director of Research and Development, Diagnostics Operations, Beckman Instruments, Inc., Fullerton, CA 92634, U.S.A.

#### THEODORE PETERS, Jr., Ph.D.

Diplomate, American Board of Clinical Chemistry; Research Biochemist, The Mary Imogene Bassett Hospital, Cooperstown, NY 13326 and Adjunct Associate Professor of Biochemistry, College of Physicians and Surgeons, Columbia University, New York, NY, U.S.A.

#### D. NOEL RAINE, B.Sc., Ph.D., M.B., B.S., F.R.I.C., F.R.C.Path.

Consultant Chemical Pathologist and Head, Department of Clinical Chemistry, The Children's Hospital, Birmingham B16 8ET, England

#### COLIN R.J. RUTHVEN, Ph.D., M.Sc., F.R.I.C., C.Chem.

Top Grade Biochemist, Bernhard Baron Memorial Research Laboratories, Queen Charlotte's Maternity Hospital, London W6 0XG, England

#### MERTON SANDLER, M.D., F.R.C.P., F.R.C.Path.

Professor of Chemical Pathology, University of London, Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, London W6 0XG, England

#### MORTON K. SCHWARTZ, Ph.D.

Vice President for Laboratory Affairs and Chairman, Department of Biochemistry, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, U.S.A.

#### OLE SIGGAARD-ANDERSEN, M.D., Ph.D.

Professor of Clinical Chemistry, University of Copenhagen and Head, Department of Clinical Chemistry, Copenhagen County Hospital, Herley, DK-2730 Herley, Denmark

# F. WILLIAM SUNDERMAN, Jr., M.D., F.A.C.P., F.C.A.P.

Professor and Chairman, Department of Laboratory Medicine, University of Connecticut School of Medicine, Farmington, CT 06032, U.S.A.

#### DONALD P. TSCHUDY, Ph.D.

Senior Investigator, Metabolism Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20014, U.S.A.

#### RICHARD W.E. WATTS, M.D., D.Sc., Ph.D., F.R.C.P., F.R.I.C.

Head, Division of Inherited Metabolic Diseases, M.R.C. Clinical Research Centre and Honorary Consultant Physician, Northwick Park Hospital, Harrow, Middlesex HA1 3UJ, England

# † J. HENRY WILKINSON, C.B.E., Ph.D., D.Sc., F.R.I.C., F.R.C.Path.

Professor of Chemical Pathology in the University of London at Charing Cross Hospital Medical School and Consultant Chemical Pathologist to Charing Cross Hospital, Department of Chemical Pathology, Charing Cross Hospital, Fulham Palace Road, London W6 8RF, England

#### DONALD S. YOUNG, M.B., Ph.D.

Professor of Laboratory Medicine, Mayo Medical School and Head, Section of Clinical Chemistry, Mayo Clinic, Rochester, MN 55901, U.S.A.

<sup>&</sup>lt;sup>†</sup> Died November 29th, 1977.

# Contents

	Preface List of affiliations	
	APTER 1: BIOLOGICAL VARIABILITY hald S. Young	1
1.1.	Introduction	3
1.2.	Genetic influences	7
1.3.	Long-term physiological influences	
1.4.	Short-term physiological influences	44
1.5.	Drug administration	75 86
1.6. 1.7.	General physiological responses In vitro effects	. 80 92
1.7.	Analytical methodology	95
1.0.	Third to a method of ogy	,,,
Refer	rences	95
	her reading	112
	APTER 2: CHEMICAL ANALYSIS OF BODY FLUIDS OTH AN BLOOD	ER
	iam Z. Borer	115
2.1.	Introduction	115
2.2.	Fluids of the central nervous system and special senses	116
2.3.	Effusion	121
2.4.	Fluids of the genitourinary system	132
2.5.	Saliva, faeces and meconium	150
2.6.	Specialized glandular secretions	159
Defer	rences	161
Further reading		179

	PTER 3: HYDROGEN IONS AND BLOOD GASES	
Ole S	iggaard-Andersen	181
3.1.	Introduction	183
3.2.	Concentration of free hydrogen ion in arterial plasma	186
3.3.	Concentration of titratable hydrogen ion in plasma, blood or extracellular fluid	198
3.4.	Partial pressure of carbon dioxide in arterial blood	205
3.5.	Concentrations of total carbon dioxide and bicarbonate in plasma	214
3.6.	Partial pressure of oxygen in arterial and mixed venous blood	219
3.7.	Partial pressure of oxygen in blood at half saturation of oxygen in haemoglobin	229
3.8.	Saturation of oxygen in haemoglobin in arterial blood	236
3.9.	Case histories	238
Refere	nces	241
Furthe	r reading	245
СПА	PTER 4: GLUCOSE METABOLISM	
	cholas Hales and Robert D.G. Milner	247
C. Ni	choias haies and Robert D.G. Millier	247
4.1.	Introduction •	248
4.2.	Normal glucose metabolism in man	248
4.3.	Investigation of glucose metabolism	256
4.4.	Investigation of insulin metabolism	260
4.5.	Investigation of glucagon metabolism	264
4.6.	Diagnosis and management of some conditions affecting glucose metabolism	264
Refere	nces	278
Further reading		279
Adden	dum	280
СНА	PTER 5: LIPIDS	
	/ Lewis	281
Duil	120 1110	
5.1.	Introduction	282
5.2.	The lipoproteins of plasma	282
5.3.	Definitions of normal lipid concentrations	285
<b>5.4</b> .	The hyperlipidaemic states	289 298
5.5.	Methods for lipid and lipoprotein analysis	298
Refere	ences	306
	er reading	309
Adder	· ·	309
CHA	PTER 6: PROTEINS	
Theo	odore Peters, Jr.	311
6.1.	The nature of proteins	312
6.2.	Metabolism of proteins	325
6.3.	Some specific plasma proteins	332
6.4.	Summarized indications for screening or for specific tests	355

		Xiii '
Refere Furth	ences er reading	357 360
Adder	<del>-</del>	361
	PTER 7: ENZYMES	
Mog	ens Hørder and J. Henry Wilkinson	363
7.1. 7.2. 7.3. 7.4. 7.5.	Materials Methodology Biochemistry and physiology of enzymes Application of enzyme measurements in clinical medicine Biological variability of enzymes	365 370 375 382 398
Refere Furth Adde	er reading	399 405 405
OII.	DEED O CALCHIN AND MACNEGUM	
Kay	W. Colston, Imogen M.A. Evans, Peter B. Greenberg, Richard G. tins and Iain MacIntyre	407
	·	
8.1.	Biochemical physiology of calcium	409 411
8.2. 8.3.	Parathyroid hormone Calcitonin	421
8.4.	Vitamin D	423
8.5.	Disorders of calcium homeostasis	426
8.6.	Metabolic bone diseases	432
8.7.	Biochemical physiology of magnesium	439
8.8. 8.9.	Measurement of serum magnesium  Disorders of magnesium homeostasis	440 440
Refer	ences	443
	er reading	450
Adde	ndum	450
CH/	APTER 9: RENAL EUNCTION	
	iglas A.K. Black and J. Stewart Cameron	453
9.1.	Normal function	454
9.2.	Aspects of renal pathology	460
9.3.	The syndromes of renal disease	466
9.4.	Tests used in the investigation of renal disease	483
9.5.	Summary statement on the place of biochemical tests in renal disease	514
Refe	rences	515
	her reading	524
Adde	endum	524

	APTER 10: LIVER FUNCTION onthony Jones and Paul D. Berk	525
10.1.	Introduction	
10.1.		528
10.3.		529 590
10.4.	B	603
10.5.	· ·	617
10.6.		642
10.7.		643
Refer	ences	646
Addit	ional references	662
CHA	APTER 11: GASTRIC FUNCTION	
Jame	es B. Elder and Provash C. Ganguli	663
11.1.	Saliva	664
11.2.	Hydrochloric acid	665
11.3.	Pepsin	673
11.4.	Gastric mucus	676
11.5.	Gastrin	677
Refere	ences er reading	684 687
СНА	PTER 12: INTESTINAL AND PANCREATIC FUNCTION	
	erek Holdsworth	689
12.1.	Nutritional assessment in gastrointestinal disease	691
12.2.	Diarrhoea	699
12.3.	Abdominal pain	703
12.4.	Malabsorption	705
12.5.	Assessment of pancreatic function	722
12.6.	Immunological tests in diagnosis	731
Refere	117	732
Furthe	er reading	734
OI .	PTER 12 THYROLD FUNCTION	
	PTER 13: THYROID FUNCTION	
Kayr	mond Hoffenberg	735
13.1.	Thyroid physiology	736
13.2.	Disease of the thyroid gland	742
13.3.	Thyroid function tests	746
Refere	ences	766
Further reading		768
Adden	dum	769

xv

v ivia	n H.T. James and Frederick L. Mitchell	771
14.1.	Introduction	772
14.2.	Group assays	773
14.3.	Measurements of individual steroids and production rates	778
14.4.	Assessment of adrenocortical function	783
14.5.	Aldosterone and the control of electrolyte metabolism	792
14.6.	Steroid metabolism in pregnancy, the perinatal period and in infancy	799
14.7	Investigation of androgen metabolism	812
Refere	nces	815
Furthe	r reading	820
Adden	dum	821
CHA	PTER 15: FERTILITY, PREGNANCY AND CONTRACEPTION	
R. Aı	ngus Harkness	823
15.1.	Introduction	824
15.2.	Methods of diagnosis	825
15.3.		826
15.4.		830
15.5.	Biochemical changes after oral contraceptives	841
15.6.	Conclusion	846
Refere	nces	846
Furthe	r reading	849
	PTER 16: HAEMATOLOGICAL BIOCHEMISTRY	851
israe	l Chanarin	831
16.1.	Interpretation of blood count values	853
16.2.	Assessment of iron status	855
16.3.	Assessment of megaloblastic anaemia	860
16.4.	Assessment of total haemopoiesis	866
16.5.	Assessment of white blood cell function	868
16.6.	Assessment in haemolytic states	869
16.7.	Assessment in bleeding disorders	872
16.8.	Anticoagulant therapy	876
16.9.	The anaemia of chronic disorders or secondary anaemia	876
Refere	nces	. 876
Furthe	er reading	878
	PTER 17: ABNORMAL HAEMOGLOBINS	
Rohi	n W. Carrell and Hermann Lehmann	879
KOUI		
17.1.	The haem group	880 882

•

17.3. 17.4. 17.5. 17.6.	Biosynthesis and mutation Diagnostic techniques Detection and identification of variants Specific haemoglobinopathies – investigation and interpretation	898 903 907 916
References Further reading Addendum		922 925 925
	PTER 18: INBORN ERRORS OF METABOLISM	927
D. NC	Ci Name	921
18.1.	Introduction	928
18.2.	Genetic considerations	928
18.3.	Pathogenetic mechanisms	931
18.4. 18.5.	Classification of inherited metabolic disease Inherited biochemical abnormalities not associated with disease	934 934
18.6.	Screening healthy populations for early detection of inherited metabolic disease	935
18.7.	Screening a patient for evidence of metabolic disease	936
18.8.		937
18.9.	Prenatal detection of an affected foetus	938
18.10.	Monitoring treatment	939
18.11.	Some groups of inherited metabolic diseases	942
Referen	nces	1002
	reading	1002
Addend	-	1007
	PTER 19: TRACE ELEMENTS Iliam Sunderman, Jr.	1009
19.1.	Introduction	1010
19.2.	Zinc	1010
19.3.	Соррег	1015
19.4.	Chromium	1022
19.5.	Manganese	1023
19.6.	Nickel	1025
19.7. 19.8.	Gold	1026 1029
19.8. 19.9.	Other trace metals	1029
•,,,,	ond had motal	
Referer		1030
Further	reading	1037
СНИ	PTER 20: PORPHYRINS	
		1039
	ld P. Tschudy	
20.1.	Porphyrin and haem chemistry and biochemistry	1039
20.2.	Classification of the porphyrias	1044 1044
20.3.	Clinical aspects of the porphyrias	1044

4.

		xvii
20.4.	Chemical findings in the porphyrias	1045
Refere	nces	1056
	Further reading	
CILA	DEED 21. DUDINGS AND MUCLEOTIDES	
	PTER 21: PURINES AND NUCLEOTIDES ard W.E. Watts	1059
21.1.	Biochemistry, physiology and pharmacology	1061
21.2.	Analytical considerations	1081
21.3.	The normal concentration of urate in plasma	1090
21.4.	The normal urinary excretion of uric acid	1096
21.5.	Gout	1097
21.6.	The Lesch-Nyhan syndrome	1100
21.7.	PRPP synthetase deficiency	1103
21.8.	Renal disease due to disorders of purine metabolism	1103
21.9.	Primary renal disease and uric acid disorders	1105
21.10.	Xanthinuria (congenital xanthine oxidase deficiency)	1105
21.11.	Xeroderma pigmentosum	1109
Refere	nces	1109
Furthe	r reading	1118
Adden	dum.	1119
	PTER 22: VITAMINS	
Hipo.	lito V. Niño	1121
22.1.	Introduction	1122
22.2.	Vitamin A	1124
22.3.	Vitamin D	1127
22.4.	Vitamin E	1131
22.5.	Vitamin K	1133
22.6.	Thiamine (vitamin B <sub>1</sub> )	1135
22.7.	Riboflavin (vitamin B <sub>2</sub> )	1138
22.8.	Niacin	1140
22.9.	Vitamin B <sub>6</sub>	1143
	Pantothenic acid	1144
	Biotin	1145
	Ascorbic acid (vitamin C)	1145
	Other compounds	1147
22.14.	Therapeutic applications of vitamins	1150
Refere		1152
	er reading	. 1158
Adden	dum	1159
CHI A	DTCD 22 TOVICOLOGY AND DDUC MONUTODING	
	PTER 23: TOXICOLOGY AND DRUG MONITORING	11/1
Stant	ey S. Brown and Alexander A.H. Lawson	1161
23.1.	Introduction	1162
23.2.	Basic principles of pharmacokinetics and pharmacology	1164

23.3. 23.4. 23.5. 23.6.	The case for drug monitoring and some examples Basic principles of clinical toxicology Prevalence of acute poisonings and some examples Conspectus	1172 1182 1188 1204
Referen	nces r reading	1205 1215
TUM	PTER 24: NEUROGENIC AMINES AND SECRETING OURS	
Colin	R.J. Ruthven and Merton Sandler	1217
24.1.	Introduction	1219
24.2.	The key role of monoamine oxidase	1219
24.3.	Catechol-O-methyltransferase	1222
24.4.	Catecholamines	1224
24.5.	Catecholamine-secreting tumours	1241
24.6. 24.7.	Other conditions associated with abnormal catecholamine production  Biochemical diagnosis of catecholamine-secreting tumours	1257 1260
24.7. 24.8.	Indolealkylamines	1272
24.9.	Biochemical diagnosis of carcinoid tumour	1276
	Conclusion	1277
Refere	1006	1277
	r reading	1291
CHAI	PTER 25: CANCER	
-	on K. Schwartz and Donald S. Young	1293
25.1.	Introduction	1295
25.2.	Enzymes	1296
25.3.	Hormones	1308
25.4.	Polyamines	1315
25.5.	Tumour-associated antigens	1317
25.6.	Proteins	1325 1331
25.7. 25.8.	Lipids Trace and other elements	1331
25.8. 25.9.	Miscellaneous compounds	1334
	Products of tumour metabolism	1336
	Population screening	· 1337
Refere	nces	1338
	r reading	1345
Adden		1346
Cuk:-	ot inday	1349
Subje	ct index	1347

#### Chapter 1

# **Biological variability**

# Donald S. Young

Department of Laboratory Medicine, Mayo Clinic, Rochester, MN 55901, U.S.A.

#### **CONTENTS**

1.1. Introduction	3
1.1.1. Composition of the body	3
1.1.2. The individual versus the population	5
1.1.3. Reference values	6
1.1.4. Mathematically derived normal values	6
1.2. Genetic influences	7
1.3. Long-term physiological influences	8
1.3.1. Ageing	8
1.3.1.1. Newborn	8
1.3.1.2. Childhood to puberty	12
1.3.1.3. Adult life	15
1.3.1.4. Old age	16
1.3.2. Sex	18
1.3.3. Race	19
1.3.4. Geographical location	21
1.3.4.1. Environmental temperature and climate	-22
1.3.4.2. Other environmental influences	23
1.3.5. Body build and obesity	23
1.3.6. Diet	25
1.3.6.1. Habitual diet	26
1.3.6.2. Vegetarianism	28
1.3,6,3. Synthetic diet	29
1.3.6.4. Malnutrition and protein calorie deficiency	29
1.3.6.5. Fasting and starvation	31
1.3.7. Pregnancy	35
1.3.7.1. Multiple pregnancy	40
1.3.7.2. Labour	40
1.3.7.3. Puerperium	40
1.3.8. Vasectomy	41
1.3.9. Occupation and social class	41
1.3.10. Season	42
1 2 11 Rlindness	43

Chemical diagnosis of disease, edited by S.S. Brown, F.L. Mitchell and D.S. Young © 1979 Elsevier/North-Holland Biomedical Press