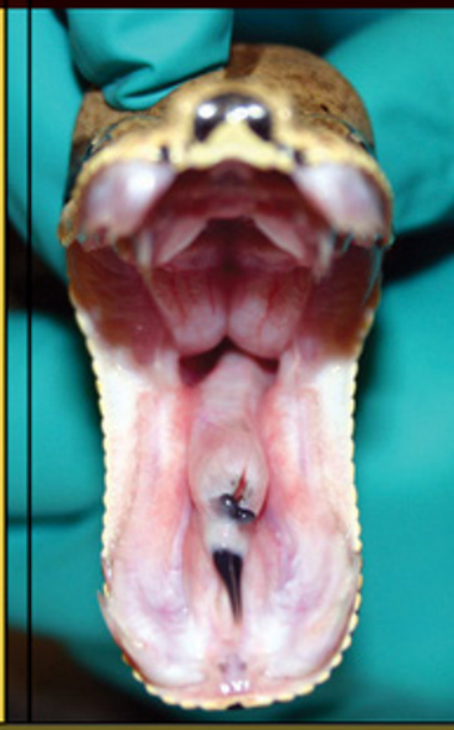
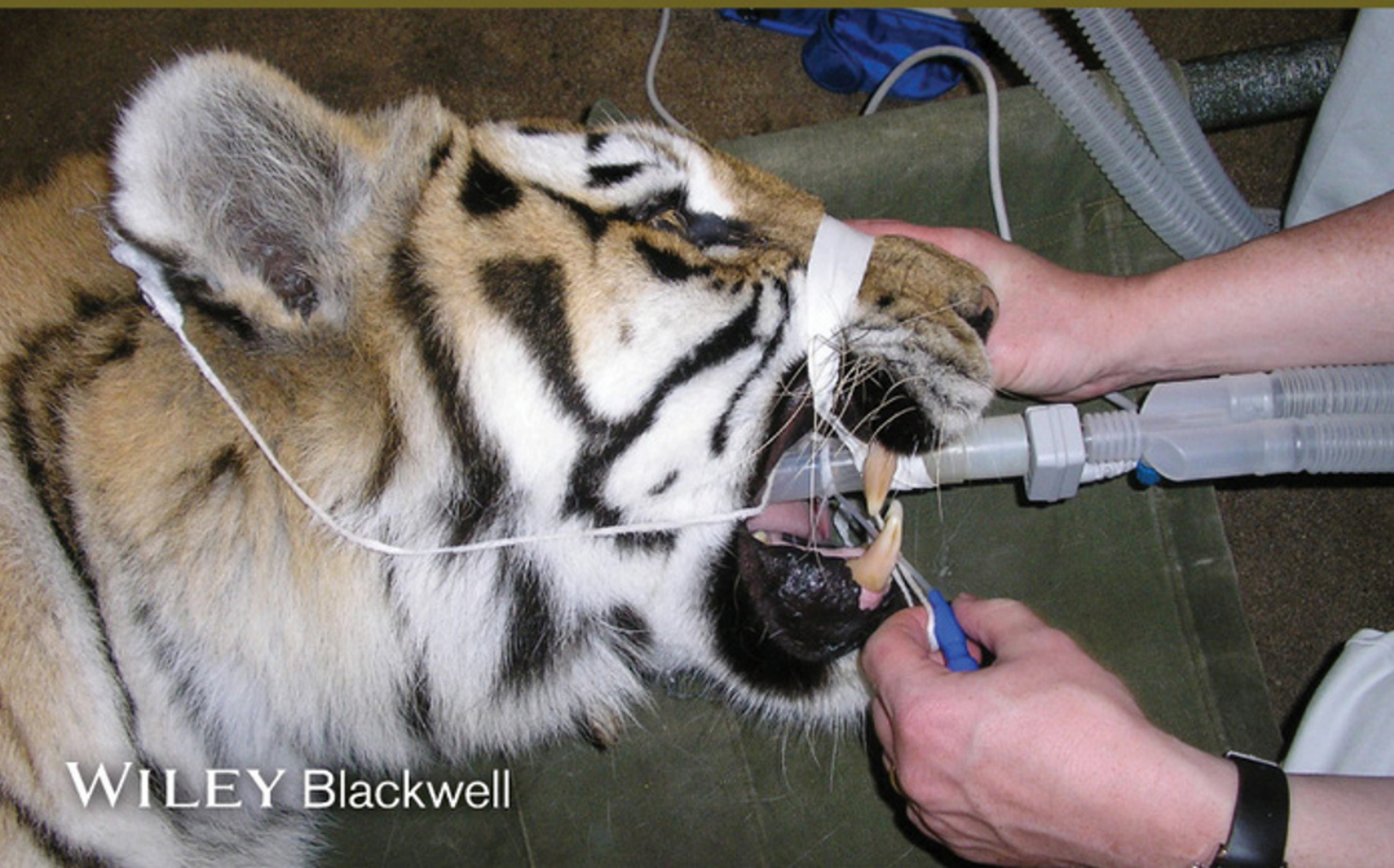
2nd Edition

# Zoo Animal and Wildlife Immobilization and Anesthesia



*Editors* Gary West, Darryl Heard and Nigel Caulkett



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# ZOO ANIMAL AND WILDLIFE IMMOBILIZATION AND ANESTHESIA

Second Edition

# ZOO ANIMAL AND WILDLIFE IMMOBILIZATION AND ANESTHESIA

**Second Edition**

**Edited by**

**Gary West, DVM, Dipl ACZM**
Phoenix Zoo

**Darryl Heard, BSc, BVMS, PhD, Dipl ACZM**
College of Veterinary Medicine
University of Florida

**Nigel Caulkett, DVM, MVetSc, Dipl ACVA**
College of Veterinary Medicine
University of Calgary

WILEY Blackwell

*Editorial offices:* 1606 Golden Aspen Drive, Suites 103 and 104, Ames, Iowa 50014-8300, USA
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
9600 Garsington Road, Oxford, OX4 2DQ, UK

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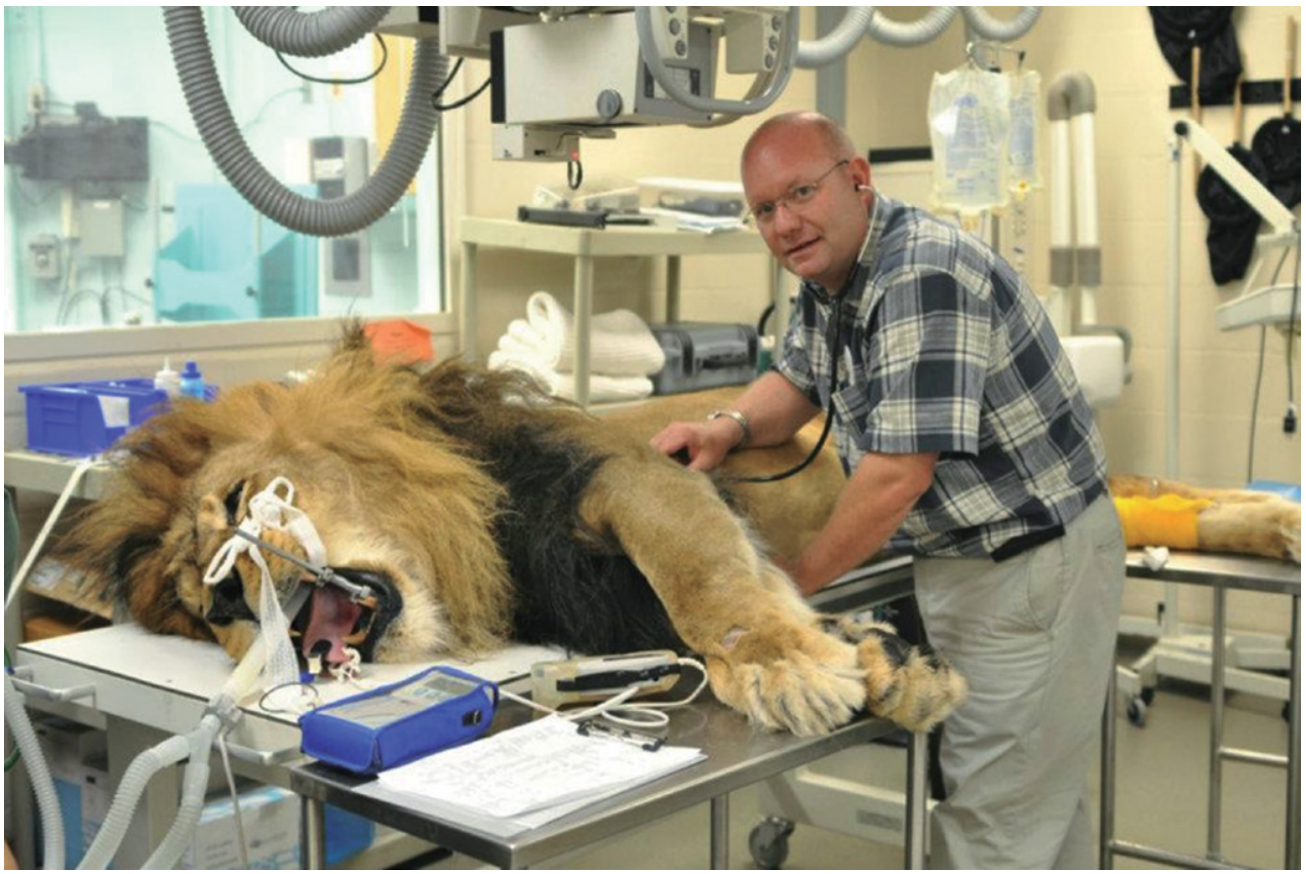
# Dedication



**The second edition of *Zoo Animal and Wildlife Immobilization and Anesthesia* is dedicated to our dear friend and colleague, Dr. Greg Fleming (March 13, 1966–March 9, 2013).**

How miserably things seem to be arranged in this world. If we have no friends, we have no pleasure; and if we have them, we are sure to lose them, and be doubly pained by the loss.

—Abraham Lincoln

(Photo credit: Department of Animal Health, Disney's Animals, Science, and Environment.)

# Contents

# Contributors


### Noha Abou-Madi, DVM, Msc
Clinical Associate Professor, Section of Zoological Medicine
Department of Clinical Sciences
College of Veterinary Medicine
Cornell University
Ithaca, NY 14853-6401
Phone: 607-253-3371
E-mail: na24@cornell.edu

### Frederick B. Antonio
Director
Orianne Center for Indigo Conservation
30931 Brantley Branch Road
Eustis, FL 32736
Phone: 407-516-7694
E-mail: fantonio@oriannesociety.org

### Douglas L. Armstrong, DVM
Director of Animal Health
Omaha's Henry Doorly Zoo and Aquarium
3701 S. 10th St.
Omaha, NE 68107
Phone: 402-738-2044

### Jon M. Arnemo, DVM, PhD, DECZM
Department of Forestry and Wildlife Management
Faculty of Applied Ecology and Agricultural Sciences
Hedmark University College, Campus Evenstad
NO-2418 Elverum
Norway
Department of Wildlife, Fish and Environmental Studies
Faculty of Forest Sciences, Swedish University of Agricultural Sciences
SE-901 83, Umeå
Sweden
Cell/work phone: +47 99585019
E-mail: jon.arnemo@hihm.no

### James Bailey, DVM, MS, DACVAA
University of Florida
College of Veterinary Medicine
Service Chief
Anesthesia and Pain Management
P.O. Box 100136
Gainesville, FL 32610-0136
Phone: 352-258-6600
E-mail: baileyj@mail.vetmed.ufl.edu

### Eric Baitchman, DVM, DACZM
Director of Veterinary Services
Zoo New England
1 Franklin Park Road
Boston, MA 02121
E-mail: ebaitchman@zoonewengland.com

### Ray L. Ball, DVM
Senior Veterinarain, Director of Medical Sciences
Tampa's Lowry Park Zoo
1101 W. Sligh Avenue
Tampa, FL 33604
Phone: 813-935-8552 ext. 349
E-mail: Ray.Ball@LowryParkZoo.com

### Mads F. Bertelsen, DVM, DVSc, DECZM (Zoo Health Management), DACZM
Staff Veterinarian
Centre for Zoo and Wild Animal Health
Copenhagen Zoo
Roskildevej 38
DK-2000 Frederiksberg
Denmark
Phone: +45 72200227
E-mail: mfb@zoo.dk

### Kate Bodley, BSc (Vet), BVSc (Hons), MVS
Melbourne Zoo
Elliott Ave.
Parkville, VIC
Australia

### Søren Boysen, DVM, DACVECC
Department of Veterinary Clinical and Diagnostic Sciences
Faculty of Veterinary Medicine
University of Calgary
3330 Hospital Drive NW
Calgary, AB
T2N 4N1
Phone: +403 210-8129
Fax: +403 220-3929
E-mail: srboysen@ucalgary.ca

**David B. Brunson, DVM, MS, DACVAA**
Senior Veterinary Specialist
Companion Animal Division, Zoetis
Adjunct Associate Professor
Department of Surgical Sciences in the School of Veterinary Medicine
University of Wisconsin
Madison, WI 53706
2780 Waubesa Ave.
Madison, WI 53711
E-mail: david.brunson@zoetis.com

**Mitchell Bush, DVM, DACZM**
Senior Veterinarian Emeritius
Smithsonian Conservation Biology Institute
Front Royal, VA

**Tracy Carter, BS, MS, PhD**
Adjunct Professor
Oklahoma State University
Department of Zoology
415 LSW
Stillwater, OK 74078
Phone: 405-744-9675
Fax: 405-744-7824
E-mail: tracy.carter@okstate.edu

**Nigel Caulkett, DVM, MVetSc, DACVAA**
Department of Veterinary Clinical and Diagnostic Science
3280 Hospital Drive NW
Calgary, AB
Canada T2N 1N4
Phone: 403 220 8224
E-mail: nacaulke@ucalgary.ca

**Shannon Cerveny, DVM, DACZM**
Oklahoma City Zoo
2101 NE 50th St.
Oklahoma City, OK 73111

**Scott B. Citino, DVM, DACZM**
Staff Veterinarian
White Oak Conservation Center
Yulee, FL

**Tonya M. Clauss, DVM, MS**
Georgia Aquarium
Atlanta, GA
E-mail: tclauss@georgiaaquarium.org

**Jonathan Cracknell, BVMS, CertVA, CertZooMed, MRCVS**
Director of Animal Operations
Longleat Safari and Adventure Park
Safari Park Office
Longleat, Wiltshire
England BA12 7NJ
Phone: +44 (0) 1985 845 413
Mobile: +44 (0) 7855 763319
E-mail: jon.cracknell@longleat.co.uk

**Christopher Dold, DVM**
Vice President of Veterinary Services
SeaWorld Parks & Entertainment
E-mail: christopher.dold@seaworld.com

**Alina L. Evans, DVM, MPH**
Department of Forestry and Wildlife Management
Faculty of Applied Ecology and Agricultural Sciences
Hedmark University College
Campus Evenstad
NO-2418 Elverum
Norway
E-mail: alina.evans@hihm.no

**Åsa Fahlman, DVM, VetMedLic, PhD, DECZM**
Department of Clinical Sciences
Faculty of Veterinary Medicine and Animal Science,
Swedish University of Agricultural Sciences,
P.O. Box 7054
SE-750 07 Uppsala
Sweden
Phone: +46 70 6106388
E-mail: asa_fahlman@hotmail.com

**Gregory J. Fleming, DVM, DACZM**
Disney's Animals, Science, and Environment
P.O. Box 10000
Lake Buena Vista, FL 32830

**Kurt A. Grimm, DVM, MS, PhD, DACVAA, DACVCP**
Owner Veterinary Specialist Services, PC
P.O. Box 504
Conifer, CO 80433
Phone: (303) 918 1321
E-mail: grimm.dvm@gmail.com

**Nina Hahn, DVM, PhD, DACLAM**
Attending Veterinarian
Lawrence Berkeley National Laboratory
Berkeley, CA

**Michelle G. Hawkins, BS, VMD, DABVP (Avian Practice)**
Associate Professor, Companion Avian and Exotic Animal Medicine and Surgery
Department of Medicine and Epidemiology
University of California-Davis
School of Veterinary Medicine
Davis, CA

**Martin Haulena, DVM, MSc, DACZM**
Vancouver Aquarium
PO Box 3232
Vancouver, BC
Canada V6B 3X8
604-659-3468
E-mail: Martin.Haulena@vanaqua.org

**Darryl Heard, BSc, BVMS, PhD, DACZM**
Associate Professor Zoological Medicine
Department of Small Animal Clinical Sciences
College of Veterinary Medicine
University of Florida
Gainesville, FL 32610-0126
E-mail: heardd@ufl.edu

**Sonia M. Hernandez, DVM, DACZM, PhD**
Assistant Professor
Warnell School of Forestry and Natural Resources and the
Southeastern Cooperative Wildlife Disease Study
University of Georgia
Athens, GA 30602

**Markus Hofmeyr, BVSc, MRCVS, MDP**
Principal Scientist, Veterinary Services
South African National Parks
P.O. Box 122
Skukuza, Mpumalanga
South Africa 1350
Phone: 27-84-7001355 or 27-13-7354239
Fax: 27-13-735-4057
E-mail: markush@parks-sa.co.za

**Peter Holz, BVSc, DVSc, MACVSc, DACZM**
Tidbinbilla Nature Reserve
RMB 141
Via Tharwa, ACT 2620
Australia
E-mail: holz@megalink.com.au.

**William A. Horne, DVM, PhD, DACVAA**
Chairperson
Department of Small Animal Clinical Sciences
Michigan State University
Room D208
Veterinary Medical Center
736 Wilson Rd.
East Lansing, MI 48824

**Ramiro Isaza, DVM, MS, MPH, DACZM**
Associate Professor of Zoological medicine
Department of Clinical Sciences
Cornell University College of Veterinary medicine
University of Florida
Gainesville, FL 32610-0126
Phone: (352) 392 4700
E-mail: isazar@mail.vetmed.ufl.edu

**Randall E. Junge, MS, DVM, DACZM**
Vice President for Animal Health
Columbus Zoo and the Wilds
Cumberland, OH

**Jeff C. Ko, DVM, MS, DACVAA**
Professor, Anesthesiology
Department of Veterinary Clinical Sciences
College of Veterinary Medicine
Purdue University
625 Harrison Street
West Lafayette, IN 47907-2026
Phone: (765) 496 9329
E-mail: jcko@purdue.edu

**George V. Kollias, DVM, PhD, DACZM**
J. Hyman Professor of Wildlife Medicine
Department of Clinical Sciences and
Janet L. Swanson Wildlife Health Center
College of Veterinary Medicine
Cornell University
Ithaca, NY 14853-6401
Email: gvk2@cornell.edu

**Terry J. Kreeger, MS, DVM, PhD**
State Wildlife Veterinarian
Wyoming Game and Fish Department
2362 Highway 34
Wheatland, WY 82201
E-mail: tkreeg@gmail.com

**Rebecca A. Krimins, DVM, MS**
Medical Director
Veterinary Imaging of the Chesapeake
808 Bestgate Rd.
Annapolis, MD 21401
Phone: (410) 224 0121
E-mail: rkrimins@vetimagingchesapeake.com

**Leigh A. Lamont, DVM, MS, DACVAA**
Associate Dean, Academic and Student Affairs
Atlantic Veterinary College
University of Prince Edward Island
550 University Avenue
Charlottetown, PE
Canada C1A 4P3
Phone: (902) 566 0374
E-mail: llamont@upei.ca

**Jennifer N. Langan, DVM, DACZM**
Clinical Associate Professor
University of Illinois
College of Veterinary Medicine
Associate Veterinarian
Chicago Zoological Society
Brookfield Zoo
8400 W 31st St.
Brookfield, IL 60513

**R. Scott Larsen, DVM, MS, DACZM**
Vice President of Veterinary Medicine
Denver Zoo
2300 Steele St.
Denver, CO 80205
E-mail: slarsen@denverzoo.org

**Gregory A. Lewbart, MS, VMD, DACZM**
NCSU-CVM
1060 William Moore Drive
Raleigh, NC 27607
Email: galewbar@ncsu.edu

**Michael R. Loomis, DVM, MA, DACZM**
Chief Veterinarian
North Carolina Zoological Park
4401 Zoo Parkway
Asheboro, NC 27205

**Michael Lynch, BVSc, PhD, MANZCVSc (Epi)**
Melbourne Zoo
Parkville, VIC
Australia

**Khursheed R. Mama, DVM, DACVAA**
Professor, Anesthesiology
Department of Clinical Sciences
Colorado State University
Fort Collins, CO 80526
Phone: 970 297 4124
Email: kmama@colostate.edu

**Michele Miller, DVM, MS, MPH, PhD**
Professor, South African Research Chair in Animal Tuberculosis
Division of Molecular Biology and Human Genetics
Faculty of Medicine and Health Sciences
Tygerberg, South Africa

**Anneke Moresco, DVM, MS, PhD**
Research Associate
Denver Zoo
2300 Steele St.
Denver, CO 80205
Phone: 720 337 1590
E-mail: anneke_moresco@hotmail.com

**Peter vdB. Morkel, BVSc**
Private Consultant
P.O. Box 260
Kakamas 8870
South Africa

**Cornelia I. Mosley, Dr Med Vet, DACVAA**
Assistant Professor
Ontario Veterinary College
University of Guelph
Guelph, ON
Canada

**Daniel M. Mulcahy, PhD, DVM, DACZM**
Wildlife Veterinarian
U.S. Geological Survey
Alaska Science Center
4210 University Drive
Anchorage, AK 99508

**Natalie D. Mylniczenko, DVM, MS, DACZM**
Disney's Animals, Science, and Environment
P.O. Box 10000
Lake Buena Vista, FL 32830
Phone (office): 407-938-3277
Cell phone: 321-299-4079
Fax: 407-938-3266
Email: Natalie.Mylniczenko@Disney.com

**Julie Napier, DVM**
Senior Veterinarian
Omaha's Henry Doorly Zoo and Aquarium
3701 S. 10th St.
Omaha, NE 68107

**Donald L. Neiffer, VMD, DACZM**
Veterinary Operations Manager
Disney's Animal Programs
P.O. Box 10,000
Lake Buena Vista, FL 32830
Phone: 407-938-2719
Fax: 407-939-6391

**Elizabeth C. Nolan, DVM, MS, DACZM**
Disney's Animals, Science, and Environment,
P.O. Box 10,000,
Lake Buena Vista, FL 32830
Email: elizabeth.c.nolan@disney.com.

**Rolf-Arne Ølberg, DVM, DVSc**
Director of Animal Care
Kristiansand Dyrepark
4609 Kardemomme By
Norway
Phone: +47 97059860
Email: rolfarne@dyreparken.no

**Larissa Ozeki, DVM, MSc**
Department of Veterinary Clinical and Diagnostic Science
3280 Hospital Drive NW
Calgary, AB
Canada T2N 1N4
Phone: (403) 466 0115
E-mail: lmozeki@ucalgary.ca

**Luis R. Padilla, DVM, DACZM**
Director of Animal Health
St. Louis Zoo
1 Government Drive
St. Louis, MO 63110

**John M. Parker, DVM**
Campus Veterinarian
Laboratory Animal Resource Center
University of California San Francisco

**An Pas, DVM**
Breeding Center for Endangered Arabian Wildlife
P.O. Box 29922
Sharjah
United Arab Emirates

**Peter J. Pascoe, BVSc**
Professor
Surgical and Radiological Sciences
University of California Davis
Davis, CA 95616

**Jessica Paterson, BSc (Hons), DVM, MVetSc**
Department of Veterinary Clinical and Diagnostic Science
3280 Hospital Drive NW
Calgary, AB
Canada T2N 1N4
E-mail: paterson_jessica@hotmail.com

**Julia Ponder, DVM**
Executive Director
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108

**Robin W. Radcliffe, DVM, DACZM**
Director Cornell Conservation Medicine Program
Adjunct Assistant Professor of Wildlife and Conservation Medicine
College of Veterinary Medicine
Cornell University
Ithaca, NY

**Edward C. Ramsay, DVM, DACZM**
Professor, Zoological Medicine
The University of Tennessee
Department of Small Animal Clinical Sciences
C247 Veterinary Teaching Hospital
Knoxville, TN 37996-4544
Ph 865-755-8219
FAX 865-974-5554
E-mail: eramsay@utk.edu

**Patrick T. Redig, DVM, PhD**
Professor of Avian Medicine and Surgery
Co-Founder and Director Emeritus
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108

**Sam Ridgway, DVM, PhD, DACZM**
National Marine Mammal Foundation
2240 Shelter Island Drive Ste 200
San Diego, CA 92106
Phone: 619-553-1374
E-mail: sridgway@UCSD.edu

**Todd L. Schmitt, DVM**
SeaWorld San Diego
500 SeaWorld Dr.
San Diego, CA 92109
E-mail: todd.schmitt@seaworld.com

**Jim Shaw, BS, MS, PhD**
Professor, Oklahoma State University
Department of Natural Resources, Ecology and Management
008 Ag Hall
Stillwater, OK 74078
Phone: 405-744-9842
Fax: 405-744-3530
E-mail: jim.shaw@okstate.edu

**Todd Shury, DVM**
Wildlife Health Specialist|Spécialiste en santé de la faune
Office of the Chief Ecosystem Scientist|Bureau de Scientifique en chef des écosystèmes
Protected Area Establishment and Conservation|Établissement et conservation des aires protégées
Parks Canada Agency|Agence Parcs Canada
Saskatoon, SK
Canada S7N 5B4
Phone: (306) 966 2930
E-mail: Todd.Shury@pc.gc.ca

**Jessica Siegal-Willott, DVM, DACZM**
Center for Animal Care Sciences
Smithsonian's National Zoological Park
Smithsonian Conservation Biology Institute
P.O. Box 37012, MRC 5502
Washington, DC 20013-7012

**Melissa Sinclair, DVM, DVSc, DACVAA**
Associate Professor in Anesthesiology
Ontario Veterinary College
University of Guelph
Department of Clinical Studies
University of Guelph
Guelph, Ontario
Canada
N1G 2W1
Phone: 519 824-4120 EXT 54450
Email: msinclai@ovc.uoguelph.ca

**Jonathan Sleeman, MA, VetMB, DACZM, DECZM, MRCVS**
Center Director
USGS, National Wildlife Health Center
6006 Schroeder Road
Madison, WI 53711
Tel: (608) 270 2401
Fax: (608) 270 2415
Email: jsleeman@usgs.gov

**M. Andrew Stamper, DVM, DACZM**
Research Biologist/Clinical Veterinarian
The Seas, Disney's Animal Programs
Walt Disney World Resorts
EC Trl. W-251
2020 North Avenue of the Stars
Lake Buena Vista, FL 32830-1000
Phone: 407-560-5576
Fax: 407-560-5750

**Mark Stetter, DVM, DACZM**
Dean
College of Veterinary Medicine and Biomedical Sciences
Colorado State University
Fort Collins, CO
Phone (office): (970) 491-7051
Email: mark.stetter@colostate.edu

**Wm. Kirk Suedmeyer, DVM, DACZM**
Director of Animal Health
The Kansas City Zoo
6800 Zoo Drive
Kansas City, MO 64132

**Gregory Timmel, DVM, MS, DACLAM**
Attending Veterinarian
Legacy Research
Portland, OR

**Alessio Vigani, DVM, PhD, DACVAA**
University of Florida
Gainesville, FL
E-mail: alessio.vigani@gmail.com

**Kent A. Vliet, PhD**
Coordinator of Laboratories
University of Florida
Department of Biology
208 Carr Hall
P.O. Box 118525
Gainesville, FL 32611-8525

**Michael T. Walsh, DVM**
Aquatic Animal Health Program
Large Animal Clinical Sciences
College of Veterinary Medicine
University of Florida
2015 SW 16th Ave.
Gainesville, FL 34787
E-mail: walshm@ufl.edu

**Chris Walzer, DECZM, Dr Med Vet, DECZM**
University Professor
Research Institute of Wildlife Ecology
Department of Integrative Biology and Evolution
University of Veterinary Medicine
Savoyenstrasse 1, A-1160
Vienna, Austria
E-mail: Chris.Walzer@vetmeduni.ac.at

**Mary L. Weldele, BA**
Associate Research Specialist
Department of Psychology
University of California Berkeley
Berkeley, CA

**Gary West, DVM, DACZM**
Executive Vice President
Animal Health and Collections
Phoenix Zoo
455 North Galvin Parkway
Phoenix, AZ 85008

**Douglas P. Whiteside, DVM, DVSc, DACZM**
Senior Staff Veterinarian
Calgary Zoo Animal Health Centre
Clinical Associate Professor
University of Calgary Faculty of Veterinary Medicine
1625 Centre Ave East
Calgary, AB
Canada T2E 9K2
Phone: (403) 232 9390
E-mail: dougw@calgaryzoo.com

**Michelle Willette, DVM**
Staff Veterinarian
The Raptor Center
College of Veterinary Medicine
University of Minnesota
St. Paul, MN 55108

**Cathy V. Williams, DVM**
Senior Veterinarian
Duke Lemur Center
Duke University
Durham, NC
Adjunct Assistant
Professor of Zoological Medicine
College of Veterinary Medicine
North Carolina State University
Raleigh, NC

**Murray Woodbury, DVM, MSc**
Associate Professor and Research Chair,
Specialized Livestock Health and Production,
Western College of Veterinary Medicine
52 Campus Drive
Saskatoon, SK
Canada S7N 5B4
Phone: 306 966 7170
E-mail: murray.woodbury@usask.ca

**Ashley M. Zehnder, DVM, ABVP (Avian)**
Postdoctoral Fellow
Department of Dermatology
CCSR Bldg., 2150
269 Campus Drive
Stanford University
Stanford, CA 94305-5168
E-mail: azehnder.dvm@gmail.com

# Preface

Welcome to the second edition of *Zoo Animal and Wildlife Immobilization and Anesthesia*. The publication of this edition occurs at a time when continual advances in wildlife anesthesia are being made. Increasingly, veterinarians, biologists, veterinary technicians, and others are challenged to provide exemplary care to threatened or endangered species. To meet these challenges, we continually strive to ensure the highest level of patient safety. The goal of this book is to provide an efficient method to access knowledge about wildlife anesthesia.

We wish to express our appreciation to all of our contributing authors. Their hard work, willingness to share their expertise, and their dedication to this field allow us to produce a high quality and clinically useful publication.

There is still much to learn about the anesthetic and analgesic management of our wildlife patients. We hope that this book can help augment educational experiences for veterinarians and veterinary students and provide important information about anesthesia in some of the most challenging species that veterinarians work with.

We recognize the monumental effort of Susan Engelken at Wiley for helping us organize the production of this book. Without her extraordinary effort and guidance, this book would not be possible.

We are very proud of our final product and feel that we have produced another excellent piece of work.

Gary West, Darryl Heard, and Nigel Caulkett

# ZOO ANIMAL AND WILDLIFE IMMOBILIZATION AND ANESTHESIA

Second Edition

# Section I
# General

# 1 Clinical Pharmacology

Leigh A. Lamont and Kurt A. Grimm

## INTRODUCTION

Pharmacology is the study of drugs and their interactions with organisms (Page & Maddison 2002). Pharmacology incorporates aspects of statistics, biochemistry, biology, pathology, and medicine. Failure to interpret the description of drugs' pharmacological properties in the context of the clinical picture (i.e., clinical pharmacology) can result in unintended outcomes.

The pharmacological data available for most drugs are mean values derived from a relatively small number of individuals (usually healthy individuals). While this approach provides a starting point for clinical use of drugs, individual responses can vary greatly due to disease states, body condition, environment, genetics, coadministered drugs, and many other factors. When the toxic dose is close to the therapeutic dose (as is often the case with drugs used for immobilization and anesthesia), careful titration of dose and patient monitoring are required. However, the nature of working with wildlife and captive nondomestic species often precludes baseline health assessment, individualization of dosing, and intensive patient monitoring. This is one factor associated with increased risk of adverse outcomes when capturing or anesthetizing nondomestic species. It should also be appreciated that advances in drug safety will likely result in only limited improvement of the safety of anesthesia and immobilization. Management of other risk factors through airway management, reduction of stress, and improvements in supportive care will also be beneficial.

## PHARMACOKINETICS

Pharmacokinetics (PK) can be generally defined as what an organism does to a drug. Absorption, distribution, biotransformation, and elimination are processes that determine the concentration of the drug at the site of action (i.e., biophase). Pharmacokinetic parameters are estimates of these processes in the group of animals studied. These estimates can be used to predict or understand the way a drug interacts with an organism. It is important to understand that pharmacokinetic parameters can vary between individual animals and can be influenced by many different drug- and organism-related factors. Additionally, pharmacokinetic parameters are derived using mathematical models selected by the investigator. There is usually no correlation between model components and anatomical structures.

## PHARMACODYNAMICS

Pharmacodynamics (PD) can be generally defined as what a drug does to an organism. PD includes intended drug effects, as well as adverse drug actions. Drugs such as opioids, alpha-2 adrenergic agonists, and antimuscarinics act by binding to relatively well-characterized receptor complexes located on cellular membranes. Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit prostaglandin production by binding to cyclooxygenase enzyme isoforms. Relating plasma drug concentrations to observed NSAIDs actions can be complex in comparison with other drugs (e.g., opioids) due to the different nature of their action. Preexisting progstaglandins, as well as their slower process of inhibiting an enzyme system, confound the relationship between drug concentration and effect. The molecular actions of inhalant anesthetics have not been completely characterized, even though their clinical use has been well described (Steffey & Mama 2007).

Pharmacodynamic effects are predictable for most clinically used drugs. However, individual animal

*Zoo Animal and Wildlife Immobilization and Anesthesia*, Second Edition. Edited by Gary West, Darryl Heard, and Nigel Caulkett.

responses can vary considerably. Additionally, the nature of capture of free-ranging and captive wildlife often makes accurate dosing and drug delivery difficult or impossible. Therefore, close monitoring of patient response and preparation for supportive care are paramount to safe immobilization and anesthesia.

## INHALANT ANESTHETICS

Inhalant anesthetics are commonly used in companion animal veterinary practice. Their use under field conditions is limited due to the requirement for specialized delivery devices and a supply of delivery gas (e.g., oxygen). However, inhalant anesthetics are used commonly in controlled settings, such as zoological parks and research laboratories, because of the ease of titration of anesthetic depth and rapidity of recovery. Inhalant anesthetics should be delivered by a well-maintained anesthetic machine and properly trained individuals. While inhalant anesthetics are relatively safe, their low therapeutic index mandates frequent and careful monitoring of anesthetic depth.

### Physics of Gases and Vapors

An understanding of the processes that influence the uptake and delivery of inhalant anesthetics allows the anesthetist to predict and respond to individual circumstances.

**Brief Review of Molecular Theory** Molecules in a liquid state have more vibrational energy than when in a solid state, and each molecule can move through the liquid. If heat is added to a liquid, each molecule gains more kinetic energy and eventually some overcome the forces exerted by their neighbors and are able to escape into the space above the liquid. This state is that of a gas or a vapor. A gas is a phase of matter that expands indefinitely to fill a containment vessel. A vapor is the gaseous state of a material below its boiling point.

A vapor is in equilibrium with the liquid beneath it. Because both gaseous and liquid molecules have kinetic energy, they are in constant motion. The molecules in the vapor phase are striking the liquid–gas interface and returning to the liquid while liquid molecules are leaving the interface to become vapor. The relationship between these two phases depends mainly on the physicochemical properties of the molecules and the temperature of the system.

Vapor Pressure Molecules in a gaseous state possess kinetic energy and collide with the walls of the containment vessel. These collisions produce a force on the walls. This force is spread over a surface area and therefore is a pressure (Pressure = Force/Area). This pressure is called the vapor pressure. Since kinetic energy increases directly with temperature, vapor pressure must always be given with reference to the temperature it was measured at (e.g., vapor pressure of water is 47 mmHg at 37°C).

**Table 1.1.** Anesthetic agent vapor pressures at 20 and 24°C

| Anesthetic Agent | Vapor Pressure at 20°C in mmHg | Vapor Pressure at 24°C in mmHg |
|---|---|---|
| Methoxyflurane | 23 | 28 |
| Sevoflurane | 160 | |
| Enflurane | 172 | 207 |
| Isoflurane | 240 | 286 |
| Halothane | 243 | 288 |
| Nitrous oxide | Gas | Gas |

*Source*: Adapted from Steffey EP, Mama RM. 2007. Inhalation anesthetics. In: *Lumb and Jones' Veterinary Anesthesia*, 4th ed. (WJ Tranquilli, JT Thurmon, KA Grimm, eds.). Ames: Blackwell.

When many gases are present in a mixture, such as with atmospheric air or during delivery of inhalant anesthetics, each gas has a vapor pressure that is independent of the other gases (Dalton's law of partial pressures). It is convention to refer to vapor pressure as partial pressure under these conditions. Partial pressure of an anesthetic agent is analogous to the concept of "free drug" and is important for determining the effect of the anesthetic (e.g., the level of CNS depression correlates directly with the partial pressure of isoflurane within the brain) (see Table 1.1) (Steffey & Mama 2007).

Vapor Concentration Vapor (i.e., partial) pressure is important for the observed pharmacological effect of inhalant anesthetics. However, almost all anesthesiologists refer to the amount of anesthetic delivered in units of volumes % (said as volumes-percent), or just percent, which is a concentration. The fundamental difference between anesthetic partial pressure and anesthetic concentration is partial pressure relates to the absolute number of molecules and their kinetic energy whereas concentration refers to the number of molecules of anesthetic relative to the total number of molecules present.

Critical Temperature The critical temperature is the temperature above which a substance cannot be liquefied no matter how much pressure is applied. The critical temperature of nitrous oxide is 36.5°C. Consequently, nitrous oxide can be (and is) a liquid below this temperature, but is a gas at greater temperatures. Placing a nitrous oxide tank near a heat source will result in volatilization of liquid nitrous oxide, resulting in a high tank pressure and danger of explosion or tank venting.

The critical temperature of oxygen is −119°C. Therefore, at room temperature, oxygen cannot be liquefied. All compressed cylinders of medical oxygen contain only gas. There are liquid oxygen tanks, but the internal tank temperature is below −119°C.

**Table 1.2.** Selected partition coefficients of commonly used anesthetic agents

| Anesthetic | Blood : Gas Partition Coefficient | Brain : Blood Partition Coefficient |
|---|---|---|
| Nitrous oxide | 0.47 | 1.1 |
| Desflurane | 0.42 | 1.3 |
| Enflurane | 1.4 | 1.4 |
| Sevoflurane | 0.69 | 1.7 |
| Methoxyflurane | 12.0 | 2.0 |
| Isoflurane | 2.6 | 2.7 |
| Halothane | 2.9 | 2.9 |

*Source*: Adapted from Steffey EP, Mama RM. 2007. Inhalation anesthetics. In: *Lumb and Jones' Veterinary Anesthesia*, 4th ed. (WJ Tranquilli, JT Thurmon, KA Grimm, eds.). Ames: Blackwell.

Henry's Law Henry's law states the solubility of a gas in a liquid is proportional to the pressure of the gas over the solution. It describes the solubility of an anesthetic in body fluids or other liquids. From it you can derive the following formula: $c = k{\cdot}P$; where $c$ is the molar concentration (mol/L) of the dissolved gas and $P$ is the pressure (in atmospheres) of the gas over the solution. For a given gas, $k$ is the Henry's law constant and is dependent on temperature.

Partition Coefficient A partition coefficient is the ratio of the concentration of a substance in one medium relative to another at equilibrium. It is related to the solubility of an agent. At equilibrium, the partial pressure is the same throughout the body, including the alveolar gas, but the concentration of total drug may be very different due to partitioning into tissues or body fluids (Table 1.2) (Steffey & Mama 2007). Partition coefficients are not absolute constants for an anesthetic agent. Tissue composition may change as a function of age, sex, body condition, and so on, and these changes may influence partitioning.

**Mechanism of Action of Inhaled Anesthetics** The specific mechanism of action of most anesthetics remains unknown. Volatile anesthetics appear to share some common cellular actions with other sedative, hypnotic, or analgesic drugs. A sound theory of anesthetic action should provide an explanation for the observed correlation of potency with the oil/gas partition coefficient, the observation that a large number of diverse chemical structures can cause anesthesia, and explain why the agents produce side effects. Experimental work has implicated a protein "target" on a diverse population of ionophores that is required for anesthetic action (Franks & Lieb 2004). The alteration in ionophore conductance may be related to direct action of the anesthetic at a two amino acid sequence within the transmembrane spanning domains.

The protein receptor hypothesis postulates that protein receptors in the central nervous system are responsible for the mechanism of action of inhaled anesthetics. This theory is supported by the steep dose–response curve for inhaled anesthetics. However, it remains unclear if inhaled agents disrupt ion flow through membrane channels by an indirect action on the lipid membrane, via a second messenger, or by direct and specific binding to channel proteins. Another theory describes the activation of gamma-aminobutyric acid (GABA) receptors by the inhalation anesthetics. Volatile agents may activate or facilitate GABA channels, resulting in hyperpolarized cell membranes. In addition, they may inhibit certain calcium channels, preventing the release of neurotransmitters and inhibit glutamate channels.

Evidence for the protein receptor theory includes the observation made by Franks and Lieb that a broad range of inhalant anesthetics inhibited the water-soluble enzyme firefly luciferase (Franks & Lieb 1984). This enzyme hydrolyzes luciferin to create light and is often a model for anesthetic action because the rank orders of potency of the anesthetics in animals parallels that of luciferase inhibition. Franks and Lieb studied the enzyme in a lipid free environment, with only the enzyme present, and observed the enzyme could be completely inhibited. This suggests the site of action is within the protein structure and is not strictly dependent on lipid. Franks and Lieb also noted that some anesthetics exist as stereoisomers and that the effects of these isomers can differ. However, when the stereoisomers are introduced into a lipid substrate, the physical effects on the lipid are identical. This is further evidence that the anesthetic is acting at a stereoselective "receptor" and would implicate a protein as the site of action.

Following up on the work by Franks and Lieb, Harrison, Harris, Mihic, and colleagues attempted to reconcile the apparent problem of the nonspecific action of anesthetics on a wide range of protein channels including glycine, glutamate, GABA, and other neurotransmitter activated channels (Mihic et al. 1997). For the anesthetic to act on all of these channels, one would expect a target amino acid sequence would be conserved among all channels or the anesthetic would be altering receptor function by distorting the surrounding environment. In their experiments, this group began making chimeric DNA encoding the c-terminal human GABA rho receptor subunit, which is an anesthetic insensitive receptor, and the N-terminal glycine-binding part of the human glycine alpha-receptor subunit that is situated in the transmembrane spanning domain. They expressed the cDNA in *Xenopus* oocytes and measured resulting chloride conductance. They determined the site of anesthetic action was within the N-terminal sequence of the third transmembrane spanning domain. The researchers then began to construct cDNA containing point mutations within this region and created receptors that were insensitive

to enflurane. They ultimately found two amino acids in the glycine receptor that abolished enflurane sensitivity when mutated. Changing the corresponding amino acids on the GABA receptor also abolished enflurane sensitivity. However, these mutations did not reduce the receptor's sensitivity to the injectable anesthetic propofol.

## Inhalant Anesthetic Pharmacokinetics

Anesthetic Uptake and Distribution A series of partial pressure gradients, beginning at the vaporizer, continuing in the anesthetic breathing circuit, the airways, alveoli, blood, and ending in the tissues, will drive the movement of an anesthetic gas. The movement of that gas will continue until equal partial pressures are present throughout the system. Since the lung is the point of entry and exit to the body, the alveolar partial pressure governs the partial pressure of the anesthetic in all body tissues. Therefore, it is most important to understand how to influence the alveolar partial pressure. Increasing alveolar minute ventilation, flow rates at the level of the vaporizer, and inspired anesthetic concentration, can speed the delivery of anesthetic and increase the rate of rise of alveolar anesthetic partial pressure. Solubility, cardiac output, and the alveolar-to-venous anesthetic gradient are factors that determine the uptake of the anesthetic from the alveoli into the blood. Solubility describes the affinity of the gas for a medium such as blood or adipose tissue and is reported as a partition coefficient. The blood/gas partition coefficient describes how the gas will partition itself between the two phases (blood and alveolar gas) after equilibrium has been reached. Isoflurane for example has a blood/gas partition coefficient of approximately 1.4 (Steffey & Mama 2007). This means that if the gas partial pressures are in equilibrium, the concentration in blood will be 1.4 times greater than the concentration in the alveoli. A higher blood/gas partition coefficient means a greater uptake of the gas into the blood, therefore, a slower rate of rise of alveolar and blood partial pressure. Since the blood partial pressure rise is slower, it takes longer for the brain partial pressure of the gas to increase resulting in a longer induction time.

Increased cardiac output exposes the alveoli to more blood per unit time. The greater volume of blood removes more inhalant anesthetic from the alveoli, therefore lowering the alveolar partial pressure. The agent might be distributed faster within the body, but the partial pressure in the arterial blood is lower. It will take longer for the gas to reach equilibrium between the alveoli and the brain. Therefore, a high cardiac output usually prolongs induction time. The alveolar to venous partial pressure difference reflects tissue uptake of the inhaled anesthetic. A large difference is caused by increased uptake of the gas by the tissues during the induction phase.

Transfer of the gas from the arterial blood into tissues such as the brain will depend on perfusion and the relative solubility of the gas in the different tissues. The brain/blood coefficient describes how the gas will partition itself between the two phases after equilibrium has been reached. Isoflurane has a brain/blood coefficient of 2.7; therefore, when the system is at equilibrium the concentration in the brain will be 2.7 times greater than the concentration in the blood (Steffey & Mama 2007). All contemporary inhalation anesthetics have high adipose/blood partition coefficients. This means that most of the gas will accumulate in adipose tissue as times goes by. The partial pressure of the gas in adipose tissue will rise very slowly since this tissue has a high capacity (as indicated by the high adipose/blood partition coefficient). Inhalation anesthetics stored in obese patients may delay awakening at the end of long periods of anesthesia. Fortunately, adipose tissue has a relatively low blood flow and does not accumulate significant amounts of anesthetic during the short periods of anesthesia commonly encountered in veterinary medicine.

Elimination of Inhaled Anesthetics The rate of induction and recovery from anesthesia with inhalant anesthetics differs between agents due to differences in tissue solubility; however, general statements can be made. During induction, all tissue partial pressures are zero. During recovery, different tissues in the body have different partial pressures of anesthetic which is governed by the tissue anesthetic content and not the alveolar partial pressure. Recovery is not as controllable as induction of anesthesia. During recovery from anesthesia, elimination occurs due to exhalation and biotransformation.

Enzymes responsible for inhalant anesthetic metabolism are mainly located in liver and kidneys. Anesthetic elimination via metabolism is approximately 50% for methoxyflurane, 10–20% for halothane, 5–8% for sevoflurane, 2.5% for enflurane, about 0.2% for isoflurane, 0.001% for desflurane, and nearly zero for nitrous oxide (Steffey & Mama 2007). The amount of anesthetic eliminated from the body during anesthesia due to metabolism is small compared with the amount exhaled. However, anesthetic metabolism accounts for a larger proportion of the anesthetic clearance after anesthetic delivery ceases. The low, but prolonged, blood partial pressure of the anesthetic found after terminating delivery is no longer overwhelming the enzyme systems (enzymes become saturated above ~1 MAC), so metabolism accounts for a larger proportion of clearance than it did during exposure to high partial pressures.

Elimination of the anesthetic via the lungs can be complex. The first point to consider is what effect an increase in alveolar minute ventilation will have on recovery. During recovery, increasing minute ventila-

tion will decrease alveolar anesthetic partial pressure and increase the gradient for diffusion from the blood to the alveoli. This increases elimination, especially for most anesthetic agents with high blood/gas partition coefficients.

Another situation to consider is what effect a change in cardiac output will have on the rate of decrease of partial pressure of the inhalant anesthetic. During induction, high cardiac output will increase the rate at which anesthetic is removed from the lung, slowing the rate of rise of anesthetic partial pressure, slowing induction. When cardiac output is reduced (e.g., cardiogenic shock), there is a slower removal of anesthetic and subsequently a faster rate of rise of alveolar partial pressure and induction occurs. During recovery, a high cardiac output will increase the rate at which anesthetic is returned to the lung for excretion. Since the partial pressure of anesthetic in the blood is determined by the tissues, the higher blood flow will shorten recovery. During low cardiac output situations, there will be a slower recovery due to the decreased rate at which tissue anesthetic partial pressure decreases.

The last major influence on the rate of induction and recovery is the solubility of the anesthetic agent. Agents with high blood/gas solubility will be partitioned into the blood to a greater extent than agents with low blood/gas solubility. The blood acts as a depot for agent maintaining anesthetic partial pressure. Agents with low blood/gas solubility do not partition into the blood to the extent of highly soluble agents, thus the decrease in partial pressure is faster and recovery time is reduced. Highly soluble agents have high blood concentrations, and it will take longer for the partial pressure to decrease if all other factors are equal. In summary, elimination of a volatile anesthetic depends on ventilation, cardiac output, and solubility of the gas in blood and tissue.

## Control of the Partial Pressure of Delivered Anesthetic

Inhalant anesthetics can be classified as either gaseous (nitrous oxide and xenon) or volatile (isoflurane, sevoflurane, halothane, methoxyflurane, and desflurane). Gaseous anesthetics are usually delivered to the anesthesia machine under pressure, and their rate of delivery to the breathing circuit is controlled by a flow meter. Volatile anesthetics are liquids at room temperature and pressure, and are usually delivered by a specialized apparatus that controls the volatilization of the liquid, and proportioning of the vapor in the fresh gas delivered to the patient. A vaporizer can be as simple as a piece of cotton soaked with agent held near the nose (not recommended), or can be as complex as the Tec 6 vaporizer for desflurane.

**The Breathing System** With most modern anesthetic machines, the outflow gas from the vaporizer will be delivered to the patient through a set of tubes and machinery collectively called a breathing system. There are many styles of breathing systems, each with a multitude of uses. It is important that the anesthetist understands how the type of breathing circuit used will impact the rate at which the anesthetic concentration can be changed and the relationship between the vaporizer setting and inspired concentration.

**Waste Anesthetic Gases** The health effects of chronic exposure to waste anesthetic gases are not completely known. The frequency of inhalant anesthetic use and the lack of significant associations between exposure, and most types of chronic toxicities (e.g., cancer, infertility, birth defects, etc.) would suggest there is only a very low risk (if any) associated with chronic exposure. However, certain individuals are highly susceptible to potentially life-threatening reactions, even with trace level exposure (e.g., malignant hyperthermia). In light of this, and with the admission that we do not completely understand all the risks associated with chronic exposure, it is generally agreed that the exposure of personnel be kept as low as reasonably acceptable (ALARA). In the United States, the Occupational Safety and Health Administration (OSHA) requires veterinary hospitals to maintain a system to prevent waste gases from building up in the area of use and can enforce exposure limits that are consistent with recommendations offered by the National Institute of Occupational Safety and Health (NIOSH). The NIOSH recommends that the maximum time-weighted average concentration of volatile halogenated anesthetics should not exceed 2 ppm when used alone or 0.5 ppm when used with nitrous oxide, and that nitrous oxide concentration should not exceed 25 ppm (American College of Veterinary Anesthesiologists 1996).

## Minimum Alveolar Concentration (MAC)

The measurement of the dose of an inhalant anesthetic is the minimum alveolar concentration (MAC) multiple. It is defined as the minimum alveolar concentration at 1 atm, required to prevent gross purposeful movement in 50% of the subjects tested, following a 60-second application of a supramaximal stimulus (Steffey & Mama 2007). One MAC is by definition the $EC_{50}$ (i.e., effective concentration in 50% of patients) for that agent. Animals awaken from anesthesia at approximately 0.5 MAC, surgical anesthesia occurs at approximately 1.3 MAC, and severe autonomic nervous system depression occurs around 2 MAC. Birds and many reptiles do not have true alveoli so the concept of MAC has been modified or redefined to be the minimum anesthetic concentration. It is not identical to MAC from other species, but closely approximates it in many ways.

**Physiological and Pharmacological Factors that Alter MAC** Minimum alveolar concentration is age dependent,

being lowest in newborns, reaching a peak in infants, and then decreasing progressively with increasing age (Lerman et al. 1983, 1994; Taylor & Lerman 1991). Increases in MAC can also occur from hyperthermia and hypernatremia, and decreases in MAC can result from hypothermia, hyponatremia, pregnancy, hypotension, and drugs, such as lithium, lidocaine, opioids, and $\alpha_2$-adrenergic agonists.

## General Pharmacological Actions of Inhalant Anesthetics

Inhalant anesthetic agents have more similarities than differences with respect to their effects on vital organ systems. The differences are primarily related to the speed and magnitude with which the changes occur. There are a few classic differences that have been included in the following synopsis.

**Central Nervous System** All inhalant general anesthetics alter consciousness, memory, and pain perception by acting on the central nervous system. Most inhalant anesthetics cause a mild to moderate decrease in the cerebral metabolic requirement for oxygen ($CMRO_2$), and they usually have minimal effects on cerebral blood flow autoregulation at low MAC multiples (Mielck et al. 1998, 1999). Patients with intracranial hypertension should not be anesthetized, with nitrous oxide because it may cause an increase in $CMRO_2$ (Algotsson et al. 1992; Hoffman et al. 1995; Roald et al. 1991). Halothane is also a poor choice because of its significant effects on cerebral blood flow autoregulation (Steffey & Mama 2007). Isoflurane, sevoflurane, and desflurane are the inhalants of choice at this time.

**Cardiovascular System** Most inhalant anesthetic agents cause direct myocardial depression. Halothane is the most depressant on contractility; however, it generally has the fewest effects on vascular resistance (Steffey & Mama 2007). Isoflurane, enflurane, sevoflurane, and desflurane cause some degree of vasodilatation, which tends to improve forward blood flow and maintain tissue perfusion. The reduction in afterload also tends to offset some of the direct myocardial depressant effects and may result in a net improvement in cardiac output. Nitrous oxide is a sympathomimetic and can improve contractility, blood pressure, and heart rate at light levels of anesthesia. Rapid changes in anesthetic concentration (especially with desflurane) may result in a sympathetic response and temporarily increase cardiac work.

**Respiratory System** All anesthetics tend to depress the chemoreceptor response to carbon dioxide leading to an accumulation of carbon dioxide and a respiratory acidosis unless ventilation is assisted or controlled. The ether derivatives tend to be the most depressant; however, all agents may cause significant depression. Most inhalant agents may interfere with hypoxic pulmonary vasoconstriction and may worsen ventilation–perfusion matching in the lung. This is most dramatic in larger animals where significant pulmonary shunting is often observed.

**Genital–Renal Systems** Most anesthetics cause a decrease in renal perfusion and an increase in antidiuretic hormone (ADH) secretion. Inhalant anesthetics may be the safest anesthetic techniques in anuric renal failure since pulmonary excretion is not dependent upon renal function.

Inhalant anesthetics may cause an increase in postpartum uterine bleeding. This is a bigger consideration in primate anesthesia due to placentation characteristics. Isoflurane, sevoflurane, desflurane, and nitrous oxide have been advocated for use during Caesarian section because of the rapid onset and termination of effect, and the transient effects on the delivered fetuses. Methoxyflurane and halothane are less desirable due to their greater solubility and slower elimination.

## Clinically Useful Inhalant Anesthetics

**Nitrous Oxide** Nitrous oxide is commonly used in combination with a primary inhalant or injectable anesthetic drug. The reason it is not useful in veterinary anesthesia as a solo anesthetic is because of its low potency. Nitrous oxide's MAC value has been estimated to be near 100% for humans and closer to 200% for veterinary patients. It is obvious that 200% nitrous oxide cannot be delivered; in fact, no more than 79% nitrous oxide can be safely delivered without creating a hypoxic gas mixture. In practice, it is common to use a 50% nitrous oxide mixture with the balance of the mix being oxygen. If 50% nitrous oxide is delivered to an animal, it is only providing approximately 0.25 MAC of anesthesia. A potent volatile anesthetic, injectable agent, or other sedative/analgesic drug must supply the remaining 0.75 MAC. Because of this limited anesthetic effect, nitrous oxide use for anesthetic maintenance is not widespread in veterinary medicine. Nitrous oxide is used by some anesthetists during induction of anesthesia for the *second gas effect*. Since nitrous oxide is present in the inspired gas mixture in a relatively high concentration and it rapidly diffuses into the body from the alveoli, the rate of rise of partial pressure of a second coadministered inhalant anesthetic is increased, and induction time can be shortened.

Nitrous oxide has a low blood/gas partition coefficient and has a rapid onset and recovery. The gas can diffuse out of the blood so rapidly that if nitrous oxide delivery is suddenly halted and supplemental oxygen is not administered, a situation known as *diffusion hypoxia* may result. Diffusion hypoxia happens when the mass movement of nitrous oxide down its partial pressure gradient results in high alveolar nitrous oxide