

Drugs 1960-1970

Drugs 1960-1970

Editor: Graeme S.Avery



S.Karger · Basel · München · Paris · London · New York · Sydney

Originally published by Australasian Drug Information Services Pty. Ltd.
559 Sydney Road, Seaforth, N.S.W. 2092, Australia

Published exclusively by
S. Karger AG, Arnold-Böcklin-Strasse 25, CH-4000 Basel 11 (Switzerland)
in the whole world with the exception of
Australia, New Zealand, North and South America and Japan

National Library Registry No. Aus69-2994
First Edition 1969



Copyright 1969 by Australasian Drug Information Services Pty. Ltd.

This book is copyright. Apart from any fair dealing for the purposes of private study, research, criticism or review, as permitted under the Copyright Act, no part may be reproduced by any process without written permission. Inquiries should be addressed to the publishers.

Printed by Clark and Matheson Ltd., 101-107 Albert Street, Auckland, New Zealand

FOREWORD

For the past 10 years the medical profession in Australia has been helped in its work by the publication of *New Ethicals*, and for five years *New Ethicals* and *Medical Progress* has been available in New Zealand. To mark this event, *Drugs - 1960 to 1970* was sent to all doctors in both countries in September, 1969. This volume contained numerous articles, by authorities in their chosen fields, on the pharmacological actions and the therapeutic application of many products which have become available in the past 10 years.

This "therapeutic explosion" has given to the medical profession many weapons which may be double edged. On the one hand diseases previously regarded as untreatable, and for which symptomatic relief only could be given, can now have their natural history appreciably prolonged, or be actually aborted. On the other hand, the powerful pharmacological actions of many of these drugs have put into the hands of doctors chemical substances the use of which may, in certain circumstances, be fraught with danger. Particularly is this the case in relation to the interactions which may occur, for various reasons, when the metabolism of one drug affects that of another, and the amount of iatrogenic disease uncovered by monitoring systems is probably only a proportion of that which is actually present. For drugs in 1970, unlike in 1870, are not inactive placebos, effective because of other activities of the doctor, but they are agents with effects that can be beneficial when used with wisdom, but, if they are used with inadequate insight into their indications, contra-indications, and hazards, great harm can result.

The publishers are therefore to be congratulated on their decision to reprint the articles from *Drugs - 1960 to 1970* in book form, so that they can be more readily and permanently available to doctors in Australia and New Zealand, and also available to doctors elsewhere. Only good can come of this project, and, in the end, it will be the patients attending these doctors who will benefit from the spirits of wisdom so expertly distilled between these pages.

ALASTAIR G. MACGREGOR,
Professor,

Department of Therapeutics and Pharmacology,
University of Aberdeen.

December, 1969.

EDITOR

Graeme S. Avery

EDITORIAL BOARD

Chairman: Gavin S. McL. KELLAWAY, Auckland

- | | |
|----------------------------------|------------------------------------|
| T. F. ACHESON, Sydney | C. T. JONES, Auckland |
| J. W. ARDAGH, Christchurch | Priscilla KINCAID-SMITH, Melbourne |
| J. A. BAIRD, Wellington | J. W. LANCE, Sydney |
| B. G. BARRATT-BOYES, Auckland | J. H. LEE, Sydney |
| D. W. BEAVEN, Christchurch | A. W. LILEY, Auckland |
| D. G. BONHAM, Auckland | M. McGEORGE, Dunedin |
| J. S. BOYD-WILSON, Wellington | E. G. McQUEEN, Dunedin |
| E. P. BRASTED, Auckland | A. D. MACALISTER, Dunedin |
| Patricia BUCKFIELD, Dunedin | J. B. MACKAY, Wellington |
| R. CARRUTHERS, Launceston | D. S. MALCOLM, Dunedin |
| W. N. CLAY, Auckland | O. R. NICHOLSON, Auckland |
| D. S. COLE, Auckland | J. D. K. NORTH, Auckland |
| W. H. J. COLE, Melbourne | R. G. PARK, Wellington |
| J. F. COPPLESTONE, Wellington | D. W. PIPER, Sydney |
| Marion D. CRIDLAND, Sydney | W. M. PLATTS, Christchurch |
| J. A. K. CUNINGHAM, Christchurch | D. E. POSWILLO, London |
| M. H. L. de GROOT, Toowoomba | M. J. RAND, Melbourne |
| P. B. DOAK, Auckland | P. C. READE, Melbourne |
| A. E. DOYLE, Melbourne | C. G. RILEY, Christchurch |
| Keitha FARMER, Auckland | R. G. ROBINSON, Sydney |
| C. R. FENTON, Wellington | B. S. ROSE, Rotorua |
| T. GEBBIE, Wellington | N. ROYDHOUSE, Auckland |
| W. I. GLASS, Auckland | M. J. W. SANDO, Adelaide |
| G. H. GREEN, Auckland | R. J. SEDDON, Auckland |
| G. P. HALLWRIGHT, Wellington | J. G. SLOMAN, Melbourne |
| D. R. HAY, Christchurch | B. C. STRATFORD, Melbourne |
| G. C. HITCHCOCK, Auckland | P. TAFT, Melbourne |
| F. C. HOLLOWES, Sydney | D. E. M. TAYLOR, Auckland |
| C. McK. HOLMES, Dunedin | A. M. O. VEALE, Dunedin |
| W. R. HOLMES, Christchurch | J. M. WATT, Dunedin |
| R. N. HOWIE, Auckland | F. A. WHITLOCK, Brisbane |
| H. K. IBBERTSON, Auckland | S. P. WRIGHTSON, Auckland |

CONTRIBUTORS

- | | | |
|--------------------|-------------------------|-----------------|
| M. ANTHONY | P. J. HEERY | L. W. POWELL |
| P. E. BAUME | J. HIRSH | B. G. RADDEN |
| J. F. CADE | F. C. HOLLOWES | M. J. RAND |
| R. CARRUTHERS | Priscilla KINCAID-SMITH | P. C. READE |
| W. H. J. COLE | J. H. LEE | R. G. ROBINSON |
| A. R. COOKE | W. G. McBRIDE | J. H. SHERREY |
| Marion D. CRIDLAND | E. G. McQUEEN | J. G. SLOMAN |
| J. T. DOWLING | M. L. MASHFORD | B. C. STRATFORD |
| A. E. DOYLE | D. W. PIPER | P. TAFT |
| R. G. ELSMLIE | | F. A. WHITLOCK |

COMPLETE TABLE OF CONTENTS

DRUGS IN ANAESTHETIC PRACTICE

INHALATIONAL ANAESTHETIC AGENTS	2
INTRAVENOUS ANAESTHETIC AGENTS	5
MUSCLE RELAXANTS AND ANTIDOTES	8
ANALGESIC DRUGS	11
NEUROLEPTANALGESIA	12
LOCAL ANALGESIC DRUGS	12
VASOCONSTRICTORS	12
ADRENALINE ANTAGONISTS	13
SUNDRY DRUGS	13

CARDIOVASCULAR DRUGS

CORONARY ARTERY DISEASE	
Prophylaxis	16
Angina pectoris	16
Acute myocardial infarction	18
CARDIAC ARRHYTHMIAS	
Ectopic arrhythmias	19
Heart block	21
HEART FAILURE	
Digitalis	22
Diuretics	24
Potassium supplements	26
TREATMENT OF SYSTEMIC HYPERTENSION	
27	
ANTI-THROMBOTIC DRUGS	
Anticoagulant drugs	35
Other drugs preventing fibrin formation	40
THROMBOLYTIC (FIBRINOLYTIC) INHIBITORS	
41	
ORAL CONTRACEPTIVES AND THROMBO-EMBOLISM	
43	

DRUGS IN ORAL MEDICINE

TRAUMATIC ULCERS	45
ACUTE ULCERATIVE GINGIVITIS	46
HERPETIC GINGIVOSTOMATITIS	46
ORAL MONILIASIS	47
APHTHOUS ULCERATION	48

ORAL LICHEN PLANUS	49
ANGULAR CHEILITIS	49
STAINING OF TEETH DUE TO ANTIBIOTIC THERAPY	49
ENZYME THERAPY IN ORAL SURGERY	50
PATIENTS ON SYSTEMIC DRUGS FOR NON-DENTAL REASONS	50

DERMATOLOGICAL TREATMENT

ACNE VULGARIS	53
PSORIASIS	54
IMPETIGO CONTAGIOSUM	54
VARICOSE ULCERS	55
ECZEMA AND DERMATITIS	55
RINGWORM INFECTION	56
NAPKIN RASHES	58
PARONYCHIA	58
HORMONAL CONTRACEPTIVES	58
RECURRENT HERPES SIMPLEX	59
WARTS	59
ROSACEA	59
PRURITUS	60
DRUG ERUPTIONS	60
PITYRIASIS CAPITIS (DANDRUFF)	61
MISCELLANEOUS	
Aphthous ulcers	61
Chloasma	61
Miliaria rubra	62
Pityriasis versicolor	62
Cutaneous xanthomata	62
Keloids	62
Hyperkeratoses	62
Basal cell carcinomata	62

DRUGS IN EAR, NOSE AND THROAT DISEASE

UPPER RESPIRATORY INFECTIONS	65
ALLERGIC RHINITIS	67
VASOMOTOR RHINITIS	70

CONTINUED OVERLEAF

OTITIS EXTERNA	70
ACUTE OTITIS MEDIA	71
SECRETORY OTITIS MEDIA	71
CHRONIC OTITIS MEDIA	71
BELL'S PALSY	71
VERTIGO	72
MENIERE'S DISEASE	72
MOTION SICKNESS	73
OTOTOXIC DRUGS	74
DYSMORPHOGENIC DRUGS	75

DRUGS AND THE EYE

INTRA OCULAR SURGERY	77
RETINAL DISEASES	
Diabetic retinopathy	77
Hypertensive retinopathy	77
Toxoplasmosis	78
Retinal vein thrombosis and retinal vasculitis	78
OPTIC NERVE DISORDERS	
Neuro myelitis optica	78
Tobacco-toxic nutritional amblyopia	78
Cranial arteritis	79
GLAUCOMA	79
CORNEAL DISEASE	80
MISCELLANEOUS	
Thyroid eye diseases	80
Orbital pseudo-tumour	81
Auto-immune diseases	81
OCULAR COMPLICATIONS OF DRUGS	81
CORTICOSTEROIDS AND IMMUNOSUPPRESSION	81
MANAGEMENT OF OCULAR INFLAMMATION AND INFECTION	82

ENDOCRINE THERAPY

DRUGS AFFECTING CARBOHYDRATE METABOLISM	
Drugs lowering blood glucose	
Oral hypoglycaemic agents	84
New insulins	87
Drugs raising blood glucose	
Glucagon	87
Thiazides and other diuretics	88
Oral contraceptives	88
Diazoxide	88
DRUGS AFFECTING GROWTH	89
GONADOTROPHIN THERAPY IN INFERTILITY	90
THYROID DISEASE	
Hypothyroidism	91

Drugs in the treatment of thyrotoxicosis	92
OBESITY	92
DIABETES INSIPIDUS	93
ADRENOCORTICAL STEROIDS (Corticosteroids)	93
SYNTHETIC ACTH	94
ANABOLIC STEROIDS	94

DRUGS IN GASTROENTEROLOGY

STOMACH AND DUODENUM

Gastro-duodenal disease	
Antacids	97
Anticholinergic drugs	98
Carbenoxolone sodium	98
Metoclopramide	99
Toxic effects of drugs on gastric mucosa	100

HEPATO-BILIARY DISEASE

Virus hepatitis	101
Active chronic hepatitis	102
Hepatic cirrhosis	102
Hepatic enzyme induction by drugs	103

HEPATIC REACTIONS TO DRUGS

THE USE OF DRUGS IN THE PATIENT WITH LIVER DISEASE	104
-------------------------------------------------------------	-----

ACUTE PANCREATITIS

Pain relief	105
Pancreatic rest	105
Antibiotics	105
Antitryptics	106
Fluids and electrolytes	106

CHRONIC PANCREATITIS

SMALL AND LARGE BOWEL DISEASE

Topical sprue	108
Bowel infections	108
Crohn's disease	108
Ulcerative colitis	109
Other conditions	
Neurogenic disorders	109
Fat malabsorption	109
Toxic reactions of drugs on small and large intestine	110

DRUGS IN NEUROLOGICAL DISEASE

FACIAL PAIN	
Trigeminal neuralgia	115

CONTINUED OVERLEAF

Post herpetic neuralgia	116
Migrainous neuralgia	116
"Lower half" headache	117
Atypical facial pain	117
MIGRAINE	117
CONVULSIVE DISORDERS	120
PARKINSONISM	125
ANTICOAGULANTS IN CEREBROVASCULAR DISEASE	129
ORAL CONTRACEPTIVES AND CEREBROVASCULAR DISEASE	131
DEMYELINATING DISEASE	
Multiple sclerosis	132
Optic neuritis	132

DRUGS IN OBSTETRICS AND GYNAECOLOGY

HORMONAL CONTRACEPTIVES	136
INDUCTION OF OVULATION	138
IMMUNOLOGICAL TESTS FOR PREGNANCY	138
DRUGS IN PREGNANCY	139
HAEMATINICS	139
DIURETICS	140
ANTIHYPERTENSIVE DRUGS	140
URINARY TRACT INFECTIONS IN PREGNANCY	141
ANTICOAGULANTS	141
PROGESTIN THERAPY IN PREGNANCY	141
OXYTIC DRUGS IN OBSTETRICS	142
INHIBITORS OF UTERINE ACTION	142
ANAESTHESIA AND ANALGESIA	142
ANTI D GAMMA GLOBULIN	143
SUPPRESSION OF LACTATION	143
ENDOMETRIOSIS	144
DRUGS IN THE MENOPAUSE	144
VAGINITIS	145
ENDOMETRIAL CANCER	146
ANTINEOPLASTICS	146

PSYCHOTROPIC DRUGS: DRUG ABUSE

CLASSIFICATION OF PSYCHOTROPIC DRUGS	148
ANTIPSYCHOTICS	149
ANTIDEPRESSANTS	150
AGENTS FOR THE TREATMENT OF MANIA	151
ANTI-ANXIETY AGENTS	151
DRUG ABUSE	152

DRUGS IN RENAL DISEASE

URINARY TRACT INFECTION	160
GLOMERULONEPHRITIS	161
NEPHROTIC SYNDROME	162
OTHER FORMS OF TREATMENT AIMED SPECIFICALLY AT THE UNDERLYING RENAL LESION	
Collagen or autoimmune diseases	163
Gout and uric acid nephropathy	164
Cystinuria	164
Hypertension	164
Diuretics	165
DRUGS IN RENAL FAILURE	
Salt	166
Anabolic steroids	166
Hyperphosphataemia	166
Dosage of other drugs in renal failure	167
RENAL TRANSPLANTATION	167
ANALGESICS	167

DRUGS IN RESPIRATORY DISEASES

BRONCHIAL ASTHMA	170
Bronchodilators	
Sympathomimetic agents	171
Xanthine derivatives	172
Corticosteroids	173
Bronchial asthma, allergy and disodium cromoglycate	174
Drug therapy and asthma—special considerations	176
CHRONIC BRONCHITIS	177
BRONCHIECTASIS AND CYSTIC FIBROSIS	178
PNEUMONIA	179
TUBERCULOSIS	180

DRUGS IN RHEUMATIC DISEASES

PAIN AND ANALGESICS	182
INFLAMMATION AND ANTI-INFLAMMATORY DRUGS	183
ANTI-GOUT DRUGS	191
DISEASE MANAGEMENT	
Rheumatoid arthritis	191
Ankylosing spondylitis	191
Osteoarthritis	191
Gout	192
ANTICIPATED PROGRESS	192

ANTIMICROBIAL AGENTS**THE DRUGS THEMSELVES**

The penicillin group of drugs	195
The cephalosporins	197
The polymyxins	198
The neomycin group of drugs	198
The macrolide group of antibiotics	200
The tetracycline group of drugs	200
Other antibiotics	
Chloramphenicol	201
Fusidic acid	201
Rifamide	201
Lincomycin	201
Vancomycin	202

CHEMOTHERAPY OF FUNGAL

INFECTIONS	202
Candida infections	202
Aspergillosis, blastomycosis, cryptococcosis, histoplasmosis, coccidioidomycosis	202
Dermatophyte infections	203

NON ANTIBIOTIC ANTIMICROBIALS

Sulphonamide derivatives	203
Trimethoprim plus sulphonamides	204
Nitrofurantoin and nalidixic acid	204

CHEMOTHERAPY OF TUBERCULOSIS

Principles	204
New drugs	205
Guide lines to use of antituberculosis drugs	206

CHEMOTHERAPY OF VIRAL INFECTIONS

Vaccines	205
Drug treatment	207

SOME FINAL COMMENTS

The Gram stain	208
Topical antibiotic therapy	208
Combined antibiotic therapy	208
The laboratory	208
Empirical chemotherapy	209

**DRUGS FOR EMPIRICAL TREATMENT
OF COMMON DISEASES****IMMUNOSUPPRESSIVE AND
ANTINEOPLASTIC DRUGS****GENERAL**

Cytotoxicity	211
Choice of drug	211
Dose schedule	212

THE DRUGS

Alkylating agents	212
Vinca rosea alkaloids	212

Antimetabolites	212
Antibiotics	213
Others	213

THE DISEASES

Acute leukaemia	213
Chronic lymphocytic leukaemia	214
Chronic granulocytic leukaemia	215
Polycythaemia vera	216
Myelofibrosis	216
Hodgkin's Disease	216
Lymphosarcoma and follicular lymphoma	217
Reticulum cell sarcoma	218
Myelomatosis	218
The carcinomas	219
Burkitt's tumour	219
Perfusion, infusion and cancer surgery	219
Non-neoplastic conditions	219
HORMONES	220

DRUG POISONING

BARBITURATES	223
FORCED ALKALINE DIURESIS IN SALICYLATE POISONING	226
PSYCHOTROPIC AGENTS	227
TRICYCLIC ANTIDEPRESSANTS	227
POISONING WITH MONOAMINE OXIDASE INHIBITORS	229
PRESCRIPTION OF PSYCHOTROPIC DRUGS	229
HALLUCINOGENIC DRUGS	230
MISCELLANEOUS DRUGS	
Paracetamol	231
Oral hypoglycaemic agents	231
Antituberculosis drugs	231
Antihistamines	231
Methaqualone with diphenhydramine	231
Iron	231

**RESEARCH IN THE
PHARMACEUTICAL INDUSTRY****DRUG RESEARCH IN THE
UNIVERSITY****DRUG TRIALS**

LIST OF CONTRIBUTORS

MICHAEL ANTHONY, M.D., M.R.C.P., M.R.A.C.P.

The Division of Neurology, Prince Henry Hospital and the School of Medicine, University of New South Wales, Sydney, N.S.W., Australia.

P. E. BAUME, M.D., M.R.A.C.P.

Honorary Assistant Physician, The Royal North Shore Hospital of Sydney, N.S.W., Australia.

J. F. CADE, M.D., M.R.A.C.P.

Respiratory Unit and Department of Medicine, Royal Melbourne Hospital, Victoria, Australia.

RONALD CARRUTHERS, M.B., Ch.B.

Honorary Dermatologist, Launceston General Hospital, Tasmania, Australia.

W. H. J. COLE, M.B., B.S., D.A., F.F.A.R.A.C.S., M.Sc.

Royal Melbourne Hospital, Victoria, Australia.

A. R. COOKE, M.B., M.R.A.C.P.

Research Fellow of the National Health and Medical Research Council of Australia, A. W. Morrow Unit of Gastroenterology, Royal Prince Alfred Hospital, Sydney, N.S.W., Australia.

MARION D. CRIDLAND, M.B., B.S., B.Sc.(Med).

Royal Prince Alfred Hospital, Sydney, N.S.W., Australia.

JOHN T. DOWLING, M.R.A.C.P.

Cardiology Department, Royal Melbourne Hospital, Victoria, Australia.

AUSTIN E. DOYLE, M.D., B.S.(Lond.), F.R.A.C.P., F.R.C.P.

Professor of Medicine, University of Melbourne, Department of Medicine, Austin Hospital, Heidelberg, Victoria, Australia.

R. G. ELMSLIE, M.D., F.R.A.C.S.

Reader in the Department of Surgery, in the University of Adelaide, Queen Elizabeth Hospital, Adelaide, South Australia, Australia.

P. J. HEERY, M.B., B.S., F.R.C.S.

The Association of Medical Directors of the Australian Pharmaceutical Industry.

J. HIRSH, M.D., M.R.A.C.P.

Department of Medicine, St. Vincent's Hospital, Victoria, Australia.

F. C. HOLLOWS, M.B., Ch.B.(N.Z.), F.R.C.S., D.O.(Lond.).

Associate Professor of Ophthalmology, Department of Ophthalmology, the Prince of Wales Hospital and the University of New South Wales School of Surgery, Sydney, Australia.

PRISCILLA KINCAID-SMITH, B.Sc., M.D., F.R.C.P., F.R.A.C.P., D.C.P.

Reader in Medicine, University Department of Medicine and Physician in Charge, Renal Unit, Royal Melbourne Hospital, Victoria, Australia.

J. H. LEE, M.B., B.S., M.R.A.C.P.

Honorary Assistant Physician, Royal Prince Alfred Hospital, Sydney, N.S.W. Australia.

WILLIAM G. McBRIDE, M.D., F.R.C.O.G.

The Womens Hospital, Sydney, N.S.W., Australia.

E. G. McQUEEN, F.R.A.C.P.

Associate Professor of Clinical Pharmacology, Department of Pharmacology and Pharmacy, University of Otago. Director, National Poisons Information Centre, Dunedin, New Zealand.

M. L. MASHFORD, M.B., B.S., M.R.A.C.P.

Reader in Applied Pharmacology in the Departments of Pharmacology and Medicine (Austin Hospital Clinical School), University of Melbourne, Parkville, Victoria, Australia.

D. W. PIPER, M.D., F.R.A.C.P.

Associate Professor of Medicine, University of Sydney and Honorary Physician, Royal North Shore Hospital of Sydney, N.S.W., Australia.

L. W. POWELL, M.D., M.R.A.C.P.

Senior Lecturer, Department of Medicine, University of Queensland, Royal Brisbane Hospital, Brisbane, Queensland, Australia.

BRYAN G. RADDEN, B.D.Sc.(W.A.), M.D.Sc., Ph.D.(Lond.), F.D.S.R.C.S.

Reader in Oral Pathology, Department of Dental Medicine and Surgery, University of Melbourne, Victoria, Australia.

M. J. RAND, B.Sc., M.Sc., Ph.D.

Professor of Pharmacology, Department of Pharmacology, University of Melbourne, Parkville, Victoria, Australia.

PETER C. READE, M.D.S.(Adel.), M.D.Sc., Ph.D.(Adel.), F.D.S.R.C.S.

Professor of Dental Medicine and Surgery, University of Melbourne, Melbourne, Victoria, Australia.

R. G. ROBINSON, M.B., B.S.

Royal North Shore Hospital, Sydney, Australia.

J. H. SHERREY, M.B., D.L.O., F.R.C.S. (C).

Honorary Surgeon to the Ear, Nose and Throat Department, Royal Hobart Hospital, Hobart, Tasmania, Australia.

GRAEME SLOMAN, B.Sc., F.R.C.P.(Edin.), F.R.A.C.P., M.R.C.P.(Lond.).
Cardiology Department, Royal Melbourne Hospital, Victoria, Australia.

BRYAN C. STRATFORD, E.D., M.D.(Melb.), M.R.A.C.P., M.C.P.A.,
M.C.Path.(Lond.).
Director of Microbiology, St. Vincent's Hospital, Melbourne, Victoria, Australia.

PINCUS TAFT, M.D., F.R.A.C.P.
Physician-In-Charge, Ewen Downie Metabolic Research Unit, Alfred Hospital,
Melbourne, Victoria, Australia.

F. A. WHITLOCK, M.A., M.D., M.R.C.P., D.P.M.
Professor of Psychological Medicine, Department of Psychological Medicine,
University of Queensland, Brisbane, Queensland, Australia.

CONTENTS

DRUGS IN ANAESTHETIC PRACTICE

W. H. J. Cole, M.B., B.S., D.A., F.F.A.R.A.C.S., M.Sc. 1

CARDIOVASCULAR DRUGS

J. F. Cade, M.D., M.R.A.C.P., John T. Dowling, M.R.A.C.P.,
J. Hirsh, M.D., M.R.A.C.P. and
Graeme Sloman, B.Sc., F.R.C.P.(Edin.), F.R.A.C.P., M.R.C.P.(Lond.) 15

DRUGS IN ORAL MEDICINE

Peter C. Reade, M.D.S.(Adel.), M.D.Sc., Ph.D.(Adel.), F.D.S.R.C.S. and
Bryan G. Radden, B.D.Sc.(W.A.), M.D.Sc., Ph.D.(Lond.), F.D.S.R.C.S. 44

DERMATOLOGICAL TREATMENT

Ronald Carruthers, M.B., Ch.B. 52

DRUGS IN EAR, NOSE AND THROAT DISEASE

J. H. Sherrey, M.B., D.L.O., F.R.C.S. (C). 64

DRUGS AND THE EYE

F. C. Hollows, M.B., Ch.B.(N.Z.), F.R.C.S., D.O.(Lond.). 76

ENDOCRINE THERAPY

Pincus Taft, M.D., F.R.A.C.P. 84

DRUGS IN GASTROENTEROLOGY

D. W. Piper, M.D., F.R.A.C.P., A.R. Cooke, M.B., M.R.A.C.P.,
L. W. Powell, M.D., M.R.A.C.P., R. G. Elmslie, M.D., F.R.A.C.S. and
P. E. Baume, M.D., M.R.A.C.P. 96

DRUGS IN NEUROLOGICAL DISEASE

Michael Anthony, M.D., M.R.C.P., M.R.A.C.P. 114

DRUGS IN OBSTETRICS AND GYNAECOLOGY

William G. McBride, M.D., F.R.C.O.G. 135

CURRENT STATUS OF PSYCHOTROPIC DRUGS AND DRUG ABUSE

F. A. Whitlock, M.A., M.D., M.R.C.P., D.P.M. 147

DRUGS IN RENAL DISEASE

Priscilla Kincaid-Smith, B.Sc., M.D., F.R.C.P., F.R.A.C.P., D.C.P. 159

DRUGS IN RESPIRATORY DISEASES

J. H. Lee, M.B., B.S., M.R.A.C.P. 169

DRUGS IN RHEUMATIC DISEASES

R. G. Robinson, M.B., B.S. 181

ANTIMICROBIAL AGENTS

Bryan C. Stratford, E.D., M.D.(Melb.), M.R.A.C.P., M.C.P.A.,
M.C.Path.(Lond.) 194

IMMUNOSUPPRESSIVE AND ANTINEOPLASTIC DRUGS

Marion D. Cridland, M.B., B.S., B.Sc.(Med.) 210

DRUG POISONING

E. G. McQueen, F.R.A.C.P. 222

RESEARCH IN THE PHARMACEUTICAL INDUSTRY

P. J. Heery, M.B., B.S., F.R.C.S. 233

DRUG RESEARCH IN THE UNIVERSITY

M. J. Rand, B.Sc., M.Sc., Ph.D. and
M. L. Mashford, M.B., B.S., M.R.A.C.P. 242

DRUG TRIALS

Austin E. Doyle, M.D. B.S.(Lond.), F.R.A.C.P., F.R.C.P. 248

SUBJECT INDEX

257

DRUGS IN ANAESTHETIC PRACTICE

W. H. J. COLE*, M.B., B.S., D.A., F.F.A.R.A.C.S., M.Sc.

Summary: The last decade has been notable for the large number of valuable drugs of all kinds which have been introduced into anaesthetic practice.

Halothane is a satisfactory inhalational anaesthetic agent which combines lack of respiratory tract irritation, rapid postoperative recovery and a low incidence of vomiting. Methoxyflurane is a respiratory tract irritant, but it has analgesic properties and the capacity to produce muscular relaxation which exceed those of halothane.

Five valuable intravenous anaesthetic agents have been developed; methohexitone, propanidid, gamma hydroxy sodium butyrate, diazepam and ketamine. Choice can now be exercised in relation to duration of action, respiratory stimulation or depression and circulatory stimulation or depression.

Alcuronium and pancuronium are two competitively blocking muscle relaxants. Both cause an increase in heart rate, but the immediate effect of alcuronium on the blood pressure is to cause a fall, while pancuronium causes an elevation.

Tacrine and hexaflurenium are anticholinesterase drugs capable of potentiating and extending the duration of action of suxamethonium.

New morphine-like analgesic drugs include phenazocine, dextromoramide, phenoperidine, fentanyl, and propoxyphene. These vary in potency, duration of action and in dependence potential. Pentazocine, an analgesic related to nalorphine, does not produce euphoria and like propoxyphene is considered non-dependence producing.

The neuroleptic drug droperidol, when given with an analgesic, usually either fentanyl or phenoperidine, produces a state of neuroleptanalgesia in which the patient is unperturbed by his surroundings and insensitive to discomfort.

New local analgesics are mepivacaine, which has a quick onset of action with a slightly longer duration of effect than lignocaine; bupivacaine which has an even longer duration of action; and prilocaine which has a lower toxicity relative to analgesic potency than comparable drugs.

Felypressin, an octapeptide vasoconstrictor used for infiltration at an operation site, does not cause as much circulatory stimulation as adrenaline and is said not to act adversely on the heart in the presence of halothane.

*Royal Melbourne Hospital, Victoria, Australia.

Propranolol and other beta-receptor blocking drugs are of value in treating the effects of accidental overdose of adrenaline or noradrenaline, or of excessive endogenous catecholamine production.

Trimeprazine has sedative, anti-emetic and antihistaminic effects intermediate in degree between promethazine and chlorpromazine. Prochlorperazine and thiethylperazine are anti-emetic drugs of considerable value in postoperative vomiting.

Doxapram, although a respiratory stimulant, is not a specific antagonist to any particular drug.

INTRODUCTION

The last decade has been remarkable for the extraordinarily large number of drugs of all types which have been introduced into anaesthetic practice. In considering the history of development of anaesthesia it can be observed that the discovery of new drugs and agents has not proceeded at a uniform rate. From 1840 to 1850 nitrous oxide, ether, chloroform and ethyl chloride were used, but it was over 80 years before any new general anaesthetic agents were added that were to have a permanent place in the practice of anaesthesia. During the years 1930 to 1935 a great increase in knowledge occurred with the introduction of hexobarbitone, thiopentone ('Intraval', 'Pentothal'), cyclopropane, and trichloroethylene ('Trilene'), with the result that anaesthesia became firmly established as a medical specialty. It is of interest that the Association of Anaesthetists of Great Britain and Ireland was founded in 1933, and the Australian Society of Anaesthetists in 1935. Since 1935 new discoveries have appeared at an accelerated rate and it is proposed to discuss those compounds introduced since 1959.

INHALATIONAL ANAESTHETIC AGENTS

HALOTHANE ('Fluothane')

Halothane was the first, and probably the most important inhalational agent to be introduced in this period. It was synthesised by Dr Suckling, in 1956, and tested on animals by Dr Raventes. Clinical trials were carried out by Johnstone (1956) in Manchester, and by Bryce-Smith and O'Brien (1958) at Oxford. Clinical testing in Australia commenced in 1957, but halothane was not available for unrestricted sale till 1959 or 1960.

Halothane has been spectacularly successful since it was introduced with the result that it has become the most widely used "potent" inhalational anaesthetic agent in the world, and the standard by which other agents are judged. The reasons for this extensive usage include the overall satisfactory properties of halothane, the lack of respiratory tract irritation which facilitates induction, the extraordinarily low rate of postoperative vomiting, and the property of non-inflammability.

Initially the matter of vaporisation of halothane proved a problem since none of the existing vaporisers were suitable. Halothane which has a boiling point of 51°C gives rise to a vapour concentration of about 30 per cent by volume at room temperature. As halothane vapour of this strength is dangerous, safe usage necessitated the development of vaporisers which

would deliver accurately known concentrations of vapour, with a maximum concentration which was limited to a strength that could be safely used. Such a vaporiser was made by the Cyprane Company of Great Britain, and marketed under the name of 'Fluotec'. It rapidly became popular and other similar vaporisers have since been made. An alternative type of vaporiser is that described by Professor Lucien Morris as the "Copper Kettle".

When administered in a suitable concentration with nitrous oxide and oxygen or oxygen alone, halothane is a quickly acting anaesthetic agent. Excitement during induction is uncommon. Halothane is not a respiratory tract irritant, and does not stimulate mucus secretion or promote bronchospasm. When surgical depth of anaesthesia has been established there is usually some depression of respiration in which tidal volume is reduced, often with an increase in rate of respiration. Blood pressure usually falls to below pre-anaesthetic levels often with a slowing of heart rate. The heart is sensitised to the action of adrenaline and noradrenaline. Muscular relaxation of the extremities is complete, but a loss of tone sufficient for abdominal surgery is attainable only with relatively high concentration of halothane.

When administration is ceased recovery occurs rapidly, unless high concentrations have been used or the administration has been prolonged. Post-operative vomiting, before the return of consciousness is rare. Shivering is apt to occur in the post-operative period, especially if the weather is cold.

In 1963 cases of post-operative jaundice occurred in which halothane was thought to have a causal relation. Subsequent exhaustive studies showed that while post-operative jaundice was a fairly common condition the use of halothane was not associated with an increased incidence. Nevertheless cases have occurred in which the association of liver damage with the inhalation of halothane has strongly suggested the occurrence of a sensitisation as in the case exhaustively reported by Klatskin and Kimberg (1969).

While halothane is usually administered from standard anaesthetic machines with or without carbon dioxide absorption it can also be given with oxygen alone or with air and oxygen from quite simple equipment. Under armed service conditions or in remote parts of the world this possibility can be a definite advantage.

In addition, halothane is easily the best inducing agent yet available for use, either with or without an intravenous anaesthetic agent, before the irritating vapours of ether, trichloroethylene or methoxyflurane. In this respect it supersedes ethyl chloride.

METHOXYFLURANE ('Penthrane')

Methoxyflurane was developed several years after halothane (Artusio et al., 1960). It is a non-inflammable halogenated ethyl, methyl ether, and like all ethers which have been used in anaesthetic practice it is a respiratory tract irritant. This feature combined with the high boiling point of 104.7°C of methoxyflurane and the consequently low vapour concentration tends to make induction of anaesthesia slow, and if the patient has poor lung function with a tendency to cough this period can be quite difficult. Fortunately the problem can be overcome, either by interposing the inhalation of halothane between the injection of an intravenous anaesthetic agent and the