

# PREFACE

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It is my hope that this book will be used both by scientists and the policymakers who determine where the research dollars are spent. Anyone who takes the time to read more than a few pages of this Handbook will encounter quite a few surprises, some good and some bad. The good news is that during the last decade, a tremendous amount has been learned about abused drugs. The bad news is that progress has not been equally rapid on all fronts. Molecular biologists and neurochemists who, perhaps not coincidentally receive the lion's share of federal funding, have made breathtaking advances. They are tantalizingly close to characterizing the basic mechanisms of addiction. Progress has been somewhat less dramatic on other fronts.

Testing workers for drugs has become a huge, competitive business. Market forces have ensured that the necessary research was done. Regulated urine drug testing is now a reliable and reasonably well-understood process. Yet, desperately needed studies to test the efficacy (as opposed to the accuracy) of workplace drug testing programs are not on the horizon, and we still do not know with any certainty whether the enormous amount of money being spent really has an effect on worker absenteeism, accident rates, and productivity.

In areas where government and industry share common interests, there has been impressive progress. Researchers interested in impairment testing have received sufficient funding to finally place this discipline on firm scientific footing. But practical workplace applications for impairment testing are hampered by the paucity of data relating blood, hair, sweat, and saliva drug concentrations with other workplace performance measures.

The use of alternate testing matrices poses a daunting challenge. Until very recently, alternate approaches to workplace testing were not permitted. There was little government interest, and no potential market in sight. With no money to be made, industry leaders saw no reason to invest in new technologies. Now it appears that pressure from private industry has altered government perceptions, and changes may be imminent. But a great deal of science remains to be done. In particular, basic pharmacokinetic research is needed to describe the disposition of abused drugs in alternate specimens. Without such data, the utility of alternate specimens is limited, and reliable interpretation of test results is nearly impossible.

Farther away from university and government laboratories, at the bedside and at the autopsy table, the picture is not quite so rosy. SAMHSA supported the development of LAAM, the long acting methadone substitute, and funding has gone into improving methadone maintenance programs. But methadone clinics are not ivory towers, and controlled studies with non-compliant patients are fiendishly difficult. Politicians intent on being "tough on drugs" have created a regulatory climate where control of treatment has largely been taken away from physicians, and political considerations outweigh reasoned scientific judgment. The recent suggestion by National Drug Control Policy Director Barry McCaffrey that physicians be allowed to prescribe methadone, may mark an important shift in the way our leaders address these problems.

Even so, research into the medical management of drug users is not exactly a priority issue. One might suppose that given the very sophisticated techniques now available for therapeutic drug monitoring, the kinetics of abused drugs would be well characterized. There are several reasons why they have not. Discounting the fact that such projects have little commercial appeal, and seem not to be a priority for our government (even though most of the important research has been done at the federally funded Addiction Research Center), the greatest handicaps are ethical and political. Drug abusers take drugs in quantities that no Institutional

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Review Board would ever approve and that doctors would refuse to administer. Whether or not the body metabolizes 50 mg of cocaine given intravenously the same way it manages 250 mg is, for the moment, at least, anyone's guess. However, the results of recent studies from the Addiction Research Center suggest that chronic oral dosing with cocaine may allow researchers to simulate the high doses used on the street.

Cocaine and heroin abuse claim the lives of more than 15,000 Americans every year, but no pathologist sits on the advisory board that passes on drug research grants, and there is no federal funding for pathology or for pathologists interested in drug abuse. The sorry state of the DAWN report (Drug Abuse Warning Network) offers a hint of the importance our government accords to the investigation of drug-related deaths; results for 1995 were finally released in May of 1997! Three-year-old epidemiologic data may be of some interest to historians, but it certainly is of little value to clinicians.

At least the epidemiologic studies get funded. Lack of federal support means that a great many promising leads are being passed up. There is mounting evidence that chronic drug abuse produces identifiable morphologic changes in the heart, brain, lungs, and liver. But there are no federal funds to support the studies needed to translate these preliminary observations into useful diagnostic tools.

Toxicologists studying postmortem materials have done no better than the pathologists. Technologic innovations in workplace testing and therapeutic drug monitoring now allow the routine measurement of nanogram quantities of drugs in tissue obtained at autopsy, but the interpretation of these measurements is not a straightforward process. Even though postmortem drug concentrations are frequently debated in court, research on the interpretation of postmortem drug levels consists of little more than a handful of case reports, published by a few dedicated researchers. During the last decade, more than 50,000 Americans have died using cocaine, but postmortem tissue levels have only been reported in a handful of cases.

Even if the tissue levels were better characterized, tolerance occurs. It is impossible to speak of "lethal" and "non-lethal" cocaine and morphine concentrations because tolerant users may be unaffected by levels that would be lethal in naive drug users. But, poorly informed physicians and attorneys continue to ignore these subtleties, just as they continue to ignore the wealth of scientific knowledge that has been accumulated on the effects of alcohol, both in the living and the dead. The same legal arguments are debated again and again, even though the science has been very well worked out.

Important research remains to be done, yet we have already learned a great deal. Unfortunately, that knowledge is not being shared effectively, not with the rest of the medical community, not with the courts, and certainly not with drug policy makers. If we can do a better job of educating, then sometime in the not too distant future, we may be able to obtain the support for the work that we know needs to be done. I hope this book helps in that process.