

METHODOLOGY for ANALYTICAL TOXICOLOGY

I. Sunshine



Methodology for Analytical Toxicology

Editor

Irving Sunshine

Chief Toxicologist
Cuyahoga County Coroner's Office
Cleveland, Ohio
Professor of Toxicology
Institute of Pathology, School of Medicine
Case Western Reserve University
Cleveland, Ohio





Published by

CRC PRESS, Inc.
2255 Palm Beach Lakes Blvd. · West Palm Beach, Florida 33409

Library of Congress Cataloging in Publication Data

Main entry under title:

Methodology for analytical toxicology.

At head of title: CRC.

Includes bibliographies and index.

1. Poisons — Analysis. 2. Toxicology — Laboratory manuals. I. Sunshine, Irving. II. Chemical Rubber Company, Cleveland.

RA1221.M44

A1221.W44

615.9'07

74-30747

ISBN 0-8493-0716-3 Former ISBN 0-87819-716-8

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© 1975 by CRC Press, Inc. 2nd Printing, April 1978 CRC Press, Inc.

Revised from CRC Handbook of Analytical Toxicology
© 1969 by The Chemical Rubber Co.

International Standard Book Number 0-8493-0716-3 Former International Standard Book Number 0-87819-716-8

Library of Congress Card Number 74-30747
Printed in the United States

Methodology for Analytical Toxicology

PREFACE TO METHODOLOGY FOR ANALYTICAL TOXICOLOGY

The current and growing interest in determinations for anticonvulsant drugs, digoxin and digitoxin, procaine amide, lidocaine, and theophylline indicates that monitoring drug therapy is an increasing challenge to clinical laboratory scientists. Physicians are anxious to have this laboratory support which they can use to better understand a patient who has not achieved the expected results from a prescribed therapeutic regimen. Among the several questions related to this problem are these. Was the patient taking the drug? Was the prescribed dose sufficient? Was the patient taking some other medication which could affect his proper utilization of the prescribed drug? (Polypharmacology is practiced by many, and seldom do they deem it necessary to inform the physician that they are taking medications other than those he prescribed.)

One of the objectives of this volume is to present acceptable methods for the analysis of therapeutic agents in biological fluids. By utilizing these procedures, the chemist can provide the physician with objective laboratory data which can be used to answer some of the questions postulated above. In the several laboratories where these analyses have been instituted the demand for them has been overwhelming. One of the contributions of this volume is to present the analyst with several methods for the analysis of therapeutic agents and present the physician with reasonable interpretations of the results.

Procedures for many substances have been included in this volume so that methods for the analysis of the many products involved in acute poisonings are more easily available to those who want to use them. The described methods are the essence of the pragmatic experience of many active analysts. They will yield a reasonable result when carried out exactly as described in the text. Subsequently, some may wish to modify these methods to suit their local needs; however, this should be done only after establishing that the proposed modifications are preferable. The exception to this rule must be those methods which use gas chromatography. Many different columns are described, and no laboratory should have access to all of them. Hence, the reader is advised to become familiar with the columns he has available and expand their use for as many substances as he can. A table of McReynold's Constants has been included in the text. Using this, one should be able to determine which column packings are comparable and interchangeable.

In many instances a given procedure is really a prototype for many other chemically related substances. The expanded index, therefore, indicates all the so-called "interferences" to a given procedure. If a substance is listed as interfering with a given determination, it may be determinable by the same procedure, providing the prototype is not present. One should verify this and then proceed with the analysis.

The problem for some laboratories dealing with the analysis of specimens from patients involved in acute poisonings is that the causative agent may not be known. To help resolve this problem the second section of this volume presents several approaches to the systematic analysis of a biological fluid. The approach one chooses depends on local facilities. To encompass most, procedures are described which require a minimum of special equipment (TLC), some commonly available instruments (spectrophotometry), or gas chromatography (a technique rapidly growing in popularity and value). The more experimental liquid chromatographic techniques and the more elegant, sophisticated combination of gas chromatography and mass spectrometry are not presented. Too few laboratories now have this potential, but probably the next revision of this material will find these techniques commonplace.

Coupled with the revised or new procedures are updated assessments of the interpretation of the laboratory values. Significant data have been elaborated in recent years. These results are included in the presentation, as are recent literature citations so that the readers so inclined may seek them out and digest them at leisure.

I.S.

PREFACE TO THE MANUAL OF ANALYTICAL TOXICOLOGY

Published by the Chemical Rubber Co., 1971.

A growing number of requests for toxicological analyses is being made by physicians in order to establish whether or not particular patients may have been poisoned. This is understandable, because the signs and symptoms seen in acutely ill patients are not pathognomonic of exposure to a specific exogenous chemical agent, and a reliable history of an exposure to a toxic chemical often cannot be obtained. Thus, a correct diagnosis of poisoning frequently depends on the result of a chemical analysis of a biological specimen obtained from a patient. Simple and reliable methods for these analyses are not readily available for use in clinical chemistry laboratories. This book proposes to assemble and present a number of such methods.

The comprehensive toxicological treatises that have been published to date present many methods for the analysis of toxic substances. Unfortunately, their multiplicity often leaves the clinical chemist perplexed. Which of the many methods should he use in his laboratory? This volume is designed to answer that question. The basic principles of the many published methods will not be discussed, but details of some carefully selected and tested procedures will be presented.

The choice of the described methods was based on many factors, including reliability, the availability of equipment and reagents, the simplicity of the procedure, and the relative speed with which an informative result can be obtained. These methods are mainly personal modifications of procedures originally developed by others. When applied exactly as described, they will produce meaningful and reliable data.

Three types of methods were planned for each substance: Type A, a simple, direct, and qualitative test; Type B, a quantitative procedure using facilities found in the average laboratory; and Type C, an elegant, precise procedure using whatever equipment may be required. This goal was not realized for many obvious reasons and remains as a challenge for subsequent volumes.

Because the interpretation of the results obtained from these analyses will not be within the common experience of many readers, a summary of the reported correlations between the clinical condition of the patient and the concentration of the toxic agent in a relevant specimen will be given. More detail can be obtained by referring to the bibliobraphy following each method. The interpretive data will interest not only toxicologists, clinical chemists, and clinical pathologists, but also all physicians who face the problem of treating a symptomatic patient purportedly poisoned by the most frequently offending drugs, household products, and economic poisons.

No extensive effort will be made to present methods that are primarily concerned with industrial toxicology and the evaluation of occupational hazards.

CONTRIBUTORS

This manual could never have been prepared without the help of the contributing authors. I and every reader of this volume are indebted to each of them for their time and effort. The procedures they contributed represent their considered judgment on an acceptable, reproducible, and reliable method for the substance involved.

John K. Abbott, B.A.

Chemist
Federal Aviation Administration, DOT
P.O. Box 25082
Oklahoma City, Oklahoma 25082

Vijay Aggarwal, B.A.

Toxicologist
Bureau of Forensic Science
1 North 14th Street
Richmond, Virginia 23219

Steve Andryauskas

Senior Chemist
Office of Chief Medical Examiner
520 First Avenue
New York, New York 10016

Joseph S. Annino, B.S.

Director Clin-Chem Laboratories 1106 Commonwealth Avenue Boston, Massachusetts 02215

David N. Bailey, M.D.

Clinical Fellow
Yale University School of Medicine
Box 1001
New Haven, Connecticut 06510

John R. Barnes, Ph.D.

Section Chief, Biochemistry Section
Haskell Laboratory of Industrial Medicine
and Toxicology
Elkton Road
Newark, Delaware 19711

Frank E. Barnhart, B.S.

Forensic Toxicologist San Diego County Coroner's Office Laboratory 5555 Overland Avenue San Diego, California 92123

Milton L. Bastos, Ph.D.

Director of Toxicology
Office of the Chief Medical Examiner
520 First Avenue
New York, New York 10016

Raymond J. Bath, Ph.D.

Chief Toxicologist
Bureau of Forensic Science
1 North 14th Street
Richmond, Virginia 23219

David J. Berry, L.R.I.C.

Chief Technician
Poisons Unit, New Cross Hospital
Avonley Road
London, S.E. 14, England

Robert V. Blanke, Ph.D.

Professor of Pathology and Director of Toxicology Laboratory Virginia Commonwealth University Box 696, MCV Station Richmond, Virginia 23298

Paul B. Bondo, M.S.

Research and Development Chemist South Bend Medical Foundation 531 North Main Street South Bend, Indiana 46601

Robin A. Braithwaite, A.R.I.C., Ph.D.

Senior Clinical Biochemist Poisons Unit, New Cross Hospital Avonley Road London, S.E. 14, England

Robert D. Budd, B.S.

Toxicologist Rancho Los Amigos Hospital 7601 East Imperial Highway Downey, California 90242

Wing Chan, M.S.

Chemist New York City Department of Health 125 Worth Street New York, New York 10013

Claude Charette, Dipl. Technol.

Chemical Technologist
Department of National Health and Welfare
Health Protection Branch
Ottawa, Ontario, Canada K1A OL2

George Cimbura, M.Sc.Phm.

Head, Toxicology Section
The Centre of Forensic Sciences
8 Jarvis Street
Toronto, Ontario, Canada M5E 1M8

John Cooper, Dipl. Technol.

Biochemical Technologist
Department of National Health and Welfare
Health Protection Branch
Ottawa, Ontario, Canada K1A OL2

Charles Russell Crane, Jr., Ph.D.

Chief, Biochemistry Research Civil Aeromedical Institute, DOT, FAA P.O. Box 25082 Oklahoma City, Oklahoma 73125

Robert H. Cravey, B.S.

Toxicologist
Office of the Sheriff-Coroner
550 North Flower Street
Santa Ana, California 92702

Bernard Davidow, Ph.D.

Assistant Commissioner for Laboratories City of New York Department of Health 455 First Avenue New York, New York 10016

Walter A. Dechtiaruk, B.S.

Chemist, Senior Associate
Department of Laboratory Medicine
601 North Broadway
Baltimore, Maryland 21205

Kurt M. Dubowski, Ph.D.

Professor, Clinical Chemistry and Toxicology, and Director, Toxicology Laboratories University of Oklahoma Health Sciences Center P.O. Box 26901 Oklahoma City, Oklahoma 73190

Leslie Eidus, M.D.

Director, Bureau of Bacteriology Laboratory Centre for Disease Control Health and Welfare Canada Ottawa, Ontario, Canada K1A 0L2

John Epton, M.Sc.

Biochemist Regional Toxicology Laboratory Dudley Road Hospital Birmingham, England

Milton Feldstein, M.A., M.S.

Deputy Air Pollution Control Officer Bay Area Air Pollution Control District 939 Ellis Street San Francisco, California 94103

Frank J. Fernandez, B.S.

Applications Chemist
Perkin-Elmer Corporation
Main Avenue
Norwalk, Connecticut 06856

Bryan S. Finkle

Toxicologist Center for Human Toxicology University of Utah Salt Lake City, Utah 84112

Arthur J. Fisk. B.S.

Director of Laboratories Dade County Medical Examiner's Office 1700 N.W. 10th Avenue Miami, Florida 33136

Robert Forney, Jr., Ph.D.

Instructor
Case Western Reserve University
2065 Adelbert Road
Cleveland, Ohio 44106

A. W. Freireich, M.D.

Consulting Toxicologist
Nassau County Medical Examiner
P.O. Box 160
East Meadow, New York 11554

James C. Garriott, Ph.D.

Chief Toxicologist
Dallas County Institute of Forensic Sciences
5230 Medical Center Drive
Dallas, Texas 75235

Franklin D. Griffith, Ph.D.

Toxicologist
3M Company
3M Center, Medical Department
St. Paul, Minnesota 55101

Jeffrev Grove, A.R.I.C.

Senior Biochemist
Nicholas Laboratories Ltd.
225 Bath Road
Slough, Berks, England SL1 4AV

J. V. Halliwell, B.Sc.

Chemist
Poisons Unit, Guy's Hospital
St. Thomas Street
London, S.E.1., England

Horace E. Hamilton, M.S.

Instructor, Department of Pathology University of Texas Health Science Center 7703 Floyd Curl Drive San Antonio, Texas 78284

Bette L. Hamman, M.S.

Chief Toxicologist National Health Laboratory 653 North Glebe Road Arlington, Virginia 22203

Keith B. Hammond, M.S.

Director and Senior Instructor in Pediatrics University of Colorado Medical Center 4200 East 9th Avenue Denver, Colorado 80220

Jesse A. Hancock, Ph.D. (Deceased)

Professor of Clinical Chemistry and Toxicology The University of Texas at El Paso P.O. Box 180 El Paso, Texas 79999

Anita Harnanansingh, B.S.

Chemist
Laboratory Centre for Disease Control
Health and Welfare Canada
Ottawa, Ontario, Canada K1A 0L2

Wayne H. Harrington, Ph.D.

Assistant Professor Chemistry Department Cleveland State University Cleveland, Ohio 44115

Norman W. Henry III, B.A.

Chemist
Haskell Laboratory of Industrial Medicine
and Toxicology
Elkton Road
Newark, Delaware, 19711

Bradford R. Hepler, B.S.

Assistant Director, Special Chemistry Branch Clinical Pathology Services Wilford Hall Medical Center Lackland AFB, Texas 78236

Jocelyn M. Hicks, Ph.D.

Acting Director Clinical Laboratories, Children's Hospital National Medical Center 2125 13th Street, N.W. Washington, D.C. 20009

Mary M. Hodgkin, B.Sc.

Chemist Laboratory Centre for Disease Control Health and Welfare Canada Ottawa, Ontario, Canada K1A 0L2

Naresh C. Jain, Ph.D.

Director of Toxicology Rancho Los Amigos Hospital 7601 East Imperial Highway Downey, California 90242

Peter Jatlow, M.D.

Associate Professor, Department of Laboratory Medicine Yale University School of Medicine 789 Howard Street New Haven, Connecticut 06504

George Johnson, Ph.D.

Clinical Chemist
The Johns Hopkins Hospital
601 North Broadway
Baltimore, Maryland 21205

Susan H. Jones, B.A.

Technician
Dallas County Institute of Forensic Sciences
5230 Medical Center Drive
Dallas, Texas 75235

David G. Kaiser, Ph.D.

Research Head, Drug Metabolism Research The Upjohn Company 301 Henrietta Kalamazoo, Michigan 49001

Gerald E. Kananen, Ph.D.

Applications Chemist Hewlett-Packard Corporation Route 41 and Starr Road Avondale, Pennsylvania 19311

Sidney Kave, Ph.D.

Professor of Toxicology, Pharmacology, and Legal Medicine School of Medicine University of Puerto Rico San Juan, Puerto Rico 00936

Leo Kazyak, M.A.

Chief Toxicologist
Walter Reed Army Institute of Research
Walter Reed Army Medical Center
Washington, D.C. 20012

Edgar W. Kivela, Ph.D.

Chief, Division of Crime Detection Michigan Department of Public Health 3500 North Logan Street Lansing, Michigan 48914

David Landau, M.S.

Toxicologist Nassau County Medical Examiner's Office P.O. Box 160 East Meadow, New York 11554

Charles J. Least, Jr., M.S.

Supervisor, Therapeutic Drug Monitoring Laboratory The Johns Hopkins Hospital 601 North Broadway Baltimore, Maryland 21205

Beverly Lorenzo, B.S.

Chemist Cuyahoga County Coroner's Laboratory 2121 Adelbert Road Cleveland, Ohio 44106

Robert Maes, Ph.D.

Professor of Toxicology University of Utrecht Voldelhaan 14 Utrecht, Holland

Robert S. Martin, B.A.

Biology, Biochemistry Assistant The Upjohn Company 301 Henrietta Kalamazoo, Michigan 49001

Arthur J. McBay, Ph.D.

Chief Toxicologist
Office of the Chief Medical Examiner
P.O. Box 2488
Chapel Hill, North Carolina 27514

Michael McGee, B.S.

Chemist Bureau of Forensic Science 1 North 14th Street Richmond, Virginia 23219

Ian J. McGilveray, Ph.D.

Head, Biopharmaceutics Section
Drug Research Laboratory, Health
Protection Branch
Health and Welfare Canada
Ottawa, Ontario, Canada K1A OL2

John J. McHugh, J.D.

Chief of Laboratory
Department of Public Safety
1010 Commonwealth Avenue
Boston, Massachusetts 02215

John M. Meola

Assistant Director, Clinical Chemistry Albany Medical Center Hospital 46 New Scotland Avenue Albany, New York 12208

Kamal K. Midha, Ph.D.

Research Scientist
Drug Research Laboratory, Health
Protection Branch
Health and Welfare Canada
Ottawa, Ontario, Canada K1A 0L2

Joseph R. Monforte, Ph.D.

Toxicologist Wayne County Medical Examiner's Office 400 East Lafayette Street Detroit, Michigan 48226

Sunil K. Nivogi, Ph.D.

Consultant 5247 North 10th Street Philadelphia, Pennsylvania 19141

Robert J. Osiewicz, Ph.D.

Toxicologist
Bureau of Forensic Sciences
401 A. Colley Avenue
Norfolk, Virginia 23507

Robert J. Perchalski, B.S.

Research Chemist Veterans Administration Hospital Medical Research Gainesville, Florida 32602

L. F. Prescott, M.A., M.D., F.R.C.P.

Consultant Physician
Department of Therapeutics
The Royal Infirmary
Edinburgh, Scotland EH39YW

Arnold O. Rathje, B.S.

Senior Industrial Hygienist General Electric Company Nela Park Cleveland, Ohio 44112

Philip C. Reynolds, B.S.

Chief Toxicologist
Institute of Forensic Sciences
2945 Webster Street
Oakland, California 94609

Fredric Rieders, Ph.D.

Laboratory Director National Medical Services, Inc. 2300 Stratford Avenue Willow Grove, Pennsylvania 19090

William Robinson, B.Sc.Phm.

Toxicologist
The Centre of Forensic Sciences
8 Jarvis Street
Toronto, Ontario, Canada M5E 1M8

Denis O. Rodgerson, Ph.D.

Chief of Clinical Chemistry
The Center for the Health Sciences
University of California at Los Angeles
Los Angeles, California 90024

Joseph I. Routh, Ph.D.

Professor of Biochemistry and Pathology University of Iowa Iowa City, Iowa 52242

Donald C. Sanders, M.S.

Research Chemist Civil Aeromedical Institute, FAA P.O. Box 25082, AAC-114A Oklahoma City, Oklahoma 73125

Phillip Santinga, B.S.

Chemist
Bendix Corporation
Box 80
Brandey Station, Virginia 22714

Bernard Searle, Ph.D.

106D Finderne Avenue Grandview Gardens, New Jersey 08876

Paul Richard Sedgwick, B.A.

Associate Toxicologist Orange County Sheriff-Coroner 550 North Flower Street Santa Ana, California 92701

Richard F. Shaw, B.S.

Chief Toxicologist
San Diego County Coroner's Office
5555 Overland Avenue
San Diego, California 92123

Theodore J. Siek, Ph.D.

Toxicologist
Northern Virginia Branch, Bureau of
Forensic Science
P.O. Box 486
Merrifield, Virginia 22116

Thomas C. Sneath, B.S.

Senior Toxicologist Rancho Los Amigos Hospital 7601 East Imperial Highway Downey, California 90242

Harvey M. Solomon, M.D.

Clinical Pathologist
The Johns Hopkins Hospital
601 North Broadway
Baltimore, Maryland 21205

F. William Sunderman, Jr., M.D.

Professor and Chairman, Department of Laboratory Medicine University of Connecticut School of Medicine P.O. Box G Farmington, Connecticut 06032

Irving Sunshine, Ph.D.

Chief Toxicologist Cuyahoga County Coroner's Office 2121 Adelbert Road Cleveland, Ohio 44106

Marjorie Q. Swift, B.S.

Senior Chemist
Department of Public Safety
1010 Commonwealth Avenue
Boston, Massachusetts 02215

James B. Terrill, Ph.D.

Research Toxicologist Haskell Laboratory, DuPont Company Elkton Road Newark, Delaware 19711

Jerry J. Thoma, M.S.

Research and Development Chemist South Bend Medical Foundation 521 North Main Street South Bend, Indiana 46601

Robert Turk, Ph.D.

Chief Toxicologist Clinical Bio-Tox Laboratories, Ltd. 1436 Old Skokie Road Highland Park, Illinois 60035

James C. Valentour, Ph.D.

Associate Toxicologist Cuyahoga County Coroner's Office 2121 Adelbert Road Cleveland, Ohio 44106

Michael Vanko, Ph.D.

Assistant Director Albany Medical Center Hospital 120 Mohawk Drive Schenectady, New York 12307

Clifford B. Walberg, Ph.D.

Clinical Chemist Toxicology Lab, LAC-USC Medical Center 1200 North State Street Los Angeles, California 90033

Jack E. Wallace, Ph.D.

Associate Professor University of Texas Health Science Center 7703 Floyd Curl Drive San Antonio, Texas 78284

John Wells, Ph.D.

Toxicologist
The Centre of Forensic Sciences
8 Jarvis Street
Toronto, Ontario, Canada M5E 1M8

Rhondda J. Wells, B.S.

Assistant Director Pediatric Microchemistry Laboratory University of Colordo Medical Center Denver, Colorado 80220

H. R. Wetherell, Ph.D.

Crime Laboratory Scientist Michigan Department of Public Health 3500 North Logan Street Lansing, Michigan 48914

B. J. Wilder, M.D.

Chief Neurology Service Veterans Administration Hospital Gainesville, Florida 32802

Louis A. Williams, B.S.

President Clin-Chem Laboratories 1106 Commonwealth Avenue Boston, Massachusetts 02215

William J. Wilson, Jr., M.Sc.

Chief Toxicologist
Office of Bexar County Medical Examiner
527 North Leona Street
San Antonio, Texas 78207

Bennie Zak, Ph.D.

Professor of Pathology Wayne State University School of Medicine 540 East Canfield Detroit, Michigan 48201

ACKNOWLEDGMENT

I would like to thank Jerry Thoma and Paul Bondo for their assistance in reviewing and editing the numerous manuscripts submitted by the authors. Their diligence and expertise contributed significantly in compiling this volume.

I would also like to thank the editorial staff of CRC Press, Inc., in particular Sandy Pearlman, for their conscientious application to the many details involved in converting the first drafts of the contributors' manuscripts to a useful and practical book.

APOLOGIA

"To err is human," Extensive efforts have been made to insure the reliability and lucidity of the material presented in this volume. The reader is encouraged to send his observation of errors of omission or commission to the editor so that subsequent volumes will be improved. Requests for additional information on procedural details will be welcomed by the editor.

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Type A: a simple, direct qualitative test.

Type B: a quantitative procedure using facilities found in the average laboratory.

Type C: an elegant precise procedure using whatever equipment may be required.

^{*}Use and Interpretation of Measurements, p. 86. Unit Conversion, p. 99.

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Type A: a simple, direct qualitative test.

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Introduction

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