CLINICAL PHARMACOKINETICS WORKBOOK

7th Edition

JOHN E. MURPHY, PharmD, FASHP, FCCP
Professor-Emeritus of Pharmacy Practice and Science
The University of Arizona College of Pharmacy
Tucson, Arizona
To patient care providers whose quest for knowledge remains an important part of life throughout their career.
# TABLE OF CONTENTS

Preface .................................................................................................................................................................................... vii  
Acknowledgments ................................................................................................................................................................. ix  

## SECTION I: SELF-ASSESSMENT AND ANSWERS

1.1. General Pharmacokinetic Applications .................................................................................................................. 3  
1.2. Medication Dosing in Overweight and Obese Patients .............................................................................................. 9  
1.3. Estimating Kidney Function ....................................................................................................................................... 13  
1.4. Renal Drug Dosing .................................................................................................................................................. 17  
1.5. Aminoglycoside Antibiotics ....................................................................................................................................... 21  
1.6. Carbamazepine .......................................................................................................................................................... 27  
1.7. Digoxin ...................................................................................................................................................................... 31  
1.8. Unfractionated Heparin and Low Molecular Weight Heparins ............................................................................ 35  
1.9. Lithium ..................................................................................................................................................................... 39  
1.10. Phenobarbital .......................................................................................................................................................... 43  
1.11. Phenyletoin/Fosphenytoin ....................................................................................................................................... 45  
1.12. Valproic Acid .......................................................................................................................................................... 49  
1.13. Vancomycin ............................................................................................................................................................. 51  
1.14. Warfarin ................................................................................................................................................................... 55  

## SECTION II: SOLUTIONS

2.1. General Pharmacokinetic Applications ..................................................................................................................... 63  
2.2. Medication Dosing in Overweight and Obese Patients ............................................................................................ 69  
2.3. Estimating Kidney Function ...................................................................................................................................... 71  
2.4. Renal Drug Dosing .................................................................................................................................................... 75  
2.5. Aminoglycoside Antibiotics ....................................................................................................................................... 77  
2.6. Carbamazepine .......................................................................................................................................................... 83  
2.7. Digoxin ...................................................................................................................................................................... 85  
2.8. Unfractionated Heparin and Low Molecular Weight Heparins ............................................................................ 89  
2.9. Lithium ..................................................................................................................................................................... 91  
2.10. Phenobarbital .......................................................................................................................................................... 95  
2.11. Phenyletoin/Fosphenytoin ....................................................................................................................................... 97  
2.12. Valproic Acid ..........................................................................................................................................................101  
2.13. Vancomycin .............................................................................................................................................................105  
2.14. Warfarin ...................................................................................................................................................................109  

DOI: 10.37573/9781585286669.FM
APPENDICES
APPENDIX A: Pharmacokinetic Symbols.............................................................. 111
APPENDIX B: Select Pharmacokinetic Terminology ......................................... 112
APPENDIX C: Select Pharmacokinetic Equations ............................................. 113
APPENDIX D: General Estimating Equations ................................................... 114
APPENDIX E: Therapeutic Ranges of Drugs in Traditional and SI Units .......... 115
Welcome to the Clinical Pharmacokinetics Workbook. The content for this work was developed over 10 years of practicing the application of pharmacokinetic principles to the care of patients ranging from fragile premature newborns to the oldest of the elderly. It is also informed by over 35 years of teaching both basic and applied pharmacokinetics to thousands of pharmacy students and pharmacists. I hope it will be of value to review content learned in the past and practiced in patient care settings as well as, perhaps, learning new areas that might not have been covered in your training.

Most of the pharmacokinetic parameters and dosing approaches used here are taken directly from specific chapters in the book Clinical Pharmacokinetics, Sixth Edition (American Society of Health-System Pharmacists, 2017). I wish to thank the authors of those chapters for their excellent work in reviewing the literature and compiling these data for use in predicting drug dosing schedules and resulting drug concentrations. However, it is important to note that this workbook is designed to test skills in using equations and application of pharmacokinetic parameters. It is not meant to be the final word on how patients should be dosed and monitored.

A few caveats will be of benefit to consider while using this material:

1. It is quite likely that other professors teaching pharmacokinetics used variations of some of the equations provided here. That is to be expected. My approach has always been to try and find the simplest approach to solving pharmacokinetic problems, although it is surely possible that others have found better ways to solve some problems. As an example of my approach, $2.3 \times \log = \ln$, so I always use $\ln$ (natural log) rather than $\log$ (to the base 10) because it saves the step of multiplying times 2.3. Other teachers like $C_1$ and $C_2$ to represent two different concentrations on a concentration-time curve. I prefer $C_i$, which would generally represent the initial (higher concentration) measured, and $C$ for any concentration that is down the curve and smaller.

2. The chapters are designed to pose calculations and other general knowledge questions with the answers given at the end of the chapter. If you get an answer right, keep moving on. If not, detailed problem solutions are shown in the second part of the book with corresponding numbers (eg, Chapter 1.3 self-assessment corresponds with Chapter 2.3 problem solutions).

3. Most self-assessment chapters will have population pharmacokinetic values and dosing approaches provided at the beginning of the chapter. These approaches and values provided are not meant to suggest that better approaches or different parameters might not be found in the literature. Although other approaches and population predictors may be used in various settings, the ones provided here must be used to end up with the same answer that will be provided.

4. Calculations have generally been done by storing multiple decimals of a portion of a formula answer to be used for the rest of the formula, while final answers may be rounded off to just one or two decimal places. If answers are rounded off early in calculations when a complex formula is used, the final answer may be somewhat different than the one listed as correct. If your answer is slightly off, examine the problem solution, and if the problem has been set up correctly, the difference may be due to early rounding.

5. Although most of the problems are based on actual patients treated over the years, some are purely hypothetical. Some of the approaches taken may not be in common use and are provided primarily as examples to illustrate points.

6. As mentioned above, I like simple approaches. Whenever a problem can be solved using ratio (eg, a 50% increase in dose can be expected to increase a steady state concentration by 50%), that approach will be shown. Using the correct equations that represent the dosing approach can solve any problem and will also be shown, but I don't think you should have to work harder than necessary to solve a problem.
I would like to recognize several chapter authors from *Clinical Pharmacokinetics, Sixth Edition*, for their excellent work creating some of the pharmacokinetic parameters and dosing approaches used as examples in this workbook. The following individuals are much appreciated:

Jacquelyn L. Bainbridge, Pei Shieen Wong, and Felecia M. Hart (Carbamazepine);
Robert E. Pachorek (Creatinine Clearance);
Robert DiDomenico and Robert L. Page, II (Digoxin);
A. Joshua Roberts and William E. Dager (Heparins);
Stanley W. Carson and Lisa W. Goldstone (Lithium);
Brian L. Erstad (Obesity);
Kimberly B. Tallian and Douglas M. Anderson (Phenobarbital);
Michael E. Winter (Phenytoin);
Dean A. Van Loo and Thomas C. Dowling (Renal Dosing);
Barry E. Gidal (Valproate);
Jeremiah J. Duby, Monica A. Donnelley, Chelsea L. Tasaka, and Brett H. Heintz (Vancomycin); and
Ann K. Witkowsky (Warfarin).

I would like to thank the wonderful editorial staff at ASHP for supporting this work and keeping me on track.

Many thanks to my ever-patient wife Debbie for letting me abuse family time for work time, even in retirement, and being so understanding about it all.