Drug and Alcohol Abuse

A Clinical Guide to Diagnosis and Treatment

Second Edition

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DRUG AND ALCOHOL ABUSE: A Clinical Guide to Diagnosis and Treatment, Second Edition
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Drug and Alcohol Abuse

A Clinical Guide to Diagnosis and Treatment

Second Edition

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To Sam who taught me how to laugh,
Lil who showed me how to love those close to me,
and to Judy, Dena, and Jordan who keep me doing both.

Foreword

When this series was conceived, a book on substance abuse, including alcohol and alcoholism, was to be of the highest priority. This priority was a reflection of my view that the subject is often inadequately or insufficiently taught in many training programs. Few clinicians have had comprehensive didactic education in this area, despite the frequency with which these problems are encountered in practice. All too often these encounters are in situations in which accurate diagnosis and rapid treatment are of critical importance. We wanted a book that would be concise and easily readable but also comprehensive in its presentation of the basic principles underlying clinical manifestations, diagnosis, and management. It was of particular importance that the book also serve as an easy reference guide in emergency situations.

Marc Schuckit, a man with impeccable credentials as a scholar and an experienced clinician in this field, produced just such a book with his critically acclaimed first edition. That volume rapidly became a resource of great significance for psychiatrists, psychotherapists, and physicians in general. It has been adopted as a text in medical schools and residency training, as well as for courses in psychology, emergency medicine, social work, and nursing.

The entire volume has been revised and updated to reflect changes in knowledge and clinical practice since the publication of the first edition and in order to keep the comprehensive references current. There is a new chapter on phencyclidine and another on caffeine and nicotine. There are chapters on CNS depressants; alcohol and alcoholism; stimulants; opiates and other analgesics; cannabinols; hallucinogens; glues, solvents, and aerosols; and over-the-counter drugs. Multidrug use is dealt with thoroughly, and there is an extensively revised chapter on rehabilitation. The rapid guide to emergency problems will continue to be of great relevance to all practitioners. Whether one's goal is an understanding of each drug class and its associated clinical problems or the need to diagnose

rapidly and treat a specific drug emergency, the reader is led step by step through all the elements underlying the mechanism of action, the clinical and laboratory findings, and the specifics of treatment.

Since substance abuse is such a complicated and prevasive problem, and one that has resisted our attempts at primary prevention, Dr. Schuckit's revised and expanded book will undoubtedly make an even greater contribution to clinical practice in medicine, psychiatry, and all the mental health disciplines.

SHERWYN M. WOODS, M.D., PH.D.
Series Editor

Preface to the Second Edition

In the intervening years between the publication of the first and second editions, this book has been used as a text for teaching in medical schools, psychology and social work courses, nursing curricula, and so on. As a result of my own efforts in this area and of correspondence from teachers in different disciplines, revisions have been carried out in every chapter. The goal has been primarily to clarify questions raised by students and to expand into areas of need. Regarding the latter, two new chapters have been added, one dealing with phencyclidine to meet the increasing use of this drug over the years and the other dealing with the two most prevalent substances of misuse, caffeine and nicotine. Additional changes include a thoroughly revised chapter on rehabilitation.

This revision could never have been carried out properly without the help of Cheyvonne Frontiero, the editorial assistance offered by Plenum Press, as well as the encouragement of Sherwyn Woods and my colleagues at the University of California, San Diego. Of course, this book could never have been written were it not for the love and happiness generated by my wife, Judy, and children, Dena and Jordan.

MARC A. SCHUCKIT, M.D.

Preface to the First Edition

This book grew out of a series of lectures developed to help the nonpharmacologist make sense out of a complex literature. The core of my approach is to learn the characteristics of drug classes, understand the usual types of difficulties associated with drugs, and then apply these general rules in clinical settings. It is hoped that the text will be a beginning place for gathering knowledge about drug types in the classroom and also a first step in handling emergency problems in clinical setting.

So that the book may properly serve as a resource for survey courses and as an emergency handbook, I have kept my comments relatively short, attempting to relate the most essential material. In order to help the reader understand drugs of abuse in greater depth, each chapter is highly referenced in the hopes that he will further expand his knowledge in this area.

I have never read a perfect manuscript or book, and (the views of my mother aside) this is not one. As with any complex endeavor, a series of compromises must be made as one decides whether to pursue Road A or Road B. My aim is to have this text strike a proper balance between the immediate needs of the clinician and those of the student looking for an introduction to substances of abuse.

I wish to extend my appreciation to Jane Ramsey, Edna Glenn, and my colleagues at the Alcoholism and Drug Abuse Institute of the University of Washington, as well as to my wife, Judy, and my colleagues at the University of California at San Diego Medical School, Department of Psychiatry, for their help in preparing this manuscript.

MARC A. SCHUCKIT, M.D.

Contents

CHAPTER 1

An Overview

1.1. INTRODUCTION

This book is written for the medical student, the physician in practice, the psychologist, the social worker, and other health professionals, or paraprofessionals, who need a quick, handy, clinically oriented reference on alcohol abuse and other drug problems. The first chapter addresses the need to learn the drug classes and the relevant problem areas from which generalizations can be made.

The book is divided into consecutive chapters dealing with specific classes of drugs. The discussion within each chapter is subdivided into sections on general information on the drugs in that class and sections covering the problems faced in emergency situations. Material on rehabilitation is presented in Chapter 15.

The text can be used in at least two basic ways:

1. If you are treating an emergency problem and know the probable class of the drug involved, you will turn to the emergency problem section of the relevant chapter. If you do not know the drug and need some general emergency guidelines, you will use the appropriate subsections of Chapters 1 and 14. Emphasis is placed on the most relevant drug-related material, and it is assumed that the reader already has some working knowledge of physical diagnosis, laboratory procedures, and the treatment of life-threatening emergencies.

Once the emergency has been handled, you will want to review the general information available on that class of drugs. At your leisure, you might then review the general information presented in Chapter 1 and go on to read the first section and some of the references cited in the bibliography of the relevant chapter.

2. If you are interested in learning about drug classes and their possible emergency problems, you should begin by skimming all the chapters. After gaining some level of comfort with the general thrust of the material, you

can then reread in detail those sections of most interest to you, going on to the more pertinent references. The first section of each chapter contains as little medical jargon as possible.

To address these goals and to make each chapter as self-sufficient as possible (in the emergency room you do not want to have to jump too much from chapter to chapter), there is some level of redundancy between book sections. I have tried, however, to strike a balance between readability and clinical usefulness.

No short handbook can answer all questions about every drug. The emergency-oriented nature of this text also tends to lead to oversimplification of rather complex problems. I give general rules that will need to be modified in specific clinical situations. Although you will not know everything about drugs after finishing the text, it is a place to start learning.

In order to present the material in the most efficient way, I have used a number of shortcuts:

1. In giving the generic names of medications, I have deleted the suffix indicating which salt form is used (e.g., *chlordiazepoxide hydrochloride* is noted as *chlordiazepoxide*) because to list them would add little useful information.

2. The specific medications recommended for treatment in the emergency room settings represent the idiosyncrasies of my personal experience as well as those of other authors in the literature. The physician will usually be able to substitute another drug of the same class so that he can use a medication with which he has had experience (for example, when I note the use of haloperidol [Haldol], the physician might substitute *comparable* doses of trifluoperazine [Stelazine]).

3. The dose ranges listed for the medications recommended for treatment of emergency situations are *approximations only* and will have to be modified for the individual patient based on the clinical setting and the patient's characteristics.

4. Although the treatment discussions are frequently offered as a series of steps (as seen in most discussions of toxic reactions), the order offered is a general guideline that is to be modified for the particular clinical setting.

5. It must be noted that the appropriate place for treating most emergency problems recorded here is in a hospital.

I have attempted to use the limited amount of space I have in a manner that reflects the frequency with which the usual clinician encounters drug problems. Therefore, the greatest amount of material is presented for the most clinically important drug, alcohol. Also, alcohol and opiates, drugs on which the most data for rehabilitation are available, are used as prototypes for the other discussions of rehabilitation.

The causes of substance abuse are not known. Nor is there evidence that knowledge of specific etiologies will help the clinician to address the

rehabilitation of patients with substance problems. It is assumed that the genesis of most alcohol and drug problems rests with a complex interaction between biological and environmental factors. Regarding the former, there is evidence that genetic factors may influence smoking and other drug-taking behaviors,[1,2] and there is excellent evidence, which is briefly alluded to in Chapter 3, that genetic factors contribute to the genesis of alcoholism. With rare exceptions, etiology will not be covered in depth in this clinically oriented text.

Another important issue is the prevalence and pattern of substance-related problems in populations, that is, epidemiology. The use of substances is widespread in most societies, and almost every individual has had some contact with nicotine and caffeine, a substantial majority having used alcohol, and a majority of younger people having tried the cannabinols, especially marijuana.[3-5] With the exception of these brief general comments, I have chosen to give epidemiological information as it relates to each specific class of drugs and thus offer no separate section on this topic.

Two final notes that reflect the sensitivities of our times are needed. To save time and space, male pronouns are consistently used in the text but are meant to refer to both genders. For similar goals of efficiency, the terms *client, patient,* and *subject* are used interchangeably.

1.2. SOME DEFINITIONS

Before we can begin, it is important to set forth a series of clinical concepts central to the discussion of substance misuse. The definitions presented are not the most pharmacologically sophisticated, but they do, I think, represent the greatest potential for use in clinical situations. To arrive at these terms, I have borrowed from a wide variety of standard texts and published studies, attempting to blend them together into a readily usable framework.

1.2.1. Drug of Abuse

A *drug of abuse* is any substance, taken through any route of administration, that alters the mood, the level of perception, or brain functioning.[6] Such drugs include substances ranging from prescribed medications to alcohol to solvents.[7-9] All these substances are capable of producing changes in mood and altered states of learning.

There are a number of other practices that I have considered for inclusion. For instance, there are parallels between obesity (i.e., the use of food to the point of abuse) and the misuse of the most usual drugs.[10,11] Similarly, the compulsion surrounding some forms of gambling have much of the "feel" of the obsessive behavior observed during substance abuse.[12] However, it is not possible for one text to cover everything, and expansion

into these interesting and related topics might jeopardize my attempts to cover clinically related topics in a succinct way in order to help the clinician in his day-to-day practice.

1.2.2. Drug Abuse

Drug abuse is the use of a mind-altering substance in a way that differs from generally approved medical or social practices.[4] Said in another way, when the continued use of a mind-altering substance means more to the individual than the problems caused by such use, the person can be said to be abusing drugs.

1.2.3. Dependence

Dependence, also called *habituation* or *compulsive use,*[9] connotes a psychological and/or physical "need" for the drug.[6,9]

1. *Psychological dependence* is an attribute of all drugs of abuse[6] and centers on the user's needing the drug in order to reach a maximum level of functioning or feeling of well-being. This is a subjective term that is almost impossible to quantify, and thus, it is of limited usefulness in making a diagnosis.
2. *Physical dependence* indicates that the body has physiologic adaptation to chronic use of the substance, with the development of symptoms when the drug is stopped or withdrawn. Although initially this concept appears to be quite simple, there is evidence that behavioral conditioning and psychological factors are important in what is usually felt to be a physical withdrawal syndrome.[13,14] There are two important aspects to physical dependence:
   a. *Tolerance* is the toleration of higher and higher doses of the drug or, said another way, the need for higher and higher doses to achieve the same effects. The phenomenon occurs both through alterations in drug metabolism, where the liver destroys the substance more quickly (*metabolic tolerance*), and through alterations in the target cells' (usually in the nervous system) functioning in the presence of the drug, where tissue reaction to the drug is diminished (*pharmacodynamic tolerance*). This is not an all-or-none phenomenon, and an individual may develop tolerance to one aspect of a drug's action and not another. The development of tolerance to one drug of a class usually indicates *cross-tolerance* to other drugs of the same class.[9]
   b. *Withdrawal* is the appearance of physiological symptoms when the drug is stopped too quickly. This phenomenon was first and most completely described for drugs like opiates or drugs that tend to depress the action of the central nervous system.

However, there is evidence that there are also withdrawal signs when drugs with different actions, such as stimulants, are used. Like tolerance, withdrawal is not an all-or-none phenomenon and usually consists of a syndrome of mixtures of a wide variety of possible symptoms.[9]

1.3. GENERAL COMMENTS ABOUT DRUG MECHANISMS

The drugs discussed here all affect the brain or the central nervous system (CNS). Unfortunately for our simplistic discussion, the actions of these drugs on the CNS tend to be highly complex. These factors are mediated through different neurotransmitters acting through a myriad of intercellular communications that strike a balance between excitatory and inhibitory functions.[15] This highly complex level of interaction, along with the drive of the nervous system to achieve equilibrium or homeostasis, makes it very difficult to generalize about specific mechanisms of drug actions. The same drug can have behavioral stimulation effects at one dose but sedation at another.

The problems of understanding what to expect with a specific drug are even more complex for drugs bought "on the street." Most of these substances are not pure, and many (almost 100% for such drugs as THC; see Section 1.4.4) do not even contain the purported major substances. Thus, one must apply the general lessons discussed in this text carefully, staying alert for unexpected consequences when treating drug abusers.

Specific drug actions depend on the route of administration, the dose, the presence or absence of other drugs, and the clinical condition of the patient. Disposition, metabolism, and sensitivity to substances are also affected by genetic mechanisms, probably both through levels of end organ sensitivity (e.g., in the CNS) and through the amount and characteristics of the enzymes of metabolism and the amount of protein binding. One important factor to consider in predicting reactions to drugs is age, as growing older is accompanied by a reduction in total drug clearance for many substances, along with increased brain sensitivity, especially for the CNS depressants.[16]

In summary, a clinically oriented text such as this one can make few valid generalizations about the mechanisms of drug actions. The reader is referred to general pharmacology texts, including one edited by Goodman and Gillman.[6,9]

1.4. ONE APPROACH TO DRUG CLASSIFICATION

It is possible to learn the characteristics of a drug class and then to apply the general rules to the specific case. There are many possible classifications, some of which are best used for research and some of which are the most pharmacologically correct. However, I present a breakdown of drugs

into classes that have particular usefulness in clinical settings and where the drug class is determined by the most prominent CNS effects at the usual doses.[15]

This drug classification is presented in Table 1.1 along with some examples of the more frequently encountered drugs of each particular class. The divisions include:

1.4.1. General CNS Depressants

The most prominent effect of these drugs is the depression of excitable tissues at all levels of the brain, along with relatively few analgesic properties at the usual doses.[15] The CNS depressants include almost all sleeping medications, antianxiety drugs (also called *minor tranquilizers*), and alcohol. The antipsychotic drugs (also called *major tranquilizers*), such as chlorpromazine (Thorazine) or haloperidol (Haldol), are *not* CNS depressants, do not resemble the antianxiety drugs in their structures or predominant effects, are not physically addictive, and are rarely used to induce a "high."

1.4.2. CNS Sympathomimetics or Stimulants

The predominant effect of these drugs at the usual doses is the stimulation of CNS tissues through blocking the actions of inhibitory nerve cells or by the release of transmitter substances (chemicals released from one brain cell to stimulate the next cell) from the cells, or by direct action of the drugs

Table 1.1
Drug Classification Used in This Text

Class	Some examples
CNS depressants	Alcohol, hypnotics, antianxiety drugs
CNS sympathomimetics or stimulants	Amphetamine, methylphenidate, cocaine, weight-loss products
Opiates	Heroin, morphine, methadone, and almost all prescription analgesics
Cannabinols	Marijuana, hashish
Psychedelics or hallucinogens	LSD, mescaline, psilocybin
Solvents	Aerosol sprays, glue, toluene, gasoline, paint thinner
Over-the-counter drugs	Contain: atropine, scopolamine, antihistamines
Others	Phencyclidine (PCP), bromides

themselves. The substances most relevant to clinical situations include all the amphetamines, methylphenidate (Ritalin), and cocaine. The related substances, nicotine and caffeine, are discussed in a separate chapter (Chapter 12) as their pattern of associated problems is limited to panic and medical difficulties.

1.4.3. Opiate Analgesics

These drugs, also called *narcotic analgesics*, are used clinically to decrease pain, and they include morphine and other alkaloids of opium as well as synthetic morphinelike substances and semisynthetic opium derivatives. Prominent examples of these drugs include *almost all* painkilling medications, ranging from propoxyphene (Darvon) to heroin and including oxycodone (Percodan) and pentazocine (Talwin).

1.4.4. The Cannabinols, or Marijuana

The active ingredient for all these substances is tetrahydrocannabinol (THC) with the predominant effect of producing euphoria, an altered time sense, and, at doses higher than those usually found in clinical situations, hallucinations. This is a "street" drug sold in the United States primarily as marijuana or hashish, as pure THC is almost never available on the "black market."

1.4.5. Psychedelics or Hallucinogens

The predominant effect of these substances is the production of hallucinations, usually of a visual nature. The hallucinogens have no accepted medical usefulness and are a second example of "street" drugs. Phencyclidine (PCP) is abused as a hallucinogen but is discussed separately because of its unique actions and problems (see Chapter 9).

1.4.6. Solvents, Glues, and Aerosols

These substances are used in various fuels, aerosol sprays, glues, paints, and industrial solutions. They are used as drugs of abuse in attempts to alter the state of consciousness, producing primarily light-headedness and confusion.

1.4.7. Over-the-Counter Drugs and Other Prescription Medications

A variety of substances are marketed for sale without prescription in the treatment of constipation, pain, nervousness, insomnia, and so on. The sedative or hypnotic medications are the most frequently abused and contain atropine-type drugs (anticholinergics) and/or antihistamines and are

taken to give feelings of light-headedness and euphoria. Finally, there are a number of other prescription drugs that are much less likely to be abused than those described above, including diuretics, antiparkinsonian drugs, and some antipsychotics.

1.5. ALTERNATE CLASSIFICATION SCHEMES

An additional breakdown of these substances, addressing a series of "schedules" developed by the federal government, is presented in Table 1.2.[17,18] The classification is based on both the degree of medical usefulness and the abuse potential of the substance, ranging from Schedule I, which includes those drugs with few accepted medical uses and a high abuse potential (e.g., heroin), to Schedule V, drugs that have a high level of medical

Table 1.2
Drug Schedules with Examples[17,18]

Schedule I (High abuse, low usefulness):	
Examples:	Heroin
	Hallucinogens
	Marijuana
Schedule II:	
Examples:	Opium or morphine
	Codeine
	Synthetic opiates (e.g., meperidine [Demerol])
	Barbiturates
	Amphetamines, methylphenidate (Ritalin), and phenmetrazine (Preludin)
	Methaqualone (Quāālude)
	PCP
Schedule III:	
Examples:	Aspirin with codeine
	Paregoric
	Methyprylon (Noludar)
	Glutethimide (Doriden)
	Diethylpropion (Tenuate)
Schedule IV:	
Examples:	Phenobarbital
	Chloral hydrate (Noctec)
	Ethchlorvynol (Placidyl)
	Flurazepam (Dalmane)
	Pentazocine (Talwin)
	Chlordiazepoxide (Librium)
	Propoxyphene (Darvon)
Schedule V (Low abuse, high usefulness):	
Examples:	Narcotic-atropine mixtures (Lomotil)
	Codeine mixtures ($<$ 200 mg)

usefulness and relatively little abuse potential. Unfortunately, it is not always possible to generalize from the schedule level to the actual drug dangers, as exemplified by the classification of marijuana and heroin at the same level and of ethchlorvynol (Placidyl) and glutethimide (Doriden) in different categories, despite their marked medicinal and abuse similarities.

Another way of looking at these drugs is to attempt to classify them by their "street" names. These differ from one locale to another and at the same place over time; therefore, Table 1.3 can be seen as only a brief list of some of the more relevant street names that are *usually* used. It is important to gain some knowledge of the specific use of drug names in your vicinity. In

Table 1.3
A Brief List of "Street" Drug Names

CNS Depressants[a]

Blue birds	Green and whites (Librium)	Seccy
Blue devil	Greenies	Seggy
Blue heaven	Nembies	Sleepers
Blues	Peanuts	T-bird
Bullets	Peter (chloral hydrate)	Toolies
Dolls[b]	Rainbows	Tranqs (Librium type)
Double trouble	Red birds	Yellow jackets
Downs	Red devils	Yellows
Goofballs	Roaches (Librium)[b]	

Stimulants[c]

Bennies	Double cross	Roses
Blue angels	Flake (cocaine)	Snow (cocaine)
Chris	Footballs	Speed
Christine	Gold dust (cocaine)	Speedball (heroin plus cocaine)
Christmas trees	Green and clears	Truck drivers
Coast to coast	Hearts	Uppers
Coke (cocaine)	Lip poppers	Ups
Copilot	Meth	Wake-ups
Crisscross	Oranges	Whites
Crossroads	Peaches	
Crystal (IV Methamphetamine)[b]	Pep pills	
Dexies	Pinks	

Analgesics

Heroin		Other	
Brown	Scat	Black (opium)	PG, or PO (Paregoric)
H	Shit	Blue velvet (Paregoric plus antihistamine)	Pinks and grays (Darvon)
H and stuff	Skag	Dollies (methadone)	Poppy (opium)
Horse	Smack	M (morphine)	Tar (opium)
Junk		Microdots (morphine)	Terp (terpin hydrate or cough syrup with codeine)

(Continued)

Table 1.3
A Brief List of "Street" Drug Names (Cont.)

Cannabinols			
Marijuanalike			Hashishlike (more potent)
Acapulco gold	MJ	Yesca	Bhang
Brick	Muggles		Charas
Grass	Pot		Gage
Hay	Reefer		Ganja
Hemp	Roach[b]		Hash
Jive	Rope		Rope
Joint	Sativa		Sweet Lucy
Key, or kee	Stick		
Lid	Tea		
Locoweed	Texas tea		
Mary Jane	Weed		

Phencyclidine (PCP)		
Angel dust	Hog	Shermans
Aurora	Jet	Sherms
Busy bee	K	Special L.A. coke
Cheap cocaine	Lovely	Superacid
Cosmos	Mauve	Supercoke
Criptal	Mist	Supergrass
Dummy mist	Mumm dust	Superjoint
Goon	Peace pill	Tranq
Green	Purple	Whack
Guerrilla	Rocket fuel	

Hallucinogens		
Acid (LSD)	Cube (LSD)	Mescal (mescaline)
	D (LSD)	Owsleys (LSD)
Blue dots (LSD)		
Cactus (mescaline)		Pearly gates (morning glory seeds)
Crystal[b]		

[a]Moderate length of action *like* secobarbital unless otherwise noted.

[b]Multiple drugs have the same name.

[c]A form of amphetamine unless otherwise stated.

the table, drugs are divided into the major classes outlined in this chapter, and the street names are given alphabetically within each class. For ease of reference, this is one of the rare places in this text where trade names rather than generic names are used.

1.6. A CLASSIFICATION OF DRUG PROBLEMS

All drugs of abuse cause intoxication, *each induces psychological dependence* (feeling uncomfortable without the drug), and all are self-administered by an individual to change his level of consciousness or to in-

crease his psychological comfort. Indeed, if people did not begin to feel at least a psychological need for the drug, it is not likely that it would have caused a problem. Each class of drugs has its dangers, with patterns of problems differing between drug classes. In this section, I present some general concepts that will be discussed in greater depth in each chapter.

There is a limited range of adverse reactions to the drugs of abuse, and it is thus possible to create a summary table of drug categories and the problems most prominent for each (see Table 1.4). This section of the chapter expands on the information in the table. For most types of problems (e.g., a panic), I first discuss the most usual history, then I note the usual physical signs and symptoms and the most prominent psychological difficulties, and finally, I give an overview of relevant laboratory tests. The generalizations presented for panic reactions, flashbacks, psychosis, and organic brain syndromes are so constant among drug categories that only a brief discussion of the clinical picture is presented within each relevant chapter. On the other hand, the toxic reactions and the withdrawal pictures seen with the different drug classes are so distinct that detailed discussions of the clinical picture are presented within each chapter.

It is important at this juncture to note that, with the exception of toxicologic screens of the urine (telling *if* the drug has been taken in the last day to week) and blood (telling *how much* of the substance, if any, is in the blood), there are few laboratory tests that help to establish a drug diagnosis. The normal laboratory result for each of the toxicologic screens is at or near zero.

In the material that follows, a hierarchy has been established to help you in addressing the most clinically significant problem first:

1. Any patient who has taken enough of a drug to seriously compromise his vital signs is regarded as having a toxic reaction. Associated symptoms of confusion and/or hallucinations/delusions can be expected to clear as the overdose is properly treated.

Table 1.4
Most Clinically Significant Drug Problems by Class

	Panic	Flashbacks	Toxicity	Psychosis	OBS	Withdrawal
Depressants	-	-	++	++	++	++
Stimulants	+	-	+	++	+	+
Opiates	-	-	++	-	+	++
Cannabinols	+	+	+	-	+	-
Hallucinogens	++	++	+	-	+	-
Solvents	+	-	+	-	++	-
Phencyclidine (PCP)	+	?	++	*a*	*a*	?
Over-the-Counter	-	-	+	-	++	-

[a]Most PCP problems appear to be related to a toxic reaction and the subsequent stages of recovery.

2. Patients who demonstrate a drug-related clinical syndrome with relatively stable vital signs, but who show strong evidence of drug withdrawal even if the syndrome includes confusion or psychotic symptoms, are labeled *withdrawal.*
3. Patients with stable vital signs and no signs of withdrawal, but levels of drug-induced confusion, are regarded as having an organic brain syndrome (OBS) even if hallucinations or delusions are part of that clinical picture. In this instance, the psychotic symptoms can be expected to clear as the OBS disappears.
4. Thus, patients who show stable vital signs, no evidence of clinically significant confusion, and no signs of withdrawal, but who show hallucinations and/or delusions without insight, are regarded as having a psychosis.
5. Most remaining patients are expected to be demonstrating a panic reaction or flashbacks.

1.6.1. Panic Reaction

1.6.1.1. The Typical History

The patient is usually a naive user who has typically taken marijuana, a hallucinogen, or a stimulant.[19] Shortly after ingestion of the drug and the onset of the "typical" drug effects, the individual acutely develops fears that he is losing control, that he has done physical harm to himself, or that he is going crazy, and he is brought in for help by friends, relatives, or the police.

1.6.1.2. Physical Signs and Symptoms

Physical findings reflect fear, anxiety, and sympathetic nervous system overactivity (for example, increased pulse and respiratory rates) occurring in the midst of a panic. This overactivity includes an elevated pulse (usually about 120 beats per minute), an elevated respiratory rate (over 20 or 25 per minute), and an elevated blood pressure. The patient may also demonstrate slightly dilated pupils and excess perspiration.

1.6.1.3. Psychological State

Fear of going crazy, developing uncontrollable behavior, or the occurrence of permanent brain or heart damage (e.g., having a heart attack) dominates the clinical picture.

1.6.1.4. Relevant Laboratory Tests

Depending on the patient's clinical picture, steps must be taken to rule out any obvious physical pathology. Thus, in addition to establishing the level of the vital signs, it is necessary to evaluate the need for an *electro-*

cardiogram (EKG) and to draw routine baseline laboratory studies (e.g., red blood cell count [RBC]; glucose, liver function, and kidney function tests; white blood cell count [WBC]; and tests of skeletal or heart muscle damage, such as creatinine phosphokinase [CPK]). Some of the more relevant tests, along with their abbreviations and *most usual* normal values, are presented in Table 1.5. Of course, when a drug reaction is suspected but no adequate history can be obtained, urine (approximately 50 ml) and/or blood (approximately 20 ml) should be sent to the laboratory for a toxicologic screen to determine which, if any, drugs are present.

1.6.2. Flashback

A flashback, also most frequently seen with the cannabinols and the hallucinogens, is the unwanted recurrence of drug effects. This is probably a heterogeneous group of problems, including the presence of residual drug in the body, psychological stress, a behavioral "panic," or the possibility of a temporary alteration in brain functioning.

Table 1.5
A Brief List of Relevant Laboratory Tests and Usual Norms

Abbreviation	Name	Usual value
	Chemistry	
	Amylase	35–160 (Somogyi) units
	Bilirubin	Total $\leqslant$ 1.0 mg/dl Direct $\leqslant$ 0.2 mg/dl
BSP	Bromsulphalein	$<$ 5% retention at 45 min
BUN	Blood urea nitrogen	8.0–23.0 mg/dl
Ca	Calcium	9.0–10.6 mg/dl
	Creatinine	0.8–1.2 mg/dl
CPK	Creatinine phosphokinase	0–140 U/l
	Glucose	70–110 mg/dl
LDH	Lactic dehydrogenase	36–200 U/l
Mg	Magnesium	1.8–2.5 mg/dl
K	Potassium	3.5–4.5 mEq/l
SGOT	Serum glutamic oxalacetic transaminase	8–30 U/l
SGPT	Serum glutamic pyruvic transaminase	5–35 U/l
Na	Sodium	135–145 mEq/l
	Blood counts	
Hgb	Hemoglobin	Men: 14–18 gm Women: 12–16 gm
Hct	Hematocrit	Men: 42–52% Women: 37–47%
MCV	Mean corpuscular volume	Volume 82–92 μm^3
WBC	White blood cell count	4.3–10.8 $\times$ 10^3 cells

1.6.2.1. The Typical History

This picture is most frequently seen after the repeated use of marijuana or hallucinogens. The typical patient gives a history of past drug use with no recent intake to explain the episode of feeling "high."

1.6.2.2. Physical Signs and Symptoms

These depend on how the patient responds to the flashback, that is, his degree of "panic." Physical pathology is usually minimal and ranges from no physical symptoms to a full-blown panic as described above.

1.6.2.3. Psychological State

The patient most typically complains of a mild altered time sense or visual hallucinations (e.g., bright lights, geometric objects, or a "trailing" seen when objects move). Symptoms are most common when the subject enters darkness or before he goes to sleep. The emotional reaction may be one of perplexity or a paniclike fear of brain damage or of going crazy.

1.6.2.4. Relevant Laboratory Tests

Except for the unusually intense or atypical case where actual brain damage might be considered (this would require a brain wave tracing or electroencephalogram [EEG], an adequate neurologic examination, X rays of the skull, and so on), there are no specific laboratory tests. The patient will probably be drug-free, and it is likely that even toxicologic screens will not be helpful.

1.6.3. Toxic Reaction

A toxic reaction is really an overdose occurring when an individual has taken so much of the drug that the body support systems no longer work properly. Clinically, this reaction is most frequently seen with the CNS depressants and opiates. A detailed discussion of this phenomenon is given within each relevant chapter, as the picture differs markedly among drug types. This diagnosis takes precedence even if signs of confusion or psychosis are present.

1.6.4. Psychosis

Psychosis, as used here, occurs when an awake and alert individual with stable vital signs and no evidence of withdrawal experiences hallucinations or delusions *without insight.*

1.6.4.1. The Typical History

Drug-induced psychoses are usually seen in individuals who have repeatedly consumed CNS depressants, or stimulants.[20] The onset of symptoms is usually abrupt (within hours to days) and represents a gross change from the person's normal level of functioning. The disturbance is dramatic and may result in the patient's being brought to a psychiatric facility or to the emergency room by police.

1.6.4.2. Physical Signs and Symptoms

There are few physical symptoms that are typical of any particular psychotic state. It is the loss of contact with reality occurring during intoxication that dominates the picture. However, during the psychosis, an individual may be quite upset and may present with a rapid pulse or an elevated blood pressure.

1.6.4.3. Psychological State

A psychosis occurs with the development of either hallucinations (an unreal sensory input, such as hearing things) or a delusion (an unreal and fixed thought into which the individual has no insight). In general, the drug-induced psychotic state lasts for a day to at most a week and is usually totally reversible. As will be discussed in greater depth in the appropriate chapters, there is little evidence, if any, of chronic or permanent psychoses being induced in individuals who have shown no obvious psychopathology antedating their drug experience.

1.6.4.4. Relevant Laboratory Tests

No specific laboratory findings are associated with the psychosis, as the patient may be drug-free and still out of contact with reality. For patients who abuse drugs intravenously, the stigmata of infection (e.g., a high WBC) and hepatitis (e.g., elevated SGOT, SGPT, CPK, and LDH) may be seen. It is also *possible* that a urine or blood toxicologic screen will reveal evidence of a drug.

1.6.5. Organic Brain Syndrome

An organic brain syndrome (OBS) consists of confusion, disorientation, and decreased intellectual functioning along with stable vital signs in the absence of signs of withdrawal.

1.6.5.1. The Typical History

Any drug can induce a state of confusion and/or disorientation (an OBS) if given in high enough doses, but at very high levels, the physical signs and symptoms of a toxic overdose predominate. There are a number of drugs, including the atropinelike substances, the CNS depressants, and PCP, that produce confusion at relatively low doses. There are, in addition, some factors that predispose a person to confusion, including physical debilitation (e.g., hepatitis), advanced age, a history of prior head trauma, or a long history of drug or alcohol abuse. These factors combine to explain the varied types of onset for organicities ranging from a very rapidly developing picture after PCP in a healthy young man to a slow onset (e.g., over days to weeks) of increasing organicity for an elderly individual taking even therapeutic levels of CNS depressants.

1.6.5.2. Physical Signs and Symptoms

As defined in this text, the OBS patient most often presents with a stable physical condition and a predominance of mental pathology. However, because an organicity is more likely to be seen in an individual with some sort of physical problem, any mixture of physical signs and symptoms can be seen.

1.6.5.3. Psychological State

The patient demonstrates confusion about where he is, what he is doing there, the proper date and time, or who he is. He has trouble understanding concepts and assimilating new ideas but usually maintains some insight into the fact that his mind is not working properly. This, in turn, may result in a level of fear or irritability. The signs of an OBS may be accompanied by visual or tactile (i.e., feeling) hallucinations.

1.6.5.4. Relevant Laboratory Tests

The first step in treating any OBS is to rule out major medical problems. Although the OBS may continue beyond the length of action of any drug (especially in the elderly), a blood or urine toxicologic screen may be helpful. It is also important to rule out aggressively all potentially reversible nondrug causes of confusion. Thus, in addition to a good neurologic examination, blood tests should be drawn to determine the status of the electrolytes (especially sodium, calcium, and potassium [see Table 1.5]); blood counts (especially the hematocrit and hemoglobin levels, as shown in the table); and liver and kidney function (including the BUN and creatinine for the kidney and the SGOT, SGPT, and LDH for the liver). It is also necessary to evaluate the need for skull X rays (to look for fractures and

signs of internal bleeding); a spinal tap (to rule out bleeding, infection, or tumors of the CNS); and an EEG (to look for focal problems as well as general brain functioning).

1.6.6. Withdrawal or Abstinence Syndrome

The withdrawal or abstinence syndrome consists of the development of physiological and psychological symptoms when a *physically* addicting drug is stopped too quickly. The symptoms are usually the opposite of the acute effects of that same drug. For instance, withdrawal from drugs that induce sleep, that can be used to help achieve relaxation, and that decrease body temperature (e.g., the CNS depressants) consists of insomnia, anxiety, and increases in body temperature and respiratory rates. The length of the withdrawal syndrome varies directly with the half-life (the time necessary to metabolize one-half of the drug), and the intensity increases with the usual dose taken and the length of time over which the drug was administered. Treatment consists of giving a good medical evaluation, offering general supports (e.g., rest and nutrition), and addressing the immediate cause of the withdrawal symptoms through administering enough of the substance (or any other drug of the same class) to markedly decrease symptoms on Day 1 of treatment and then decreasing the dose over the next 5–10 days.

Clinically significant withdrawal syndromes are seen for the CNS depressants, the opiates, and the stimulants. Because these syndromes differ for each specific kind of drug, the reader is encouraged to review each relevant chapter.

1.7. A GENERAL INTRODUCTION TO EMERGENCY AND CRISIS TREATMENT

The emergency care of the drug-abusing patient is covered within each chapter and in a general review in Chapter 14. The treatment approaches represent commonsense applications of those lessons learned about the drug category, the probable natural course of that class of difficulty, and the dictum of "First, do no harm."

1.7.1. Acute Emergency Care

One must first address the life-threatening problems that may be associated with toxic reactions, psychoses, organic brain syndromes, withdrawal, and medical problems. The approach to emergency care begins by first establishing an adequate airway, supporting circulation and controlling hemorrhage, and dealing with any life-threatening behavior.

1.7.2. Evaluation

After the patient has been stabilized, it is important to carry out evaluations of other serious problems through gathering a good history from the patient and/or a resource person (usually a relative), doing careful physical and neurologic examinations, and performing the relevant laboratory tests.

1.7.3. Subacute Care

1. It is then possible to begin the more subacute care, attempting to keep medications to a minimum, especially for symptoms of *panic* and *flashbacks*, which tend to respond to reassurance.
2. For *toxic reactions*, the subacute goal is supporting the vital signs until the body has had a chance to metabolize the ingested substance adequately.
3. The transient nature of the *psychoses* indicates that the best care is suppression of any destructive behavior during the several days necessary for the patient to recover.
4. Evaluation of an *OBS* requires carefully diagnosing and treating all life-threatening causes.
5. *Withdrawal* is usually treated through an adequate physical evaluation to rule out associated medical disorders, giving rest and good nutrition, and slowly decreasing the level of the addictive substances.
6. *Medical problems* must be handled individually.

1.8. ONWARD

You have now been introduced to my general philosophy involving drugs, drug problems, and their treatment. I now proceed with a detailed discussion of the CNS depressants, which is followed by two chapters on alcohol and the treatment of alcoholism, serving as a prototype for the remaining chapters in the text. Each of the clinically relevant drug types is then discussed, with the two final chapters emphasizing emergency problems of substance misusers in general and an introduction to rehabilitation.

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CHAPTER 2

The CNS Depressants

2.1. INTRODUCTION

The central nervous system (CNS) depressant drugs include a variety of medications, such as hypnotics, antianxiety drugs (also called *minor tranquilizers*), and alcohol. The general anesthetics will not be discussed here, as time and space constraints force me to limit the discussion to the substances most clinically important in drug abuse. One anesthetic agent, phencyclidine (PCP), is abused as a hallucinogen and is discussed in Chapter 9.

The CNS depressants all have clinical usefulness and most have an abuse potential. When used alone, they cause an intoxication or "high" similar to alcohol, but they can also be mixed with other drugs, such as stimulants, in attempts to modify some of the effects or side effects of those drugs.

As indicated by the high rate of prescriptions, a major avenue of supply is through the physician. In addition, many of the legally manufactured depressants find their way into the street marketplace.

The prototypical depressant drug is the barbiturate. These medications have been available since the 1860s[1] and have been prescribed for a wide variety of problems. The generic names of all barbiturates in the United States end in *-al,* and in Britain in *-one.*[1] The most widely prescribed class of CNS depressants, the benzodiazepines (Bz), have some unique characteristics. Therefore, whenever appropriate, they will be discussed separately.

2.1.1. Pharmacology

2.1.1.1. General Characteristics

The different CNS depressants possess markedly different lengths of action, as discussed below. Blood levels depend on the physical redistribution of the drug between various parts of the body; metabolic breakdown of the substance, usually in the liver; and excretion via the kidneys.

2.1.1.2. Predominant Effects

With the exception of the Bz's, the specific pharmacologic mechanisms by which these drugs exert their effects are not completely known, but theories are discussed in other texts.[1] The depressants result in reversible depression of the activity of all excitable tissues—especially those of the CNS—with the greatest effects on the synapse (the space between two nerve cells).[1,2] The resulting depression in activity ranges from a slight lethargy or sleepiness, through various levels of anesthesia, to death from breathing and heart depression. It should be noted that, paradoxically, the hypnotics and the antianxiety drugs sometimes cause extreme excitement when given to children and elderly patients (a *paradoxical reaction*).

2.1.1.3. Tolerance and Dependence

2.1.1.3.1. Tolerance

The tolerance of these drugs is clinically important and occurs through both increased metabolism of the drug after its administration (*drug dispositional* or *metabolic tolerance*) and apparent adaptation of the CNS to the presence of the drug (*pharmacodynamic tolerance*).[1] However, metabolic tolerance also results in the enhanced metabolism of a variety of other substances, including the anticoagulant medications, with resulting altered blood levels. As is true of all medications, tolerance is not an all-or-none phenomenon, and most individuals do not demonstrate enhanced toleration of lethal doses of the depressants (with the possible exception of alcohol).[2]

An important aspect of tolerance occurs with the concomitant administration of additional depressant drugs. If the second drug is administered in the absence of the first drug, cross-tolerance will probably be seen, at least in part, because of the expansion of the liver's capacity to metabolize depressant drugs. However, if the second depressant drug is administered *at the same time* as the first, the two drugs compete for metabolism within the liver, neither is metabolized properly, and the toxic effects of one drug appear to multiply the toxic effects of the second. As an example, the patient regularly abusing alcohol who undergoes surgery while in an alcohol-free state is likely to show significant cross-tolerance to preanesthetic and anesthetic medications. The same patient, however, who tries to abuse a barbiturate or an antianxiety medication while intoxicated with alcohol is likely to show potentiation of the effects of both drugs, with the possibility of a resulting unintentional toxic reaction or overdose. Therefore, even an individual with tolerance to one drug can have a fatal overdose with a concomitantly administered second drug, a common clinical circumstance with barbiturates and alcohol.

2.1.1.3.2. Dependence

All CNS depressants, including the benzodiazepines like chlordiazepoxide (Librium) and diazepam (Valium), produce a withdrawal state when stopped abruptly after the relatively continuous administration of high doses. The withdrawal picture *resembles* a rebound hyperexcitability characterized by body changes in a direction opposite to those seen with the administration of the drug (this may not be the actual pharmacologic mechanism).[2]

It is possible to see signs of withdrawal after several weeks of intoxication,[2] but, in general, the severity of the withdrawal syndrome parallels the strength of the drug, the doses taken, and the length of administration.[3] The actual dosage varies with the drug and the individual, but for a drug like pentobarbital, for example, the administration of 400 mg a day for three months results in definite withdrawal EEG changes in at least one-third of the individuals taking the drug; 600 mg for one to two months results in a mild to moderate level of withdrawal in half of the individuals, with 10% going on to severe withdrawal, including seizures; and 900 mg for two months results in seizures in 75% of the individuals, with most demonstrating a confusion–disorientation syndrome (organic brain syndrome [OBS]).[2,3] With a drug like meprobamate (Miltown or Equanil), one can see severe withdrawal in an individual taking 3–6 gm daily over 40 days. As a general rule, abuse of 500 mg of a barbiturate or an equivalent dose of other drugs will result in a risk of withdrawal seizures.[4,5] For the benzodiazepines, minor to moderate withdrawal symptoms can be seen with individuals taking two or three times the usual clinical dose for only 16 weeks.[2,5]

2.1.1.4. Specific Drugs

Tables 2.1 and 2.2 give numerous examples of members of the different classes of hypnotic and antianxiety drugs. The actions of members of two major subclasses of drugs can overlap greatly. For example, antianxiety drugs in high enough doses induce sleep, whereas the hypnotics, for many years, were labeled *hypnosedatives* and were administered to treat anxiety. In addition, some of the hypnotics are used as general anesthetic agents.

2.1.1.4.1. The Hypnotics

As shown in Table 2.1, some commonly used hypnotics are the barbiturates, the barbiturate drugs, and three other hypnotics.

1. The first subclass of *barbiturates* consists of the rarely abused *ultrashort* drugs (used to induce anesthesia) with lengths of action of minutes (e.g., sodium pentothal and hexobarbital). The *short-to-*

Table 2.1
CNS Depressants

Drug type	Generic name	Trade name
HYPNOTICS		
Barbiturates		
Ultra-short-acting	Thiopental	Pentothal
	Methohexital	Brevital
Intermediate-acting	Pentobarbital	Nembutal
	Secobarbital	Seconal
	Amobarbital	Amytal
	Butabarbital	Butisol
Long-acting	Phenobarbital	Luminal
Barbituratelike		
	Methaqualone	Quāālude
	Ethchlorvynol	Placidyl
	Methyprylon	Noludar
	Glutethimide	Doriden
Others		
	Temazepam	Restoril
	Flurazepam	Dalmane
	Chloral hydrate	Noctec
ANTIANXIETY DRUGS[a]		
Carbamates		
	Meprobamate	Miltown
		Equanil
	Tybamate	Salacen
		Tybatran

[a]See Table 2.2 for the benzodiazepines.

intermediate-acting barbiturates exert their major effect for a period of approximately four hours, so that they are ideal for helping people to get to sleep. These include the drugs most frequently prescribed and abused as hypnotics, such as secobarbital (Seconal) and pentobarbital (Nembutal). Finally, the *long-lasting* drugs, exemplified by phenobarbital, are most often used to treat chronic conditions such as epilepsy. These drugs are relatively rarely abused.

2. The *barbituratelike drugs* (e.g., glutethimide [Doriden] and methaqualone [Quāālude]) were almost all introduced as "nonaddictive and safe" substitutes for the barbiturates. They were developed in an attempt to overcome some of the drawbacks of barbiturate hypnotics, such as the morning-after "hangover," residual sleepiness, drug-induced disturbances in sleep patterns (especially in rapid-eye-movement [REM] sleep), and the highly lethal overdose potential of barbiturates. However, most barbituratelike hypnotics share the dangers of the barbiturates. Two drugs are *especially*

dangerous in overdoses as they are highly fat-soluble and resistant to excretion; offer few clinical advantages; and should be prescribed rarely, if at all. These are ethchlorvynol (Placidyl) and glutethimide (Doriden).[7] Another drug, methaqualone (Quāālude), has been especially widely abused.[8]

3. The third and final group of hypnotics discussed here is exemplified by paraldehyde and chloral hydrate (Noctec), drugs that share most of the dangers outlined for the barbiturate and barbituratelike hypnotics. Two other drugs, representing the only departure from these general drawbacks, are the benzodiazepines flurazepam (Dalmane) and temazepam (Restoril). Although these drugs do disturb sleep patterns,[9] the ratio between the effective dose and the lethal overdose is huge, so that they are relatively safe.

4. In summary, the hypnotics share serious drawbacks. They disturb the natural sleep pattern; they are extremely dangerous if taken in an overdose (with the probable exception of temazepam and flurazepam); and all have an abuse potential. Two of the drugs, ethchlorvynol and glutethimide, have additional dangers of delayed metabolism, which make their prescription even more dangerous than that of the usual drug.

It appears that all hypnotic medications lose their effectiveness if taken nightly for more than two weeks.[9,10] Therefore, considering their potential as suicide agents and their limited time of efficacy when used daily, there is a serious question about the wisdom of prescribing these medications for anything more than a short-term, acute crisis. If a hypnotic is required for an acute anxiety situation, I use temazepam or flurazepam, but rarely for more than two weeks at a time.

Numerous other approaches to handling insomnia are available and are discussed in detail in other texts.[11] For instance, after carefully ruling out problems to which insomnia might be secondary,[12] I prescribe a schedule of going to bed and getting up at the same time each day, no caffeinated beverages, and no naps. Milk at bedtime can be a useful adjunct, perhaps because of its tryptophan content.

2.1.1.4.2. The Antianxiety Drugs

The two classes of drugs most frequently prescribed for anxiety are the benzodiazepines (e.g., diazepam, or Valium) and the carbamates (e.g., meprobamate, or Equanil), as shown in Tables 2.1 and 2.2. These drugs have been demonstrated to be highly effective in handling *acute* anxiety,[13] but no well-controlled study has yet proved that they work for more than one or two months when taken daily.

The major dangers include a disturbance in sleep pattern and a change in affect (increased irritability, hostility, and lethargy). In addition, the carbamates are highly lethal when taken in overdose. Most members of this drug subclass have a length of action that exceeds the usual time between

the administration of doses. I never prescribe the carbamates (Miltown, Equanil, or Tybamate) because of their much higher addictive potential and greater possibility of fatal overdosage than the benzodiazepines.

2.1.1.4.3. The Benzodiazepines (Bz)

Although the drugs in this antianxiety subclass are definitely CNS depressants, they are discussed separately because of our level of understanding of their mode of action, because of their widespread use, and because of their asset of producing significantly less physiological impairment and less intense toxic reactions or overdose. These drugs are used as muscle relaxants (e.g., after strains or disc disease); as anticonvulsants (usually for non-grand-mal seizures and/or for status epilepticus); and as antianxiety agents. Their usefulness in treating anxiety states is best limited to short-term (two or three weeks) help for severe situational problems. The more long-term and chronic major anxiety disorders (e.g., agoraphobia or obsessive-compulsive disease) are not usual targets for Bz treatment, as these drugs are not effective over a long enough period of time, and there is a possible rebound increase in symptoms when the drugs are stopped. The limited use of the Bz's in treating anxiety is discussed elsewhere.[10,14]

The specific drugs are listed in Table 2.2. Although there are individual variations between the drugs (especially related to their half-lives), the Bz's have great clinical similarities.[10] Compared with other types of sedative/hypnotics, these drugs are relatively safe in overdose; are less like-

Table 2.2
Benzodiazepines (Bz)

Generic name	Trade name	Half-life (hr)	Usual adult daily dose (mg)
Alprazolam	Xanax	11–15	0.75–4
Chlordiazepoxide	Librium	5–30	5–25
Clonazepam[a]	Clonopin	20–50	0.5–10+
Clorazepate	Tranxene	30–60	15–60
Diazepam	Valium	20–50	2–15
Flurazepam[b]	Dalmane	50–100	15–30HS[c]
Lorazepam	Ativan	10–20	2–9
Nitrazepam[b]	Mogodan	24	5–10HS[c]
Oxazepam	Serax	5–20	10–40
Prazepam	Verstran: Centrax	50–80	20–60
Temazepam[b]	Restoril	4–8	15–30HS[c]
Triazolam	Halcion	3–5	0.25–2.5

[a]Used only as an anticonvulsant.
[b]Used only as a hypnotic.
[c]HS indicates use at bedtime.

ly to lead to metabolic tolerance; induce less significant changes in sleep stages; and appear to be less likely to produce physical addiction. All drugs of this class can be administered orally, and most are better absorbed by mouth than by injection (diazepam can be given intravenously and lorazepam is well absorbed intramuscularly).[14,15] They usually reach peak blood levels in 2–4 hours after oral administration, and most have active metabolites (except oxazepam and lorazepam). The frequency of administration varies with the half-life, with the result that oxazepam and lorazepam may need to be given four times a day to be effective, whereas clorazepate and diazepam may be used once per day (usually at bedtime). Most of the Bz's (with the exception of those having shorter half-lives—these are the same drugs that have no active metabolites) tend to accumulate in the body, reaching a steady state in 7–10 days, with the result that clinicians must be certain that sedative side effects do not progressively interfere with life functioning.

The pharmacological mechanisms of the Bz's are interesting. A unique attribute relates to the discovery of high-affinity selective receptors for Bz substances in the brain, with actions that correlate closely with levels of anxiety or seizure activity.[16] This discovery indicates the probable existence of endogenous ligands (probably purines) for those specific receptors.[17,18] The Bz receptors are probably distinct from but interact closely with receptors for a brain neurotransmitter, gamma aminobutyric acid (GABA), with a mutual enhancement of effects.[16,18] Although a direct link between Bz receptors and the actions of other CNS depressants has not been found, there is evidence that in physiological doses at least one barbiturate, pentobarbital, increases binding at Bz receptors.[19]

2.1.2. Epidemiology and Pattern of Abuse

The CNS depressants are prescribed in great quantities, as approximately 90% of hospitalized medical/surgical patients receive orders for hypnotic and/or antianxiety medication during their inpatient stay,[20] and in excess of 15% of American adults use these drugs during any one year.[21] Thus, it is not surprising that it has been estimated that up to 10% of general medical/surgical patients and 30% of individuals with serious psychiatric histories have, at some time, *felt* psychologically dependent on antianxiety or hypnotic drugs, with outright abuse seen for between 5% and 10%.[22]

Among the CNS depressants, the Bz's receive the widest use. In one year, over 2 billion tablets of diazepam alone were prescribed in the United States.[22] In a recent study, 9% of adults had taken a Bz in the last year for at least one month, as had 13% of college students.[23] Although use is certainly widespread, these figures do not necessarily indicate abuse, as these drugs are very effective on a short-term basis.[20,24,25]

In simple terms, depressant-drug abusers fall into the two classes of those who receive the drugs on prescription and those who (belonging to a "street culture") primarily misuse illegally obtained medications. One survey has revealed that between one-fourth and one-third of abusers of illegally obtained medications report using hypnotics or antianxiety drugs over the prior month, usually periodic ingestion of 30–80 mg of diazepam (Valium), frequently in combination with other drugs. For both types of abusers, at least 10% of all "drug mentions" in emergency rooms and crisis clinics are of diazepam.[26]

Thus, misuse of these drugs should be considered in the evaluation of almost any patient seen in a usual medical setting, an emergency room, or a crisis clinic. In light of the limited time that these medications stay effective when taken daily, there is rarely a valid clinical need to prescribe them for more than 2–4 weeks.

2.1.3. Establishing the Diagnosis

Identification of the individual misusing or abusing CNS depressants requires a high index of suspicion, especially for patients with an OBS or paranoid delusions and for all patients who insist on receiving prescriptions for any of these medications. It is imperative that these drugs not be given to patients who are not known to the physician, and that, when they are prescribed, only relatively small samples be given (both to decrease the suicide overdose potential[27] and to discourage misuse); that no "repeats" be allowed; that bottles be labeled as to contents; and that past records be evaluated to determine how long the patient has been on the medication.

2.2. EMERGENCY PROBLEMS

The outline given below follows the general format presented in Table 1.4, reviewing the possible areas of difficulty seen in emergency rooms, the outpatient office, and crisis clinics. The most common problems seen for the depressants are toxic overdose, withdrawal, and temporary psychosis.

2.2.1. Panic Reaction (See Sections 1.6.1, 5.2.1, 7.2.1, and 8.2.1)

Panic reactions (high levels of anxiety due to the fear of either going crazy or coming to physical harm as a result of the normal effects of the drug) are most frequently seen with stimulants and hallucinogenic drugs. They are rarely noted as part of the reaction to sedating drugs, such as CNS depressants and opiates.

2.2.1.1. Clinical Picture

The closest one comes to seeing a panic reaction is the hyperexcitability (paradoxical reaction) seen in some children and elderly individuals receiv-

ing depressant drugs, where the patient is frightened and excited, cannot sleep, and has excessive energy.[28,29] Problems begin in the first hour or so after taking the drug and remain for the length of action of the substance.

2.2.1.2. Treatment

In this instance, the clinical picture tends to clear within hours, with only general support and reassurance. It is best to avoid administering other drugs.

2.2.2. Flashbacks

These are not known to occur with CNS depressants. If a patient reports them, other diagnoses (especially emotional or neurologic diseases) should be considered.

2.2.3. Toxic Reactions (See Sections 4.2.3, 6.2.3, and 14.4)

The most usual toxic reaction seen with the depressant drugs occurs with either a deliberate or an inadvertent overdose.

2.2.3.1. Clinical Picture

2.2.3.1.1. The History

The toxic reaction usually develops over a matter of hours, and the patient often presents in an obtunded state with or without evidence of recent drug ingestion. This reaction can be seen when an individual mixes depressants together (usually alcohol and hypnotics); develops a confused organic state that results in inadvertent repeated administration of the drug (an automatism[30]); unintentionally takes too high a dose of street drugs; or makes a deliberate attempt at suicide.

2.2.3.1.2. Physical Signs and Symptoms

Toxic reactions are characterized by various levels of anesthesia and decreased CNS, cardiac, and respiratory functioning. An overdose of a depressant drug is very serious. The physical signs must be carefully evaluated in a manner similar to that reported in Section 6.2.3 for opiates and as suggested by other authors.[31] Examination includes:

1. A careful evaluation of the vital signs and the reflexes, with the findings depending on the drug dose, the time elapsed since ingestion, and any complicating brain conditions, such as hypoxia.[31]
2. The neurologic exams will help establish the degree of coma. Important aspects include:

a. *Pupillary reflexes.* Usually midpoint and slowly reactive, except with glutethimide (Doriden), where pupils tend to be enlarged.
b. *Corneal reflexes.* Present only in mild coma.
c. *Tendon reflexes and pain reflexes.* Tend to be depressed.[31]

3. Cardiac arrhythmias may be present, especially with the short-acting barbiturates.[31]
4. The lungs may be congested from heart failure or from positional or infective pneumonia.

2.2.3.1.3. Psychological State

Because the patient often presents in a stupor or a coma, there are usually few other distinctive psychological attributes.

2.2.3.1.4. Relevant Laboratory Tests (See Section 6.2.3.1.4)

As with any shocklike state or comparable medical emergency, it is important to carefully monitor the vital signs and the blood gases (arterial oxygen and CO_2) to evaluate the need for a respirator. A toxicologic screen on either urine (50 ml) or blood (10 ml) should also be carried out to determine the specific drug involved and the amount of the substance in the blood, and baseline blood chemistries and blood counts should be taken as outlined in Table 1.5. If the cause of the stupor or coma is not obvious, a thorough neurologic evaluation for ancillary damage (including an EEG, skull X rays, a spinal tap, and so on) must be done.

2.2.3.2. Treatment (See Section 6.2.3.2)

Treatment begins with emergency procedures to guarantee an adequate airway, to make sure that the heart is functioning, and to deal with any concomitant bleeding. The general goal is to support the vital signs until enough of the drug has been metabolized so that the patient is stable,[32,33] following the general approach presented in Table 2.3. The specific emergency maneuvers will depend upon the clinical status of the patient. These may range from simple observation for mild overdoses to starting an intravenous infusion (IV), placing the patient on a respirator, and admitting him to an intensive care unit.

Although toxic reactions involving the Bz's should not be taken lightly, the clinical picture tends to be relatively mild, and less than 5% of patients require intensive-unit care for 48 hours or more.[34] Deaths are relatively rare (less than 1%), and especially rapid recovery is to be expected with the short-acting Bz's such as lorazepam and oxazepam, even if the blood levels are initially high.[34,35]

Table 2.3
Treatment of the Depressant Toxic Reaction

Diagnose	History, clinical signs
First steps	Airway, assist respiration Cardiac Check electrolytes Treat shock Lavage (use cuff if obtunded; activated charcoal; castor oil?)
Consider	Forced diuresis (limited value) Hemodialysis
Avoid	CNS stimulants

The steps for approaching the patient with a toxic reaction to CNS depressants, not given in any fixed order, include the following:

1. Establish a *clear airway, intubate* (use an inflatable cuff in case you want to do a gastric lavage) if needed, and place on a *respirator* if necessary. The respirator should use compressed air (oxygen can decrease the respiratory drive) at a rate of 10–12 breaths per minute.
2. Evaluate the *cardiovascular status* and control *bleeding;* treat shock with plasma expanders, saline, dextran, or the relevant drugs,[33] administer *external cardiac massage/defibrillation/ intracardiac adrenaline,* if needed.
3. Begin an IV (large-gauge needle), replacing all fluid loss (e.g., urine), *plus* 20 ml for insensible loss (from respiration and perspiration), each hour.
4. Establish a means of measuring *urinary output* (bladder catheter, if needed). Send 50 ml of urine for a toxicologic screen.[33]
5. Carry out *gastric lavage* if oral medication was taken in the last 4–6 hours.[33] Carry out lavage with saline until you get a clear return. You may give 60 ml of *castor oil* via the stomach tube, especially if fat-soluble drugs like glutethimide (Doriden) were taken.[30,33]
6. Recognizing that analgesics can cause a similar picture and that the patient may have ingested more than one type of medication, consider the possibility of a narcotic overdose. This is easily tested for through the administration of a narcotic antagonist such as *naloxone* (Narcan) at a dose of 0.4 mg, given either intramuscularly (IM) or IV. If the patient has ingested narcotic analgesics to the point of obtundation, a rapid reversal of the picture should be demonstrated.

7. Carry out a more thorough *physical* and *neurologic exam.* This must include *pupils, corneal reflexes, tendon reflexes,* presence of *pathologic reflexes* (e.g., snout reflex), *pain perception* (use Achilles tendon), and level of *awake/alert status.* (See Sections 6.2.3 and 14.4.)
8. Draw *bloods* for arterial blood gases, general blood tests to evaluate liver and kidney functioning, blood counts, and toxicologic screen.
9. Gather a thorough *history* of the following:
   a. Recent drugs (type, amount, time)
   b. Alcohol
   c. Chronic diseases
   d. Allergies
   e. Current treatments

   Obtain this information from the patient and/or any available resource person.
10. For the comatose patient, protect against *decubital ulcers* by frequent turning, and *protect the eyes* by taping the lids closed if necessary.
11. Establish a *flow sheet* for the following:
    a. Vital signs
    b. Level of reflexes (Number 7 above)
    c. Urinary output
    d. IV fluids

    These should be recorded every 30 minutes. An example is given in a reference text.[4]
12. Consider *forced diuresis.* This is not needed for patients with stable vital signs or for those who present deep tendon reflexes (e.g., Grade I or II coma[31]) and rarely helps for chlordiazepoxide (Librium) or diazepam (Valium).[4] If either diuresis or dialysis is used, special care must be taken to maintain proper electrolyte levels and to avoid precipitating congestive failure. If diuresis is needed, you may use the following:
    a. Furosemide (Lasix), 40–120 mg, as often as needed to maintain 250 ml or more per hour.
    b. IV fluids, with the general approach being to give enough saline and water with glucose to maintain urinary output in excess of 250 ml per hour.
13. Hemodialysis or peritoneal dialysis can be considered for the patient in a deep coma, but this is rarely needed. Hemoperfusion may be helpful for patients who have Grade IV coma with associated apnea and hypotension; patients showing a deterioration despite supportive treatment; individuals in prolonged coma

with cardiorespiratory complications; or patients with very high plasma drug levels.[34]

14. Evaluate the need for *antibiotics.* Do *not* use these prophylactically.
15. Do *not* use CNS stimulants.
16. For the unresponsive patient who requires admission to an intensive-care unit, it is possible to establish a prognosis by observing the levels and the degree of change in systolic pressure, the central venous pressure, and the acid–base balance (pH), as described in the reference.[33] A special word of warning is required regarding the ability of the depressant drugs to produce a temporary flat electroencephalogram (EEG), which reverses within a matter of days.[2]
17. There are some special CNS depressant pictures, but most of these generalizations would hold for any drug. However, one might expect a longer period of coma with the fat-soluble drugs like glutethimide (Doriden) and ethchlorvynol (Placidyl). These patients may enter an emergency room looking alert or may be treated in a hospital and appear to come out of their coma only to relapse into a deep level of obtundation.

2.2.4. Psychosis (See Sections 1.6.4, 4.2.4, and 5.2.4)

2.2.4.1. The Clinical Picture

The depressant drugs can produce a temporary psychosis characterized by an acute onset, a clear sensorium (the patient is alert and oriented), auditory hallucinations, and/or paranoid delusions (e.g., thinking that someone is plotting against or trying to harm him). This picture has been more clearly described as it relates to alcohol and thus is discussed in greater depth in Section 4.2.4. However, similar pictures can be expected with the abuse of any CNS depressant.[36] It is probable that the generalizations presented for alcohol hold for the other depressants as well.

2.2.4.2. Treatment

The psychosis will probably clear within two days to two weeks with supportive care. Medications should not be given unless the paranoia and/or hallucinations create a serious danger to the patient or those around him. Then, antipsychotic drugs—e.g., haloperidol (Haldol), 1–5 mg four times a day (QID) or thioridazine (Mellaril), 25–100 mg four times a day (QID)—can be used *until* the clinical picture clears.

2.2.5. Organic Brain Syndrome (See Section 1.6.5)

The OBS can result as part of intoxication or an *overdose*, or during withdrawal. The confusion associated with intoxication tends to be mild and transient and thus will not be discussed here in great depth.

2.2.5.1. General Comments

One special case of OBS needs further discussion. Individuals with decreased brain functioning (e.g., the elderly and those who have had brain damage in the past following trauma, infections, and so on) are probably more sensitive to the effects of all CNS depressants, including the Bz's. Thus, such individuals might be expected to show a clinically significant and relatively persistent, although rarely permanent, state of confusion whenever they take hypnotics, alcohol, or antianxiety drugs. Use or abuse of CNS depressants should be considered as part of the differential diagnosis for all confused states of recent onset or for anyone demonstrating a rapid deterioration in his usual state of cognition.

Another important topic involves the recognition of possible neuropsychological deficits in abusers of CNS depressant drugs. Clinical and anecdotal information reveals significant memory problems in many Bz and hypnotic-drug abusers. These observations are corroborated by the demonstration of psychological test deficits (e.g., on the Halstead–Reitan Battery) in approximately a third or more of depressant abusers, deficits that remain after three weeks to three months of abstinence.[37] Interference with memory and learning can be demonstrated with these drugs even after a single dose.[38]

The treatment of a CNS-depressant–induced OBS involves a series of commonsense steps. First, the patient should be evaluated for any life-threatening causes of the OBS. These include trauma (e.g., a subdural hematoma), serious infections in the CNS or elsewhere, blood loss, electrolyte imbalances, hypoglycemia, and so on. Next, all CNS depressants should be stopped, and the patient should be observed over the next several weeks to document possible improvement. As with alcohol, it is possible that some patients may demonstrate more permanent neuropsychological deficits, although this has not been documented.

The discussion will now highlight two specific categories of OBS in greater detail.

2.2.5.2. Overdose

2.2.5.2.1. Clinical Picture

An overdose short of a coma is characterized by abnormal vital signs and confusion, disorientation, decreased mentation, and impaired memory-

processing. This picture closely resembles that seen during high-level alcohol intoxication. It may develop at even low doses in individuals at high risk for confusion, such as the elderly.[39,40]

2.2.5.2.2. Treatment

The confusional state is best treated with observation, usually in an inpatient setting where the patient is protected from wandering or harming himself. For younger individuals, the confusion usually clears within a matter of hours to days, but for older people, it might require an extended period of treatment of two weeks or longer. In either instance, it is best to avoid the concomitant administration of any drug.

2.2.5.3. Withdrawal

2.2.5.3.1. Clinical Picture

A rapidly evolving OBS can be seen during withdrawal from these drugs. It is usually temporary, rarely lasting more than a few days even without treatment. When it develops, signs of withdrawal are usually prominent, but one must take care to rule out other potentially lethal causes of OBS, including trauma, occult bleeding, or brain damage.

2.2.5.3.2. Treatment

This is discussed in Section 2.2.6.2.

2.2.6. Drug Withdrawal Syndrome (See Sections 4.2.6 and 6.2.6)

The depressant withdrawal syndrome consists of a constellation of symptoms that *might* develop in an individual taking any of these drugs daily in excessive doses. The final clinical picture is usually a mixture of any or all of the possible symptoms, running a time course that tends to last three to seven days for the short-acting drugs like alcohol (the most frequently abused CNS depressant[41]), but it may be longer for longer-acting drugs like diazepam (Valium).

Although probably less likely to cause physical addiction, the Bz's can do so.[42] These drugs are less often selected as the "street" drug of choice; tend to be avoided by drug-naive college students in experimental settings; and have a low level of self-administration when offered to animals IV.[23] As is true of all CNS depressants, the development of physical dependence relates to the drug dose and the period of time over which it was administered. Thus, physical withdrawal has been reported with diazepam in

clinical dose ranges (e.g., 10–20 mg per day) or lorazepam (4 mg per day) when taken over a period of years.[23] When two to three times the normal maximal doses are ingested, physical dependence can probably be induced in a matter of days to weeks.[23]

2.2.6.1. The Clinical Picture

2.2.6.1.1. History

A CNS-depressant withdrawal syndrome must be considered in any individual who presents with autonomic nervous system dysfunction along with agitation and who asks the physician for a CNS depressant drug. This syndrome can be seen in both the "street" addict, who may be abusing the drug either orally or IV, and the middle-class abuser, who obtains the drug on prescription but takes more than prescribed. The syndrome begins slowly over a period of hours and may not peak until Day 2 or 3 for alcohol and Day 7 for Bz's.

The time course for the withdrawal of barbiturates, such as pentobarbital, or a drug like meprobamate (Miltown or Equanil) is outlined in Table 2.4. This table can be used as a general outline for what might be expected,

Table 2.4
Time Course of Acute Withdrawal for Short/Intermediate Barbiturates and Meprobamate[2–4]

Time (after last dose)	Symptom	Severity
12–16 hours	Intoxicated state *Onset:* Anxiety, tremors, anorexia, weakness, nausea/vomiting, cramps, hypotension, increased reflexes	Mild
24 hours	Weakness, tremors, increased reflexes, increased pleading for drug	Mild
	High risk for grand mal seizures Delirium	Severe
24–72 hours	Peak intensity	
3–7 days	Symptoms gradually disappear	
1 week–6 months	Some anxiety, sleep disturbance, autonomic nervous system irregularities	Mild

showing the beginning of symptoms within a half day of stopping or decreasing the medications, a peak intensity at 24–72 hours, and a disappearance of acute symptoms sometime before Day 7. The time course of withdrawal is probably a good deal longer for the longer-acting barbiturates and the antianxiety drugs, such as chlordiazepoxide (Librium), where it has been reported that seizures and delirium can begin as late as Day 7 or 8.[3]

The wide range of half-lives for the Bz's demonstrates the correlation between the length of drug action and the timing of withdrawal symptoms. Thus, with the longer-acting Bz's, such as chlordiazepoxide, withdrawal can be expected to begin on Day 3 or 4, to peak on Days 5–8, and to disappear on Days 9–14,[43] but secondary abstinence symptoms of a lesser degree of severity may continue for months.[44] The shorter-acting Bz's without known potent active metabolites (e.g., lorazepam and oxazepam) might demonstrate a time course more similar to alcohol, with symptoms such as nausea beginning within hours, the withdrawal syndrome peaking on Day 2 or 3, and a great deal of improvement by Day 4 or 5.[23,43]

2.2.6.1.2. Physical Signs and Symptoms

The withdrawal symptomatology consists of a strong mixture of both psychological and physical problems. The patient usually develops a fine *tremor, gastrointestinal (GI) upset, muscle aches,* and problems of the *autonomic nervous system* (e.g., increased rates for pulse and respiration, a fever, and a labile blood pressure).[22,23,45] More atypical withdrawal syndromes can also be seen, especially with the Bz's, and may include headache, malaise, and abrupt weight loss.[23,45] With any CNS depressant, but especially the barbiturates, somewhere between 5% and perhaps 20% of the individuals will develop grand mal *convulsions*—usually one or at most two fits and rarely going on to demonstrate a state of continued seizures known as *status epilepticus.*

2.2.6.1.3. Psychological State

The withdrawal symptomatology includes moderate to high levels of *anxiety* and a strong drive to obtain the drug. In addition, somewhere between 5% and 15% of individuals develop an OBS and/or a *hallucination/delirium* state. With the barbiturates, probably at least one-half of people showing convulsions during withdrawal go on to a delirium if not treated.[3] Similar problems as well as hallucinations or delusions can be noted during withdrawal from Bz's.[23,46] The withdrawal psychotic states are differentiated from those described in Section 2.2.4 above by the autonomic nervous system dysfunction and the confusion seen during withdrawal.

2.2.6.1.4. Relevant Laboratory Tests

Because the CNS withdrawal syndrome is potentially *more severe than any other type of drug withdrawal,* it is essential that an adequate physical examination be carried out and that all baseline laboratory tests (including most of the chemistries and blood counts listed in Table 1.5) be considered. A toxicologic screen (10 cc blood or 50 cc urine) may or may not reveal evidence of the drug, depending on the length of time since the last drug dose and the specific substance involved. It is imperative that the physical condition be carefully monitored throughout the acute withdrawal syndrome.

2.2.6.2. Treatment (See Sections 4.2.6 and 6.2.6.2)

An important aspect of treatment is prevention. Thus, patients should never be placed on a daily CNS depressant for more than two to three weeks, and even then, the drug should be tapered off slowly rather than being stopped abruptly.[23]

The treatment of depressant withdrawal follows a relatively simple paradigm, consisting of a good *physical evaluation, general supportive care,* and *treatment of the actual withdrawal* itself (including recognition that symptoms have occurred because a depressant drug was stopped too quickly).[2,4,47] The comments below apply to depressants other than alcohol. Alcoholic withdrawal is discussed in Section 4.2.6.

1. Because of the possibility of the development of an OBS or convulsions, it is probably safest to carry out withdrawal in a *hospital setting.*[3] (See Section 4.2.6.3.2 for an exception.)
2. The poor physical condition of many drug abusers necessitates that each patient receive an adequate *physical examination* and general *screening laboratory procedures.*
3. Assuming that there has been a good physical evaluation and that good nutrition, rest, and *multivitamins* are being offered the patient, treatment of the *actual withdrawal* itself can begin. The two most usual withdrawal regimens (neither of which is clearly superior) are outlined in Table 2.5. At this point, it is a good idea to develop a *flow sheet* of all symptoms as evaluated every four hours, along with the drug doses given.[4]
   a. The pentobarbital (short-to-intermediate-acting barbiturate) method.[4,47]
      i. This involves utilizing an *oral test dose of 200 mg* of the drug (usually pentobarbital) and evaluating the individual 1–2 hours later. If the patient is sleeping at that time, he is probably not addicted to depressant drugs, and no active medication will be needed.[4]

Table 2.5
Treatment of Depressant Withdrawal[4,41,47,48]

I. Pentobarbital method
Test dose: 200 mg
If patient falls asleep, no treatment needed.
If no reaction, repeat dose Q 2 hr.

Determine dose for 24 hr. Divide QID.

Stabilize for 2 days.

Decrease by 100 mg/day.

II. Phenobarbital method
Calculate needed dose. Give 30 mg phenobarbital for each 100 mg pentobarbital or equivalent.

Stabilize for 2 days.

Give QID.

Decrease by 30 mg each day.

ii. If, after two hours, the individual is showing severe tremors, orthostatic hypotension, or other signs of withdrawal, it is assumed that severe withdrawal is imminent, and an alternate schedule of withdrawal is established, as discussed under Number v below.

iii. If, at two hours, the individual looks normal, it is possible to wait 2–5 hours, retest with 200 mg of an oral intermediate-acting barbiturate, and to continue with test doses during the day to establish the final level needed during the first 24 hours.

iv. In this instance, the barbiturate is then withdrawn by approximately 100 mg each day. If serious withdrawal symptoms recur, withdrawal is proceeding too quickly, and the patient should be administered an extra 200-mg dose of the barbiturate IM; he should be restabilized at the needed dose; and withdrawal should be begun once more.

v. For those patients who demonstrate severe signs of withdrawal after the administration of a 200-mg short-to-intermediate-acting barbiturate test dose, Sapira and Cherubin[4] recommend that the patient be given 400 mg of oral barbiturates, be reevaluated every two hours, and be carefully titrated in order to determine the probably high dependent dose.

b. The second withdrawal regimen utilizes a *longer-acting barbiturate, phenobarbital* (Luminal), which has a half-life of 12–24

hours.[41] This approach is based on the ease with which stable blood levels of this longer-acting drug can be reached—but suffers the drawback of some difficulty in titrating the original dose accurately.

i. One begins by estimating the dose of the drug abused and giving approximately 32 mg of phenobarbital for each 100 mg of estimated abused barbiturates; each 250 mg of a drug like glutethimide (Doriden); each 400 mg of meprobamate (Equanil); each 5 mg of diazepam (Valium); and each 25 mg of chlordiazepoxide (Librium). The total dose of phenobarbital is divided into portions to be given four times per day, with extra given if the patient begins to demonstrate signs of withdrawal.
ii. One or two doses (or more) are withheld if the patient appears too sleepy or demonstrates some signs of intoxication, such as nystagmus[26] or ataxia.
iii. The required dose is then utilized for two days, given in divided doses at 6 A.M., noon, 6 P.M., and midnight—the largest dose (approximately 1.5 times the other dose) being given at midnight.
iv. After this, the dose is decreased by approximately 30 mg per day—a 200-mg IM dose is used if needed to control the emergence of serious withdrawal symptoms.[48] If the patient looks sleepy or confused, the next dose should be withheld until he clears.[26]

In utilizing either regimen, it has not been shown that it is necessary to include phenytoin (Dilantin).[49] It also must be emphasized that the information presented in Table 2.5 is a rough outline and that the individual dose must be titrated for the specific patient. The goal is to reach a drug level at 24 hours that decreases withdrawal symptomatology without intoxicating the patient or making him overly sleepy. As with any drug that has a half-life of more than a few hours, it is important to recognize that the drug could accumulate in the body over time. This danger is especially important in elderly patients.

2.2.7. Medical Problems

There are few medical disorders known to be unique to depressant abusers. The conditions developed depend on the specific drug taken and the route of administration. A few "special" problems are discussed below.

1. There is much anecdotal information on the ability of these drugs to *decrease memory* over an extended period of time—perhaps even per-

manently. However, this phenomenon has not been well worked out, although there is a possibility of permanent neurologic damage.[50,51]

2. IV users can be expected to develop any of the problems that can result from contaminated needles. These include hepatitis, tetanus, abscesses, and so on, as described in Section 6.2.8, for opiates.

3. A special problem can result from the (usually inadvertent) injection of these drugs into an artery. The resulting painful muscle and nervous tissue necrosis can necessitate amputation of the limb.

4. A major difficulty with any of the CNS depressants, including the Bz's, is *sedation.* This may result in impaired judgment and work and motor performance, problems of special importance for the longer-acting drugs, which may accumulate in the body over time. The difficulty is enhanced in the presence of liver disease or decreased albumen in the blood, but all patients should be warned to avoid activities demanding high levels of alertness and/or motor performance if they are experiencing sedation side effects.

5. In the usual doses, these drugs are not likely to induce serious *cardiotoxic* symptoms in the average healthy individual—a problem especially unlikely with the Bz's, as they have less CNS brain-stem depressant activity.[32] However, all CNS depressants can suppress respirations (with the Bz's less prominent) and thus might precipitate respiratory failure in individuals with chronic obstructive lung disease.[32]

6. Serious *psychological* sequelae of moderate drug use are not likely. However, all of these drugs do tend to decrease inhibitions, and thus, they have been anecdotally reported to increase the possibility of angry outbursts.[23] There is also the possibility that some depressed patients will react to CNS depressants (even the Bz's) with an increase in their prior symptomatology (e.g., hostility).[23]

7. *Drug interactions* are a potential problem with all medications. The CNS depressants are likely to potentiate the side effects of tricyclic antidepressants and phenytoin and (through a possible interference with liver metabolism) may increase blood levels of digoxin.[38,52] The actions of L-dopa may be inhibited by this class of drugs, and cimetidine may interfere with Bz metabolism and excretion.[38,53] Of course, the interaction between two or more CNS depressants can be severe, and an enhancement of Bz actions may be noted as long as 10 hours after an individual drinks ethanol.[38] Long-term contraceptive use can also interfere with Bz metabolism, and antacids can interfere with absorption.[54]

8. Similarly, no drug can be considered totally safe for *pregnant* women. Although there is some controversy and other CNS depressants such as thalidomide are highly toxic to the fetus, there is no strong evidence of any teratogenicity in most of the currently used CNS depressants.[55]

Prenatal exposure to one CNS depressant, phenobarbital, has been shown to permanently decrease testosterone in male offspring.[55] Because this class of drugs is rarely necessary for sustaining life functioning, pregnant women should be told to avoid these medications, especially during the first trimester. This caveat probably extends to the neonatal period for women who are breast-feeding, as there is evidence that Bz's pass through the mother's milk to the baby and may be responsible for an increase in the accumulation of bilirubin.[56]

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CHAPTER 3

Alcoholism: An Introduction

3.1. INTRODUCTION

3.1.1. General Comments

Alcohol, nicotine, and caffeine are the most widely used drugs in Western civilization, alcohol being the most potent and destructive of the three. Probably reflecting this, there is a great deal of information available on the epidemiology, the natural history, and the treatment of alcohol-related disorders; thus, this drug is used as a prototype for the discussion of other pharmacologic agents. Information on alcohol is presented in two chapters: Chapter 3 covers the pharmacology of alcohol, definitional problems surrounding this drug, the epidemiology of drinking patterns and problems, the natural history of alcoholism, and some data on etiology; Chapter 4 is an overview of treatment of acute problems.

3.1.2. Some Definitions

3.1.2.1. General Comments

It is important at this point to note the distinction between studies of *drinking practices* and studies of *alcoholism.* The vast majority of Americans drink, and a substantial minority (one-third or more) of young men drink to the point of getting into temporary difficulties.[1] However, these young men usually do not go on to develop the persistent, serious alcohol-related difficulties that might be termed *alcoholism.* Therefore, the less serious problems, such as arguments with friends or missing occasional work or school because of drinking, due to their high prevalence, cannot in themselves be used to predict future alcohol-related problems.[1,2] Although these difficulties must be seen in almost every alcoholic early in the development of the disorder, they are seen in such a significant percentage of people who do not go on to develop alcoholism that they have little if any prognostic significance in themselves.

I diagnose to indicate prognosis and to select treatment. For this purpose, the entity must be clearly defined by objective criteria that can be utilized by different clinicians in different settings; people with the syndrome must have a somewhat homogeneous, predictable course (seen in follow-up); and the disorder must not represent the prodrome of yet another diagnosis.[3,4] To be used to maximal benefit, the diagnostic criteria should have been applied to individuals randomly assigned to different treatments to determine which is the most effective and the least dangerous approach.

Unfortunately, the second *Diagnostic and Statistical Manual* of the American Psychiatric Association (DSM-II) did not use objective terms nor demonstrate any predictive validity for the syndromes outlined under alcoholism, with the result that the labels tended to be applied in an inconsistent manner.[5,6] The next edition of the DSM (DSM-III) improves on the situation, presenting a definition for alcoholism requiring life problems as well as evidence of psychological or physical dependence.

The DSM-III lists alcohol-related states of confusion—for example, alcoholic intoxication, pathological intoxication (termed *alcohol idiosyncratic intoxication*), and alcoholic withdrawal, as well as alcoholic hallucinosis—in a manner not dissimilar from prior editions.[7] It then goes on to list some "alcoholisms," noting that both alcohol abuse (coded 305.0X) and alcohol dependence (303.9X) encompass both a pattern of "pathological alcohol use" (e.g., the need for daily use, repeated efforts to control, binges, alcoholic blackouts, and continuation of drinking despite the problems) *and* impairment in social or occupational functioning due to alcohol (e.g., alcohol-related violence, absence from work, legal difficulties, and arguments with significant others). This is similar to the definition given below, which uses life problems related to drinking. The difference between alcohol abuse and alcohol dependence is that the latter requires evidence of tolerance and a demonstration of some withdrawal symptoms after the cessation of or a reduction in drinking. Although resembling the definition given below, the prognostic implications of the specific DSM-III criteria and the benefits of differentiating between abuse and dependence have not been fully established. The next section reviews diagnostic choices for alcoholism, while more limited problems associated with alcohol abuse (e.g., alcoholic hallucinosis and pathological intoxication) are discussed in Section 4.2.

3.1.2.2. My Preferred Definition of Alcoholism

To be clinically useful, the diagnostic criteria must be stated in relatively objective terms, avoiding such judgments as "He drinks too much" or "I *feel* that he is becoming too psychologically dependent." There is no one best definition of alcoholism, and the different criteria overlap a great deal.

1. The *quantity–frequency–variability* (QFV)[8] approach attempts to gather accurate information on drinking patterns and then to place an individual in a "deviant" category when the alcohol intake differs statistically from the average. Although this scheme has great relevance to studies of drinking practices, its usefulness is limited by the difficulty of obtaining good information about alcohol intake because of the reticence of the individual to admit his pattern and because of his decreased memory at rapidly rising blood-alcohol levels.[9]

2. The second rubric, *psychological dependence*, is based on the occurrence of a series of subjective experiences relating drinking to such problems as stockpiling liquor, taking drinks before going to a party, and otherwise demonstrating that the individual is psychologically uncomfortable unless there is alcohol around. It is very difficult, if not impossible, to quantify this approach objectively.

3. A third diagnostic scheme, fairly widely used by physicians, centers on the occurrence of *withdrawal* or *abstinence* symptoms when an individual stops taking alcohol.[10] However, between 85% and 95% of people experiencing withdrawal have only the more minor symptoms.[11] In this mild form, it can be difficult to distinguish withdrawal from a hangover or a case of the flu. In any event, this definition is restrictive, as many individuals who have serious life-impairment and medical problems and who may suffer an alcohol-related death have never demonstrated obvious signs of physiological withdrawal.

4. The definition that probably has the greatest usefulness to clinicians centers on the occurrence of serious social or health *problems related to alcohol.*[3,12,13] Using this approach, each clinician can briefly review areas of life problems (e.g., work, accidents, marital problems, and arrests) with every patient—a review that takes less than three to five minutes. Once a pattern of problems has been established through information from the patient and/or a significant other, the connection between the life difficulties and alcohol can be broached. Subsequently, the pattern of drinking and the associated quantity and frequency can be ascertained.

The research criteria note the occurrence of any major life problem related to alcohol, including a marital separation or divorce, or multiple arrests, or physical evidence that alcohol has harmed health (e.g., a cardiomyopathy or cirrhosis), or the loss of a job or a layoff related to drinking.[14] As is true of any clinical diagnosis, the criteria must be "bent" for an individual who comes close but does not quite fit the research definition and is thus labeled a "probable" alcoholic. For instance, an individual who is self-employed and whose spouse appears to be "long-suffering and never complaining" and who appears to be at low risk for arrest (he could either be in a powerful position or live in a small community where he knows the police) may have many alcohol-related life problems but may not fulfill the

research diagnostic criteria. In this instance, the patient would be labeled a probable alcoholic and receive the same general treatment as the definite alcoholic, but I constantly recheck my diagnosis and recognize the lowered level of certainty in predicting the future course.

Proper diagnosis can be facilitated by understanding the effects that alcohol has on various body systems. Thus, as described in Section 3.2.2, there are various patterns of laboratory results and physical signs and symptoms that, although not diagnostic, can raise the clinician's suspicion regarding the presence of alcoholism. Similarly, there is a variety of simple paper-and-pencil tests asking about alcohol-related life problems that can help in establishing the diagnosis.[15] The most widely used is the 25-item Michigan Alcohol Screening Test (MAST), as well as its shorter 10-question counterpart.[16] Although screening tests like this can be most helpful, they do not diagnose alcoholism by themselves and cannot take the place of a clinical history carefully obtained from the patient and a relevant resource person.

3.1.2.3. Primary versus Secondary Alcoholism (See Figure 3.1)

To use diagnosis for prognosis and selection of treatment, it is important that one look separately at those cases that *might* be a complication of another disorder (secondary) and those that are more straightforward

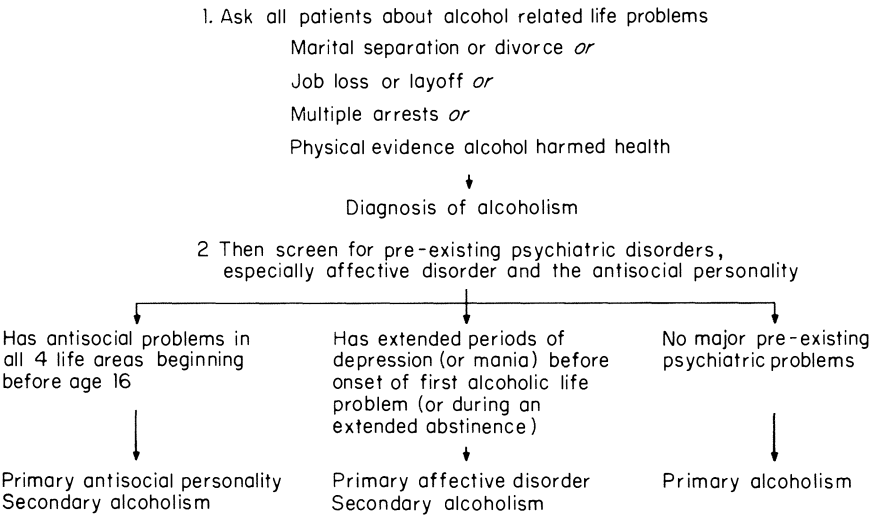

Figure 3.1. The diagnosis of alcoholism. From Schuckit, M. A. Treatment of alcoholism in office and outpatient settings. In J. H. Mendelson & N. K. Mello (Eds.), *Diagnosis and Treatment of Alcoholism.* New York: McGraw-Hill, copyright © 1979. Reprinted with permission of McGraw-Hill Book Company.

alcoholism (primary). The paradigm is similar to that used for patients with pneumonia: one case might be related to an immune deficiency; another pneumonitis might be secondary to trauma; yet another might reflect the consequences of congestive heart failure. Each exemplifies *secondary* pneumonia, where the prognosis and the major treatment efforts are dictated by the primary illness (e.g., the trauma or the heart failure).

In psychiatry or behavioral medicine, there is no specific symptom that is in itself diagnostic.[17] For instance, hallucinations and/or delusions can occur in many psychiatric disorders (e.g., affective disorders or major depressions, schizophrenia, or organic brain syndromes or major confused states), each of which has its own prognosis and most effective treatment. As a result, patients presenting with both repeated alcohol intoxication and serious psychotic symptomatology either could have primary alcoholism with secondary psychotic symptoms (in which case, the psychoses can be expected to clear within several days to several weeks with abstinence) or might have primary schizophrenia or primary major depressive disorder of a psychotic nature with secondary alcoholism (in which case, the psychotic symptoms can be expected to persist and to respond only to proper pharmacological interventions, e.g., lithium for manic-depressive disease or antipsychotic medication for schizophrenia).[3,17] In following the approach of diagnosis for prognosis and treatment, the proper label is derived by considering the constellation of symptoms and the time course or chronology. Psychiatric symptoms such as hallucinosis or confusion occurring *after* the onset of alcoholism or drug abuse, for instance, would be considered secondary manifestations and would be expected to clear on their own without active pharmacological intervention once abstinence is achieved.

Thus, a patient who develops alcohol abuse after the onset of another major psychiatric disorder has *secondary alcoholism,* whereas one who shows no evidence of a preexisting major psychiatric problem would be labeled a *primary alcoholic.*[13,18] It is the primary alcoholics, representing 70% or more of alcohol patients, who can be thought of as having the "disease" alcoholism and who are most likely to fit the natural history outlined below.[13,18]

Secondary alcoholism can occur in the midst of almost any psychiatric picture, but it is most likely to be seen with the antisocial personality and in individuals with primary affective disorder. The remaining personality syndromes noted in the DSM-III are not stated clearly enough to be clinically useful here.

3.1.2.3.1. Primary Antisocial Personality with Secondary Alcoholism

The antisocial personality or sociopath can be defined as being an individual who demonstrates antisocial life problems in *all four* life areas of family, school, police, and peers, beginning before age 16 and before the

onset of alcohol and drug abuse.[3,13,19] The sociopath runs a course of serious violence and criminal behavior, thus carrying a prognosis different from that of the primary alcoholic. Evaluations of both public and private inpatient alcoholic programs indicate that approximately 20% of male alcoholics and 5% of female alcoholics have primary antisocial personalities with secondary alcoholism.[13,20]

3.1.2.3.2. Primary Affective Disorder with Secondary Alcoholism

Disorders of mood, or affect, can entail either a serious depression or an episode of euphoria, hyperirritability, grandiosity, and disorganized thinking that is termed *mania.*[3] Because most people with primary affective disorder have depressions only (unipolar affective disorder), the major discussion here will center on depression, not mania.

When an episode of sadness that represents a change from the person's normal level of functioning persists for at least two weeks, occurs all day every day, and is accompanied by changes in body functioning (e.g., insomnia, lethargy, and constipation) and changes in mind functioning (e.g., inability to concentrate, the future looking hopeless, and loss of interest in usual activities), the diagnosis of depressive disorder can be made. This episode of sadness is quite different from the normally transient grief reaction or other despondencies accompanying a loss. When the depressive episode occurs in the absence of preexisting psychiatric disorders, including alcoholism, the label of *primary affective disorder* can be assigned, with its implications for prognosis and treatment.[3]

On the other hand, serious depressions (even with associated delusions and/or hallucinations or suicidal ideation) can occur (and frequently do) in the midst of heavy drinking.[18] Primary affective disorder of either the unipolar or the bipolar type can be diagnosed only for affective episodes lasting two or more weeks and interfering with life functioning *and* occurring either before the onset of the first major life problem related to alcohol or during a period of three or more months of abstinence. The differential between the primary affective disorder with secondary alcoholism and the primary alcoholism with secondary affective disorder has important prognostic implications, as it is only the primary affective disorder that will require antidepressants or lithium—there is no evidence that such medications benefit the course of the usual primary alcoholic.[3,18,20]

Studies of inpatient alcoholics have shown that about 15%–20% of women and 5% of men meeting the criteria for alcoholism have had affective disorder episodes either *before* their first major alcoholic life problem or during a period of three or more months when they were not actively drinking.[13,18,20] Such individuals would be labeled *primary affective disorder* and *secondary alcoholics.*

3.1.2.3.3. Other Diagnoses

When careful diagnostic criteria are used,[3] alcoholism is rarely secondary to disorders other than the antisocial personality or the primary affective disorder. Less than 10% of alcoholics demonstrate schizophrenia (the very slow onset of social withdrawal, hallucinations, and/or delusions that are persistent and seen during an extended abstinence[3]) or other psychiatric disorders such as hysteria (Briquet's disease) and anxiety neurosis. In other words, these problems do not seem to occur in alcoholics more frequently than in the general population. The confusion in the literature on the relationship between alcoholism and schizophrenia[21] occurs when investigators use loose criteria for schizophrenia whereby relatively benign or transient paranoid or hallucinatory psychoses, which may accompany the heavy use of alcohol (see Section 4.2.4), are mislabeled as schizophrenia.

The key to accurate labeling is taking a very careful history of the chronology of the development of psychiatric symptoms from both the patient and a resource person such as the spouse. Primary sociopathy is easily distinguished from primary alcoholism through gathering information on the extent of antisocial problems occurring before age 16. The primary schizophrenic should demonstrate persistent and serious social withdrawal and hallucinations/delusions that occurred before the onset of serious alcohol problems and that remain throughout extended periods of abstinence.

To summarize, all patients, no matter what their chief complaint, should be queried for their pattern of life problems and subsequently for the relationship of alcohol (and other drugs) to these difficulties. Once a diagnosis of definite or probable alcoholism has been established, it is necessary to distinguish between the 70% of primary alcoholics and the 30% or so who have alcoholism secondary to another major preexisting psychiatric disorder. This distinction is made by asking all possible alcoholics about their pattern of life problems beginning before the age of 16, their pattern of drug-related difficulties, and the presence of any major psychiatric symptoms (e.g., serious depression or psychotic symptoms) occurring before the onset of their first alcohol-related life problem or during a period of three or more months of abstinence.

3.2. PHARMACOLOGY OF ALCOHOL

3.2.1. General Comments

This widely used drug is a central nervous system (CNS) depressant that, in high enough doses, is an anesthetic. It adversely affects almost all body systems, interfering with either cell membrane functioning, intra-

cellular respiration, or energy processing in most body cells, especially those in the CNS.[22-24] Although the primary action of alcohol on the CNS is depression, at lower doses behavioral stimulant properties predominate, a fact that may be related to a direct stimulant effect of alcohol or a differential depression of inhibitory neurons at relatively low blood-alcohol concentrations.[25] The CNS depression occurs at all levels of the brain, with the first noted actions occurring in the reticular activating system and those areas most closely involved with complex functions—the cortex.[25]

The final level of behavioral impairment depends on the person's age, weight, sex, and prior experience with alcohol, as well as on his level of tolerance. Table 3.1 gives a rough outline of what can be expected in a nontolerant individual, with results ranging from minor impairment in motor coordination, sensation, and mood at low doses to amnesia and Stage 1 anesthesia for blood levels exceeding 300 mg of alcohol per 100 ml of blood (mg %). Doses of 400–700 mg % can cause coma, respiratory failure, and death,[25] although tolerant individuals may be awake and able to talk at blood levels exceeding 780 mg %.[25,26] Note that 100 mg % is equivalent to 0.1 gm/100 ml.[27] The usual drink contains about 10 gm of absolute alcohol and (for those watching their weight) a minimum of 70 calories.

3.2.2. Effects on the Body

Alcohol is a very attractive drug as its immediate effects at modest doses are perceived by the user as pleasant. In addition, for nonalcoholic individuals who are not taking medications and are in good physical condition, alcohol has the beneficial effects of increasing socialization, possibly stimulating the appetite, perhaps decreasing the risk of cardiovascular disease through an increase in high density lipoproteins (HDLs), and so on.[27,28]

Table 3.1
Rough Correlation between Blood-Alcohol Level and Behavioral/Motor Impairment[21]

Rising blood-alcohol level in mg/100 ml blood (mg %)	Expected effect
20–99	Impaired coordination, euphoria
100–199	Ataxia, decreased mentation, poor judgment, labile mood
200–299	Marked ataxia and slurred speech, poor judgment, labile mood, nausea and vomiting
300–399	Stage I anesthesia, memory lapse, labile mood
400 and above	Respiratory failure, coma, death

When alcohol is taken in moderation by such individuals in good health, most pathological changes that do occur are reversible. However, at higher doses or in individuals who are ill, damage to various body systems can be more serious, and early signs of some of these changes can be used by the clinician to increase his level of suspicion that the patient being seen may be alcoholic. Because the physiological toxicity of alcohol has been reviewed in depth in other texts, only a very brief review is given here.[22,29]

The average alcoholic is likely to appear in clinical settings in a sober state, looking well groomed and having no smell of alcohol about him. He or she will complain of any of a variety of medical and emotional problems, which must be properly diagnosed if the clinician hopes to avoid unexpected calls in the middle of the night and nonresponse to ill-advised treatments that should never have been given in the first place (e.g., sleeping pills). Thus, it is in the clinician's best interest to identify the alcoholic in order to be certain that the maximal amount of care at the minimal risk is being offered.

Changes in body systems that can be expected in the course of alcoholism include the following:

1. The easiest and most obvious screening tests involve simple *blood markers.* Many alcoholics have a mild elevation in uric acid, free fatty acids, mean corpuscular volume (MCV) of approximately 95 or 100, and/or an elevation in gamma-glutamyl transferase (GGT levels of 30–50 or more).[30,31] The first test to change is likely to be the GGT, elevations tending to occur long before other liver function tests show a rise, probably in response to the actual induction of this enzyme by ethanol. A related approach is to evaluate the pattern of 25 commonly used blood tests, which, according to one report, may be plugged into a mathematical formula to identify over 85% of alcoholics versus controls.[32] Although many clinicians may be unwilling to use such complex formulas, the simple combination of the brief MAST and observation of the blood tests specifically noted above may be very useful.[33]

2. In the *digestive system,* alcohol is associated with high rates of cancers of all levels of the digestive tract, especially the esophagus and the stomach as well as the head and neck[34,35]; high rates of ulcer disease[36]; and elevated rates of inflammation of the stomach (gastritis) or pancreas (pancreatitis), fatty liver, alcoholic hepatitis, chronic active hepatitis, and cirrhosis.[23,37] Even at low doses, alcohol disturbs the ability of the liver to produce sugar (gluconeogenesis) and shunts building blocks into the production of fats.[23]

Most of the problems in the liver may be secondary to the use of alcohol by liver cells as a "preferred fuel," with resultant scarcity of nicotinamide adenine dinucleotide (NAD) as a hydrogen receptor.[23] The liver problems appear to progress from fatty liver (probably seen with

repeated blood-alcohol levels of 80 mg/dl or more), to alcoholic hepatitis (probably not directly related to the fatty liver), and to subsequent cirrhosis, which may begin with early fiber deposition around the central veins, that is, central hyaline sclerosis. In reviewing this material, however, the average clinician must remember that only 1 in 5 or so alcoholics actually present with clinically significant cirrhosis.

3. In the *neurologic system,* the chronic intake of alcohol results in deterioration of both the peripheral nerves to the hands and feet (a peripheral neuropathy seen in 5%–15% of alcoholics)[38] and temporary as well as permanent organic brain syndromes associated with both the direct effect of alcohol and specific vitamin deficiencies, such as the thiamine-related Wernicke–Korsakoff syndrome[39] (seen in less than 5% of alcoholics). It has been estimated that between 15% and 30% of nursing-home patients with organic brain syndromes are alcoholics whose alcohol-induced organicity has become permanent.[40] Additional problems associated with the CNS involve a rapidly developing permanent uncoordination (cerebellar degeneration), which is seen in less than 1% of alcoholics,[41] and other more dramatic but even rarer neurologic disorders that can result in rapid death.[38]

As recognized by the DSM-III, the most prevalent form of alcohol-related confusion, however, is intoxication. Although most individuals show a clearing of clouded consciousness over a matter of hours, those with preexisting brain damage (e.g., some elderly and those with prior brain trauma) may show confusion lasting for days or weeks. Thus, alcohol must be considered a part of the differential diagnosis of all fairly rapid-onset states of confusion.[17]

The association between alcoholism and more permanent decreased intellectual functioning is less clear. The majority of alcoholics presenting for detoxification show some signs of intellectual impairment, and 40%–70% may show increased brain ventricular size (possibly indicating decreased brain tissue).[42] Although some investigators feel that there is a correlation between increased brain ventricles and decreased functioning on psychological testing, not all agree, and it is probable that most alcoholics will recover in both parameters after months of abstinence.[42,43] The etiology of these psychological changes is not known, but it probably represents the combination of trauma, vitamin deficiencies, and a direct neurotoxic effect of alcohol on the brain.

4. It has also been estimated that one-quarter of alcoholics develop diseases of the heart or *cardiovascular system,*[44] as alcohol, a striated-muscle toxin, produces a heart inflammation or myocardiopathy and hypertension and elevates blood fats, including cholesterol.[22,45] In addition, alcohol in doses as low as one drink can decrease the cardiac output of blood in nonalcoholics with heart disease and can diminish the warning

signs of pain while increasing the potential heart damage or ischemia in patients with angina.[46] Alcoholism must also be considered in all individuals demonstrating mild elevations in blood pressure (e.g., 145/95), especially if the pressure appears to fluctuate with time (e.g., higher early in the week).[47]

5. Alcohol also decreases the production of all types of *blood cells*, with resulting large red blood cell anemia (a macrocytosis, probably related to folic acid deficiency), decreased production and efficiency of white cells (probably leading to an increased predisposition toward infection), and decreased production of clotting factors and platelets (probably related to increased bruising and gastrointestinal bleeding[44,48,49]). There is also a decrease in thymus-derived lymphocytes, which might relate to the increased rates of cancers seen in alcoholics.[40]

6. *Body muscle* is also sensitive to alcohol, and an alcoholic binge can result in muscle inflammation or, in chronic abusers, muscle wasting, primarily in the shoulders and hips.[49]

7. Through a variety of mechanisms, alcohol induces a number of other *blood test* abnormalities, including those of liver function, glucose, blood components, creatinine phosphokinase (CPK), and uric acid.[31–33]

3.2.3. Effects on Mental Processes

In addition to the physiological changes that occur with alcohol, there are a number of important emotional consequences. With modest intake, at peak or decreasing blood-alcohol levels, most people (alcoholics and "normals") experience sadness, anxiety, irritability, and a whole host of resulting interpersonal problems.[18,50–52] At persistent higher doses, alcohol can cause almost any psychiatric symptom, including temporary pictures of intense sadness, auditory hallucinations and/or paranoia in the presence of clear thought processes (a clear sensorium), and intense anxiety. These are discussed in Sections 4.2.4, 4.2.5, and 4.2.8 and in another text.[17]

Insomnia can occur with simple alcohol intoxication, as this drug tends to fragment the sleep, and there is a resulting decrease in deep sleep stages and also frequent awakenings—problems that can be expected to persist in alcoholics for 3–6 months as part of a "protracted" abstinence phase.[50] *Sexual functioning* is also disturbed, with decreased sperm production and motility (through the direct effects of ethanol on the testes); a decreased production of testosterone and the production of impotence (through psychological mechanisms as well as perhaps via a temporary or more permanent peripheral neuropathy involving the perineal nerves and/or the direct destruction of the testes, with resulting testicular atrophy after many years of heavy drinking); and menstrual irregularities in women.[51] The effects of alcohol on the developing fetus—various stages of the fetal alcohol syndrome (FAS)—are described further in section 4.2.8.2.

3.2.4. Alcohol Metabolism

Alcohol is fully absorbed from the lining or membranes of the digestive tract, especially in the stomach and the proximal portion of the small intestine. Only 5%–15% is excreted directly through the lungs, sweat, and urine, with the remainder being metabolized in the liver at a rate of approximately one drink per hour, the equivalent of 7 gm of ethanol per hour, with 1 gm equaling 1 ml of 100% alcohol.[48,51] The usual route of metabolism is via the enzyme alcohol dehydrogenase, although some additional alcohol is metabolized in the liver microsomal system, as shown in Figure 3.2. Thus, the major product of alcohol metabolism is acetaldehyde, a very toxic substance that, fortunately, is quickly metabolized to carbon dioxide and water through a variety of mechanisms.

Alcohol and aldehyde dehydrogenases are used by the body for a variety of purposes in addition to the metabolism of ethanol. Both enzymes are under genetic control, and the former (ADH) has eight or more isoenzymes in humans, each with different metabolic properties and with different patterns in various national groups.[53] The latter, ALDH, possesses at least four clinically significant isoenzymes in humans, and the most physiologically active regarding acetaldehyde, ALDH I, is absent in perhaps up to 50% of Orientals. This finding may be responsible for the higher rate of facial flushing (probably acetaldehyde-mediated) when some Oriental

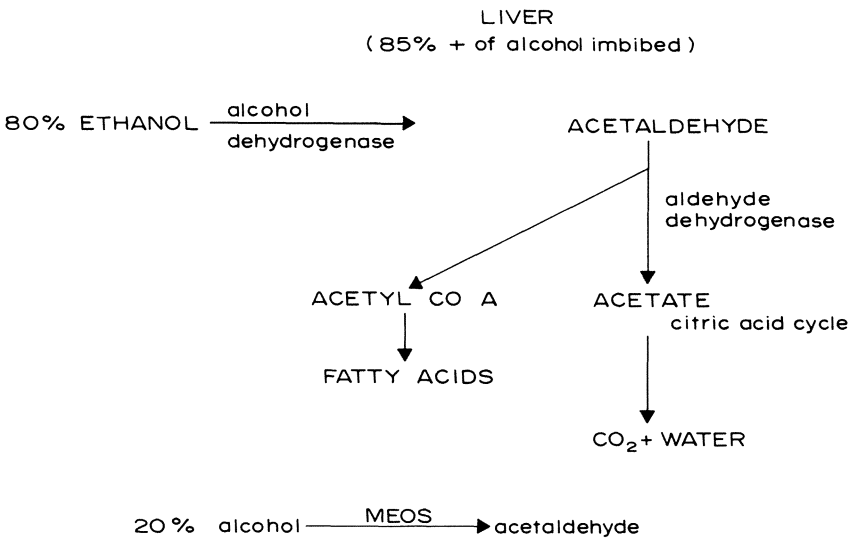

Figure 3.2. The metabolism of alcohol.[21,22]

people drink.[54] Various authors have tried to tie in this finding with the purported lower level of alcoholism in Oriental groups, although such speculations do not take into consideration the high rate of both flushing and alcoholism among another related group, North American Indians and Eskimos. These brief comments are mentioned here to give the interested reader the opportunity of reviewing other references and because these enzymes and their genetic control may have an impact on a genetic predisposition toward alcoholism, as discussed in Section 3.5.4.

3.2.5. Tolerance and Physical Dependence

Toleration of higher doses of ethanol occurs rapidly and parallels what has already been discussed about the depressants in Section 2.1.1.3. This tolerance is both metabolic, primarily through a slight increase in the liver microsomal ethanol-oxidizing system (MEOS), and pharmacodynamic, the apparent result of a direct adaptation of CNS tissues to alcohol.[25] As is true of most drug mechanisms, behavioral factors play a role as well in the development of tolerance and physical dependence.[55] Regarding the latter, animals given a potentially lethal dose of a drug in an environment where they have previously received sublethal drug doses are more likely to survive the drug challenge than animals with similar histories given the same dose in an environment unrelated to prior drug exposure. Cross-tolerance to other CNS-depressing drugs occurs, but it must be remembered that the concomitant administration of two or more CNS depressants may potentiate the effects of both.

Alcohol also produces a level of physical addiction that results in a withdrawal syndrome almost identical to that described for the depressants.[56] This withdrawal syndrome is discussed in Section 4.2.6.

3.3. EPIDEMIOLOGY OF DRINKING AND ALCOHOLISM

Most people drink, and many have minor problems, but few demonstrate a lifestyle centered on alcohol (i.e., alcoholism).

3.3.1. Drinking Patterns

Over two-thirds of American men drink more than just occasionally, with a male-to-female ratio of approximately 1.3 to 1.[57] The peak years, with the highest percentages of drinkers and the greatest per capita consumption, are probably between 16 and 25, and then there is a decrease with age. At any stage of life, the chances of being a *drinker* (not an alcoholic) are higher for people with higher levels of education, higher socioeconomic status, and Italian or Jewish heritage.[2,58]

The average adult consumes 2.7 gallons of absolute alcohol per year, with a resultant total expenditure of many billions per year in the United

States—representing almost 3% of total personal expenditures.[58,59] Between a quarter and a half of young men experience transient alcohol-related problems, such as arguments with friends, missing time from work, or a drunk-driving arrest.[1] These problems alone do not predict future alcoholism, and most individuals drift away from these problems with increasing age.[1,2]

Thus, the average person in our society is a drinker. He tends to have his first alcohol-related experience (i.e., drinking on his own—not just sipping from an adult's glass) between the ages of 12 and 15, his first experience of drunkenness by the mid-teens, and, especially for males, his first temporary alcohol-related life problem at age 18–25 (e.g., missing school or work because of drinking, having an argument with a friend, driving while drunk, or receiving a single drunk-driving arrest).[58] Regarding the latter, most individuals who have had only a single alcohol arrest do not qualify for the diagnosis of alcoholism, nor on follow-up, do they demonstrate a course consistent with that disorder; however, multiple drunk-driving arrests are associated with more pervasive and persistent future problems.[60] It is probably in the late 20s to early 30s that the average drinker decreases his frequency and quantity of intake, whereas the alcoholic maintains or even increases his drinking pattern, and the resulting diagnosis is alcoholism.

3.3.2. Alcoholism

With the use of a rigorous criterion for alcoholism centering on serious life problems (see Section 3.1.2), it has been estimated that between 5% and 10% of the adult male population in the United States will demonstrate alcoholism at some time during their lives.[58,61] Because of the high level of physical pathology associated with heavy drinking, 20%–35% of male general medical or surgical patients are alcoholic.[15,58]

The highest rates of *alcoholism* are seen in men aged 30–50 years, and the rates increase with lower socioeconomic strata, with lower income and education, and among Catholics—especially French and Irish.[58] However, it is important to recognize that alcoholism is a problem of all socioeconomic strata, all ages, all religions, all parts of the country, and both sexes.

The armed services have a reputation for high rates of alcohol problems, an observation that implies possible high rates of alcoholism.[62] These findings must be considered from the perspective that the military has a high percentage of young males (i.e., those at highest risk for alcohol-related difficulties). Indeed, once one controls for age, sex, and socioeconomic stratum, the rate of probable alcoholism (about 5%–10%) and that of additional alcohol-related problems (approximately 10%) are not significantly different from those of the population in general.

Controlling for socioeconomic strata, most racial or ethnic groups

show similar rates of alcoholism. Possible exceptions include Orientals (with low rates of alcoholism—perhaps related to their high propensity for flushing and to societal norms regarding drunken behavior), low rates of persistent alcohol problems in Jews, and probable high rates in North American Indians and Eskimos.[58,63] It is not known whether these differences are related to social factors, either protecting from heavy drinking or encouraging drunkenness (for lower or higher rates, respectively) and/or genetically influenced factors.

Another group of great interest is young drinkers. As briefly discussed above, drinking is the "norm" in most Western societies, and adolescence is the time of learning to assume adult roles. However, most teenagers drink approximately two times per week, with an average intake of less than four drinks per occasion (defining a drink as 12 oz of beer, 4 oz of nonfortified wine, or 1½ oz of 80-proof beverage).[58] Those individuals drinking daily (perhaps 10% of youth by the end of high school) and/or those demonstrating serious alcohol-related pathology are very likely to have associated multiple drug problems and/or to fulfill the criteria of the antisocial personality as described in Section 3.1.2.3.[64] Although 10% daily drinkers by the end of high school is an alarming statistic, this figure has not changed much over the last 10–15 years, and there is some evidence of an actual decrease in the prevalence of drinking among youth during that time period.[65] Once again, this observation points out how unwise it might be to equate drinking, drinking problems, and alcoholism and demonstrates the need to view statistics on alcoholism from a longitudinal perspective.

3.4. NATURAL HISTORY OF ALCOHOLISM

3.4.1. General Comments (See Table 3.2)

Once the diagnosis of primary alcoholism has been carefully established, it is possible to estimate the prognosis or the natural course of the disorder. The average primary alcoholic, male or female, demonstrates the first major alcohol-related life problem in the late 20s to early 30s, and most alcoholics present for treatment in their early 40s—after more than a decade of difficulties.[66,67] Consistent with these findings, it is likely that by age 31 approximately half of those who will fulfill the criteria for alcoholism have already done so.[66]

If alcohol problems continue, the alcoholic is likely to die 15 years earlier than the general population,[67–69] with the leading causes of death (in approximately decreasing order of importance) being heart disease, cancer, accidents, and suicide. These leading death causes do not include the series disorders found at markedly higher rates in alcoholics than in the general population, such as cirrhosis, pancreatitis, and infections. As alluded to

Table 3.2
The Natural History of Primary Alcoholism

1. Age of first drink[a]	12–14
2. Age first intoxicated[a]	14–18
3. Age first minor alcohol problem[a]	18–25
4. Usual age of onset First major problem	23–33
5. Usual age entering treatment	40
6. Usual age of death Leading causes: Heart disease Cancer Accidents Suicide	55–60
7. In any year, abstinence alternates with active drinking "spontaneous remission" rate or response to nonspecific intervention	¼–⅓

[a]These ages are about the same in the general population.

earlier in Section 3.2, these findings reflect the diverse organ systems affected by ethanol. Thus, in one series, over 93% of alcoholics coming in for treatment had important medical problems, including 15%–25% with hypertension, ulcer disease, or chronic obstructive lung disease; approximately 10% with gastritis, epilepsy, or peripheral neuropathy; and less than 5% with cardiomyopathy.[70]

The course of alcoholism is a *fluctuating* one, with very few, if any, alcoholics staying persistently drunk until they die. The usual alcoholic is a blue-collar or white-collar worker who alternates periods of abstinence (and times when he is drinking very little) with periods of serious alcohol misuse. In any given month, one-half of alcoholics will be abstinent, with a mean of four months of being dry in any one-year to two-year period.[72] Thus, the average alcoholic has spontaneous periods of abstinence and marked decreases in drinking, which appear to alternate with heavy drinking times.

The question of an alcoholic's returning to "controlled" or nonproblem drinking has been hotly debated.[71] The problem has centered on the definition of *controlled drinking*, with some reports including individuals drinking as many as eight drinks per day and accepting self-reports without thorough record checks or interviewing of additional relatives. However, both anecdotal information and follow-ups of groups of subjects have indicated that perhaps 1%–5% of alcoholics may achieve a state, for years, of drinking low amounts of ethanol without associated problems. These people are likely not to have fulfilled the more rigorous criteria for alcoholism at intake (i.e., they probably had less severe and pervasive alcohol-related problems).[66] Therefore, it is best to advise alcoholics that abstinence is the only relevant

goal of treatment because 95% or more of alcoholics are unlikely to achieve any long period of controlled drinking; because short periods of drinking without problems are part of the natural course of most alcoholics but usually give way to serious problems; because of the low percentage of alcoholics who can achieve stable controlled drinking; and because of the difficulties in picking out those who will be able to do this successfully.

Alcoholism is not a hopeless disorder. Not only can one expect improvement with treatment, but there is good reason to estimate that 10%–30% of alcoholics learn to abstain or to seriously limit their drinking without any exposure to a formal treatment regimen.[66,68,69,72,73] The chance of demonstrating spontaneous remission probably increases with the same factors that indicate a good prognosis for those entering treatment (e.g., having a job, living with a family, and having no police record).

3.5. ETIOLOGY

As noted in Chapter 1, a clinically oriented handbook has little room to discuss etiologic theories in great depth. I turn to this topic now to demonstrate both how difficult etiology is to study and how people erroneously tend to state tentative hypotheses as proven fact. As we shall see, a theory that makes sense is not necessarily true, and a demonstration that Factor A is related to Factor B does not mean that the former caused the latter.

3.5.1. Psychological Theories

These usually involve comparisons of alcoholics and nonalcoholics on performance on psychological tests. The approach at times neglects the possibility that the psychological attributes of alcoholics who have been drinking heavily for 10 years may be the consequence of their lifestyle rather than the original cause. Proponents of psychological theories may also fail to differentiate between studies of why people drink and why people become alcoholic.

These theories include the "tension-reduction hypothesis," which (despite the fact that most physiological evidence indicates that alcohol increases tension) states that alcoholics drink in an attempt to decrease their levels of stress.[74] A second set of important theories centers on the premise that people begin to drink, drink abusively, or remain alcoholic because alcohol, in some way, reinforces or rewards their behavior through inducing pleasure, removing discomfort, enhancing social interactions, and fulfilling the need to feel powerful or, on the other hand, helping them to self-destruct or to abolish unpleasant memories.[74] Studies of personality characteristics and levels of anxiety in nonalcoholic young men at high risk for the future development of alcoholism versus controls have demonstrated few significant differences between the two groups.[75,76]

3.5.2. Sociocultural Theories

A second approach centers on sociocultural theories, which use observations of similarities and differences between cultural groups and subgroups as they relate to drinking practices.[77] The major importance of this approach is heuristic, and no factors that are purported to be important in the development of alcoholism in one culture have been shown to generalize to most other cultures. An example would be the statements that Jews and Italians have low rates of alcoholism *because* children are introduced to alcohol within the home setting and alcohol is used as part of religious ceremonies—a theory that ignores the very high rate of alcoholism among the French, for whom both factors also operate.[74]

3.5.3. Biological Theories

A series of biological theories is found in the literature, including the possibility that alcoholics are seeking relief from an innate hypoglycemia, that they have allergies to alcohol or the congeners found in alcoholic beverages, or that a differential brain responsiveness to alcohol exists in alcoholics.[74] Once again, it has not been established whether the physiological abnormalities of alcoholics were the initial cause of the heavy drinking or resulted from a lifestyle of relatively poor nutrition, high stress, and high doses of ethanol.

One theory, which has had a great impact in the field by developing a focus on the chemical changes in nervous-system functioning that result from alcohol, is the possibility that alcohol may produce a morphinelike substance in the brains of certain individuals that may subsequently be responsible for the level of addiction.[78] These substances (tetrahydropapaveroline or beta-carbolines) can be found in the condensation of acetaldehyde and brain neurotransmitters such as dopamine or serotonin in the test tube. Such observations have opened an important area of research, but it is not likely that levels of these materials capable of functioning as false neurotransmitters are actually formed in the brain after heavy drinking.[78] These findings may tie into a genetic propensity toward alcoholism, as alcoholics have been shown to have higher levels of acetaldehyde after drinking and it is possible that similar findings may occur in individuals at higher risk for the future development of alcoholism.[79,80] At present, these findings are only of theoretical interest and will require much more work before their validity can be established.

3.5.4. Genetic Factors

A series of studies has established the probable importance of genetic factors in the genesis of primary alcoholism. This disorder has been shown to run strongly within *families*, and the rate of concordance (or sameness)

for alcoholism in identical *twins* is much higher than in nonidentical twins or same-sex siblings. A number of potential genetic *markers* (such as blood types) have been found to be associated with alcoholism, and some biological factors that influence the patterns of alcohol consumption in animals have been identified.[74] The most important information, however, comes from *separation* or adoption-type studies done in both the United States and Denmark, demonstrating that the children of alcoholic biological parents separated from their parents early in life and raised without knowledge of their natural parents have markedly elevated rates of alcoholism, whereas the children of nonalcoholics adopted into the homes of alcoholics do not show elevated rates of alcohol problems as adults.[81,82] The four- to five-fold higher risk for alcoholism in the adopted-out children of alcoholics when compared with controls was subsequently corroborated in a variety of studies for men, as well as in one study for women.[81–84]

Thus, the best data to date indicate that alcoholism is a genetically influenced disorder with a rate of heritability (i.e., the chance of inheriting the disorder) similar to that expected for diabetes or peptic ulcer disease. This finding may have great importance in helping to elucidate the psychological, social, and cultural factors impacting on the genesis of alcoholism. It may now be possible to study prospectively groups of individuals at high risk for alcoholism and to identify those factors that determine whether the predisposition is expressed and to identify other causative factors.

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CHAPTER 4

Alcoholism: Acute Treatment

4.1. INTRODUCTION

Alcohol is the most commonly abused substance creating serious medical and psychological problems. I will present an overview of *emergency problems* here, but the extensive discussion of rehabilitation that serves as a prototype for the rehabilitation of substance abusers in general is presented in Chapter 15.

4.1.1. Identification of the Alcoholic

The "obvious" alcoholic who calls in the middle of the night drunk or who has signs of cirrhosis represents a minority of individuals with alcoholism. The usual alcohol-dependent patient is a middle-class family man or homemaker presenting with complaints of insomnia, sadness, nervousness, or interpersonal problems. Because 5%–10% of adult men develop alcoholism (the rate for women being approximately one-third of that) and the rate of alcohol problems in medical and surgical inpatients may be over 25%, it is important to consider alcoholism a part of the differential diagnosis for every individual. The index of suspicion should be even higher for those with some of the more typical medical problems, including high blood pressure, ulcer disease, elevated uric acid, a macrocytosis, a high GGT, or any fluctuating medical condition that is otherwise difficult to explain (see Section 3.2.2).

Therefore, I take the two or three minutes necessary to query *each* patient about alcohol-related life problems. I begin by asking about general areas of difficulty, including: "How are things going with your spouse?" "Have you had any accidents since I last saw you?" "How are things going on the job?" and "Have you had any arrests or traffic tickets?" If there is a general life problem, I then try to determine what role, if any, alcohol may have played in that problem, and I go on to questions about the quantity and frequency of drinking. If the patient appears evasive or if I have any further doubts, I privately interview the spouse.

4.1.2. Obtaining a History

Once I have established either a definite or a probable diagnosis of alcoholism, I must determine whether or not there are any preexisting primary psychiatric disorders (as outlined in Figure 3.1). Thus, I first do a brief review of antisocial problems early in life, including such questions as "How did you do in school?" "What was the highest grade you completed?" "Did you ever run away from home overnight before you were 16?" "Did you have any police record prior to age 16?" and "When you were in junior high school or high school, did you get in a lot of fights and did you ever use a weapon in a fight?" Next, I ask about any depression that has occurred daily, all day, for periods of at least two weeks or that has been associated with the body and mind changes described in Section 3.1.2.3. If these have occurred, I then determine whether they existed prior to the first major alcohol-related life problem or occurred during a time when the individual had been abstinent for at least three months.

These steps are well worth my time, as complex and perplexing medical and psychological problems associated with alcoholism can be very confusing and can lead to serious complications through improper diagnosis and treatment. I can practice good preventive medicine and save myself a number of middle-of-the-night calls into the emergency room by maintaining a high level of suspicion of alcoholism.

4.2. EMERGENCY SITUATIONS

The most frequent emergency situations for alcoholics involve toxic reactions and accidents. Almost 8% of all emergency room patients have alcohol problems as part of their mode of presentation, rates that increase to 33% for accident victims.[1] Recognition of the presence of alcohol (whether alcoholism is involved or not) is important, as this drug alters the patient's reactions to emergency procedures.

4.2.1. Panic Reaction (See Section 1.6.1)

4.2.1.1. The Clinical Picture

Alcohol is a depressant drug and thus is rarely involved in acute panics. One possible exception, based on the increased level of anxiety that can be seen during alcohol imbibition as well as during withdrawal, is the induction of acute anxiety attacks characterized by nervousness, hyperventilation, and palpitations.

4.2.1.2. Treatment

After taking an EKG, doing a physical examination, and evaluating to

be sure that acute withdrawal is not likely, the cornerstone of treatment is reassurance and education. Of course, I will probably refer these patients for alcohol counseling.

4.2.2. Flashbacks

Flashbacks are not noted with alcohol.

4.2.3. Toxic Reactions (See Sections 1.6.3, 2.2.3, 6.2.3, and 14.4)

Toxic reactions to alcohol are usually the result of the narrow range between the anesthetic and the lethal doses of this drug, or they reflect the potentiating interaction seen between alcohol and other CNS depressants (see Section 13.2.3).

4.2.3.1. The Clinical Picture

The overdose from alcohol results from CNS depression to the point of respiratory and circulatory failure. The danger is heightened when alcohol is taken in combination with other CNS-depressing drugs, such as any of the hypnotics or antianxiety drugs; but it can also occur with drugs of other classes, such as the opiates. The clinical picture of an ethanol overdose is basically similar to what has been described for the depressants in Section 2.2.3.

4.2.3.1.1. The History

The patient usually presents smelling of alcohol with a history of a recent ingestion of high doses of alcohol, perhaps accompanied by other CNS depressants, such as sleeping pills (e.g., the barbiturates or flurazepam [Dalmane]) or the antianxiety drugs (e.g., chlordiazepoxide [Librium] or diazepam [Valium]). If no history can be obtained directly from the patient, a friend or relative might supply the relevant information, or there may be obvious evidence of drug ingestion (e.g., empty bottles).

4.2.3.1.2. Physical Signs and Symptoms

These are identical to the physical manifestations reported for other CNS depressants in Section 2.2.3. Basically, the patient presents with depressed functioning of the CNS and changed vital signs, including a slow pulse, a lowered respiratory rate, and a low blood pressure.

4.2.3.1.3. Psychological State

This also resembles the picture described for the other CNS depressants in Section 2.2.3, including signs of severe intoxication (i.e., the person is very drunk) along with confusion and irritability of mood.

4.2.3.1.4. Relevant Laboratory Data

The diagnosis, resting with the history and the physical examination, is aided by the toxicologic screen (10 ml blood or 50 ml urine) for both alcohol and other CNS depressants. The remaining laboratory tests are those necessary to properly exclude other causes of stupor (e.g., low glucose) and to monitor the physical status (e.g., blood counts and, if the patient is very stuporous, blood gases, as shown in Table 1.5).

4.2.3.2. Treatment

A fatal toxic reaction has been reported with blood-alcohol levels as low as 350 mg % in nontolerant individuals.[2] The treatment procedures follow those outlined for CNS depressants in Section 2.2.3.2, but there are a few differences.

1. Treatment involves carrying out the necessary emergency procedures to guarantee adequate ventilation, circulation, and control of shock; making a careful evaluation to rule out ancillary medical problems, such as electrolyte disturbances, cardiac disorders, associated infections, and subdural hematomas; and then establishing general supportive measures while the body metabolizes the alcohol.

2. Some investigators report that oral or intravenous (IV) fructose can enhance the rate of ethanol metabolism by 25% or more.[3,4] The mechanism is probably via an increased rate of reoxidation of the hydrogen receptor NAD so that more is available for ethanol. However, oral administration of this substance can result in abdominal colic and IV use may contribute to lactic acidosis.[3,4] Therefore, this approach is rarely used in clinical situations.

3. If you suspect that opiates were also ingested, naloxone (Narcan) (0.4 mg, intramuscular [IM] or intravenous) should be given. If, as outlined in Section 6.2.3.2, the patient does not respond to two doses given within one-half hour, it is almost certain that opiates were not part of the respiratory and cardiac depression. There is some anecdotal evidence that alcohol toxic reactions uncomplicated by opiate misuse may themselves respond to 0.4 mg of naloxone IV, which can be repeated twice in 10 minutes. However, laboratory experiments have failed to confirm these findings in animals or humans.[5]

4.2.4. Psychosis (See Sections 1.6.4, 2.2.4, and 5.2.4)

4.2.4.1. The Clinical Picture

The chronic ingestion of alcohol can cause a suspiciousness that can progress to the point of frank paranoid delusions, that is, *alcoholic paranoia.* Similarly, alcohol can cause persistent hallucinations, usually

voices accusing the patient of being a bad person or a homosexual (although at times the hallucinations can be visual or tactile), an example of *alcoholic hallucinosis.* Both pictures can develop in the midst of a drinking bout; occur in an otherwise clear sensorium (i.e., there is no organic brain syndrome); begin during alcoholic withdrawal; or have an onset within several weeks of the cessation of drinking. Both run a course of complete recovery within several days to several weeks if no further drinking occurs.[6,7] Clinically the syndrome resembles the stimulant-induced psychosis (see Section 5.2.4) and psychoses associated with other depressant drugs (see Section 2.2.4). It is not a form of schizophrenia, as there is no increased family history of that disorder in these individuals, and there is no evidence that alcoholic paranoia or hallucinosis progresses to schizophrenia.[8]

As was mentioned in Section 3.1.2.3, alcohol can induce serious states of depression in alcoholics or nonalcoholics. This depression looks cross-sectionally identical to the major affective disorders.[7,9] However, primary alcoholism with secondary depression is likely to show a clearing of the depressed mood after several days or weeks of abstinence without active treatment, whereas primary affective disorder may require intervention with antidepressants or (for manic-depressive disease) lithium.

In addition, states of violence are frequently associated with alcohol intoxication. An individual with a history of violence unrelated to alcohol may demonstrate severe aggression as he becomes tired, agitated, and perhaps hypoglycemic in the midst of heavy drinking. Thus, alcohol is associated with crimes of violence although many such violent individuals are probably antisocial personalities and/or drug abusers who are also using alcohol abusively. One specific form of alcohol-related violence, pathologic intoxication, is discussed in Section 4.2.8.1.

4.2.4.2. Treatment

1. If the patient has no insight into his delusions or hallucinations (i.e., if he believes that they are real), he should be hospitalized so that he is protected from acting out his delusions.

2. Treatment should be aimed at giving the patient insight and at evaluating and treating any medical problems associated with his heavy intake of alcohol.

3. Although the picture will clear spontaneously within a few days or several weeks, an antipsychotic agent like haloperidol (Haldol) at 1–5 mg per day (but up to 20 mg each day, if needed) by mouth, or IM if needed, may help keep the patient comfortable until the psychosis clears. There is no indication for continued use of these drugs, and they should be stopped within two weeks. If the patient has demonstrated delusions and/or hallucinations before the onset of heavy drinking or has a history of the

psychosis's persisting despite abstinence, the diagnosis of primary schizophrenia with secondary alcohol problems should be entertained and antipsychotic medications continued.[10]

4.2.5. Organic Brain Syndrome (See Sections 1.6.5 and 2.2.5)

4.2.5.1. The Clinical Picture

Alcohol can cause mental confusion and clouding of consciousness through the direct effects of the drug, alcohol-related vitamin deficiencies, and indirect consequences of alcohol intake, such as trauma and metabolic disturbances. Therefore, states of serious confusion can be seen during alcohol intoxication; during withdrawal from alcohol; as a complication of vitamin deficiency (e.g., thiamine); as the result of trauma (e.g., a subdural hematoma); and probably as the result of many years of heavy drinking.[7] The latter is probably the result of a combination of factors, including the direct toxic effect of ethanol on neurons.

4.2.5.1.1. Alcohol's Direct Effects

1. *Acute.* At relatively low doses (i.e., one or two drinks), judgment and performance are impaired, but at blood-alcohol levels in excess of 150 mg %, a picture of confusion and disorientation occurs for most nontolerant people. The OBS can be seen at even lower doses for the elderly and for individuals with preexisting brain disorders, such as those with prior head trauma and subsequent unconsciousness. The course is *usually* relatively benign, and a clearing of confusion occurs as blood-alcohol levels decrease. However, in the elderly and those with prior brain damage the state confusion may last for days or longer, and alcohol intoxication may thus be an important part of the differential diagnosis of acute-onset confusion.

2. *Chronic* heavy doses of alcohol are associated with a number of organic pictures, some of which may be permanent. As noted previously, 15%–30% of nursing-home patients with chronic OBS have histories of alcoholism. This OBS may result in part from the deleterious effects of alcohol on nerve cells, but it is also probably the combined result of alcohol, vitamin deficiencies, and trauma. A number of studies have corroborated the direct toxic effects of ethanol on neurons even when other aspects of nutrition are controlled.[11] The clinical picture and the treatment would be similar to those for vitamin-related organicities, as discussed below.

4.2.5.1.2. Vitamin Deficiencies

In the presence of alcohol, the body does not absorb thiamine ade-

quately and uses what thiamine there is at a faster rate. This fact may be of great importance, especially to individuals with inefficient thiamine-dependent enzymes.[12] The result is a syndrome consisting of a mixture of neurologic problems, such as ataxia, nystagmus, and the paralysis of certain ocular muscles, which characterize *Wernicke's syndrome,* and psychological symptoms like markedly decreased recent memory, confusion, and a tendency to make up stories to fill in memory deficits (confabulation), known as *Korsakoff's syndrome.* The Wernicke–Korsakoff syndrome (or variations thereof) runs an unpredictable course, with a tendency toward rapid and complete improvement of most neurologic signs with the administration of adequate thiamine, but with a slower resolution of the mental clouding and a possibly permanent OBS.[13]

4.2.5.1.3. Other Causes of Organicity in Alcoholics

Any individual presenting with confusion, disorientation, and decreased intellectual functioning should receive a thorough evaluation for trauma (and resultant subdural hematomas), infections, and metabolic abnormalities (especially glucose, magnesium, and potassium problems). Regarding glucose, alcohol interferes with gluconeogenesis as well as with the actions of insulin and may cause pancreatic damage; thus, alcoholics may show hyper- or, more frequently, hypoglycemia when they enter treatment. These problems tend to revert toward normal after several weeks of abstinence.

4.2.5.2. Treatment

1. The cornerstone of treatment rests with finding and treating the physical causes (e.g., infection, electrolyte abnormalities, and consequences of trauma).

2. All patients should receive thiamine in doses of 100 mg IM daily for at least three days, followed by oral multiple-vitamin preparations. Persisting signs of confusion, especially when difficulties with recent memory are out of proportion to those expected from the global mental status and/or where confusion is associated with neurologic problems such as a VIth-cranial-nerve palsy, should be met with continued thiamine for two or more months, as the Wernicke–Korsakoff syndrome may continue to improve over a long period of time.[13]

3. Patients should be given good general nutrition and lots of opportunity to rest.

4. Although improvement in the level of organic impairment is to be expected, the mental confusion may clear slowly, and it may not be possible to establish the exact degree of permanent intellectual deterioration for several months.

4.2.6. Alcoholic Withdrawal (See Section 1.6.6, 2.2.6, and 6.2.6)

4.2.6.1. The Clinical Picture

This is an example of the *depressant withdrawal syndrome* and is almost identical to the discussion given under CNS depressants in Section 2.2.6. Figure 4.1 outlines a simple approach to the symptomatology expected during withdrawal.

4.2.6.1.1. History

Some withdrawal symptomatology can be expected in any alcoholic who has been drinking daily—even if he has not become intoxicated every day. The intensity of the symptoms is difficult to predict with any degree of certainty, but the common pattern described in this section may be helpful.

The alcoholic may present with a clear history of alcohol abuse, but more often, he comes to the physician with a variety of psychological or physical complaints, as described in Section 4.1.1. It is wise to have a high index of suspicion for possible alcoholic withdrawal in all new patients, especially for those presenting with any of the more obvious stigmata of alcoholism, ranging from a high red blood cell MCV (see Table 1.5) to liver failure, cancer of the esophagus, or cancer of the head and neck. When a patient presents with any of the physical problems often associated with alcoholism or demonstrates a tremor and gives a history of alcohol misuse, the possibility of withdrawal must be carefully considered.

Symptoms	Treatment
Begin in hours, peak day 2 or 3, subside day 4 or 5	Thiamine (100 mg IM x 3 days)
Anxiety	Physical exam
Malaise	Multiple vitamins
A N S dysfunction	Food and rest
Insomnia	
Convulsions	Depressant drugs
O B S	
Hallucinations (visual or tactile)	

Figure 4.1. Detoxification. From Schuckit, M. A. Inpatient and residential treatments of alcoholism. In J. H. Mendelson & N. K. Mello (Eds.), *Diagnosis and Treatment of Alcoholism.* New York: McGraw-Hill, copyright © 1979. Reprinted with permission of McGraw-Hill Book Company.

4.2.6.1.2. Physical Signs and Symptoms

The final clinical picture is a combination of any of the problems listed in Figure 4.1. Almost all individuals show some degree of anxiety, a drive to drink, a tremor, and autonomic nervous system (ANS) dysfunction (e.g., a pulse of 100–120, a temperature of 99°–100°F orally, respirations of about 25, and an unstable blood pressure). Only between 5% and 15% of the alcoholics going through withdrawal develop the more serious sequelae, including convulsions (these are drug-induced seizures not related to idiopathic epilepsy and not requiring chronic treatment) and OBS or hallucinations (usually visual or tactile and rarely auditory).[14–16]

The etiology of alcoholic withdrawal is not totally understood although it has definitely been established that it depends on the direct effects of alcohol. However, the severity of the symptoms may relate to the level of acidosis achieved or to either direct or indirect disturbances in the electrolytes, including magnesium.[17]

4.2.6.1.3. Psychological State

This is as dramatic as the physical problems and consists of nervousness, a feeling of decrease of self-worth, and a high drive to continue drinking. For the 5%–15% mentioned above, it can include an obvious OBS or hallucinations.

4.2.6.1.4. Relevant Laboratory Tests

There are no laboratory tests that are pathognomonic for alcoholism. For an individual entering withdrawal, however, it is necessary to rule out all serious physical problems. Thus, it is important to perform an adequate neurologic examination, to determine the cardiac status through an EKG, and to do any of the relevant laboratory procedures outlined in Table 1.5 Abnormalities in liver function and kidney function, as well as in glucose levels, should be monitored throughout withdrawal. They can be expected to return to normal within a week in most individuals, unless serious permanent damage in the relevant organs has occurred.

4.2.6.2. Treatment

Therapy is rather simple and can be divided into identifying problems, offering general support, and carrying out active detoxification.

1. One of the most important steps is an adequate *medical examination* to rule out preexisting medical disorders that might complicate withdrawal and threaten life. There is a high risk of mortality if an

individual with serious physical damage enters a rather strenuous withdrawal without adequate treatment. It is important to note the possibility of cardiac disorders, intracranial trauma, infections, and electrolyte abnormalities requiring specific treatment.

2. All individuals should be offered good general support, including adequate rest, good nutrition, and a generally supportive milieu.
3. The usual alcoholic going through withdrawal (except for those who evidence bleeding, persistent vomiting, or diarrhea) is *over*hydrated, not dehydrated.[18] Therefore, with rare exceptions, intravenous fluids *should not* be used and *ad lib* oral fluids should be relied on to maintain adequate hydration.
4. It is especially important that all alcoholics receive thiamine in doses of 100 mg IM for one to three days (or up to two months for actual Korsakoff patients) along with routine daily oral multiple vitamins.[13]
5. It is possible at this point to begin education about the alcoholic process and to attempt to convince the alcoholic to begin rehabilitation.
6. None of these generally supportive measures addresses the actual withdrawal syndrome. As is true in any physical addiction, one must recognize that physiological symptoms have occurred because the individual stopped the drug too abruptly. Therefore, one can administer the drug of addiction, or a cross-tolerant drug, in doses high enough to abolish symptoms and then decrease the drug slowly (in the case of alcohol, that can be a decrease of approximately 20% of the first day's dose each day). This point is especially important in dealing with the 5%–15% of alcoholics who demonstrate convulsions, OBS, or hallucinations.

   Although any depressant drug, including alcohol, can be used,[19] I choose the benzodiazepines because of their relatively low rate of respiratory and blood pressure depression. Using chlordiazepoxide (Librium) as an example:

   a. I generally establish a prescribed oral dose of 25 mg three to four times a day initially.
   b. If the patient demonstrates obvious signs of withdrawal, such as a tremor, within an hour after administration of the drug, and if his blood pressure is relatively stable and he is awake and alert, an "as needed" (PRN) dose of 50 mg orally is given (the drug is poorly absorbed intramuscularly).[20]
   c. Each patient is titrated with PRN doses given for signs of withdrawal, but all doses are withheld if the patient develops a drop in blood pressure or excessive sleepiness. The total dosage

on the first day is usually between 100 and 300 mg of chlordiazepoxide. Rarely, patients need even higher doses.

d. The drug needed to diminish symptoms on the first day is then decreased by 20% each following day, so that a patient requiring 200 mg on Day 1 would receive 160 mg on Day 2, 120 mg on Day 3, 80 mg on Day 4, and so on.
e. One advantage of chlordiazepoxide or diazepam (Valium) is the relatively long half-life, which (while necessitating special care to observe blood pressure depression and sleepiness in order to avoid overmedicating the patient) allows for a slow, steady decrease in blood drug levels and a resulting smooth withdrawal.

Other authors have suggested the use of the shorter-acting benzodiazepines because, reflecting the short half-lives, these drugs do not accumulate in the body.[21] Such medications are certainly preferred for patients with serious liver damage or, for lorazepam, those who require IM drugs. One potential drawback is the difficulty in developing a smooth decrease in CNS depressant blood levels, as the short action may result in prominent peaks and valleys of both blood levels and symptoms and a subsequent increase in the risk of seizures.

One additional comment about this CNS depressant withdrawal is worthwhile. All of the material on withdrawal presented to this point assumes that the patient is not showing signs of agitated confusion (i.e., delirium). Once this serious state begins, there are few data on how the withdrawal syndrome can best be handled. The goal is to control behavior and to stop the patient from hurting himself or others, and the confusion is not likely to disappear for three to five days no matter what treatment is used. Some clinicians recommend the use of enough benzodiazepines to control behavior, and others use antipsychotic medications (e.g., haloperidol, or Haldol, 5 mg TID), but the latter may decrease the seizure threshold and actually increase the possibility of convulsions. Thus, I generally choose to use a benzodiazepine in an attempt to control agitation and decrease the probability of convulsions. Regarding other medications, there is *no* evidence that phenytoin is effective in prophylaxis against seizures in CNS depressant withdrawal.[22]

4.2.6.3. Some Withdrawal Treatment Variants[23]

4.2.6.3.1. The Social Model

The use of depressant drugs in treating the alcohol withdrawal syndrome requires that a physician and a registered nurse be available. In an ef-

fort to avoid the expense of such procedures, some programs choose to screen out patients with medical problems or those who appear to be heading for serious withdrawal and refer them to a hospital setting. This procedure leaves the program with individuals who are likely to do relatively well without hospitalization (although showing signs of minor withdrawal) and who will respond to good general supportive care and milieu. In this model, although there is the possibility of serious medical complications, many more patients are reached at a lower cost than in a hospital setting.

4.2.6.3.2. Outpatient Detoxification

This approach to alcohol withdrawal also aims at saving money by the use of an *outpatient* alcohol withdrawal program. If one chooses to carry out detoxification outside a hospital, it is imperative that *all patients be screened* for serious medical problems.[24,25] Next, a prediction of the final degree of withdrawal symptomatology is achieved by correlating the present symptoms with the blood-alcohol level. Thus, an individual showing severe shakes and autonomic dysfunctioning with a rapidly decreasing blood-alcohol level of approximately 100 mg % can be expected to enter serious withdrawal and should be hospitalized, whereas another patient showing only minor tremors with a 0 blood-alcohol level is probably a good candidate for outpatient withdrawal.

During withdrawal, the patient is treated in a day-hospital setting and receives medication both at the hospital and from a friend or relative at home with medical backup by phone, if needed. A paradigm using chlordiazepoxide and a generally supportive milieu can be established similar to that outlined above for inpatient detoxification. Outpatient detoxification should not be used in patients with histories of withdrawal seizures.

4.2.7. Medical Problems

The deleterious effects of alcohol on alcoholics are so ubiquitous that it is impossible to discuss adequately all the resulting medical conditions in this short handbook. One is faced with recognition of the complications described in Section 3.2.2 and discussed in greater depth in other texts.[26]

It is also important to consider alcohol-induced complications in *nonalcoholics* with chronic disorders. Examples include the increased chance of bleeding in individuals with ulcer disease; respiratory depression in people with emphysema; the adverse effects of alcohol on the livers of people with infectious hepatitis; the interference with normal pancreatic functioning for those who already have pancreatitis[1]; the deterioration in sugar metabolism that might adversely affect diabetics; and the impairment of cardiac functioning in individuals with heart disease.[27]

Alcohol also adversely affects the metabolism and the efficacy of a wide variety of medications, including potentiation of the adverse effects of analgesics, adverse interactions with antidepressants, and interference with the proper actions of all psychotropic medications.[7] The problems extend to antihypertensive drugs, as alcohol may potentiate orthostatic drops in blood pressure, and to hypoglycemic agents and anticoagulants because of the induction of liver metabolic enzymes.

4.2.8. Other Problems

4.2.8.1. Pathologic Intoxication

4.2.8.1.1. The Clinical Picture

This syndrome (which is probably both overdiagnosed and understudied) consists of the development of violent behavior at low doses of alcohol, usually followed by exhaustion and amnesia for the episode.[28,29] Although this diagnosis may be included as part of a legal defense for individuals committing violent acts under the influence of ethanol, it is a relatively rare phenomenon and is seen primarily in individuals with evidence of organic brain damage.

4.2.8.1.2. Treatment

Although no specific treatment regimen has been worked out, there are a number of commonsense suggestions.

1. The patient should be evaluated for a CNS epileptic focus, especially temporal lobe epilepsy.
2. Treatment in the midst of an episode is symptomatic and involves firm attempts to control behavior, such as using antipsychotics (such as haloperidol [e.g., 5 mg IM]), which may be repeated in one hour, if necessary.
3. All patients with this picture should be warned to abstain from drinking or at least to avoid alcohol when they are tired, hungry, or under stress. They should be told that they are legally responsible for violent acts committed after voluntarily imbibing ethanol.

4.2.8.2. The Fetal Alcohol Syndrome

4.2.8.2.1. The Clinical Picture

This syndrome consists of a combination of any of a number of components, including multiple spontaneous abortions; a baby with a low birth weight for gestational stage (a smaller size that is never "caught up"); malformations in facial structure, including shortened palpebral fissures, a flattened bridge of the nose, and an absent filtrum; ventricular septal defects

of the heart; malformations in the hand and feet (especially syndactyly); and levels of mental retardation that may be mild or moderately severe. The exact amount of ethanol involved, the timing of the drinking, the possible role of associated nutritional deficiencies, and other aspects of the clinical situation required to produce the FAS are unknown.[30,31]

The exact role of alcohol in producing specific impairment in the developing fetus has not been conclusively proved. However, the information available to date favors either a direct or an indirect role of alcohol in problems in fetal development. First, there is ample evidence, described in Section 3.2.2, that alcohol is capable of causing bodily damage in almost all systems, including the heart, the muscles, and the nervous system. Second, ethanol and acetaldehyde (the first breakdown product of ethanol; see Section 3.2.4) readily cross to the fetus. Third, the developing baby does not have efficient alcohol- or acetaldehyde-metabolizing systems, and the result is that these substances are likely to stay with the baby over an extended period of time.[32] Thus, the clinical observations of the possibility of a fetal alcohol syndrome along with this theoretical information are enough to convince most prudent parents that it is unwise for pregnant women to drink excessively, and as is true of all substances, it is probably safest for them to take no alcohol at all.

4.2.8.2.2. Treatment

The only treatment is prevention, and women should be advised not to drink at any time during pregnancy or, if they must drink, to keep the alcohol intake as low as possible.

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CHAPTER 5

Stimulants

5.1. INTRODUCTION

Stimulants are widely prescribed and greatly misused medications that have very limited bona fide medical uses. It is important that the clinician know these drugs well, as their misuse can mimic a variety of medical and psychiatric syndromes.

Nonmedicinal use of stimulants has occurred for many centuries, beginning even before the discovery of coca leaves by natives of the Andes in their effort to decrease hunger and fatigue.[1,2] Cocaine itself was first isolated in Germany in 1857, and its local anesthetic assets were applied to ophthalmology in the 1880s.[3,4] Amphetamine was first synthesized in 1887, and its clinical properties were recognized in about 1930, but until the middle 1950s or early 1960s stimulants were felt to be generally safe. These claims were made despite evidence of the widespread misuse of cocaine in Germany after World War I[5] and epidemics of the misuse of stimulants in Japan after World War II.[6]

5.1.1. Pharmacology (See Section 11.7 and Chapter 12)

5.1.1.1. General Characteristics and Background

The stimulants encompass a variety of drugs (some of which are outlined in Table 5.1), which share the ability to stimulate the CNS at multiple levels.[4] I will limit this discussion to those substances that are the most clinically important, avoiding other stimulants (such as strychnine) that are not usually abused. Two other important stimulants, nicotine and caffeine, are consumed in large amounts, but because of their relatively low potency, they are discussed separately, in Chapter 12.

As a group, the stimulants work, at least in part, by causing the release of neurotransmitters (chemicals that stimulate neighboring neurons), such as norepinephrine, from nerve cells. Some, in addition, mimic the functions of transmitters like norepinephrine through a direct effect on the nerve cells themselves.

Table 5.1
Some Commonly Abused Stimulants

Generic	Trade
Amphetamine	Benzedrine
Benzphetamine	Didrex
Caffeine	
Chlorphentermine	Pre-Sate
Cocaine	
Dextroamphetamine	Dexedrine
Diethylpropion	Tenuate, Tepanil
Fenfluramine	Pondimin
Methamphetamine	Desoxyn, Fetamin
Methylphenidate	Ritalin
Phenmetrazine	Preludin
Phentermine	Ionamin, Wilpo

Cocaine's effects occur through a variety of mechanisms, including the blocking of initiation or conduction of peripheral nerve impulses (contributing to its local anesthetic effect), direct stimulation of the CNS, and blockade of catecholamine uptake (norepinephrine more than epinephrine) at nerve terminals.[7] The special emphasis given cocaine in this text reflects the relatively widespread use of this substance in recent years. Coke is sold on the "streets" as an impure powder, most frequently being expanded with procaine. It is well absorbed through all modes of administration,[7] but it is most often used intravenously or through snorting (intranasally or IN). For the latter, powder is arranged on a glass in thin lines, 3–5 cm long, each with approximately 25 mg of the active substance, which is then inhaled through a straw or rolled paper via the nose.[4]

Recently, the drug has been smoked on tobacco although such use is inefficient, as cocaine sulfate has a melting point of almost 200°C.[8] As a result, cocaine "freebase" has been developed to lower the melting point to 98°C for use sprinkled over tobacco or smoked in special pipes. The freebase is produced by adding a strong base (e.g., buffered ammonia) to an aqueous solution of cocaine and then extracting the alkaline freebase precipitate.[9]

The blood levels of this CNS stimulant are fairly similar whether it is taken IN, through smoking, or orally,[10] although the half-life may differ with the different routes. Through most modes of administration, the peak blood levels develop rapidly (within 5–30 minutes). Most of the drug disappears over two hours (a half-life of approximately one hour), although some activity persists for four or more hours.[11,12] The longest-lasting effects are probably seen after IN ingestion, as the active drug appears to remain in the nasal mucosa for three or more hours, probably reflecting local con-

striction of the blood vessels.[12] The actual amount ingested varies with the purity of the preparation, but the usual cigarette has approximately 300 mg.[13] Most of the active drug is metabolized in the liver, but some is acted on by plasma esterases, and a small amount is excreted unchanged in the urine.[3,7]

Because of the high cost of coke on the streets, a number of cocaine "substitutes" (not truly related to cocaine itself) have been developed.[14,15] Some (e.g., iceberg, rock crystal, and snort) contain benzocaine and/or procaine, whereas others contain about 75 mg of caffeine (e.g., cocaine snuff, coca snow, and incense) or other mild stimulants (e.g., zoom). The effects of these drugs would be expected to resemble those of caffeine, and the reader is referred to Chapter 12 for further information.

5.1.1.2. Predominant Effects

The most obvious actions of stimulants are on the CNS, the peripheral nervous systems (outside the CNS), and the cardiovascular systems. Clinically, the drugs cause euphoria, decrease fatigue and the need for sleep, may increase feelings of sexuality, interfere with normal sleep patterns, decrease appetite, increase energy, and tend to decrease the level of distractibility in children with a hyperkinetic syndrome.[4]

Physically, the drugs produce a tremor of the hands, restlessness, and a rapid heart rate. Most of the substances have actions similar to amphetamine, although methamphetamine (Desoxyn) has fewer cardiac effects (especially at low doses), and methylphenidate (Ritalin) and phenmetrazine (Preludin) have lower levels of potency.[4] Cocaine is quite potent, having effects similar to those of intravenous (IV) amphetamine.[4,7,16]

If we use cocaine as an example, it is possible to look at the predominant effects more closely. The CNS actions show a biphasic response, lower doses tending to improve motor performance but higher doses causing a deterioration, with subsequent severe tremors and even convulsions.[3,7] Additional CNS effects include nausea and possible emesis, dilated pupils, and an increase in body temperature, probably reflecting both direct actions on the brain and indirect actions through muscle contractions.[7] Regarding the muscles, there is no evidence that cocaine produces an increase in strength, but there is a decrease in fatigue, probably mediated through CNS effects.[7] The cardiovascular results are also biphasic, smaller doses tending to produce a decrease in heart rate via actions on the vagus nerve but higher doses producing both an increased heart rate and vasoconstriction, with a resulting elevation in blood pressure.[3,7] The actions on the heart may produce arrhythmias both directly through the effects of the drug and indirectly through catecholamine release.[7]

5.1.1.3. Tolerance and Dependence

5.1.1.3.1. Tolerance

Tolerance to stimulant drugs develops within hours to days. It is the result of *metabolic* tolerance (an alteration in drug distribution and metabolism perhaps related to increased acidity of the body [acidosis] or an increased rate of metabolism), *pharmacodynamic* tolerance (as exemplified by toleration of injections of up to 1 gm of methamphetamine IV every two hours), and behavioral tolerance.[4,7,16]

The topic of tolerance is especially important in relation to cocaine, for which a very rapid development of acute tolerance is noted. For example, both the euphoric and the cardiovascular manifestations of the substance diminish much more rapidly than the plasma levels.[4,11] The magnitude of the final level of tolerance may be quite large, as it has been reported that humans have taken up to 10 gm of cocaine a day and monkeys have self-administered doses after several days that would have produced convulsions and cardiorespiratory complications in naive animals.[17,18] Although the metabolic tolerance noted for cocaine is large (the plasma half-life has been reported to decrease from 93 minutes to 48 minutes with repeated administration in animals), pharmacodynamic and *behavioral* tolerance are also shown to be important.[17]

On the other hand, an important phenomenon of *reverse tolerance* can also be noted demonstrating once again that drug actions vary with drug history and clinical circumstances. Some individuals show an increasing effect of repeated doses of the medications, perhaps related to a CNS process similar to enhanced cellular sensitivity or kindling.[19] Although there is a cross-tolerance between most of the stimulant drugs, it is not known whether it generalizes to cocaine.[4,7]

5.1.1.3.2. Physical Dependence

We are used to thinking of withdrawal symptoms as they relate to depressant and opiate drugs, expecting individuals to show anxiety, anorexia, loss of appetite, sleeplessness, and so on. As a result, there has been a debate about whether actual physical withdrawal can be expected with stimulants; however, most investigators and clinicians feel that such a syndrome exists. This syndrome is described in detail in Section 5.2.6.

5.1.1.4. Purported Medical Uses

This section and Table 5.2 are included to reinforce the fact that despite the claim that stimulants are effective for many medical disorders, in most instances the potential benefit *does not* outweigh the potential harm. This is true, at least in part, because of the rapid development of tolerance to

Table 5.2
Purported Medical Uses of Stimulants

Use	Comment
Depression	Stimulants can make the picture worse.
Dysmenorrhea	No proven usefulness.
Fatigue	Rule out medical diseases or depression. Stimulants do not work.
Hyperactive child syndrome	Very much overdiagnosed. Responds to stimulants or antidepressants.
Narcolepsy	A *rare* disorder that responds to other REM-suppressing drugs as well.
Obesity	Stimulants result in *temporary relief.* Dangers far outweigh assets.

stimulants, which seriously limits their ability to maintain a level of clinical usefulness.

Problems for which stimulants have been prescribed include:

5.1.1.4.1. Narcolepsy

This disorder—characterized by falling asleep without warning, through the development of rapid eye movement (REM) or "dreamtype" sleep at any time of the day or night—is associated with falling attacks (catalepsy). Stimulants can both modify and prevent attacks,[4] in part by decreasing REM sleep. However, narcolepsy may be a very rare disorder and should be diagnosed only with brain-wave or EEG studies, and other REM-decreasing drugs are available, including most of the antidepressants. Stimulants should be used very carefully, if at all, for this disorder.

5.1.1.4.2. The Hyperkinetic Child Syndrome (HS)

This syndrome of children, and perhaps adults, is characterized by a short attention span and an inability to sit quietly, with resultant difficulty in learning, and may be associated with signs of minimal brain damage.[20] However, hyperactivity is a common reaction to stress in childhood, and the diagnosis should not rest solely with the rapid evolution of a symptom of overactivity, especially when it occurs in relationship to a life problem.[21] This disorder, which appears before age 6, becomes much more incapacitating once school begins. For a bona fide HS, stimulants have been shown to be effective in decreasing symptomatology and in increasing the ability to learn. In addition, carefully prescribed medication does not predispose the child to go on to drug abuse.[21] This is probably the only

disorder for which stimulants are the primary drug of choice, but alternate modes of pharmacotherapy, including antidepressants, are available.[22]

5.1.1.4.3. Obesity

Stimulants do decrease the appetite, but only temporarily, with activity lasting *at most* three or four weeks.[23] In almost all controlled investigations, weight lost while on stimulants reappears within a relatively short period of time after the drug is stopped. Thus, considering the abuse potential of these drugs, their use in weight reduction is contraindicated.

5.1.1.4.4. Other Problems

The stimulants have also been used for *fatigue, depression, menstrual pain* or *dysmenorrhea,* and some *neurologic disorders.* Controlled studies have demonstrated that the drugs are not effective for these problems, and their potential dangers outweigh their usefulness.

5.1.2. Epidemiology and Patterns of Abuse

Enough stimulants are manufactured legally to give 50 doses each year to every man, woman, and child in the United States, with an estimated one-half of this drug finding its way into illegal channels.[24] This availability, when added to that of the drugs that enter the country illegally (e.g., cocaine) and other drugs coming from illegal manufacturing sources, allows for high levels of stimulant abuse.

Although they are extremely dangerous, the stimulating and euphoria-producing properties of the stimulants make them very appealing drugs. It has been estimated, for example, that the major limiting factor in the abuse of cocaine in the United States has been its high cost and limited availability. Nonetheless, at least 15% of all psychoactive drugs sold in the United States are amphetamines, and 15% of patients admitted to metropolitan psychiatric hospitals have traces of amphetamine in their urine.[6]

Precise figures on the pattern of cocaine abuse are not available, but this drug is taken by members of all social strata. In one recent survey in Ontario, Canada, approximately 5% of students and 3% of adults had taken cocaine. The highest use was among young males who also took other drugs.[25] The rapid increase in the desirability of freebase is demonstrated by a more than doubling of the percentage of abusers who reported ever smoking the substance, from 14% in 1977 to almost 39% in 1978.[26]

As with CNS depressants, abusers of stimulants other than cocaine can be rather simplistically divided into those more middle-class individuals receiving the drug on prescription from one or a variety of physicians (medical abusers) and the predominantly young population primarily

misusing drugs obtained from street suppliers or friends (street abusers). Either group may use the drugs alone or in an attempt to modify the effect of other substances, usually CNS depressants as described in Chapter 13. These drugs also appear to be used more and more in middle-class social settings as part of an attempt to increase a party "high."

5.1.2.1. Medical Abusers

These individuals usually begin using the medications to reduce weight, to treat fatigue or dysmenorrhea, to study for exams, or to aid in long-distance drives. The patient may get all the drug from one physician, attempting to obtain multiple or refillable prescriptions, or may receive simultaneous supplies from a variety of medical resources. In this setting, anecdotally, abuse tends to begin with a slow escalation of the dose, perhaps in response to the sadness, fatigue, and increased appetite that are seen when tolerance develops. Attempts to stop the medication result in fatigue and an increased need for sleep (hypersomnia), leading, in turn, to drug dose escalation.

A related pattern of social abuse is seen in students, individuals working odd hours, truck drivers, and other people with abnormal sleep cycles or the need to get a large job done in a short period of time without much sleep. Under these circumstances, fatigue and depression secondary to the use of the stimulants are almost certain to develop, and some individuals also demonstrate paranoia, emotional lability, and even violence.

5.1.2.2. Street Abusers

Here, an individual is attempting to achieve an altered state of consciousness by taking oral, IV, or inhaled drugs. In one pattern, the person chronically misuses the drug either alone or in combination with depressant medications. In another mode, the person initiates repeated periods of "runs" of amphetamines or cocaine,[26] taking the drug around the clock for two to four days. Problems with withdrawal and psychosis can occur with any method of drug administration and pattern but are most likely to be seen with the IV method during a "run."

5.1.3. Establishing the Diagnosis

Any substance that so thoroughly mimics other medical and psychiatric emergencies and that is so readily available both on prescription and "on the street" must be considered part of the differential diagnosis in most psychiatric emergency room situations. As with the other drugs of abuse, one must have a high index of suspicion or the diagnosis will be missed.[1,21] Because it is important to gather a careful history from both the

patient and any available resource person about the use of stimulant drugs, I ask each patient about his pattern of prescription and illegal drug-taking.[27] I ask specifically about stimulants when an individual presents with any of the following problems[28]:

1. A restless, hyperalert state
2. An anxietylike attack (usually nervousness plus a rapid pulse)
3. A high level of emotional lability or irritability
4. Aggressive or violent outbursts
5. Paranoia or increased levels of suspiciousness[29]
6. Hallucinations, especially auditory or haptic (touch)
7. Confusion or an organic brain syndrome
8. Depression
9. Lethargy
10. Any evidence of IV drug use, such as needle marks or skin abscesses
11. Abnormalities in the nasal lining or mucosa such as might be expected with inhaling stimulants
12. Worn down teeth (from tooth grinding while intoxicated)

Also, in an emergency room, any individual presenting with *dilated pupils, increased heart rate, dry mouth, increased reflexes, elevated temperature, sweating,* or *behavioral abnormalities* should be considered a possible stimulant-drug misuser.[17] Under such circumstances, or if there is a hint of stimulants from either the patient or the family, it is a good idea to take blood or urine for a toxicologic screen.[30]

5.2. EMERGENCY PROBLEMS

Drug-induced psychiatric disturbances are probably more prevalent among abusers of CNS stimulants than among the users of any other type of drug.[31] The difficulties can include maniclike states, serious psychoses resembling schizophrenia, depressions almost identical to major affective disorders (especially during withdrawal), and panic states. These all tend to be transitory and disappear over a period of hours or days when the drug is stopped. The most frequently seen clinical problems associated with stimulant abuse are the panic reaction (frequently presenting as "pseudoheart attack"), a temporary psychosis, and medical problems.[3,32]

5.2.1. Panic Reaction

5.2.1.1. Clinical Picture (See Sections 1.6.1, 7.2.1, 8.2.1, and 14.2)

Stimulant drugs can give rise to at least two related forms of panic. In the first instance, the individual, even when taking stimulants in relatively

"normal" doses, can experience a rapid heart rate, palpitations, anxiety, nervousness, and hyperventilation (the last resulting in altered blood carbon dioxide [CO_2] levels). The subsequent chest pains, in combination with anxiety and palpitations as well as shortness of breath, can give the individual the feeling that he is having a heart attack.[1]

The second rather classical picture relates to the psychological anxiety and nervousness that can be associated with stimulants. In such instances, the individual may "panic," feeling that he is losing control or going crazy.

5.2.1.2. Treatment

Treatment involves careful evaluation to rule out medical or psychiatric disorders, reassurance, and time.

1. The patient should be evaluated for bona fide medical illness, including the possibility of a heart attack or hyperthyroidism.
2. A careful history should be taken to rule out preexisting psychiatric disorders, especially anxiety neurosis or affective disorder.[33]
3. Bloods (10 ml) should be drawn or a urine sample taken (50 cc) for toxicologic tests.
4. If the first two points are negative, the patient should be told that his reaction is a result of the drug and that the effects should wear off over the next two to four hours.
5. The patient should be reassured that he will recover totally.
6. Of course, if stimulant misuse is a regular occurrence for the patient, he should be referred for evaluation and counseling to an outpatient drug treatment program or an interested health professional.
7. Medications should be used sparingly, if at all. If needed, the antianxiety drugs (e.g., chlordiazepoxide [Librium], 10–25 mg by mouth, repeated several times in 30–60 minutes, if necessary) may be helpful.

5.2.2. Flashbacks

The relatively short length of action and the rapid metabolism of stimulants does not make them conducive to the development of flashbacks.

5.2.3. Toxic Reaction (See Sections 2.2.3, 4.2.3, 6.2.3, and 14.4)

5.2.3.1. The Clinical Picture

5.2.3.1.1. History

The patient usually is a member of the "street" culture, where abuse

may be oral or IV, has a high-risk job (e.g., is a truck driver or a student at exam time), or has a history of some "medical" use of stimulants. The clinical picture may develop within minutes (e.g., with IV use or "snorting") or more slowly over hours to days, as with oral use in cross-country truck drivers.

5.2.3.1.2. Physical Signs and Symptoms

Evidence of sympathetic nervous system overactivity dominates the clinical picture for toxic reactions of all stimulants, including cocaine.[7,34] Thus, the patient presents with a rapid pulse, an increased respiratory rate, and an elevated body temperature. At high levels of overdose, the picture progresses to *grand mal convulsions*, markedly elevated blood pressure, and a very high body temperature—all of which can lead to cardiovascular shock.[28] It has been estimated that between 100 mg and 200 mg of dextroamphetamine and similar doses of cocaine can be lethal in a nontolerant individual, but chronic users may tolerate 1 gm or more, and the use of up to 10 gm of cocaine per day has been reported.[3,16,17] Death, though infrequent, is usually related to a strokelike CNS vascular picture, cardiac arrhythmias, or high body temperature.[28] There may also be signs of IV drug use (e.g., needle marks or abscesses), or if the patient takes the drug nasally, there may be an inflammation of the nasal mucous membranes or, with cocaine, a destruction of all or part of the nasal septum.

5.2.3.1.3. Psychological State

Taken in excessive doses, stimulants produce restlessness, dizziness, loquaciousness, irritability, and insomnia. These may be associated with headache, palpitations, and the physical signs and symptoms listed above. As the dose increases, toxic behavioral signs develop, including a high level of suspiciousness, repetitive stereotyped behaviors, grinding of the teeth (bruxism), repetitive touching and picking at various objects and parts of the body (stereotypy), and the repetitious dismantling of mechanical objects, such as clocks.[7,32]

5.2.3.1.4. Relevant Laboratory Tests

With the exception of a toxicologic screen and the usual vital sign changes expected with stimulants, there are rarely dramatic laboratory test results.

5.2.3.2. Treatment

The treatment chosen will depend on the clinical condition of the patient at the time he comes for treatment.

1. Emergency care to ensure a clear *airway, circulatory* stability, and treatment of *shock* should be carried out as described in Sections 2.2.3.2, 6.2.3.2, and 14.4.3.
2. For an *oral overdose,* gastric lavage should be carried out through either a nasogastric tube (for a conscious patient) or after intubation (for a comatose patient).
3. *Elevated body temperature* must be controlled, with all fevers above 102°F orally being treated with cold water, ice packs, or, at higher temperatures, a hypothermic blanket (see also Item 7 below).
4. *Repeated seizures* should be treated with IV diazepam (Valium) of from 5 to 20 mg injected *very slowly* intravenously over a minute and repeated in 15–20 minutes as needed. In this instance, intubation should be strongly considered, as IV diazepam could result in laryngospasm or apnea.
5. A major elevation in *blood pressure* (e.g., a diastolic pressure of over 120 mm) lasting for over 15 minutes requires the usual medical regimen for malignant hypertension, which may include a phentolamine (Regitine) IV drip of 2–5 mg given over 5–10 minutes. Failure to treat this symptom vigorously could result in CNS hemorrhage.
6. To help *excretion* of the stimulant, the urine should be acidified with ammonium chloride with the goal of obtaining a urinary pH below 6.6. This usually requires 500 mg orally every three to four hours.[27]
7. *Hyperthermia* and marked *agitation* can be treated with a dopamine-blocking agent such as haloperidol (Haldol), beginning with doses of 5 mg orally per day, but the dose might have to be a good deal higher for some individuals.[35] An alternate drug is chlorpromazine (Thorazine) in doses of 25–50 mg IM or orally, to be repeated in 30–60 minutes, if needed, but in this instance, one must be especially careful to avoid precipitating an anticholinergic crisis (see Section 11.9.1) or a severe drop in blood pressure.[28] This danger, once again, underscores my preference for avoiding medications unless absolutely needed.
8. Patients rarely require dialysis, even though most of these drugs would respond to such measures if needed (see Section 14.4.3.2).
9. For cocaine (and possibly other stimulants as well) propranalol (Inderal) 1 mg/min IV up to 5–8 mg total might help control blood pressure, pulse, and respiratory effects,[36] but not all authors agree.[34]
10. Bloods and urines should be drawn for baseline studies and toxico-

logic tests, which will help you to rule out the concomitant use of other medications.

11. Once the patient begins to recover or if the overdose was not medically very serious, he should be placed in a quiet room with a minimal amount of stimulation.
12. Treatment of unintentional overdoses by children requires basically the same approach.[37]

5.2.4. Psychosis (See Sections 1.6.4, 2.2.4, and 4.2.4)

The stimulant-induced psychosis gives a temporary but potentially dramatic picture. The clinical state can be seen with *all* the major stimulants, including methylphenidate, pemoline, the amphetamines, prescription (and some nonprescription) weight-reducing products, and cocaine.[30,32]

5.2.4.1. The Clinical Picture

A high level of suspiciousness and paranoid delusions in a *clear sensorium* (the patient is alert and oriented) developing after an individual takes stimulants is called an *amphetamine* or *stimulant psychosis*.[6,26–32] This picture usually develops gradually with chronic abuse, although it can be seen acutely with one very large amphetamine dose. The psychosis has been noted in normal volunteers when 10 mg of dextroamphetamine was given in slowly escalating doses,[28,29,30] and pictures resembling human psychoses have been seen in animals after the administration of stimulants.[39–41] The paranoia is usually associated with hallucinations, either auditory or haptic (the individual feels things crawling on him), but it can also be seen with visual hallucinations or illusions and is usually accompanied by a very labile mood.[27,28,32] This picture often contains repetitive compulsive behavior.

The paranoid delusions can be very frightening to the patient. The level of insight or understanding is usually limited or nonexistent, and the suspiciousness has been known to result in unprovoked violence to the point of murder.[42] For instance, it has been reported that in the midst of the epidemic of amphetamine abuse in Japan, 30 of the 60 convicted murder cases in a two-month period were related to the abuse of amphetamines.

With cessation of the stimulants, the psychosis usually clears within two days to a week, the hallucinations disappearing first and the delusions later.[7,28,32] This is followed by increased sleep (often accompanied by disturbing dreams) and a depression that may last two weeks or longer.[28]

The psychosis mimics an acute schizophrenic picture or mania. However, schizophrenia, as defined by Goodwin and Guze,[33] has a relative-

ly slow onset and is usually associated with a stable, somewhat bland mood; also, a schizophrenic rarely shows abnormal physical findings. On the other hand, a physical evaluation of the amphetamine psychotic can reveal severe weight loss, excoriations (from scratching at nonexistent bugs), needle marks, and elevated blood pressure, heart rate, and temperature.[27] These physical findings are quite variable, and their absence does not rule out amphetamine psychosis.

The cocaine psychosis (basically identical to that of the other major stimulants) has been noted for many years, having been thoroughly described by Freud.[13,26] There is probably a progression from "snow lights" (seeing colored lights when cocaine is administered) to hallucinations of geometrical forms and on to tactile hallucinations. Frank visual and/or auditory hallucinations are most likely to occur in psychologically vulnerable individuals, in those taking the drug for an extended period of time, or in those taking relatively high doses.[13,26]

Hallucinations are reported by only a minority of stimulant abusers, with 15% relating histories of visual hallucinations, 13% tactile, 7% olfactory (usually of an unpleasant nature), 4% auditory, and 4% gustatory in one series.[13,26] An important part of the sensory change involves a perception that bugs are crawling under the skin, or formication.[13,26,32] It is worthy of note that any of the stimulants can produce serious paranoid delusions without insight and either with or without accompanying hallucinations.[43,32] In dealing with these patients, it is important to recognize that no matter how prominent their hallucinations, this is *not* schizophrenia and is likely to clear relatively quickly even if no antipsychotic medications are used.[32]

5.2.4.2. Treatment

Treatment of the stimulant psychosis is relatively straightforward, as, even without active therapy, the pathologic picture tends to disappear within days to a week.[7,28,32]

1. If the individual is out of contact with reality, it is best to hospitalize him.
2. The patient should be carefully screened for any signs of serious physical pathology, as psychotic symptoms can be part of an overdose. A discussion of the treatment of the overdose is given above in Section 5.2.3.2.
3. Vital signs must be carefully recorded, and blood pressures, especially those over 120 diastolic, should be treated with drugs such as phentolamine (Regitine) in doses of 2–5 mg given over 5–10 minutes. Special care must be given to avoid precipitating hypotension.[44]
4. In evaluating the clinical picture, consider the possibility that the

individual may have also been abusing a depressant, and check for signs of depressant withdrawal.

5. In general, the patient should be placed in a quiet, nonthreatening atmosphere and should be treated with the general precautions one would extend to any paranoid patient (e.g., not performing any procedures without thorough explanation, not touching the patient without permission, and avoiding any rapid movements in the patient's presence).[27]
6. The treatment personnel should assume an appearance of self-confidence, but the possibility of unprovoked or assaultive behavior should be noted.[28]
7. As is true in a toxic reaction, it is possible that the administration of ammonium chloride (500 mg every three to four hours) to acidify the urine might help cut the psychosis short.[27]
8. A careful history of preexisting psychoses, especially schizophrenia or a serious manic or depressive disorder, should be taken from the patient and available resource people.
9. Although my preference is to avoid medications, if behavior cannot otherwise be controlled drugs can be considered.
   a. Some authors recommend chlorpromazine (Thorazine) in doses of 50–150 mg by mouth or 25–50 mg IM,[44] to be repeated up to four times a day, if needed, with special care to avoid anticholinergic problems or hypotension.[16,35] I avoid this drug, as it tends to increase the half-life of amphetamine.[35]
   b. Others recommend the use of haloperidol (Haldol) in doses beginning with 5 mg per day up to 20 mg daily given orally or IM.[35] As would be true of chlorpromazine, the drug need be given for only three to four days.
   c. Some authors recommend the use of diazepam (Valium) in doses of 10–30 mg orally or 10–20 mg IM to control anxiety or overactivity.[44] However, I feel that there is no place for CNS-depressant drugs in treating the amphetamine psychosis, and they may increase the risk of violence.[35]
10. Patients should be referred after discharge to a drug treatment center to help them deal with their drug problems and to rule out the existence of other psychiatric disorders.

5.2.5. Organic Brain Syndrome

Confusion and disorientation can develop when an individual takes so much of the drug that his normal mental processes are disturbed.

5.2.5.1. The Clinical Picture (See Section 1.6.5)

The organicity tends to be a transient problem consisting of any of the

following symptoms including confusion, disorientation, hallucinations, delusions, paranoia, loose association of ideas, and behavioral problems of bruxism and repeated touching or stereotypic behavior.[7] It should be noted that the stimulants may cause cerebrovascular changes when taken chronically, and there are reports of increased rates of cerebral hemorrhage, subarachnoid bleeding, subdural hematomas, and vascular lesions resembling periarteritis nodosa in stimulant misusers.[30] There is also some *anecdotal* evidence that abusers of amphetamines and other stimulant drugs demonstrate a potentially permanent decrease in mentation and concentration, and there is good evidence that some neuropsychological deficits can be seen for weeks and even up to three months of abstinence.[45,46] Thus, the abuse of stimulant drugs should be considered a part of the differential diagnosis of any individual presenting with signs of CNS organicity, and it is important that one carefully evaluate the neurologic functioning of all stimulant misusers seen in practice.

5.2.5.2. Treatment

1. Because the organicity tends to be transient, the general approach is to give supportive care following the guidelines offered in Section 5.2.4.2.
2. However, one must be certain to carry out an adequate neurologic examination to rule out all of the possible causes of an OBS, including a focal CNS lesion or intracranial bleeding.
3. One can roughly estimate the prognosis by determining which, if any, preexisting psychiatric disorder is present or if evidence of brain malfunctioning was present before the onset of the drug-induced problem.

5.2.6. Withdrawal

5.2.6.1. The Clinical Picture

5.2.6.1.1. History

Depending on the type of abuse involved (e.g., "street" versus medical), the patient may give an obvious history of drug abuse, or a great deal of probing and gathering information from friends and relatives may be required to establish the accurate diagnosis. The withdrawal may begin insidiously, with the patient having no idea why he is depressed, lethargic, or irritable, or it may have a more dramatic onset.

5.2.6.1.2. Physical Signs and Symptoms

There is usually no specific physical pathology present, other than the usual type of medical problems seen in any abuser. The withdrawal syndrome can begin while the individual continues to take stimulants as

tolerance develops, and it may include a variety of nonspecific muscular aches and pains.[7]

5.2.6.1.3. Psychological State

The repeated administration of stimulants results in bad dreams as a result of the body's need to make up for the rapid-eye-movement (REM) sleep deprivation caused by stimulants. Feelings of sadness and hopelessness can be severe, sometimes leading to suicide, and the apathy and fatigue can last up to four weeks or more.[27] It is possible (but not definite) that some sadness and lethargy persist as a secondary abstinence syndrome over a period of months.

5.2.6.1.4. Relevant Laboratory Tests

There are no specific laboratory tests that will help here. Of course, all IV drug abusers should be screened for possible hepatitis (e.g., the liver function tests listed in Table 1.5) and signs of occult infection (a white blood count as listed in Table 1.5), and they should be given a good neurologic examination. A toxicologic screen may be helpful, but the signs of withdrawal might not appear until the stimulant drugs have been metabolized.

5.2.6.2. Treatment

Treatment is simply addressing the *symptoms,* as the major acute syndrome tends to dissipate in one to three days on its own (except for the depression and lethargy, which may remain for several weeks).

1. The patient must be given a careful neurologic and physical examination.
2. The possibility of the concomitant misuse of other drugs, especially depressants, must be considered. Blood and urine samples should be sent for toxicologic screening, and the patient should be carefully queried about other drug use.
3. A careful history of the drug misuse pattern and prior psychiatric disorders must be obtained.
4. The patient should be placed in a quiet atmosphere and allowed to sleep.[27]
5. If the patient is markedly despondent, (temporary) suicide precautions should be considered.
6. Although, once again, I prefer to avoid medications, some authors suggest the use of haloperidol (Haldol), up to 5 mg a day (rarely up to 20 mg) for three days to a week to help modify symptoms.[27,28]
7. In general, allowing the person several days to recover and having him sleep and eat as much as he needs will usually result in the disappearance of all symptoms.

5.2.7. Medical Problems

The medical problems associated with overdose have been described in Section 5.2.3. Additional problems that must be considered are as follows:

1. Complications from the use of contaminated needles include endocarditis, tetanus, hepatitis, emboli, abscesses, and so on (see Section 6.2.8).
2. Apparent signs of a stroke can accompany the strong contraction of blood vessels caused by stimulants.
3. A related phenomenon occurs in those individuals who sniff cocaine. The constriction of blood vessels in the nasal mucosa can be so severe that the nasal septum is destroyed.[3]
4. Another problem after snorting or smoking coke is possible aspiration subsequent to laryngeal or pharyngeal anesthesis.[3]
5. The elevated blood pressure that can accompany the use of stimulant drugs can cause an intracranial hemorrhage.
6. The stereotyped behavior during intoxication can include grinding of the teeth (bruxism), which can wear down the teeth and cause dental difficulties.
7. A variety of skin problems, including scratches (secondary to delusions about bugs in the skin) and skin ulcers, can be noted.

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CHAPTER 6

Opiates and Other Analgesics

6.1. INTRODUCTION

This chapter is concerned with those pain-killing drugs (analgesics) that are most likely to be misused, ranging from propoxyphene (Darvon) through the synthetic, opiatelike drugs to the major opiates, including morphine and heroin. The generalizations made here apply to almost all prescription painkillers, with the possible exception of the newer prescription anti-inflammatory medications. The material will also be relevant to the newer opiate-type drugs, including the mixed agonist/antagonist butorphanol (Stadol or Borphanol), which is similar to buprenorphene and nalbuphene, as well as fentanyl (Sublimaze). Most of these newer medications have not yet met the test of time to determine their actual propensity to develop adverse reactions, including addiction.[1,2]

Historically, the widespread opiate abuse observed in Europe and the United States at the turn of the century was the result of legally purchased morphine and related compounds, primarily in middle-class women.[3,4] The preponderance of medical abusers of opiates continued until the drugs were placed under legal control in the early 1900s, after which the "street" misuse of these substances began, primarily in young men from poor areas. Since the mid-1960s, however, abuse of these substances has spread once again to the middle class, where the drugs are obtained through both physicians and the "black market."

6.1.1. Pharmacology (See Section 11.5 for over-the-counter analgesics.)

6.1.1.1. General Characteristics

The major opiates include natural substances, such as opium, morphine, and codeine; semisynthetic drugs produced by minor chemical alterations in the basic poppy products (e.g., heroin, hydromorphone [Dilaudid], and oxycodone [Percodan]); and synthetic analgesics, such as

Table 6.1
Opiate Analgesics

Drug type	Generic name	Trade name
Analgesics		
	Opium	
	Heroin	
	Morphine	
	Codeine	
	Hydromorphone	Diluadid
	Oxycodone	Percodan
	Methadone	Dolophine
	Propoxyphene	Darvon
	Meperidine	Demerol
	Diphenoxylate	Lomotil
	Pentazocine	Talwin
		Fortral
Antagonists		
	Naloxone	Narcan
	Nalorphine	Nalline
	Levallorphan	Lorfan
	Cyclazocine	
	Naltrexone	

propoxyphene (Darvon) and meperidine (Demerol), as shown in Table 6.1. The relative potency of these drugs has been described in other texts and can be roughly gauged by the usual dosage, with a standard of 10 mg of morphine producing analgesia for the average individual.[6]

These drugs undergo similar metabolism in the body but differ in their degree of oral absorption (ranging from a low for heroin to a high for propoxyphene). Heroin is rapidly converted by the body into morphine. Detoxification occurs primarily in the liver, and the resulting metabolites are excreted through the urine and the bile. Over 90% of the excretion of doses of these drugs (with the exception of a very long-acting substance such as methadone) occurs within the first 24 hours, although metabolites can be seen for 48 hours or more.[6]

6.1.1.2. Predominant Effects

These substances all produce analgesia, drowsiness, changes in mood, and, at high doses, a clouding of mental functioning through the depression of CNS and cardiac activity.[6] Although there are some major differences in the way these drugs affect particular systems,[7] the actions are homogeneous enough to allow for some generalizations.

6.1.1.3. Tolerance and Dependence

6.1.1.3.1. Tolerance

Tolerance develops rapidly to most opiates, particularly the more potent analgesics, but the changes in organ sensitivity develop unevenly.[8] Almost all the opiates exhibit cross-tolerance to other members of the class.[8]

6.1.1.3.2. Dependence

These substances are very addicting (i.e., have attractive effects and quickly produce tolerance and dependence), and physical dependence develops after relatively short-term use. The degree of dependence varies directly with the potency of the particular drug, the doses taken, and the length of exposure. Therapeutic doses of morphine given twice a day for two weeks or four times a day for three days can result in a mild withdrawal syndrome, especially if precipitated by a narcotic antagonist.[7]

6.1.1.4. Recent Findings on Brain Mechanisms

Recent discoveries on the pharmacology of opiates have been very exciting and are worthy of mention here. The work began with the hypothesis that there might be opiate receptors in specific areas of the brain. Logically, if there are endogenous opiate receptors, there might be endogenous opiates to occupy those receptors. This line of reasoning has resulted in the discovery of a series of substances (the endorphins and enkephalins) that are present in various parts of the body, especially the CNS, and that appear to function in regulating the perception of pain. These substances have also been hypothesized to have some importance in the regulation of normal mood states, the development of psychoses, and the mediation of action of other misused substances. This series of investigations may lead to important breakthroughs in our understanding of the mechanism of action of these drugs, which might, in turn, lead to important information on the causes and treatment of substance misuse.[9–10]

6.1.2. Epidemiology and Pattern of Abuse

Simplistically, users divide into those who misuse analgesics in a medical setting (*medical abusers*) and those who take opiates obtained from nonmedical sources (*street abusers*). The medical abusers tend to be older, middle-class, and well established in comparison to the street abusers, but there is much overlap between the two groups. Nonetheless, for clarity, the characteristics of street and medical abusers are (somewhat artificially) separated in this section.

6.1.2.1. Street Abuse

6.1.2.1.1. Pattern of Use

The sale of illicit opiates is a very profitable business. Most of these drugs enter the United States illegally as part of a highly complex economic/manufacturing ladder beginning in the Orient, the Middle East, or Mexico. The socioeconomics of heroin misuse have been outlined by Stimmel, demonstrating that 10 kg of opium grown from poppy plants at a cost of $250 results in street heroin worth $400,000 in the United States after a series of steps of manufacture and dilution with adulterants.[11] The resulting opiates are abused through all routes of administration, including oral (primarily the synthetic and semisynthetic opiates); intranasal (snorting); smoking (usually opium); and intravenous (especially heroin).[5]

The usual street abuser begins using opiates occasionally but may progress to daily use, with tolerance and physical dependence rapidly following. This pattern is certainly the one most likely to come to the attention of medical and mental health personnel as well as the police.

However, there are a number of individuals who continue to take the drug only occasionally over an extended period of time, even when used IV. The exact number of people "chipping" these drugs is not known, but it is probable that they show a much higher level of life stability, having family, friends, and job, than is true of the general user.[12]

A related phenomenon is seen in a number of physically addicted individuals who manage to hold jobs and to function fairly well socially.[13] Another important observation grew out of Vietnam, where large numbers of soldiers with little or no prior experience with opiates found themselves in a situation of high stress and with drugs readily available.[14] Under such circumstances, as many as one-half of those given the chance tried opiates. Although many became physically addicted, those who had not used drugs before Vietnam tended to return to a drug-free status when back in their home communities.[15]

In more recent years, there is evidence that the prevalence of opiate misuse has stabilized in middle-class populations.[16] Analyses of both direct and indirect indices of "street" use in New York have shown what appears to be a decrease since 1970 in new "intensive" users, that is, those requiring treatment.[17] These data have shown a decrease in the number of felony-related opiate arrests from 22,000 in 1970 to 4,000 in 1978; a parallel decrease in opiate misdemeanor arrests per year from 16,000 to 2,000; decreases in both infectious hepatitis (from 3,000 to 500) and serum hepatitis (from 1,500 to 500); and a decrease in overall drug mortality (from 800 to 250) during the same time period. The number of new admissions to methadone maintenance treatment has also decreased from a high of 19,000

in 1972 to 2,000 in 1978, and readmissions to methadone maintenance have decreased from 6,000 in 1976 to 3,500 in 1978.[17] According to one report, it is felt that the most likely explanation for the decrease is a change in attitude toward heroin, as the indices began to shrink *before* street drug supplies became less plentiful.

6.1.2.1.2. The Natural History

The average street user tends to be young, a member of a minority group, and male.[18] He usually demonstrates a prior history of delinquent behavior (the more severe the antisocial problems, the greater the chance of continued drug use).[15] One study of a group of black addicts demonstrated that the average age of first use of any drug (usually marijuana) was 14; the first arrest for *any* problem occurred at 16.5; the first use of heroin at age 18; the first evidence of physical dependence at age 20, with the first heroin-related arrest following within about six months; and the first treatment at approximately age 26.[18] Almost 80% of opiate addicts in treatment had early school problems, and 90% reported truancy, two-thirds had been suspended from school, and 80% had dropped out before graduating high school.[18] As was true in the discussion of alcoholism, individuals who qualify for the careful diagnosis of the antisocial personality (based on their antisocial behavior before age 16 and before the onset of serious drug misuse[19]) carry a much worse prognosis for violent behavior and continued drug and antisocial problems than the "average" street abuser.

The short-term prognosis for these individuals is relatively poor, with almost 90% returning to drugs within the first six months after treatment, but this return is followed by a trend toward an increasing percentage achieving abstinence over time.[20] Long-term follow-ups (up to 20 years) have demonstrated that a third or more of opiate abusers, even those severely enough impaired to be treated in a jail/hospital setting like the federal facility in Lexington, Kentucky, are finally able to achieve abstinence. Most addicts tend to show exacerbations and remissions similar to those repeated by alcoholics.[21]

The course for the remainder was far from benign, with one-quarter of the original total dead at follow-up and one-quarter still addicted.[22,23] The mortality rate for opiate abusers is about 5–10 per thousand, with especially high levels of death due to suicide, homicide, accidents, diseases such as tuberculosis, and peripheral infections.[5] The morbidity and mortality appear to reflect complications from "dirty" needles and impure drugs more than the effects of the opiates themselves.[21] If remission is going to occur, it is probably seen after the age of 40, but there is no absolute fixed age.[22,24] When an addict remains abstinent for three or more years, there is a very

good chance that he will not go back to drugs.[22] Good prognostic signs for opiate addicts include a history of relatively stable employment, being married, a history of few delinquent acts, and few criminal activities unrelated to drugs.[15,20,22]

One additional aspect of the natural history of opiate abuse, the rate of associated alcohol problems, requires emphasis. Most opiate abusers began their substance problems with tobacco and alcohol and then progressed to marijuana and other drugs of misuse as described in other references and elsewhere in this text.[24,25] These "stages" of abuse are not mutually distinct, and most periods involve a combination of other drugs with alcohol. Thus, because ethanol is legal, is readily available, and rarely leads to dismissal from drug treatment programs, it makes sense that many opiate abusers will turn to alcohol abuse when their primary drug is not available, as alcohol can be used to boost the effects of other drugs. Although many opiate addicts demonstrate periods of time both "on the street" and during outpatient treatment when their alcohol use is relatively moderate (e.g., in one survey approximately 50% of methadone-maintenance patients reported three to four drinks per day on the average),[26] perhaps as many as 50% of male and 25% of female addicts meet the criteria for alcohol dependence within the first five years after active drug treatment.[27] The prevalence of alcohol misuse is higher in drug treatment dropouts than it is in those who stay with therapy, and abuse is more likely in individuals who have a history of alcohol misuse before being identified as drug addicts.[26–28] Although active education regarding alcohol and attempts to prevent alcohol misuse should be included in treatment programs for drug abusers, successful drug therapy without specific efforts aimed at alcohol can result in a decreased use of alcohol over time.[26]

6.1.2.2. Medical Abuse

The medical-setting abusers have not been well studied, probably because their use of opiates is not associated with a very high rate of unexpected death, serious crimes, or violence. What data there are indicate a preponderance of middle-class individuals, women, and those with pain syndromes.[29] The misuse is frequently one of multiple drugs, including depressants and stimulants as well as analgesics.

Two groups of individuals stand out as being at high risk for this syndrome. First, it has been suggested that a majority of those individuals with pain syndromes misuse their prescribed drugs.[29] The second important subgroup, health-care professionals (especially physicians and nurses), may have the highest rate of analgesic drug abuse of any middle-class population.[22] Possible explanations include the stresses of caring for other people's problems, the manner in which their job interferes with their ability to

relate to their families, the long hours of their jobs, and the ready availability of drugs.[30]

6.1.3. Establishing the Diagnosis

Diagnosis in either the "street" or the "medical" group requires an awareness of the possibility of misuse with all patients[5] and a good medical history. In addition, there are a number of physical symptoms, signs, and behavioral patterns to watch for. These include:

1. *Increased pigmentation* over veins.
2. Evidence of clotted or *thrombosed veins.*
3. Other *skin lesions* and *abscesses.*
4. *Constricted* or small *pupils.*
5. *Swollen nasal mucosa* (if the drug was "snorted").
6. *Swollen lymph glands.*
7. An *enlarged liver.*
8. Abnormal laboratory tests, including *decreased globulins,* a positive *latex fixation test (VDRL), liver-function test* abnormalities, and a relatively high *white blood count.*
9. Evidence of visiting *multiple physicians* (perhaps to get a supply of drugs), a *complex medical history* that is hard to follow, or a *de novo* visit with complaints of *severe pain* (e.g., kidney pain, back pain, headache, or abdominal pain), even with physical signs, as these are easy to produce at will (e.g., by placing a drop or two of blood in a urine sample).
10. Any *health professional* being seen for a syndrome for which analgesics might be prescribed.

6.2. EMERGENCY PROBLEMS

The most frequently occurring emergency difficulties seen with the opiates are toxic reactions and medical problems.

6.2.1. Panic Reactions (See Section 1.6.1)

As is true of all the sedating drugs of misuse, individuals tend to be slowed down rather than panicked. Thus, panic reactions rarely, if ever, occur.

6.2.2. Flashbacks

The relatively short half-life of most of these drugs and the rapid disappearance of the drug and the active metabolites make a flashback a rare phenomenon.

6.2.3. Toxic Reactions (See Sections 2.2.3 and 14.4)

6.2.3.1. Clinical Picture

6.2.3.1.1. History

The opiate overdose is usually an acute, life-threatening event. The patient is likely to be found in a semicomatose condition with evidence of a recent IV injection (e.g., a needle in the arm or nearby) or empty bottles. The picture includes both pharmacological effects of the drug and a response to behavioral factors.[31] In support of the contribution of behavioral forces is the observation of increased toxic-reaction mortality in animals given the drug in an environment unassociated with prior drug use when compared with those challenged in the presence of stimuli associated with sublethal drug doses in the past.

6.2.3.1.2. Physical Signs and Symptoms

The physical condition dominates the clinical picture. The specific symptomatology depends on the drug, how long ago it was taken, and the patient's general condition. The range of symptomatology can include:

1. Decreased respirations.[32]
2. Blue lips and pale or blue body.
3. Pinpoint pupils (unless there is brain damage, in which case the pupils may be dilated).
4. Nasal mucosa hyperemia (for a patient snorting a drug).
5. Recent needle marks or perhaps a needle still in the arm.[32,33]
6. Pulmonary edema characterized by gasping, rattling respirations of unknown etiology (not related to heart failure), and a state of shock.[25]
7. Cardiac arrhythmias and/or convulsions, especially seen with codeine, propoxyphene (Darvon), or meperidine (Demerol).[33]
8. Death appears to occur from a combination of respiratory depression and pulmonary and/or cerebral edema.[6] The pulmonary edema may be related to an idiosyncratic reaction to the opiate or may be an allergic response to either the drug or one of the adulterants (such as quinine) in the injected substances. There is no evidence that it is related to either a fluid overload or heart failure.[34] An alternate hypothesized mechanism is the possible development of cardiac arrhythmias, perhaps related to histamine release.

6.2.3.1.3. Psychological State

The patient is usually markedly lethargic or comatose.

6.2.3.1.4. Relevant Laboratory Tests (See Section 2.2.3.1.4)

It is necessary to rule out all other causes of coma, such as head trauma (with a physical exam, a neurological exam, skull X rays, and so on) and glucose or electrolyte abnormalities (as shown in Table 1.5). The level of cardiac functioning must be established with an EKG and the level of brain impairment with an EEG, if appropriate. A toxicologic screen may be helpful.

6.2.3.2. Treatment (See Section 2.2.3.2)

It has been suggested that the medical needs of the overdosed opiate abuser can be divided into emergency, acute, and subacute stages.[33,35] As outlined in Table 6.2, the general support given first addresses problems expected in any medical emergency. The levels of care listed here are not in a rigid order.

1. Establish an adequate *airway; intubate* and place on a *respirator* if necessary, using compressed air at a rate of 10–12 breaths per minute unless pulmonary edema is present.
2. Be sure the *heart* is beating; carry out external cardiac massage, defibrillate, or administer intracardiac adrenaline if needed; also, give 50 ml of sodium bicarbonate by IV drip for serious cardiac depression.
3. Prevent *aspiration* either by positioning the patient on his side or by using a tracheal tube with an inflatable cuff.
4. Begin an IV (large-gauge needle), being prepared to replace all

Table 6.2
Opiate Overdose: Symptoms and Treatment

Symptoms
Unconscious and difficult to arouse.
Blue lips and body.
Small pupils.
Needle marks.
Pulmonary and/or cerebral edema.
Hypothermia.
Decreased respiration.
Treatment
Clear airway.
Artificial respiration.
Treat hypotension with expanders or pressors.
Treat arrhythmias.
Positive-pressure oxygen.
Naloxone 0.4 mg (1 ml) IV; repeat Q 2–3 hr as needed.
Monitor 24+ hr.

fluids lost to urine plus 20 ml per hour for insensible loss if the coma persists.

5. Deal with *blood loss* or hypotension with plasma expanders or pressor drugs as needed.
6. Treat *pulmonary edema* with positive-pressure oxygen, but beware of giving too much oxygen and thus decreasing the respiratory drive.
7. Treat *cardiac arrhythmias* with the appropriate drug.
8. Administer a *narcotic antagonist:*
   a. *Naloxone* (Narcan) is the preferred drug, given in doses of 0.4 mg (1 ml) or 0.01 mg/kg IV and repeated in 3–10 minutes if no reaction occurs. Because this drug wears off in 2–3 hours, it is important to monitor the individual for at least 24 hours for heroin and 72 hours for methadone. Be prepared to deal with a narcotic abstinence syndrome, should you precipitate one with the narcotic antagonist (see Section 6.2.6.2).
   b. If naloxone is not available, use *nalorphine* (Nalline), 3–5 mg IV (1 cc = 5 mg), repeated as necessary.
   c. If neither of these drugs is available, use *levallorphan* (Lorfan), giving 1 mg (1 cc) IV,[35] repeating the dose in 10–20 minutes, if needed.
9. Draw arterial *blood gases* if there are respiratory problems.
10. Draw bloods for baseline *laboratory tests,* including CBC and the usual blood panel series, as well as a toxicologic screen (10 ml). If *hypoglycemia* is involved, administer 50 cc of 50% glucose IV.
11. Establish *vital signs* every 5 minutes for 4 hours, with continued careful monitoring for 24–72 hours.
12. The more *subacute* and *chronic care* involves careful patient monitoring, dealing with *withdrawal signs,* treating *infections* (over one-half of individuals with pulmonary edema go on to develop pneumonia, but prophylactic antibiotics are not justified). You should continue to monitor vital signs and laboratory tests, and it is suggested that *tetanus* immunization be given.
13. It is very important in treating the overdose to beware of the possibility of *mixed drug ingestion.* This may require special measures, including the possible need for dialysis (see Section 14.4.3.2).

6.2.4. Psychosis and Depression (See Section 1.6.4)

Unlike most other drugs, the opiates are not known to produce any type of temporary psychosis.[36,37] The major psychiatric symptom likely to be noted in opiate abusers is sadness, similar to that reported for alcohol. Thus, at the time of entrance into treatment, between one-third and two-

thirds of opiate addicts are likely to demonstrate significant elevations on cross-sectional depression measures, such as the D scale of the Minnesota Multiphasic Personality Inventory, the Zung, or the Beck.[27,38] Perhaps as high as 20% may meet the criteria for major depressive disorders at intake, but these figures decrease to 10% showing major depressions and 33% minor depression at three to six month follow-ups, with only 2% of the sample demonstrating significant depression at both points.[27,38] Thus, it appears that the depression associated with opiate misuse may be pharmacologically and/or situationally induced and that it tends to disappear within a relatively short period of time without active antidepressant treatment.[39] Such pictures are perhaps twice as likely to be seen in female than male addicts at treatment intake, but follow-ups show no differences between the sexes.[27] It should be remembered, however, that if depressions persist more than 10 days to two weeks and still meet the criteria for major affective episodes, a judicious use of antidepressants should be considered (see Section 3.1.2.3 on alcohol-related depressions).[38]

6.2.5. Organic Brain Syndrome (See Section 1.6.5)

This is unusual with opiates except as part of an obvious toxic overdose.

6.2.6. Opiate Withdrawal in the Adult (See Sections 2.2.6 and 4.2.6)

The opiate withdrawal syndrome, seen for all of the analgesics discussed in this chapter including propoxyphene (Darvon), was, along with alcohol withdrawal, one of the first well-described abstinence pictures. A somewhat arbitrary distinction between phases of withdrawal is outlined in Table 6.3. However, it is important to note that these phases overlap greatly.

6.2.6.1. The Clinical Picture

6.2.6.1.1. Acute Withdrawal

1. *History.* The onset of withdrawal usually begins at the time of the next scheduled drug dose, ranging from four to six hours for heroin to a day or more for methadone. The accurate diagnosis may be fairly obvious when the patient demonstrates the physical signs and symptoms as well as the psychological state described below and requests opiates, but frequently the clinician must have an index of suspicion and probe for potential "street" or medical abuse.

The most usual withdrawal syndrome of the "street" abuser is a relatively benign mixture of emotional, behavioral, and physical symptoms.[40] This is due to the variability in the potency of heroin obtained on the street, ranging from 0% to 77% (with most around 3%). Adulterants,

Table 6.3
Acute Opiate Withdrawal (Heroin)[8]

Marked drive for the drug	Begins in hours, peaks in 36–72 hours.
Tearing Running nose Yawn Sweat	Begins 8–12 hours, peaks in 48–72 hours.
Restless sleep	Begins 12–14 hours, peaks in 48–72 hours.
Dilated pupils Anorexia Gooseflesh Irritability Tremor	Begins 12 hours, peaks in 48–72 hours.
Insomnia Violent yawn Weakness GI upset Chills Flushing Muscle spasm Ejaculation Abdominal pain	At peak.

such as lidocaine, procaine, quinine, and lactose, make up most of the substances sold as street opiates.[41]

2. *Physical signs and symptoms.* Although much variability can be expected, it is possible to make the following generalizations for heroin:

a. Within 12 hours of the last dose, there is usually the beginning of *physical discomfort,* characterized by tearing of the eyes, a runny nose, sweating, and yawning.
b. Within 12–14 hours, and peaking on the second or third day, the patient moves into a *restless sleep* (a "yen").
c. Over the same time period, other symptoms begin to appear, including *dilated pupils, loss of appetite, gooseflesh* (hence, the term, *cold turkey*), *back pain,* and a *tremor.*
d. This picture gives way to *insomnia;* incessant *yawning; a flulike* syndrome consisting of weakness, GI upset, chills, and flushing; *muscle spasm; ejaculation;* and *abdominal pain.*
e. In the acute phases of withdrawal, the syndrome *decreases* in intensity and is usually greatly reduced by the fifth day, disappearing in one week to 10 days.

3. *Psychological state.* This is as important as the physical problems and includes a strong *"craving"* along with emotional *irritability.*

4. *Relevant laboratory tests.* As the patient's degree of physical impairment tends to be less severe than that noted for the CNS depressants, it is usually enough to carry out a good physical exam and to establish the baseline laboratory functions described in Table 1.5. A toxicologic screen may be helpful in establishing the recent use of opiates and analgesics.

6.2.6.1.2. Protracted Abstinence

The acute abstinence phase is followed by a more protracted abstinence, with two probable subphases.[5,8]

1. The early phase of protracted abstinence lasts from approximately *Week 4 to Week 10* or longer and consists of a mild increase in blood pressure, temperature, respirations, and pupillary diameter.

2. This is followed by a later phase lasting 30 *weeks or more,* consisting of a mild decrease in all of the above measures and a decrease in the respiratory center response to carbon dioxide. It is possible to see differences in autonomic nervous system responses to opiates as long as one year after acute withdrawal is complete.[42]

Thus, what we recognize most clearly as withdrawal is only the acute phase. The protracted abstinence, consisting of physiological as well as behaviorally mediated aspects, goes on for many months. It is possible that this long-term syndrome produces a vague discomfort that may play an important role in driving the addict back to drug use.

6.2.6.2. Treatment (Review Section 2.2.6.2, as well)

Treatment of the opiate withdrawal syndrome in adults is briefly outlined in Table 6.4 and in references 5, 8, 41, and 43. Helping the patient

Table 6.4
Treatment of Opiate Withdrawal

General support
Physical and laboratory exam.
Rest.
Nutrition.
Reassurance.
Honest appraisal of what is to be expected.
Keep one doctor in charge.
One type of specific treatment
E.g., methadone $\leq$ 15–20 mg orally as a test.
Determine dose on Day 1 or 2.
Give dose BID.
Decrease by 20%/day or over 2 weeks.

to achieve relative comfort during this period may be associated with a higher rate of retention of patients in rehabilitation.[44]

1. The first phase of therapy involves a good medical examination, as these patients have high rates of medical disorders as discussed below.
2. The physician must do all he can to develop a positive physician–patient contact to maximize patient comfort and cooperation. It is important that one physician be in charge.
3. After estimating the probable degree of dependence and thereby deciding whether active treatment of withdrawal is needed, it is important to explain carefully to the patient the symptoms he can expect and the fact that these cannot be totally eliminated. However, he should be reassured that you will do everything you can to minimize his discomfort.
4. You should establish a flow sheet of symptom severity and the treatments.[41]
5. The treatment of the physical withdrawal symptoms begins with the readministration of an opiate to the point where symptoms are greatly reduced, after which the drug dose is slowly decreased over a period of 5–14 days. Most states have rather severe restrictions on the prescription of opiates to addicts. Unless the physician or clinic possesses a special license for opiate prescription, treatment is usually limited to 72 hours, and then only in case of a medical emergency.[45] Even if a permit is granted, detoxification is usually limited to a month or less. Therefore, although I will first outline detoxification using opiates (the most "physiological" way to treat the syndrome), I will then discuss other alternatives.
   a. Any opiate can be used, but most authors recommend oral methadone.
      i. Give a test dose of 20–50 mg of methadone orally and repeat the dose if the symptoms are not alleviated, thus determining the minimum dose needed to control symptoms during the first 24–36 hours. Note that 1 mg of methadone roughly equals 2 mg of heroin or 20 mg of meperidine (Demerol).
      ii. Most addicts achieve some comfort at doses of 20 mg of methadone the first day. The necessary drug is then divided into twice-daily doses, with daily decreases of 10%–20% of the first day's dose, depending on the development of symptomatology.
   b. An alternate approach is to administer 10 mg of methadone IM and observe the effects, reexamining the patient in eight hours and monitoring the amount of drug necessary to abolish the

symptoms.[41] This procedure makes it possible to determine the amount of drug needed to control the symptoms in the first 24 hours, after which the doses can be given orally two to three times a day and can be decreased as described above.

c. It is possible to administer any opiate, establishing the necessary first-day dose and decreasing the drug by 10%–20% per day. One example is propoxyphene (Darvon) treatment, where an initial detoxification dose of 600–800 mg per day has been used in a 21-day withdrawal program.[46] Propoxyphene hydrochloride can be administered in doses of 110–220 mg by mouth given three or even four times a day whereas the napsylate may need to be given in slightly higher doses of 165–330 mg by mouth three times a day; 600 mg of the hydrochloride a day are roughly equivalent to 20–25 mg per day of morphine subcutaneously or 10 mg per day of oral methadone.[47]

d. A special case occurs when an individual has been taking part in a methadone maintenance program. Under these circumstances, it is advisable to decrease the drug slowly to minimize the chance of the development of symptoms. This usually means a diminution of approximately 3 mg from the daily dose each week, but even at this rate, some symptoms will be seen.

6. Recognizing the need to develop nonopiate approaches to both outpatient and inpatient detoxification, Tennant and Uelmen described a "cocktail" of medications, giving the usual dose administered on Day 1 in an attempt to decrease the symptoms (but not to abolish them) and then decreasing the dose to zero over the next 10–14 days. This regimen includes carisoprodol (Soma) 300 mg QID for muscle pain and tension as needed; prochlorperazine (Compazine) 10 mg QID by mouth for nausea as needed; and a relatively mild opiate that is legal for such use in many states, pentazocine (Talwin), 50 to 100 mg every four to six hours by mouth for pain.[45]

Another symptom-oriented nonopiate approach to withdrawal utilizes clonidine (Catapres). This drug decreases sympathetic nervous system overactivity during withdrawal by blocking alpha-2 receptors, especially in the locus ceruleus area of the brain and perhaps in spinal sympathetic neurons.[48,49] When the drug is given in doses of approximately 5 μg per kg (the average adult patient receiving approximately 0.3 mg four times a day), most patients undergoing opiate withdrawal report a decrease in autonomic nervous system dysfunction.[50,51] However, clonidine is inferior to opiates in the relief of subjective discomfort and pain, and it produces high levels of sedation and hypotension and thus is often not well tolerated by patients.[52] In the final analysis, this mode of treatment

may be inferior to the use of opiates in relieving most withdrawal symptoms.

Additional treatments of potential interest are the use of acupuncture, hypnosis, or any other mechanism for possibly increasing the body's own opiates, the endorphins and enkephalins.[53] However, few if any controlled data on the use of these approaches to treating opiate withdrawal are available.

7. During detoxification, it is very important that some thought be given to plans for rehabilitation. It should be recognized that many patients enter detoxification solely to decrease their high drug levels or in response to immediate life problems. Under such circumstances, the individual may not want to participate in a rehabilitation program—only 10% of those who complete a detoxification program seek long-term care.[54] However, for those who might consider rehabilitation, the detoxification period is an excellent time to introduce the need for permanent abstinence, and counseling should be offered to *everyone.*

6.2.7. Opiate Withdrawal in the Neonate

A special case of opiate withdrawal is seen in the newborn, passively addicted by the mother's drug misuse during the latter part of pregnancy.[5,8] This addiction might develop in the children of 50%–90% of heroin-dependent mothers and carries a mortality of between 3% and 30%. However, when more accurate instruments are used to measure the level of symptomatology, it may be that as few as 25% of the infants of methadone-maintenance mothers may require active treatment, and this for usually less than two weeks. Therefore, the reader is advised to carefully evaluate the levels of symptoms before actively beginning treatment.[55]

6.2.7.1. The Clinical Picture

The syndrome consists of *irritability, crying,* a *tremor* (seen in 80%), increased *reflexes,* increased *respiratory* rate, *diarrhea, hyperactivity* (seen in 60%), *vomiting* (seen in 40%), and *sneezing/yawning/hiccuping* (seen in 30%).[56] The child usually has a *low birth weight* but may be otherwise unremarkable until the second day, when the symptoms usually begin.

6.2.7.2. Treatment

1. A first step should be prevention. For those pregnant addicts on methadone maintenance, it is important that the drug be reduced to 20 mg a day or less during the last six weeks of pregnancy.[57]
2. Of course, symptoms may indicate other disorders as well, and the

clinician must carefully rule out hypoglycemia, hypocalcemia, infections including those of the CNS, CNS trauma, or anoxia and must aggressively treat any such syndromes uncovered.[55]

3. Treatment of neonatal withdrawal consists of general support and observation, including keeping the child in a warm, quiet environment and observing electrolytes, glucose, etc.
4. In addition, the child with moderate to severe symptoms should be treated with any one of the following: *paregoric,* 2–4 drops per kg; *or methadone,* 0.1–0.5 mg per kg; *or phenobarbital,* 8 mg per kg; *or Valium,* 1–2 mg every 8 hours.[6,58] Medications should be given for 10–20 days, the amounts being decreased toward the end of that period.
5. Following all of the caveats mentioned above, the clinician may also consider attempting to control the symptoms with clonidine. In this approach, the infant may be given a test dose of 0.5–1.0 μg per kg, which, if tolerated well and producing a reduction in symptoms, can be followed 24 hours later with 3 μ g per kg per day by mouth divided into six hourly doses and continued over 10–16 days in decreasing amounts.[56]
6. It is also possible to treat, at least primarily, the addicted infants of mothers on methadone maintenance by having them breast-feed while they continue to take their methadone. Additional drugs can be given to the child as needed.

6.2.8. Medical Problems

Opiate abusers, especially those taking street drugs, frequently present for care in some sort of medical crisis.[59] This may be an overdose or other serious medical problem as a consequence of the adulterants in opiate mixtures or the poor hygienic practices involved in the use of needles. A variety of texts have covered the medical problems and their treatment in detail.[41,59] These will be mentioned only briefly here. My goal is to increase your level of awareness of the problems so that you can then use the proper medical procedures.

Some of the more common problems include:

1. Abscesses and other infections of the skin and muscle
2. Tetanus or malaria
3. Hepatitis and other liver abnormalities
4. Gastric ulcers
5. Heart arrhythmias
6. Endocarditis
7. Anemias
8. Electrolyte abnormalities, especially hyperkalemia

9. Bone and joint infections
10. Eye-ground abnormalities, as they reflect emboli from the adulterant added to the street drug[59]
11. Kidney failure secondary to infections or adulterants
12. Muscle destruction
13. Pneumonia
14. Lung abscesses
15. Tuberculosis

In addition, addicts may present with a series of emotional and social problems, including:

16. Depression, frequently seen during methadone maintenance as described above[60]
17. Sexual functioning abnormalities, which may partially reflect the transiently low testosterone level seen during chronic administration and lasting at least a month after the opiate is stopped[61]
18. Police problems
19. Social and interpersonal problems

These problems point out the absolute necessity for a careful evaluation of medical and emotional problems in *any* opiate abuser undergoing treatment.

6.3. REHABILITATION

After identification and acute treatment of the opiate abuser, all such individuals should be advised of the need for rehabilitation to try to help them achieve abstinence. Such rehabilitation is usually done through methadone-maintenance clinics, drug-free residential programs, or a variety of outpatient approaches. In keeping with my emphasis on acute drug problems, rehabilitation is discussed in a separate section (see Chapter 15).

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CHAPTER 7

Cannabinols

7.1. INTRODUCTION

Marijuana is second only to alcohol as the most widely used of the drugs described in this text. The health care problems involved with delta-9-tetrahydrocannabinol, or THC (the most active ingredient in marijuana and hashish), include panic reactions, toxic reactions, and a great deal of anxiety in the general population about possible mental and physiological damage to young users. Because, as health care deliverers, you will be called on to give information about this drug to worried parents and to teenagers attempting to make decisions about future use, this chapter presents information on the history, the physiology, and the medical effects of the cannabinols.

THC is an ancient drug; its use dates back to at least 2700 B.C.[1,2] It has been used in many cultures, including the Middle East, the Orient, and Western countries, where it has had a variety of names, ranging from hashish to charas, bhang, ganja, dogga, and so on. In North America, THC is obtained as marijuana or hashish. (Pure THC is not available "on the streets," and samples so labeled are usually LSD or PCP—see Chapters 8 and 9.) At low to moderate doses, THC produces fewer physiological and psychological alterations than do most other classes of drugs, including alcohol. However, the fact that this drug does affect the nervous system, and that the peak age of use occurs in late adolescence when the brain is still developing, makes the substance a legitimate concern.

Diagnosing the misuse or abuse of marijuana poses many of the same problems seen with alcohol. Although, in contrast to alcohol, marijuana is illegal, its acceptance by the general population and the high prevalence of users make it important to differentiate among use, misuse (implying temporary problems that may disappear), and abuse (implying a high potential for future problems).

Using that approach, no one has developed objectively stated criteria for cannabinol abuse that have been tested through follow-ups to

demonstrate that they predict pervasive and persistent future difficulties. One exception may be a five-year follow-up of a moderate size sample reported by Weller and Halikas[1] using criteria for cannabinol abuse based on the presence of problems in at least three out of four areas. Potential difficulties include (1) adverse physical and psychological reactions to the drug (e.g., health problems and signs of physical addiction); (2) problems with control of use (e.g., using the drug in the morning and going on binges of heavy use for days); (3) social or interpersonal problems (e.g., arrests, traffic accidents, and fights); or (4) the opinion of the patient or significant others that use has been too high. The authors found a correlation between the diagnosis of abuse and the frequency of use, the level of initial intake, early age of onset, and future drug problems.

7.1.1. Pharmacology

THC comes from the marijuana plant, *Cannabis sativa*, which grows readily in warm climates; the percentage of active THC produced parallels the amount of sunlight received by the plant. Marijuana, the less potent source of THC, is the dried plant leaves, and hashish and other more potent sources of the drug are the resins of the plant flowers.

7.1.1.1. General Characteristics

Although this drug is sometimes called a hallucinogen, at the doses most frequently taken the predominant effects are euphoria and a change in the level of consciousness without frank hallucinations. The drug can be ingested through smoking, eating, and (rarely) intravenous injection. The average cigarette contains 2.5–5.0 mg of the most active THC, delta-9-THC; however, only one-half of the drug is absorbed through this route of administration.[2] The potency of a cigarette depends on the quality of the marijuana used (whether from the stems, leaves, or flowering tops, in increasing order of potency) and the amount of time elapsed since the plant was harvested (there is a decrease in potency over time[3]).

When it is smoked, the peak plasma level is reached within 10–30 minutes, with intoxication usually lasting between two and eight hours, depending on the dose.[4] When the plant is eaten, a greater percentage of the drug is absorbed, and the result is a longer (but less predictable) "high." Here, the onset is seen in one-half to one hour, a peak blood level is reached in two to three hours, and the effects last up to eight hours.

Other forms of cannabinols and related substances have been manufactured and tested for their psychopharmacological properties. Each has been developed for oral administration. The drugs include nabilone, a synthetic analogue with modest antiemetic properties, sedative side effects, but few euphorogenic attributes.[5,6]

There is no readily available manner of measuring THC levels in the blood. Once ingested, the drug tends to disappear from the plasma rapidly, becoming absorbed in tissues, especially those with high levels of fat, such as brain and testes.[2] The half-life is believed to be seven days,[7] primarily a result of THC in tissues, and active ingredients are found for as long as eight or more days.[8] The drug is first metabolized to an 11-hydroxylated derivative with some psychoactivity; however, the remaining metabolites do not change levels of consciousness. THC is excreted primarily as metabolites, mostly in the feces, but also in the urine.[8] Although the mechanism of action of THC is not well understood, there is some evidence of disruption of cellular metabolism and prevention of the proper formation of proteins, including DNA and RNA.[7]

7.1.1.2. Predominant Effects

The greatest effects of THC are on the brain, the heart or cardiovascular system, and the lungs. Most, if not all, changes occur acutely and appear to be reversible.

The changes in mood seen with THC depend not only on the amount of drug but also on the setting in which the substance is taken and, as with any more "mild" drug, what one expects to happen.[9] In addition to euphoria, the individual usually experiences a feeling of relaxation, sleepiness, and heightened sexual arousal; is unable to keep accurate track of time; experiences hunger; and exhibits decreased social interaction. The user develops problems with short-term memory and may demonstrate an impairment in the ability to carry out multiple-step tasks.[2,10] Intoxication may be associated with mild levels of suspiciousness or paranoia along with some loss of insight.[11] If intoxication occurs during a state of high stress, a heightened level of aggressiveness may occur; however, most frequently, one sees a decrease in this attribute.[10] At higher doses, frank hallucinations may occur, usually visual, sometimes accompanied by paranoid delusions. Like any toxic reaction, this can be associated with confusion, disorientation, and panic, as described in Section 7.2.

A variety of physiological problems accompany moderate intoxication. These include fine shakes or tremors, a slight decrease in body temperature, a decrease in muscle strength and balance, a decreased level of motor coordination, dry mouth, and bloodshot eyes (injected conjunctivae).[2,10,12] Some individuals experience nausea, headache, nystagmus, and mildly lowered blood pressure.[10,13] THC may also precipitate seizures in epileptics.[14]

Along with an increased breathing rate, the respiratory effects of an acute administration of THC include increased diameters of bronchial tubes, of potential significance in treating asthma.[10,14] However, chronic

use results in a decreased rather than an increased diameter and a worsening of breathing problems.[7,15]

Marijuana affects the heart by increasing the heart rate, resulting in an increased cardiac work load. Thus, this drug can be dangerous for individuals with preexisting cardiac disease.[16]

7.1.1.3. Tolerance and Dependence

7.1.1.3.1. Tolerance

Neither tolerance nor physical dependence is a major clinical problem with marijuana. Toleration of increasing doses of the drug does develop through both metabolic and pharmacodynamic mechanisms, but the most important aspect is the mild level of cross-tolerance to alcohol that has been demonstrated.[2,17,18]

7.1.1.3.2. Dependence

There is some debate about whether there is an actual withdrawal syndrome from marijuana. If it does occur, the strength probably parallels the amount of and length of exposure to the drug and consists of nausea, lowered appetite, mild anxiety, and insomnia.[17,19] It is possible, however, that with higher doses a syndrome resembling mild opiate withdrawal may be noted.[19]

7.1.2. Epidemiology and Pattern of Abuse

The usual distinction made in this text between medical use and "street" use is not as relevant to marijuana as it is to many other drugs. Although some medical use of this drug is being evaluated, all but an infinitesimal amount of use of THC-containing substances takes place illegally.

Marijuana is used as a "recreational drug" at all strata of society, reaching into all job levels and ages, although the predominant use is among younger people. It has been tried on at least one occasion by 50 million Americans, an increase of nearly 100% since 1971.[17,20] In fact, during the last decade, the use of most substances has tended to level off or even decrease (with the exception of PCP and a few other drugs), whereas the prevalence of marijuana intake has steadily increased.[20–22] During the same time period, daily use has fluctuated: one survey has reported that 6% of the general population in 1975 used the drug daily, 11% in 1978, and similar figures for 1980, with a possible decrease back to approximately 7% in 1981.[22]

The average user is in the 18- to 25-year age range. In this category, 60% of college students (approximately 65% of men and 55% of women) have reported recent marijuana intake. Among this age group, approx-

imately a third reported using the drug less than once a week, 10% once or twice per week, and 14% two times per week or more.[21]

The use of these drugs usually begins early. Once started, the usual pattern is smoking several times a week to several times a month. Those individuals most likely to use marijuana frequently tend to demonstrate other life problems, including delinquency and polydrug misuse, and they are less likely to be closely affiliated with a religion.[17,22,23]

7.1.3. Medical Uses

The purported medicinal properties of THC resulted in wide general use until legislation limiting its availability was introduced shortly after the turn of the century.[2] The drug was listed in the *Pharmacopeia* until the 1930s as having antibacterial activity, decreasing intraocular pressure, decreasing the perception of pain, helping in the treatment of asthma, containing anticonvulsant properties (although recent evidence disputes this[14]), increasing appetite, and helping with general morale.[2,15] Currently, THC is being used experimentally for glaucoma, which has been otherwise resistant to therapy, and for terminal cancer.

Recent interest in the medicinal properties of these drugs has resulted in their being tested as antianxiety agents, antidepressants, analgesics, and antitumor substances; the results have been basically negative.[15,22] However, their ability to lower intraocular pressure in glaucoma has been substantiated by controlled research, and they may be of at least temporary help in treating acute asthma attacks.[5,15,22,24] Their greatest therapeutic usefulness has been in controlling the severe nausea often associated with cancer chemotherapy. The doses change with the specific substance administered, but in one paradigm, delta-9-THC was given at 10 mg per square meter of body surface every three hours for a total of five doses, to help with nausea.[24] Although the long-term use of some of the synthetic cannabinols, such as nabilone, may be toxic,[5] most (although not all) researchers do report that this drug is of benefit during chemotherapy.[5,24]

7.1.4. Establishing the Diagnosis

Recognizing whether psychiatric and medical problems are associated with marijuana and hashish use requires knowledge of the drug and an adequate history. Although THC is thought to exacerbate depression and to intensify any preexisting psychosis,[25] there are no known pathognomonic physical signs and no available laboratory tests to help. Again, the key is having a high index of suspicion.

7.2. EMERGENCY PROBLEMS

The vast majority of individuals presenting with marijuana-related

problems show either panic or toxic reactions.[13] These involve high levels of anxiety and/or confusion.

7.2.1. Panic Reaction (See Sections 1.6.1, 5.2.1, 8.2.1, and 14.2)

7.2.1.1. The Clinical Picture

This is a classic drug-induced panic, lasting at most five to eight hours.[4] The clinical picture includes an exaggeration of the usual marijuana effects, which commonly are perceived as threatening by the naive or inexperienced user.[13] The feeling of anxiety, the fear of losing control or going crazy, and the fear of physical illness can be seen in individuals with no preexisting psychopathology as well as in those demonstrating a history of erratic or maladaptive behavior.[26]

7.2.1.2. Treatment

Treatment is predicated on careful diagnosis, ruling out the involvement of other drugs and preexisting psychopathology,[25] and gentle reassurance.

1. A physical examination is necessary to rule out signs of other drugs of intoxication and preexisting medical disorders. It is advisable to draw bloods (10 ml) or collect urine (50 ml) for a toxicologic screen.
2. A quick history should establish the dose taken and the individual's prior experience with the drug.
3. The individual should be reassured that his problems will clear within the next four to eight hours.
4. It helps to place the patient in a quiet room, constantly reassuring him, and allowing friends to help "talk him down."[3,26]
5. The level of intoxication may fluctuate over the next five hours or so, as the active drug is released from the tissues.
6. No specific type of drug should be used to treat every panic reaction. If, however, the anxiety cannot be controlled in any other manner, the drugs of choice would be antianxiety medications, such as chlordiazepoxide (Librium), 10–50 mg orally, which may be repeated in an hour, if needed.
7. Because of the persistence of THC metabolites in the body, patients should be warned that they may experience some mild feelings of drug intoxication over the next two to four days.
8. If the reaction is unusually intense, the patient, as well as the family, should be advised to seek evaluation for the possibility of preexisting psychopathology. Referral to a physician or a health care practitioner experienced with drug problems is best.

7.2.2. Flashbacks (See Sections 1.6.2 and 8.2.2)

7.2.2.1. The Clinical Picture

Flashbacks involve the spontaneous recurrence of feelings and perceptions experienced in the intoxicated state. They are classically seen for marijuana and the hallucinogens,[4] in both frequent and infrequent users.

The clinical picture involves a change in time sense or a feeling of slowed thinking, generally at a lower level of intensity than that experienced when the user is high. Because flashbacks tend to be time-limited (usually lasting only minutes), the major difficulty comes if the individual panics, fearing brain damage. It has also been reported that marijuana may "induce" flashbacks in individuals who have taken hallucinogens in the past.[13] In rare instances, the symptoms may be "chronic" or persistent, but this is so unusual that the presence of additional neurologic or psychiatric disorders should be evaluated.

7.2.2.2. Treatment

The treatment for a flashback is simple reassurance, following all of the steps outlined in the treatment of the panic reaction (as outlined above).

7.2.3. Toxic Reactions (See Section 1.6.3)

7.2.3.1. Clinical Picture

When an individual takes a high level of marijuana, toxic reactions can occur but are usually characterized by an OBS and/or paranoia as discussed in Sections 7.2.4 and 7.2.5. The relatively low potency of marijuana and the lack of availability of more toxic forms, such as ganja, in the United States combine to make this an infrequent problem. Life-threatening overdose is very rare for the cannabinols, even hashish.[19]

7.2.3.2. Treatment

The treatment is identical to that outlined for panic reactions (Section 7.2.1). The approach involves offering good general support and reassurance and allowing the passage of time in a room with no excessive external stimuli. It is best to treat this disorder symptomatically, avoiding the administration of other drugs.

7.2.4. Psychosis and Other Related Symptoms (See Sections 1.6.4 and 8.2.4)

A *temporary* psychotic state, characterized by paranoia and hallucina-

tions without confusion, can be seen with marijuana, but there is no evidence that it results in permanent mental impairment.

7.2.4.1. The Clinical Pictures

The temporary paranoid state accompanied by visual hallucinations is probably a reaction to excessive doses of the drug.[11,27] Retrospective studies indicate bizarre behavior, violence, and panic in some heavy users in India, but this reaction appears to be temporary.[21,28]

If a frankly psychotic state does not clear within hours to days, the patient generally has a prior psychiatric disorder, as marijuana probably worsens prior psychotic problems.[28–31] In addition, I have seen a number of people who had clear evidence of prior depressions or who demonstrated a prior psychotic picture, who complained that their present symptoms were caused by marijuana. In taking a history from the individual and relatives, the preexisting illness became obvious, and in some instances, the history of drug ingestion was a delusion.

Anecdotal reports indicate the development of apathy, decreased self-awareness, impaired social judgment, slow thinking, and a decrease in goal-directed drives in chronic THC users.[2,4,31,32] However, these reports do not address any changes in personality occurring *before* marijuana use, perhaps predisposing users to heavy doses of the drug. An equally acceptable explanation is that individuals who are becoming apathetic and withdrawing from competition and from society in general also find the chronic use of marijuana attractive.[17,22] However, although no cognitive deficits have been objectively demonstrated in chronic users,[10,33] it is possible (although unlikely) that an *amotivational syndrome* exists, in which the person loses interest in tasks and accomplishments.

7.2.4.2. Treatment

It is imperative that a history of prior psychiatric problems be obtained for all individuals presenting with what appears to be a marijuana-induced psychosis.[13] Any underlying prior psychiatric diagnosis (e.g., affective disorder or schizophrenia, as described by Goodwin and Guze[34]) is an important factor to be addressed in treatment.

1. If the individual is out of contact with reality, a short-term hospitalization can keep him out of trouble until the psychosis clears.
2. Understanding and reassurance are the cornerstone of treatment of these disorders. The individual should be told that his problem is temporary, and attempts should be made to help him with reality

testing by, for example, giving him insight into his hallucinations and delusions.

3. Antipsychotic medication can be initiated on a short-term basis if behavior control is absolutely necessary. You might use haloperidol (Haldol) at approximately 5 mg per day in divided doses (rarely up to 20 mg daily) or chlorpromazine (Thorazine) at 25–50 mg IM or 50–150 mg by mouth.
4. Anyone demonstrating a grossly psychotic reaction that lasts more than a day should be carefully evaluated for other major psychiatric disorders. The most frequent will probably be schizophrenia or affective disorder, as described in Goodwin and Guze.[34]

7.2.5. Organic Brain Syndrome (See Section 1.6.5)

7.2.5.1. The Clinical Pictures

1. Temporary clouding of mental processes, consisting of impaired and dull thinking, impaired tracking ability, decreased short-term memory, decreased concentration, and impaired learning can occur with marijuana and hashish. This is really a toxic reaction and clears fairly rapidly.[17,22,35]

2. More startling is a report of cerebral ventricular dilation (which may indicate cerebral hemisphere shrinkage) in 10 heavy drug users whose major drug was marijuana[36]—but attempts to replicate these findings have failed.[3,17,22] To date, no convincing evidence of permanent decreased brain functioning in heavy users of THC substances has been shown.[37,38]

7.2.5.2. Treatment

The temporary type of clinical picture and the relatively mild level of impairment make the center of treatment careful observation and reassurance. Treatment involves the same steps outlined for the panic reaction in Section 7.2.1.2.

7.2.6. Withdrawal

It is not certain whether any form of withdrawal of clinical significance occurs with marijuana and hashish. If symptoms develop, the picture can be expected to be limited and to clear with time alone.

7.2.7. Medical Problems

No drug can be taken into the body with complete safety. The medical disorders associated with the frequent use of marijuana tend to be relatively

mild and transient. However, because of the purely recreational nature of this drug, it is hard to justify its use even if the possibility of serious medical complications is remote. Despite the long history of use of marijuana, it has been only in recent years that serious research has been carried out into the possible medical consequences.

The risk of adverse consequences, of course, increases with increasing amount, frequency of intake, and length of exposure to these drugs. Some of the more important areas of possible damage are presented below, primarily to help you in answering questions from patients and their relatives.

7.2.7.1. Effect on the Lungs[7,10,15]

1. Marijuana and other inhaled compounds are irritating and produce a bronchitis that usually disappears with the discontinuation of drug use.
2. Although the acute administration of marijuana causes dilatation of the bronchial tree, chronic administration is thought to cause constriction, with a resulting asthmalike syndrome.
3. The chronic use of any substance that irritates the lungs can cause a temporary or permanent destruction of lung architecture, and there is evidence of a decreased vital capacity in chronic smokers—even healthy young men.[10]
4. Although it is extremely difficult to document accurately, there is some evidence that heavy marijuana smokers have increased rates of precancerous lung lesions. Marijuana has 50% higher levels of carcinogenic hydrocarbons than tobacco, and animal experiments have corroborated a possible increased rate of cancer after many years of heavy marijuana intake.[15,22]

7.2.7.2. Nose and Throat

A chronic inflammation of the sinuses (sinusitis), as well as pharyngitis, has been reported in heavy smokers of marijuana.[15,22] There is also the possibility (without any good direct evidence) that heavy marijuana smokers have the same increased risk of cancers of the head and neck as heavy tobacco smokers.

7.2.7.3. Cardiovascular System

Marijuana produces an increased heart rate and a decreased strength of heart contractions.[17,22] This reaction is dangerous for heart patients, as there is an associated decrease in oxygen delivery to heart muscle and a decrease in the amount of exercise an individual can tolerate before the onset of heart pain or angina.[16]

7.2.7.4. Immunity

Some research indicates that lymphocytes are sensitive to THC, which decreases their ability to carry out the usual immune responses.[15,22] It has not yet been determined whether this impairment results in a clinically significant increase in infections in marijuana users. A related problem is possible contamination of the drug with pathogens such as salmonella.[39]

7.2.7.5. Reproduction

THC has been demonstrated to impair sperm production in heavy users[7] and has been associated with an increased rate of chromosomal breakage. Chronic marijuana use in humans has also been shown to be associated with a decrease in the size of the prostate and testes in males and to block ovulation in females, although these changes are reversible.[15,22] In mice, chronic exposure to marijuana in the perinatal period decreases the reproductive functioning of adult males.[40] The clinical importance of these findings has not yet been demonstrated, and the purported teratogenic action of the cannabinols has also been questioned.

7.2.7.6. Hormone Levels

Decreased levels of various hormones, including testosterone, have been demonstrated in heavy marijuana smokers,[15,22,27] but these abnormalities appear to be temporary and are usually seen only after three weeks of regular use. It is also possible that growth-hormone production is decreased in heavy marijuana smokers, but the clinical significance of this finding has not been established.

7.2.7.7 The Brain

CNS problems have been briefly discussed in Sections 7.2.3 and 7.2.5. Heavy marijuana smokers may show changes in EEG tracings that may last for three months or more after chronic use, and in animals, some ultrastructural brain changes have been reported.[7,41] THC has also been noted to act on the septal area of the limbic system—an area important in the control of emotions. These findings may have some importance for brain disease, especially in adolescents, with their rapidly growing brains.[15,22]

7.2.7.8. Diabetes

The use of marijuana by diabetics can result in a potentially life-threatening alteration in the body's acid–base metabolism, ketoacidosis.[42]

Thus, THC is not a benign drug, and individuals choosing to use this substance should recognize the potential dangers. On the other hand, in

educating people about THC, it is important to portray the dangers accurately and to avoid scare tactics that might lead the young user to mistrust all information about the drug.

7.2.8. Other Emergency Problems

7.2.8.1. Accidents

One of the greatest known dangers of marijuana is accidents as a consequence of the decreased judgment, the impaired time and distance estimation, and the impaired motor performance that follow use.[15,22] These problems are similar to the effects of alcohol, and it appears that the two substances may potentiate each other.[2,10] Thus, there is impressive evidence that marijuana smoking significantly decreases automobile-driving ability and impairs the faculties necessary to fly airplanes.[43,44] The associated drug problems have been shown to persist for four to eight hours after the feeling of intoxication has disappeared.[18,22] With wider use of this drug, one can expect greater loss of property and lives from driving under the influence of marijuana and related substances.

7.2.8.2. Precipitation of Use of Other Drugs

A brief notation is necessary to deal with public fears that the use of marijuana is the first step on the road to more dangerous drugs, such as heroin. Such exaggerated reports have been prevalent since the 1920s and have done little to establish the credibility of individuals teaching that THC-containing substances have some real dangers.

The data in this area are very complex, as marijuana (as well as tobacco and alcohol) *is* frequently one of the first drugs taken by those who go on to the use of stimulants, depressants, or heroin.[45] There is, however, no convincing evidence that marijuana plays a role in "causing" the use of more potent substances. Rather, it is likely that individuals with characteristics leading them to use drugs like heroin also tend to use marijuana (and alcohol, caffeine, and so on).

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CHAPTER 8

The Hallucinogens and Related Drugs

8.1. INTRODUCTION

Both marijuana and the hallucinogens produce a change in the level of consciousness, and both are capable of inducing hallucinations. However, in the usual doses taken, the predominant effect of cannabis is to alter the "feeling state" without frank hallucinations, whereas the drugs discussed in this chapter produce abnormal sensory inputs of a predominantly visual nature (illusions or hallucinations) even at low doses.

This chapter covers a variety of substances, as shown in Table 8.1. These drugs are structurally similar; many resemble amphetamine; some (e.g., LSD) are synthetic, and others are plant products of cacti (e.g., peyote or mescaline) and fungi (e.g., psilocybin). Hallucinogens have no medical uses in which their assets are known to outweigh their liabilities.[1]

The hallucinogens are by no means new substances. They have been used as part of religious ceremonies and at social gatherings by native Americans for over 2,000 years[2] and are still utilized by some native groups.[3,4]

8.1.1. Pharmacology

All drugs of this class are well absorbed orally, exert effects at relatively low doses, and have adrenergic (e.g., adrenalinelike) properties. Lysergic acid diethylamide (LSD) is the prototype, and the generalizations given for this drug can be assumed to hold for the other drugs as well, unless specifically noted.

The exact mechanism of action of these substances is not known, but much study has centered on their structural similarities to the brain transmitters, especially serotonin.[5–7] The term *psychotomimetic* has also been used, implying a possible relationship between the hallucinogen psychoses and schizophrenia. The visual hallucinations and the strong emotional state seen with these substances, however, do not resemble the

Table 8.1
Some Hallucinogenic Drugs[26]

Indolealkylamines
LSD
Psilocybin
Psilocyn
Dimethyltryptamine (DMT)
Diethyltryptamine (DET)
Phenylethylamines
Mescaline (peyote)
Phenylisopropylamines
2,5-dimethoxy-4-methylamphetamine (DOM or STP)
Related drugs
Phencyclidine (PCP) (See Chapter 9)
Nutmeg
Morning glory seeds
Catnip
Nitrous oxide
Amyl or butyl nitrite

auditory hallucinations accompanied by the flat (or unchanging) affect seen in schizophrenics.[8]

The hallucinogens differ in length of action, with the "high" from LSD lasting as long as 6–12 hours and most others acting for 2–4 hours. The rate of metabolism tends, of course, to parallel the length of action, the half-life for LSD being approximately 3 hours.[9]

8.1.1.1. Predominant Effects

The state induced by these substances (also called *psychedelic drugs*) includes an increased awareness of sensory input; a subjective feeling of enhanced mental activity; a perception of usual environmental stimuli as novel events; altered body images[10]; a turning of thoughts inward; and a decreased ability to tell the difference between oneself and one's surroundings.[9] This group of related drugs tends to produce adrenalinelike or adrenergic effects in addition to hallucinations. Thus, the intoxicated individual usually exhibits dilated pupils, a flushed face, a fine tremor, increased blood pressure, elevations in blood sugar, and an increase in body temperature.[11–13]

8.1.1.2. Tolerance and Dependence

8.1.1.2.1. Tolerance

Toleration of larger and larger doses develops rapidly after as little as three or four days at one dose per day and disappears within four days to a

week after stopping use. Cross-tolerance exists between most of the hallucinogens, including LSD, mescaline, and psilocybin, but this cross-tolerance does not appear to extend to marijuana.[4,13,14]

8.1.1.2.2. Dependence

There is no known clinically significant withdrawal syndrome with the hallucinogens.

8.1.1.3. Specific Drugs

Thus far in this text, most of the drugs described are readily available on the street and are usually the drugs that the seller advertises them to be (a notable exception has been the virtual nonexistence of pure THC). This, however, is *not* the case for the hallucinogens. Studies have demonstrated that, although 87% of LSD samples are pure, as high as 95% of mescaline or peyote units contain either no drug, phencyclidine (PCP—see Chapter 9), or LSD; and similar figures probably exist for the other hallucinogens.[15] In addition, even those samples that actually contain the noted substance usually also contain an adulterant, such as amphetamines.[11–16] Thus, it is *not* safe to assume that one can predict the reaction just by knowing what substance the individual *thinks* he has taken.

Briefly, the more common drugs include:

8.1.1.3.1. LSD

This is a very potent drug that produces frank hallucinations at doses as low as 20–35 μg, with the usual street dose ranging from 50 to 300 μg.[4] At doses as low as 0.5–2.0 μg/kg, the individual experiences dizziness, weakness, and a series of physiological changes that are replaced by euphoria and hallucinations lasting from 4 to 12 hours. The actual "high" depends on the dose, the individual's emotional set, the environment, prior drug experiences, and psychiatric history.

LSD can be purchased as a powder, a solution, a capsule, or a pill. The colorless, tasteless substance is also sold dissolved on sugar cubes or pieces of blotter. Although the drug is usually taken orally, it has been known to be administered subcutaneously (SQ) or intravenously (IV). LSD may be placed on tobacco and smoked, but the intoxication obtained by this method is usually quite mild.[4]

8.1.1.3.2. Mescaline or Peyote

The hard, dried brown buttons of the peyote cactus contain mescaline, the second most widely used hallucinogen.[4] Mescaline effects have a slower onset than those of LSD and are frequently accompanied by unpleasant side

effects, such as nausea and vomiting. The hallucinations usually last 1–2 hours after a usual dose of 300–500 mg.

8.1.1.3.3. Psilocybin

Psilocybin is obtained from mushrooms, many of which grow wild in the United States, and the resulting hallucinations are similar to those noted for LSD and mescaline. It is usually taken by mouth and has a rapid onset: effects are demonstrated within 15 minutes after a 4–8 mg dose. Reactions peak at about 90 minutes and begin to wane at 2–3 hours, but they do not disappear for 5–6 hours. Larger doses tend to produce longer periods of intoxication.[4]

8.1.1.3.4. DOM or STP

This is a synthetic hallucinogen, bearing a structural resemblance to both amphetamine and mescaline and resembling LSD in its effects.[4] The usual dose is 5 or more mg; thus, the drug is between 50 and 100 times less potent than LSD. The onset of effects is usually within 1 hour of ingestion, and peak effects occur at 3–5 hours, disappearing by 7 or 8 hours.[4] The physiological changes are adrenalinelike, paralleling those of LSD. It may be that the effects of this substance are intensified following the administration of chlorpromazine (Thorazine).[4]

8.1.2. Epidemiology and Patterns of Abuse

The hallucinogens were, along with marijuana, the first of the "middle-class" street drugs to cause public concern in the 1960s. Although it is impossible to be certain of the extent of abuse, studies of the street culture, as well as emergency room admissions, indicate a peak prevalence in 1966–1967, with a subsequent leveling off and decline.[4,12] Hallucinogens remain in general use but have been somewhat replaced in popularity by the stimulants and the depressants.

These drugs are probably used on an occasional basis by approximately 20% of the youth population.[17] With the exception of native Americans' utilizing peyote as part of religious ceremonies, the "ritual" use of hallucinogens by various subcultural groups has diminished.

8.2. EMERGENCY PROBLEMS FOR LSD-TYPE DRUGS

The most common hallucinogen-related difficulties seen in emergency rooms are panic reactions, flashbacks, and toxic reactions. In addition, temporary psychoses (actually, probably toxic reactions) and a limited number of medical problems have been noted and need to be discussed.

8.2.1. Panic Reaction (See Sections 1.6.1, 5.2.1, 7.2.1, and 14.2)

8.2.1.1. Clinical Picture

Because these drugs cause both stimulation and hallucinations at relatively low does, it is not surprising that the most common problem connected with hallucinogens seen in emergency room settings is the high level of anxiety and fear that characterize the panic reaction.[9] In the panic state, the individual is highly stimulated, frightened, hallucinating, and usually fearful of losing his mind. This is one example of a "bad trip," the other being the toxic reaction seen in individuals who have taken higher than the usual clinical dosages (see Section 8.2.3).

Panic reactions are usually found only in people with limited prior exposure to hallucinogens. The emotional discomfort tends to last for the length of action of the drug, for example, up to 12 hours for LSD and closer to 2–4 hours for mescaline and peyote.

8.2.1.2. Treatment

1. Therapy is based on reassurance[9] by explaining the process of a panic reaction to the individual and reassuring him that he will totally recover.
2. For added comfort, care should be given if possible in the presence of friends or family members.[18]
3. It is important that a supportive, nonthreatening environment be established where constant verbal contact can be maintained.[19]
4. Hospitalization is not usually needed if a temporary, quiet, safe atmosphere can be arranged.[20]
5. Medications are usually *not* needed. However, if it is impossible to control the patient otherwise, most authors suggest the use of an antianxiety drug such as:
   a. Diazepam (Valium), 10–30 mg orally, repeated in 1–2 hours as needed,[12] or
   b. Chlordiazepoxide (Librium) in doses of 10–50 mg orally, which may be repeated in 1–2 hours.[21]
   c. Do not use chlorpromazine (Thorazine) or any other antipsychotic drug because of the possibility that the hallucinogen might be STP (see Section 8.1.1.3.4) or that the antipsychotics might increase any anticholinergic effects of adulterants in the ingested drug.[19]
6. It is important to obtain a clear history of drug misuse and prior psychiatric disorders and to establish a differential diagnosis, particularly ruling out mania and schizophrenia.[19,22]
7. It is suggested that a follow-up visit be arranged to help the in-

dividual deal with his drug-taking problems and to rule out any major coexisting psychiatric disorder.[19]

8.2.2. Flashbacks (See Sections 1.6.2 and 7.2.2)

8.2.2.1. Clinical Picture

This relatively *benign* condition usually comes to the attention of the health care practitioner because an individual becomes concerned that the recurrence of drug effects represents permanent brain damage.[23] Experiences that have been termed *flashbacks* include simple visual images, lines or tracing of objects, and complex emotional experiences similar but not identical to the prior drug experience.[24] In the midst of such a state, the patient may demonstrate sadness, anxiety, or even paranoia, which may recur periodically for days to weeks after taking the drug.[25] It is thought that this recurrence of hallucinogen effects represents, in part, residual drug metabolites and may be set off by taking a milder drug such as marijuana or by an acute crisis.

The actual incidence of flashback experiences depends on the specific definition used and the study methods invoked. The prevalence of such problems probably increases with the number of times an individual has taken the hallucinogen, but it is probable that somewhere between 15% and 30% of users have at some time had a discrete flashback of some sort.[24]

The person usually notes a feeling of euphoria and detachment, which is frequently associated with visual illusions (actual sensory inputs that are misinterpreted by the individual) lasting several minutes to hours.[12] The hallucinations are usually lights or geometric figures seen out of the corner of the eye, often when entering darkness or just before falling asleep, or a trail of light following a moving object. Only rarely do they interfere with an individual's ability to function. Other types of flashbacks, including isolated feelings of depersonalization or a recurrence of distressing emotional reactions experienced while under the drug effects, can also occur.[12] The incidence of these reactions is not known, but they have been estimated to occur in as many as 5% of users.[12]

8.2.2.2. Treatment

Therapy for the self-limited picture is relatively simple[12]:

1. Care is based on reassurance that the syndrome will gradually decrease in intensity and disappear.
2. The subject should be educated about the course and the probable causes (e.g., residual drug) of the flashback.

3. It is important that all other medications, especially marijuana, antihistamines, and stimulants, be avoided.[11]
4. If medication is needed to relax the individual during the experience (I usually choose to use no medication), use diazepam (Valium) in doses of 10–20 mg orally, repeated at 5-mg doses if the flashback recurs,[12] or comparable oral doses of chlordiazepoxide (e.g., 10–30 mg).
5. As is true in any drug-related disorder, in an emergency situation it is important to consider the possibility that the problem is a reflection of a preexisting psychiatric disorder and not really a flashback. Therefore, a careful *history of prior psychiatric problems and a family history of psychiatric illness* (which may indicate a propensity toward illness for this individual) must be taken.

8.2.3. Toxic Reactions (See Sections 2.2.3, 5.2.3, 6.2.3, and 14.4)

8.2.3.1. The Clinical Picture

8.2.3.1.1. History

The usual toxic reaction consists of the rapid onset (over minutes to hours) of a loss of contact with reality and the physical symptoms described below for an individual taking a hallucinogen. The markedly disturbed behavior usually leads friends or relatives to bring the patient in for care.

8.2.3.1.2. Physical Signs and Symptoms

Although the psychological state dominates the picture for the average patient, abnormalities in the vital signs that are consistent with the state of anxiety and panic are also seen. These include palpitations, increases in blood pressure and temperature, perspiration, and possibly blurred vision. Very high levels of overdose may include exceedingly high body temperatures (greater than 103 °F orally), shock, and convulsions.[25–27]

8.2.3.1.3. Psychological State

This is an exaggeration of the effects of a panic reaction. The individual, frequently an experienced user, has taken a higher than usual dose of the drug, with a resulting high anxiety state along with frank hallucinations and loss of contact with reality.[28] Depersonalization, paranoia, and confusion are often demonstrated.[12] The clinical picture diminishes as the drug is metabolized, but the symptoms tend to wax and wane over the subsequent 8–24 hours.[26]

8.2.3.1.4. Relevant Laboratory Tests

There are no specific laboratory tests to be noted except for the possible use of a toxicologic screen (10 ml of blood or 50 ml of urine). It is important to monitor the vital signs, especially the blood pressure and the body temperature. If signs of organicity are present, it is necessary to rule out ancillary causes, including head trauma and infection.

8.2.3.2. Treatment (See Sections 2.2.3.2, 5.2.3.2, and 6.2.3.2)

1. Although quite rare, the overdose may involve markedly elevated drug levels, and the patient may present with convulsions or hyperthermia. The treatment steps for any life-threatening drug emergency must be carried out.[27] These include:
   a. Careful observation of vital signs
   b. Establishing an airway
   c. Treatment of convulsions with anticonvulsants and a slow injection of diazepam (5–20 mg IV), if needed (see Section 5.2.3.2)
   d. The use of ice baths or a hypothermic blanket
   e. Cardiac monitoring, support of blood pressure by medications, if needed (see Sections 6.2.3.2 and 14.4.3), and so on
2. For the usual patient with relatively stable vital signs, a rapid physical examination, including a neurologic evaluation, should be carried out. The vital signs should be monitored for at least 24 hours.[26]
3. It is important to gain the patient's confidence with an understanding but firm approach. Consistent verbal contact and reality-orienting cues must be given, generally for up to 24 hours.
4. The rapid absorption of most of these drugs would indicate that gastric lavage is of little use and may only serve to frighten the patient.[23]
5. Once again, I prefer to avoid medication, but when necessary, I usually fall back on:
   a. Diazepam (Valium), 15–30 mg orally, repeating 5–20 mg every four hours as needed, *or*
   b. Chlordiazepoxide (Librium), at 10–50 mg orally, followed by up to 25–50 mg every four hours as needed.
   c. *Avoid* chlorpromazine (Thorazine) or any other antipsychotic drug.
6. If the clinical problem does not clear within 24 hours, suspect that the drug ingested was STP (which might last for several days to two weeks) or PCP, as discussed in Chapter 9. Treatment in this situation is very similar to that outlined above; however, the vital signs must be carefully monitored.

8.2.4. Psychosis (See Sections 1.6.4, 5.2.4, and 7.2.4)

8.2.4.1. Clinical Picture

In my experience, hallucinogen-induced psychoses (most often marked by visual hallucinations) clear within hours to days and (for STP) certainly within a matter of weeks. The clinical symptoms can range from paranoid delusions to hallucinations and may even encompass maniclike pictures.[29] As the patient often realizes that the drug caused the symptoms (i.e., he has insight), this picture rarely meets the criteria for a drug induced psychosis given in Section 1.6.4. The literature substantiates that those rare individuals for whom the psychosis does not clear usually have a preexisting psychiatric problem, often mania, schizophrenia, or a psychotic depression.

If a state of psychopathology persists for a month or more, it probably relates to a preexisting psychiatric disorder. The prognosis is not always benign, and perhaps as many as 50% of these individuals have long-term psychiatric difficulties.[16]

The causes of hallucinogen psychoses are difficult to study and are frequently complicated by multiple drug use.[30] As would be expected, the psychotic syndrome has a wide variety of presentations, including depression, panic, uncontrolled hallucinations, and/or intensification of a preexisting paranoid picture.[9,31]

One special area for consideration is a crime committed under the apparent influence of LSD or other hallucinogens. If the criminal act is a well-thought-out, goal-oriented one, and especially if criminal behavior is consistent with the individual's prior experiences and activities, I would tend to discount the role played by LSD in the commission of the crime.[32]

8.2.4.2. Treatment

The actual treatment must depend on the clinical picture.

1. If on reevaluation one finds an intense panic or toxic reaction, the treatment is as described in Sections 8.2.1.2 and 8.2.3.2.
2. In an individual with a preexisting affective disorder, obvious schizophrenia, and so on, emergency treatment for a psychotic reaction resembles that outlined in Section 8.2.3.2, but the most important therapy is aimed at the specific psychiatric disorder.[22]
3. A drug-induced psychosis occurring in an individual without a preexisting psychiatric disorder is treated with reassurance, education, and comfort in a manner similar to that outlined in Sections 8.2.1.2 and 8.2.3.2.[11] Hospitalization may be required if the loss of contact with reality is severe.
4. If the psychosis does not clear within 24 hours and no prior psychiatric disorder is apparent, it is imperative that the individual

be carefully evaluated for any neurologic damage, that a thorough physical examination and laboratory tests be carried out, and that the practitioner recognize the unusual nature of the syndrome. As with any atypical picture, treatment is symptomatic, requiring careful observation, good history-taking, and constant reevaluation for possible underlying pathologic diagnoses. There is no set procedure in this instance, and antipsychotic drugs, if used, should be carefully monitored.

8.2.5. Organic Brain Syndrome (See Section 1.6.5)

8.2.5.1. Clinical Picture

An organic picture can develop in the midst of a toxic reaction or a severe overdose, or it can be part of a drug-induced psychosis. The treatment of these syndromes has been outlined above in Section 8.2.4.2.

A second major concern is that prolonged exposure to these drugs may cause decreased intellectual functioning and even an organic brain syndrome. People chronically taking hallucinogens have been noted to demonstrate a syndrome similar to the purported "amotivational syndrome" already discussed in relation to marijuana in Section 7.2.4. It is extremely difficult to establish a "cause-and-effect" relationship, as persons likely to use these drugs regularly may have tended toward social withdrawal, lack of motivation, and even brain impairment before the drug use was begun. The problem of establishing cause and effect is even more acute when multiple substances are taken.

There is some evidence, however, of a decrease in abstract reasoning in heavy users,[9] but this has not been corroborated in all groups studied.[33] Brain damage should be considered in the evaluation of any chronic abuser of hallucinogens, but the probability of clinically significant impairment is remote.

8.2.5.2. Treatment

The individual suffering possible organic brain damage from continued hallucinogen use should be dealt with symptomatically. The treatment should include a recommendation of abstinence from drugs and all other medications (including alcohol), a reevaluation of the degree of impairment over time, and vocational or educational rehabilitation, if appropriate.

8.2.6. Withdrawal

No clinically significant withdrawal picture is known for the hallucinogens.

8.2.7. Medical Problems

Evaluation of chronic users of hallucinogens has rarely demonstrated unique physiological impairment directly related to the drugs.[34,35] One area of great concern has been the possibility of *chromosomal damage.*[36] Although broken chromosomes have certainly been demonstrated with LSD-type drugs, and birth abnormalities have been seen in the offspring of mothers using hallucinogens (especially LSD in the first trimester), the nature of the relationship has not been established. Many substances (including aspirin) cause chromosomal breakage but have not been demonstrated to have definitely affected the fetus. Nonetheless, these are very potent substances, and there may be a danger of fetal abnormality when they are used by pregnant women.[36–38]

8.3. RELATED DRUGS

It is necessary to discuss separately a series of drugs that produce effects similar to the more common substances but whose structures do not allow for generalizations. The more exotic (and usually less potent) substances that require mention include *nutmeg, morning glory seeds, catnip, nitrous oxide,* and *amyl* or *butyl nitrite.* The active ingredients of most "hallucinogenlike" plants and mushrooms are usually LSD-like or atropinelike substances. The reader is advised to review Section 8.2 of this chapter as well as the anticholinergic syndrome and its treatment as presented in Section 11.9.

8.3.1. Nutmeg

The nutmeg plant can be ground up and either inhaled or ingested in large amounts to produce a change in consciousness.[9] The unpleasant side effects of these substances (including vomiting) limit their use to places where other drugs are not available, such as prisons.[9,39] The oral ingestion of two grated nutmeg pods will produce, after a latency of several hours, a feeling of heaviness in the arms and legs, a feeling of not being oneself (depersonalization), a feeling of unreality (derealization), and apprehension. Along with this reaction come physiological changes such as dry mouth, thirst, increased heart rate, and flushing.[9,39–41]

The specific mechanism of the action of nutmeg is not known, but it is felt that it might inhibit prostaglandin. One of the side effects of chronic use may be constipation.[40]

The usual recovery from signs of intoxication occur within 24–48 hours. No specific treatment for the toxic reaction is needed. None of the other categories of drug misuse problems is known to occur with nutmeg.

8.3.2. Morning Glory Seeds

The seeds of the more common varieties of morning glory flowers contain an LSD-related substance,[42,43] which, if ingested in high enough amounts, can produce a mild hallucinatory state. The usual effect of these substances, known as *heavenly blue* or *pearly gates*, is a change in self-awareness and visual hallucinations, which may be accompanied by paranoia. Taken intravenously, this drug can be very dangerous and has been shown to produce a lethal, shocklike state.[43]

The treatment of any panic, toxic, or potential psychotic reactions would follow that outlined for the hallucinogens, as given in Sections 8.2.1.2, 8.2.3.2, and 8.2.4.2.

8.3.3. Catnip and Locoweed

Catnip is derived from the plant *Nepeta cataria* (a member of the mint family) and has a long history as a folk-medicine prescription for abdominal irregularities.[9] The plant contains a variety of substances, including tannin and atropinelike drugs. It can be obtained in pet stores and has been given to cats to make them appear happy, contented, and somewhat intoxicated. When used by humans, usually smoked, the intoxication can be quite similar to that from marijuana. Visual hallucinations, euphoria, and fairly rapid changes in mood are frequently associated with headaches, but these tend to clear rather quickly. There is no known treatment needed for the panic or toxic state that can be noted with the substance.

An interesting and somewhat related substance is locoweed (*Astragalus* and *Oxytropis*), which is widely distributed in the western United States.[44] This plant is usually associated with accidental ingestion in animals, the result of which is a clinical picture of incoordination, depression, and difficulty in eating, as well as an exaggerated reaction to stress. The active ingredients involved are indolizidine alkaloids that have some characteristics in common with the hallucinogens described in this section.

8.3.4. Nitrous Oxide (N_2O)

This is a relatively weak general anesthetic that is either used as an adjunct to other agents or given on its own by dentists and/or obstetricians.[9,45] Abuse of this inhalant tends to occur among professionals, but one recent case study indicated the abuse of N_2O used as a propellant for canned whipped cream.[46] Use of the drug for a number of months on a daily basis can result in a paranoid psychotic state accompanied by confusion. As would be expected, this clears fairly rapidly when the drug use is stopped.[47]

8.3.5. Amyl or Butyl Nitrite

These potent vasodilators appear to be widely used in homosexual groups in an attempt to postpone and enhance orgasm during sexual intercourse.[48–50] The substance is marketed under a variety of names, including Vaporole, and is sold in "adult bookstores" as rush, kick, belt, and so on. Although medically the drug dilates the blood vessels and has been used in the treatment of angina, it now has limited medical usefulness.[50] It is reported in the street culture that the nitrites cause a slight euphoria and flushing and may slow down time perception, in addition to having subjective effects during intercourse.

In one recent survey, approximately 60% of a series of 150 homosexuals admitted using amyl nitrite, including almost 20% of the total who took the substance once to twice a week or more often. Heavier use was associated with urban residents and, either directly or indirectly, with greater evidence of promiscuity, group sexual practices, and heavy intake of alcohol.[48] Regarding the latter, approximately 48% of the heavier amyl nitrite users versus 23% of light or nonusers reported being drunk at least weekly over the prior year.

Recently, a questionable association between amyl nitrite and Acquired Immune Deficiency Syndrome (AIDS) has been explored. The drug appears to produce a depression of cell-mediated immunity with a resulting possible increased risk for unusual forms of pneumonia and a rare form of cancer, Kaposi's sarcoma.[51,52]

The most common clinical problems of intoxication are a toxic reaction and a panic reaction, which are expected to clear spontaneously with simple reassurance. In addition, the drug can cause nausea, dizziness, and faintness, associated with a drop in blood pressure. Theoretically, it can also change the red blood cell pigment hemoglobin to methemoglobin and result in impairment in the oxygen-carrying capacity of the blood.

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CHAPTER 9

Phencyclidine (PCP)

9.1. INTRODUCTION

In the years intervening between the first and second editions of this text, the use and misuse of PCP has continued to expand. Phencyclidine is now one of the most widely misused drugs in the Western cultures (other than alcohol, tobacco, and caffeine), being taken both deliberately as a drug of intoxication and inadvertently by individuals who believe that they are buying another substance.

This interesting substance was first introduced as a general anesthetic for both humans and animals (Sernyl or Sernylan, Ketamine, Ketalar, Ketaject, and Ketavet). In both instances, it has the benefit of allowing anesthesia (lack of pain) through a dissociative state in which the subject is not in a deep "coma." Thus, it produces relatively little depression of blood pressure, respiration, and other vital signs.[1] However, its use soon became limited in humans after the recognition that approximately 20% of individuals developed agitation and even hallucinations during the immediate postoperative period.[1]

The drug soon became widely misused as an adulterant of other, more expensive street drugs. One of the major attractions on the illegal market is the relative ease of synthesis in the "kitchen" laboratory, with the result that by the mid-1970s a majority of the drugs marketed as more esoteric substances (e.g., tetrahydrocannabinol, or THC) were really PCP.

In its own right, the drug has become widely misused as a "hallucinogen" known on the street by a variety of names, as indicated in Table 9.1. In addition to its wide use as an adulterant or a substitute for other street substances, PCP can be smoked or ingested orally or injected intravenously or sprayed on other drugs, such as marijuana.[2] The most usual routes of administration, however, are smoking and oral ingestion.

Table 9.1
Some Street Names for PCP

Angel dust	Hog	Shermans
Aurora	Jet	Sherms
Busy bee	K	Special L.A. coke
Cheap cocaine	Lovely	Superacid
Cosmos	Mauve	Supercoke
Criptal	Mist	Supergrass
Dummy mist	Mumm dust	Superjoint
Goon	Peace pill	Tranq
Green	Purple	Whack
Guerrilla	Rocket fuel	

9.1.1. Pharmacology

This drug affects the basic brain centers, probably through interference with the synaptic transmission between cells. It has been noted to have indirect dopamine and acetylcholine agonistic properties and to depress nerve cell firing in a number of brain regions, including the locus ceruleus.[1]

PCP is readily absorbed by mouth or intravenously, as well as by smoking or snorting.[1] It is estimated that the average tobacco, marijuana, or parsley cigarette with PCP powder contains 12–25 mg of this substance.[1,3] Metabolism is primarily in the liver. There is no known pharmacological activity for metabolites, and excretion is through hydroxylation and conjugation with glucuronic acid, as only a small amount of the active drug is excreted directly in the urine.[1,2]

This crystalline, water-soluble, and lipophilic substance penetrates easily into fat stores and thus has a long half-life (e.g., half of a fairly large dose may be present three days later).[1] PCP, an arylcycloalkylamine, is moderately attractive as a drug of abuse and will be self-administered by animals whereas other "hallucinogens" will not.[1,3,4]

The drug has relatively complex interactions with a number of different systems. It has been shown to be *sympathomimetic*, increasing CNS catecholamines, with a subsequent rise in blood pressure, heart rate, respiratory rate, and reflexes—the latter probably resulting in muscle rigidity.[5] PCP also has *cholinergic* effects, increasing CNS acetylcholine, with resulting sweating, flushing, drooling, and pupillary constriction. CNS serotonin systems might also be affected, and effects on the cerebellum are fairly prominent, with resulting dizziness, uncoordination, slurred speech, and nystagmus.[1,6,7]

The behavioral toxicity of PCP is dose-related, and the effects range from mild intoxication to lethal overdoses.[1,8] Doses of 1–5 mg produce in-

coordination, a floating feeling of euphoria, and heightened emotionality, along with mild increases in heart rate, sweating, and lacrimation. A dose of 10 mg results in a drunken state, with possible numbness of the extremities and perceptual illusions (misconceptions of sensory inputs).[1,9,10] The toxic effects noted at doses above 10 mg are described in greater detail in Section 9.2.3, but can include signs of psychosis along with moderate to severe physical toxicity.

9.1.2. Epidemiology and Pattern of Abuse

The pattern of *both* deliberate and inadvertent misuse of this substance makes it difficult to determine accurate statistics on its epidemiology. An additional complicating factor is that most PCP users rarely take only one drug.

There is indirect evidence of widespread misuse. The substance appears to be taken by people in all ethnic groups and at all socioeconomic strata, and it may be one of the most commonly used substances available on the "street."[7,11] It is one of the few drugs that has shown little sign of a leveling off or decrease in use during the last decade.[11]

The study of patterns of intake has been advanced by the development of detection techniques that can measure 5 pg per ml in the blood.[12,13] Use patterns increase with age, and it has been estimated that approximately 3% of young people in the 12–17 age range have taken PCP, with 10%–15% or more of those over the age of 18 having used the substance at least one time, often having taken PCP with other substances.[1,10] Because of the high rate of both medical and psychiatric pathology, the rates increase when individuals attending urban emergency rooms are studied, as between one-third and one-half have detectable blood levels of PCP.[3,12] The importance of the blood determinations is demonstrated by the fact that only half of those with positive blood levels admitted use, and only 20% of the population of users had been correctly diagnosed by staff before the blood or urine results were made available.[3,7,12] In one recent study, up to 80% of the acute psychiatric admissions to the central Los Angeles hospital had PCP levels detectable in their blood.[13]

The average user detected in psychiatric facilities has taken the drug for four years.[7] Most ingest the substance as smoke at an average daily cost of approximately $25.[7] The most usual pattern of intake is relatively casual (one ingestion per week), but some individuals report "runs" of over two or three days of continuous intake.[1]

9.2. EMERGENCY SITUATIONS FOR PCP

Knowledge of the pharmacology and the behavioral toxicity of this substance can be used to predict its pattern of problems.

9.2.1. Panic and Violence

9.2.1.1. The Clinical Picture

Any drug with sympathomimetic properties can produce a state of panic. However, most PCP patients presenting in a hyperstimulated state have some level of associated confusion and a decrease in behavioral controls. Thus, an important aspect of a "panic" can be violence.

A history of physical or verbal aggressiveness, often impulsive, bizarre, and unprovoked, is prevalent among chronic PCP users.[14] Clinical observations have indicated a possible progression from anger and irritability to violence as PCP use is continued, and a history of physical acting out has been reported by up to 75% of chronic misusers.[3,8,14]

9.2.1.2. Treatment

The treatment of violence is symptomatic. As is discussed below, physical restraints should be avoided if at all possible, because of fear of muscle damage, but inactivation through holding by personnel may be required. Of course, as is true in all panic-type syndromes, it is best to avoid medication and to attempt to reason with a patient not showing signs of obvious toxicity or psychosis and to use medication only as a last resort. The medications that can be used are discussed in Section 9.2.3.2, Item 10.

9.2.2. Flashbacks

Although not well documented, anecdotal reports indicate that a recurrence of mild drug effects (e.g., feelings of unreality or mild sympathomimetic symptoms) can occur.[15] These are generally not disturbing to the patient and are probably best treated with reassurance, although antianxiety drugs (e.g., chlordiazepoxide, 10–20 mg orally, or diazepam [Valium], 5–10 mg) can be used on a one- or, at most, two-dose schedule.

9.2.3. Toxic Reactions

9.2.3.1. Clinical Picture

PCP has marked medical and psychological effects that vary greatly among individuals, social settings, doses, and whether the patient is being observed on the rising or falling PCP blood levels. There is a narrow range between the amount responsible for the usual "mild" intoxication and the dose causing a life-threatening toxic reaction. Thus, in attempting to understand the clinical picture, it is important that the clinician review all relevant parts of Section 9.2.3.

Medically, the toxic reaction consists of a combination of sympathetic and cholinergic overactivity, and symptoms appear at oral doses as low as 5–10 mg. The intensity of the symptoms varies directly with the clinical

dose, although the lipophilic nature of this drug makes reliance totally on blood or (even worse) urinary levels hazardous, as the active substance may be repeatedly released from fat stores. Longitudinal monitoring of urinary levels appears to be of little direct help.[16]

Although some level of confusion and prominent psychological changes are often noted even with low doses, each of these symptoms intensifies with higher blood levels. Moderate doses (i.e., 10 mg and above) can result in catalepsy, mutism, and even a "light" level of coma with associated stupor. The vital signs and autonomic changes intensify at the higher doses, and anything in excess of 25–50 mg is capable of producing a coma and/or convulsions.[5] At these levels, the blood pressure may be alarmingly high; the increase in deep tendon reflexes (DTRs) can progress to muscle rigidity and thence convulsions; and the changes in heart and respiratory rate can progress to failure in both systems.

Although moderate to severe toxic reactions may develop rather rapidly, the clinical picture is likely to clear less quickly. One can expect a progression of recovery from severe intoxication (e.g., coma) through more moderate intoxication and on to light levels of impairment, with the entire picture taking perhaps two to six weeks to clear. Thus, the coma may progress to a severe organic brain syndrome with or without psychotic symptoms, which then, in turn, slowly disappears. Therefore, a toxic reaction to PCP not only is life-threatening but tends to be the longest-lasting of any drug of abuse.[3,17,18] The combination of a comalike state, open eyes, nystagmus, increased tendon reflexes, decreased brain perception, and temporary periods of excitation should raise suspicion that a PCP toxic state is being observed.[6,15]

9.2.3.2. Treatment

There are no specific antagonists to PCP intoxication.[3] Treatment of the toxic state follows the commonsense rules of offering general support while avoiding the use of other medications unless absolutely necessary. When a second medication is chosen to treat the PCP intoxication, the side effects must be kept in mind, and low doses should be used over as short a period of time as possible. Thus, the treatment is symptomatic, but the clinical picture may take many weeks to clear.

The most important part of treating this "medical emergency" is support of the vital signs. In dealing with patients, it is important to have some general understanding of the treatment of toxic conditions, as outlined in Sections 2.2.3, 4.2.3, 6.2.3, and 14.4. The necessary steps (with the exception of the first several lifesaving procedures) are not given in any rigid order and are to be executed in as quiet an atmosphere as possible.

1. Support vital signs. Respiratory depression should be treated with a respirator if needed (take care to avoid laryngospasm).[3]

2. Serious hypertension may be treated with hydralazine or phentolamine (Regitine)—the latter as an IV drip of 2–5 mg over 5–10 minutes.

3. Serious hyperthermia should be addressed with a hypothermic blanket or ice.[1]

4. Rule out all other possible causes of the obtunded condition and physical impairment. This procedure will require an accurate neurologic evaluation and drawing blood (10 ml) or obtaining a urine sample (50 ml) for a toxicologic screen. A test injection with naloxone (0.25 mg IV, subcutaneously, or IM) may be advisable to rule out the possibility that opiates were involved.

5. When PCP has been taken orally, gastric lavage should be considered, including a rinsing with saline until a clear return is seen. Of course, the precaution of using an inflatable cuff for the tracheal tube should be taken to prevent aspiration in patients who are in coma.

6. Copious salivation may need to be treated with oral suction.[1]

7. As is true in any emergency situation, an IV should be begun with a large-gauge needle, as it may be necessary to replace fluid lost in the urine (along with 20 ml per hour of insensible loss).

8. Acidification of the urine can be helpful. Cranberry juice, vitamin C, and/or ammonium chloride can decrease the half-life of PCP from 72 to 24 hours—if the pH of the urine is kept less than 5.0.[1] Ammonium chloride should be given at doses of 500 mg every three to four hours, and urine acidification may be required for as long as one to two weeks for longer-lasting toxic states.[7]

9. Although some authors have recommended diuresis either through the use of furosemide (Lasix) at doses of 40–120 mg as often as is necessary to maintain 250 ml or more of urinary output per hour *or* through the use of excessive IV fluids, there is little evidence that this treatment actually increases the excretion of PCP.[1,3,5] Thus, it is probably not advisable to use diuresis.[6,15]

10. Control of behavior may be difficult and poses a number of clinical dilemmas, especially in light of the desire to avoid physical restraints. Chemical restraint using phenothiazines has been advised, but these drugs may result in excessive orthostatic hypotension; may increase the risk of seizures; and may enhance the cholinergic imbalance.[19,20] However, this drug has been used in clinical settings, and there are anecdotal reports that toxic reactions that had not responded to other therapies may improve rapidly with neuroleptics.[16,19] The butyrophenones (e.g., haloperidol, or Haldol) may have less effect than phenothiazines on the cholinergic systems but have been reported to be associated with potentially greater muscle damage.[1,3]

Other clinicians have suggested the use of benzodiazepines to decrease the risk of convulsions while helping to keep patients calm, but these run the theoretical risk of slowing down the excretion of PCP (although one

study found no evidence of this[1,3]). In the final analysis, no "perfect" chemical restraint is available, and the clinician might be best advised to use benzodiazepines, keeping the doses as low as possible for the shortest time possible (e.g., diazepam at 5–10 mg every four hours, as needed) while taking care to avoid accumulation of the drug over time.

11. Other drugs have been recommended in the treatment of PCP toxic reactions, but little data are available to back up clinical claims. For instance, control of the heart rate and other signs of sympathetic nervous system overactivity may be approached with propranolol (Inderal) in doses of 20–40 mg by mouth up to three times a day. Anticholinergic problems may also be reversed with physostigmine, 2 mg IM, which may be repeated as needed, as the drug tends to wear off every two hours.[3,19] However, in keeping with the general bias of this text, these medications should be avoided unless absolutely needed.

9.2.4. Psychosis

9.2.4.1. Clinical Picture

The psychotic picture with PCP can occur with moderate intoxication and is rarely seen in the presence of a totally clear sensorium (i.e., a true PCP psychosis in a clear sensorium is rare). Also, hallucinations and/or delusions (usually in a clouded sensorium) are to be expected during the process of improvement from a serious toxic reaction. With PCP, the state may fluctuate, so that many individuals who developed the toxic reaction or OBS will "improve" to the point of demonstrating what appears to be a psychosis alone.[15,21]

The psychotic picture may consist of paranoia and/or manic behavior (for example, grandiosity, hyperactivity, and rapid thoughts and speech).[21,22] The patient may show great emotional changes, including hostility accompanied by violent outbursts as described above for the panic reaction.[6,15] The degree and persistence of the psychosis appears to relate to the amount of the drug ingested, and it can last from 24 hours to one month.[21] In one group of psychiatrically hospitalized PCP abusers, 94% reported histories of feelings of unreality in the past; 75% reported various levels of paranoia; and 62% related a history of hallucinations.[7,12]

9.2.4.2. Treatment

Because the psychosis is part of a continuum with the toxic reaction, the treatment parallels that outlined in Section 9.2.3.2. The best approach is to offer the patient a quiet, sheltered environment where his psychosis is not likely to lead to harm to himself or to those around him (i.e., a closed psychiatric ward). Care should include acidification of the urine as described

above; a sparing use of physical restraints, with a preference for holding the patient rather than using leather or cloth immobilization; and the judicious use of IM or oral antipsychotics or benzodiazepines (e.g., diazepam in doses up to 60 mg or chlordiazepoxide in doses up to 100 mg per day, if needed). Of course, the adequate treatment of any psychotic state requires a careful evaluation to rule out preexisting psychiatric disorders that may require treatment (e.g., manic-depressive disease or schizophrenia).

9.2.5. Organic Brain Syndrome

A state of confusion and/or decreased intellectual functioning is a usual part of the toxic and psychotic reactions. Thus, the reader is referred to Sections 9.2.3 and 9.2.4. The confusion may last for four or more weeks and may be associated with violence.[7,14]

9.2.5.1. Withdrawal

Because of the structure of PCP (i.e., resembling the CNS depressants), there could theoretically be a withdrawal syndrome after chronic administration. However, this has not yet been reported in the literature, and there is no evidence of withdrawal in monkeys who have been maintained on the drug for up to two months.[1] However, a "rebound" can be expected after abrupt discontinuation of any medication (even aspirin), and patients may relate some level of discomfort, although there is no evidence that active treatment is required.

A related problem concerns the high rate of relapse observed in chronic PCP users. This could reflect a chronic abstinence phase similar to that seen with opiates or alcohol (see Chapters 4 and 6). Because of this, some authors have recommended aggressive treatment of possible withdrawal symptoms over two weeks or more with trycyclic antidepressants (e.g., desipramine, 50–100 mg on the first day, decreasing over the next two weeks).[23] Until further evidence is presented, I do not use this approach.

9.2.5.2. Medical Complications

It is not yet known whether the chronic misuse of this very toxic substance is associated with the failure of any major organ system. Most of the data to date come from studies of the toxic reactions described in Section 9.2.3.

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CHAPTER 10

Glues, Solvents, and Aerosols

10.1. INTRODUCTION

10.1.1. General Comments

This short chapter deals with a heterogeneous group of industrial substances[1] that share the ability to produce generalized CNS depression.[2] Although the intermittent use of solvents was noted in the last century,[2] more widespread misuse began with the inhalation of model airplane glue in the early 1960s.[3] Despite the efforts of the hobby industry to modify their products by removing some of the more toxic substances and adding an irritating smell, the abuses have continued, and intoxication through inhalation has spread to aerosol propellants and industrial solvents.[2]

The more frequently abused agents and their contents, presented in Table 10.1, include cleaning solvents such as carbon tetrachloride, toluene, gasoline, lighter fluids, nail polish remover, and the fluorinated hydrocarbons used in aerosols. These products are popular because they induce euphoria and are readily available, cheap, legal, and easy to conceal. The onset of mental change occurs rapidly and disappears fairly quickly, and, with the exception of headache, serious hangovers are usually not seen.[4]

Table 10.1
Some Commonly Used Agents[1,2,12]

Glues	Toluene, naphtha, acetates, hexane, benzene, xylene, chloroform, etc.
Cleaning solutions	Trichloroethylene, petroleum products, carbon tetrachloride
Nail polish removers	Acetone, etc.
Lighter fluids	Naphtha, aliphatic hydrocarbons, etc.
Paints and paint thinners	Toluene, butylacetate, acetone, naphtha, methanol, ethanol, etc.
Aerosols	Fluorinated hydrocarbons, nitrous oxide, etc.
Other petroleum products	Gasoline, benzene, toluene, petroleum ether

10.1.2. Pharmacology

10.1.2.1. General Characteristics

The solvents are all fat-soluble organic substances that easily pass through the blood–brain barrier to produce a change in the state of consciousness similar to the more mild Stage I or II levels of anesthesia.[1] It is difficult to make detailed generalizations, as the substances themselves are diverse in structure and most commercial products contain a combination of solvents along with other chemicals.[5] The metabolism of most solvents occurs in both the kidneys and the liver.

10.1.2.2. Predominant Effects

The usual "high" begins within minutes and lasts a quarter to three-quarters of an hour, during which the individual feels giddy and lightheaded.[2] Most users report a decrease in inhibitions along with a floating sensation, misperceptions or illusions, clouding of thoughts and drowsiness, and occasionally amnesia during the height of the inhalation episode.[1–3]

Acute intoxication is accompanied by a variety of potentially disturbing physiological symptoms, as noted in Table 10.2, including irritation of the eyes, sensitivity to light, double vision, ringing in the ears, irritation of the lining or mucous membranes of the nose and mouth, and a cough.[6,7] The abuser may also complain of nausea, vomiting, and diarrhea and may become faint or (especially with a fluorinated hydrocarbon aerosol) may demonstrate cardiac beating irregularities or arrhythmias.[2,8] Intoxication is usually associated with a slowing of the brain waves on the electroencephalogram to an 8–10/sec pattern.[1]

Table 10.2
Common Signs and Symptoms of Acute Intoxication[1,2,14]

Sensory	Light sensitivity
	Eye irritation
	Double vision
	Ringing ears
Respiratory	Sneezing
	Runny nose
	Cough
Gastrointestinal	Nausea
	Vomiting
	Diarrhea
	Loss of appetite
Other	Chest pain
	Abnormal heart rhythm
	Muscle and joint aches

10.1.2.3. Tolerance and Dependence

A toleration of higher doses of solvents appears to develop fairly quickly, but there is little evidence of cross-tolerance between substances.[2] Withdrawal symptoms do not develop, even with protracted use.[1,2]

10.1.3. Epidemiology and Patterns of Abuse

Solvents are usually taken intermittently and often as part of a "fad" among adolescents in their early teens.[1,2,9–11] Teenagers tend to abandon the use of solvents after a year or two as they mature and move on to other substances, but a small percentage continue with solvents as their drug of choice for periods of 15 years or more.[10,12] Although the actual scope of the use of solvents is unknown, a survey done in the 1970s indicated that as many as 20% of adolescent girls and 33% of adolescent boys in an urban setting had used solvents at least once, with the percentage of continuing users *decreasing* from junior high school to high school and into college.[13]

Solvents are usually taken by groups of young people, using any one of a variety of modes of administration. For the glues, it is common to inhale from a paper or plastic bag, perhaps increasing the intensity of the fumes by gentle warming. Unfortunately, this procedure also markedly increases the chances of suffocation, especially when plastic bags are used.[1,2] Liquids, such as the industrial solvents and paint thinners, can be inhaled directly from a container or by sniffing a cloth or placing the cloth in the mouth. Gasoline is sometimes inhaled directly from gas tanks.[1,2,4] Propellants may be inhaled directly, but most users attempt to separate out the particulate contents by straining the gases through a cloth.[2,4] In the survey alluded to above, 75% of users reported inhaling a substance from a plastic bag, and over 50% used paint, 40% glue, 37% gasoline, 27% nail polish, and 25% lacquer.[13]

10.2. EMERGENCY PROBLEMS

The most common emergency situations seen with the solvents are toxic reactions, organic brain syndromes, and medical complications.

10.2.1. Panic Reactions (See Section 1.6.1)

Because the period of intoxication is short (15–45 minutes), panic states usually abate by the time an individual would seek professional care.

10.2.2. Flashbacks (See Section 1.6.2)

With the exception of possible residual organic brain syndromes, flashbacks are not known to occur with these drugs.

10.2.3. Toxic Reactions (See Section 14.4)

10.2.3.1. The Clinical Picture

10.2.3.1.1. History

The patient usually experiences a very abrupt onset (within minutes) of severe physical distress while inhaling a solvent. This is usually done as part of a group activity involving young teenagers.

10.2.3.1.2. Physical Signs and Symptoms

A life-threatening toxic picture characterized by respiratory depression and cardiac arrhythmias can follow the administration of solvents. The result may be a rapid loss of consciousness and sudden death.[14] There is also a chance of death from suffocation in those individuals who inhale deeply from a plastic bag, which then collapses.[2]

10.2.3.1.3. Psychological State

The physically ill individual may present with anxiety and some level of mental impairment, ranging from OBS to coma.

10.2.3.1.4. Relevant Laboratory Tests

These are rarely helpful in establishing the diagnosis. It is important, however, to carry out a thorough physical examination and to establish baseline vital signs. It is also necessary to monitor cardiac functioning through an EKG and to establish red and white blood cell counts (see Table 1.5), as well as the level of liver function and kidney function (see Section 10.2.7).

10.2.3.2. Treatment

There are no specific antidotes for the solvent overdose. The treatment consists of offering good supportive care, symptomatically controlling arrhythmias, and aiding the respirations. Thus, the therapy would be similar to the general life supports outlined for opiates in Section 6.2.3, except that naloxone (Narcan) has no use here.

10.2.4. Psychosis

Any change in mentation occurring with the solvents is likely to involve an organic brain syndrome, not the delusions and/or hallucinations that might be seen with stimulants or depressants. One possible exception is the occasional violent outburst during intoxication from solvents that may be analogous to alcohol-related pathologic intoxication[4] (see Section

4.2.8.1). The treatment is aimed at controlling behavior for the short period of intoxication through reassurance and physical or pharmacologic controls, such as diazepam (Valium), 15–30 mg or more by mouth, or chlordiazepoxide, 25–50 mg or more, which can be repeated in one hour, if needed.

10.2.5. Organic Brain Syndrome

10.2.5.1. The Clinical Picture (See Section 1.6.5)

Frequently, individuals abusing solvents present with a rapid onset of confusion and disorientation. The patient may have a rash around the nose or mouth from inhaling, may have the odor of a solvent on his breath, and may have been found in a semiconscious state with solvents near him. Or he may be brought in by somebody who knows that he has been taking solvents.

The most frequent neurologic positive finding is an EEG pattern of diffuse encephalopathy with an otherwise basically normal clinical neurologic examination.[10] There is evidence that protracted long-term misuse can result in brain damage as demonstrated by a course tremor, a staggering gait, and scanning speech.[10] This brain damage may be accompanied by disorders of thought, such as tangentiality, but is usually without evidence of gross delusions or hallucinations. At this stage, nystagmus may be observed. Although long-term follow-ups have not been carried out, this type of brain damage picture has been observed for five or more months after abstinence and may be permanent.

10.2.5.2. Treatment

This is usually a short-lived organic brain syndrome clearing within a matter of hours. As for any delirium state, treatment centers on reassurance; the elimination of any ambiguous or misleading stimuli, such as shadows or whispers; protection of the patient from the consequences of hostile outbursts; and the provision of a generally supportive environment.

10.2.6. Withdrawal

No clinically relevant withdrawal syndrome from solvents has been described.

10.2.7. Medical Problems

10.2.7.1. Clinical Picture

These substances interfere with the normal functioning of most body systems. However, because abuse is generally intermittent and relatively

short-lived and the typical user is young and healthy, permanent sequelae are relatively rare. Nonetheless, the range of problems must be noted, as deaths do occur. The medical disorders associated with the solvents include the following:

1. Cardiac irregularities or arrhythmias can be seen with inhalation, especially with aerosol use.[8]
2. Hepatitis with possible liver failure has been noted following chronic exposure to solvents.[2,14,15]
3. Kidney failure may be seen with chronic abuse of toluene and benzene.[2,6,13]
4. Transient impairment in tests of lung functioning may be noted immediately after inhalation.[16]
5. Decreased production of all types of blood cells may occur and may result in a life-threatening aplastic anemia.[6,15]
6. Skeletal muscle weakness may develop as a result of muscle destruction, especially with toluene abuse.[6]
7. Transient mild stomach or gastrointestinal upsets can be seen with any of these substances.[6]
8. Peripheral neuropathies have been reported, especially lead-induced nerve damage to the hands and feet associated with the chronic inhalation of gasoline.
9. There is *anecdotal* evidence that these substances produce permanent CNS damage,[2,4] but reports in the literature are not consistent.[1]
10. Because of the probability that the solvents easily cross to the developing fetus, there is evidence that the chronic inhalation of solvents during pregancy can be associated, either directly or indirectly, with infant abnormalities.[17,18]

10.2.7.2. Treatment

Most of these disorders are transient and disappear with general supportive care. In the case of severe liver or kidney damage, the treatment is the same as that used for insults to these organs from any source. Any patient presenting with an encephalopathy should be carefully evaluated for other causes of the OBS, including intracranial bleeding.

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CHAPTER 11

Over-the-Counter (O/C) and Some Prescription Drugs

11.1. INTRODUCTION

11.1.1. General Comments

Almost any substance has the potential for abuse (if we define abuse as the voluntary intake to the point of causing physical or psychological harm).[1] As was discussed in Chapter 1, this potential is especially true if the drug has the capacity for altering an individual's perception of his environment. In the present chapter, brief mention will be made of the misuse of some prescription drugs, including the antiparkinsonian medications, diuretics, and the antipsychotics. However, the focus of this chapter is on the over-the-counter (O/C) drugs.

The O/C drugs discussed in this chapter include (1) nonprescription hypnotics (containing antihistamines); (2) nonprescription antianxiety drugs (usually containing substances similar to the O/C hypnotics); (3) nonprescription cold and allergy products; (4) bromides; (5) O/C analgesics (containing aspirin, phenacetin, and aspirinlike products); (6) laxatives; (7) nonprescription stimulants; and (8) diet pills. Because of the wide array of substances involved, each subsection represents a minichapter following the usual chapter format.

The history of O/C medications is a long one. Controls on drug availability are relatively recent, and at the turn of the century, anyone could purchase opium, cocaine, and other potent substances without a prescription.[2,3] Currently, there are many nonprescription drugs that have been poorly evaluated and consequently are of questionable efficacy. On the other hand, many are capable of producing physical and emotional pathology when taken either in excessive doses or in combination with other medications or alcohol. Many contain substantial amounts of alcohol themselves.[3]

Unfortunately, health care practitioners and the general public have limited knowledge of the dangers of these substances. Most people receive their information from advertisements or pharmacists, rather than from physicians.[4] The result is the very heavy use, and the frequent misuse, of these drugs, with resulting pathology coming to light in both emergency and general practice settings. Because of these common problems and the large variety of substances involved, the reader is encouraged to review other discussions of the O/C drugs.[5,6]

11.1.2. Epidemiology and Pattern of Misuse

There are more than 500,000 different O/C preparations.[4] At least 28% of the adult population of the United States uses these substances (not including aspirin), 12% taking caffeinated stimulants, 11% sleep medications, and 5% antianxiety drugs.[7] Many users combine O/C products with prescription drugs and alcohol.

Over-the-counter substances are used by all elements of society and must be considered a part of the differential diagnosis of emergency room problems in any patient; however, the most frequent user tends to be the white, middle-class woman.[2] Use of O/C substances is noted in 7%–10% of emergency room cases, two-thirds of these involving analgesics, and 17% sedatives.[2,3] The O/C drugs accounted for approximately 2% of the accidental overdose deaths and almost 3% of the suicides in one locale.[3]

11.2. ANTIHISTAMINIC DRUGS (SEDATIVES/HYPNOTICS)

11.2.1. General Comments

All of the O/C sleep medications now contain 25 mg of an antihistamine. With the exception of Unisom, which has doxylamine succinate, the others (e.g., Sominex, Sleep-Eze, and Miles Nervine Nighttime) contain pyrilamine maleate, and some (e.g., Quiet World) also contain aspirin (227 mg) and acetaminophen (162 mg). In the past, many of these drugs (e.g., Sleep-Eze and Sominex) contained scopolamine (0.125–0.5 mg), but in recent years, the atropine-type drugs have been deleted from these medications.

Controlled studies indicate that O/C sleep aids and sedatives (such as Compoz) are probably no more effective than placebo or aspirin, and they are significantly less effective than the benzodiazepines, such as temazepam (Restoril).[8] However, when Compoz was compared with aspirin and placebo, patients taking Compoz had increased rates of side effects, including sleepiness and dizziness.

11.2.2. Pharmacology

The antihistamines are rapidly absorbed when taken orally and have a rapid onset of action. As the name implies, they work by antagonizing the actions of histamine released by the body during allergic reactions.[9] Their usefulness in treating anxiety and insomnia takes advantage of their sedative side effect.

11.2.3. Epidemiology

It has been estimated that 18 million Americans have used O/C hypnotics or sedatives, and at least 4 million have taken one of the substances in the prior six months. The rate of use is higher in women: two-thirds of users are over age 35 and 50% over age 50.[3] For the O/C tranquilizers, the average user tends to be younger, usually under age 35.

11.2.4. Emergency Situations

Emergencies usually result from inadvertent overdose, deliberate misuse of the drugs in an attempt to achieve hallucinations, the combination of an antihistamine (e.g., pyrabenzamine) with a drug of abuse (e.g., pentazocine or Talwin—a mixture known as *T's and Blue*), or multiple-drug interactions.[10] Therefore, the most frequently noted syndromes in the emergency room are toxic reactions and organic brain syndromes. In addition, there are a few, usually reversible, medical problems.

11.2.4.1. Panic Reactions (See Section 1.6.1)

A panic occurring at normal drug doses is unlikely, although a patient might present with complaints of muddled thinking related to these drugs. Reassurance should be enough to allay the patient's fears and to decrease the level of discomfort.

11.2.4.2. Toxic Reactions (See Sections 1.6.3, 2.2.3, 6.2.3, and 14.4)

The toxic reaction for the O/C antianxiety and hypnotic drugs is usually time-limited, disappearing in 2–48 hours. The clinical picture can be confusing to the clinician and life-threatening to the patient if multiple substances have been taken. The onset of symptoms varies from a few minutes, as seen in an overdose, to the more gradual evolution of signs of confusion and physical pathology in an elderly patient regularly consuming close to the "normal" doses of an O/C sedative. The patient, rarely a member of the "street culture," usually presents in a state of agitation or may evidence varying degrees of an OBS.

Therapy for the toxic reaction involves general support.

11.2.4.3. Psychoses (See Section 1.6.4)

Although this topic is discussed separately for ease of reference, the psychosis here is simply an intense toxic reaction. It consists of sedation and confusion.[10] The treatment and the prognosis are the same as outlined under the toxic reaction.

11.2.4.4. Organic Brain Syndrome (See Section 1.6.5)

A patient presenting with confusion and marked sedation could be labeled as having a toxic reaction. The entire clinical picture, course, and treatment are identical to those outlined in Section 11.2.4.2.

11.2.4.5. Medical Problems

11.2.4.5.1. Clinical Picture

There are reports that in animals the chronic oral administration of antihistamines may be associated with a heightened risk for liver tumors.[11]

11.3. COLD AND ALLERGY PRODUCTS

These substances contain antihistamines, analgesics, decongestants, expectorants, and cough suppressants. The major clinical syndromes are similar to those seen for the antihistamines.[12]

Treatment is usually symptomatic. In addition, CNS depression, especially respiratory impairment, may follow excessive doses of cough suppressants, as some contain codeinelike substances. In that instance, one can expect to see a mild form of some of the reactions noted for the opiates (see Section 6.2.3). Finally, many decongestants contain adrenalinelike substances (e.g., ephedrine), the abuse of which can exacerbate psychiatric syndromes, including depression.[13]

11.4. BROMIDES

11.4.1. General Comments

This element has been in use since approximately 1860, when it was one of the only anticonvulsant and antianxiety drugs available. Problems of misuse have been noted since the 1920s, and in the 1940s and 1950s, bromide intoxication was felt to be a major precipitant of psychiatric hospitalization.[14] Until recent years, a variety of O/C substances used as sedatives contained bromides, including Miles Nervine and Bromo Seltzer.

11.4.2. Pharmacology

With chronic bromide use, psychopathology is likely to develop slowly, reflecting a half-life of approximately 12 days. If an individual were to take 16.5 mEq of bromide a day (the maximal amount allowable in O/C medications), he could be expected to develop intoxication in eight days, or sooner in children or patients with renal problems.

11.4.3. Emergency Problems

Although bromides have not been proved to be effective O/C sleep aids, they were, *until recent years,* widely available. They are no longer on the market.

11.4.3.1. Toxic Reactions (See Section 14.4)

11.4.3.1.1. Clinical Picture

1. *History.* The usual patient with bromide intoxication presents with the very gradual onset (over days, weeks, or months) of both physical and psychological impairment resulting from the chronic ingestion of O/C preparations containing bromide. Even with the phasing out of bromides in medications, cases still persist from the ingestion of drugs stored in the medicine cabinet or from contaminated water.[15]

2. *Physical signs and symptoms.* These are usually mild and consist of a fine tremor, a macular-papular skin rash, along with *neurologic problems* such as slurred speech, impaired coordination, and dizziness.

3. *Psychological state.* Toxic disturbances include any of a wide variety of emotional problems. These range from irritability to all grades of confusion (culminating in an organic brain syndrome), to any level of depression, and even maniclike behavior (hyperactivity and inability to organize thoughts.)

4. *Relevant laboratory tests.* As with all organicities, especially in the elderly, it is necessary to rule out physical abnormalities through the proper blood chemistries and counts (see Table 1.5) and through an adequate physical and neurologic examination, as well as an evaluation of CNS and cardiac functioning. A bromide level over 10–20 mEq/l indicates probable toxicity, and definite impairment is noted at 80 mEq/l.

11.4.3.1.2. Treatment

Treatment consists of general supportive care and the intravenous (IV) administration of either sodium or ammonium chloride. One can also use normal saline, at a rate of 330 ml per hour for 2 liters, which (for younger healthy individuals) is then alternated with 5% dextrose in saline.[16]

11.5. O/C ANALGESICS

11.5.1. General Comments

These drugs usually contain aspirin, aspirinlike substances (such as phenacetin or acetaminophen), and caffeine. They are used for relief from minor pains, such as headache, and—for aspirin and aspirin compounds—for the treatment of some chronic inflammatory disorders such as arthritis. Abuse reflects psychological dependence, as these drugs are not physically addicting and do not produce hallucinations or changes in the level of consciousness.

11.5.2. Pharmacology

Aspirin is both an analgesic and an anti-inflammatory substance that is readily absorbed orally; phenacetin and acetaminophen are analgesic but not anti-inflammatory. Caffeine is discussed separately in Chapter 12 and below under the O/C stimulants in Section 11.7. Some of the analgesics also contain antiacidic compounds such as sodium bicarbonate (e.g., Bromo Seltzer and Vanquish).

11.5.3. Epidemiology and Pattern of Misuse

Analgesic use has doubled in the last 10 years,[17] with a resulting 33 million users in the United States, 20 million of whom take the drug each month. In one survey of almost 3,000 individuals, 15% of the women and 18% of the men ingested aspirin daily,[17,18] with the rate of administration exhibiting no marked age or sex pattern. In a survey of drug-involved emergency room visits, 64% of those with a major problem with analgesics were taking aspirin, and 46% of those drug-involved emergencies were suicide attempts. There are now more than 300 products containing aspirin in the O/C market.[3]

11.5.4. Emergency Situations

The major emergency problems for analgesic users are toxic overdoses and medical disorders resulting from chronic use. Older individuals are especially liable to misuse analgesics and are at high risk for adverse reactions.[19]

11.5.4.1. Panic Reactions

These are virtually nonexistent with these drugs.

11.5.4.2. Flashbacks

These are not noted with the analgesics.

11.5.4.3. Toxic Reactions (See Section 1.6.3)

11.5.4.3.1. Clinical Picture

Overdose of O/C analgesics containing aspirin usually results in a profound acid–base imbalance, ringing in the ears, and electrolyte problems. This picture is most often seen in adolescents engaging in a deliberate overdose, usually in a spur-of-the-moment reaction to a life situation.

11.5.4.3.2. Treatment

The picture tends to be relatively benign, responding to general supportive measures. Diuresis (see Section 2.2.3.2) is rarely needed. However, as in any emergency situation, unforeseen complications, such as hospital-acquired infections or kidney failure, can occur and may be fatal.

11.5.4.4. Psychoses

Psychoses are rarely, if ever, seen with these drugs.

11.5.4.5. Organic Brain Syndrome (See Section 1.6.5)

An OBS occurring with O/C analgesics is usually the result of acid–base or electrolyte imbalance. It is temporary and will clear with supportive care.

11.5.4.6. Medical Complications

11.5.4.6.1. Clinical Picture

The medical problems seen with analgesics vary from acute, usually benign, reactions, to more permanent responses due to chronic drug misuse. Acutely, aspirin may cause gastrointestinal upset, bleeding, gastric ulcers, minor changes in blood coagulability, asthmatic attacks, and skin reactions.[3] When combined with moderate to high doses of ethanol over a period of time, acetaminophen can (at least, theoretically) produce a toxic metabolite that can result in liver cell damage.[20]

Chronic use of O/C analgesics can be associated with anemia, peptic ulcers, upper gastrointestinal bleeding, renal disease, and possibly a neuropathy.[21] Phenacetin, in chronic high doses, can produce kidney failure and chronic anemia.

11.5.4.6.2. Treatment

The treatment is symptomatic and supportive, based on the individual clinical picture.

11.6. LAXATIVE ABUSE

11.6.1. General Comments

Laxatives consist of a wide variety of substances that act through diverse methods, including increasing bulk in the colon and increasing colon motility. They can be generally subdivided into salines, bulk producers, emolients, lubricants (e.g., mineral oil), and hyperosmotic agents (e.g., glycerin).[22]

11.6.2. Pharmacology

The pharmacology, of course, differs with the specific laxative. Those most likely to cause systemic problems contain phenolphthalein, which, when absorbed, can cause cardiac and respiratory distress in susceptible individuals.

11.6.3. Epidemiology and Pattern of Misuse

Laxative use has become entrenched in Western societies, especially in elderly individuals.[23,24] It has been estimated that more than 30% of people over age 60 take a weekly dose of a cathartic with the goal of achieving daily bowel movements.

11.6.4. Emergency Situations—Medical Disorders

Laxatives are not physically addicting, do not cause changes in level of consciousness, and have no direct effect on the CNS; consequently, the major problems are medical.

1. The effects of laxative misuse include diarrhea, abdominal pain, thirst, muscular weakness, cramps secondary to hypokalemia, and the characteristic radiological appearance of a distended and flaccid colon.
2. Mineral oil laxatives may impede the absorption of some minerals and fat-soluble vitamins, thus producing a hypovitaminosis syndrome.
3. Saline cathartics can also result in dehydration and electrolyte imbalance, with important consequences for individuals with preexisting cardiac disorders.
4. Other disorders that can be seen after a chronic overuse of laxatives include melanosis coli, fecal impaction from a flaccid colon, osteomalacia, and protein loss.[23,24]

11.7. STIMULANTS (See Chapters 5 and 12)

11.7.1. General Comments

These substances, usually containing caffeine as their major active ingredient, are mostly used by people who work unusual hours, such as cross-country truck drivers and students preparing for exams. Similar emergency problems can be seen for the O/C asthma products, especially those containing stramonium.

11.7.2. Pharmacology

Caffeine is a drug whose properties have been recognized for centuries.[3] Found naturally in teas, coffees, colas, and cocoa, caffeine produces mild stimulating effects. With doses in excess of 100 mg (1–2 cups of coffee contain 150–250 mg), people begin to experience a slightly increased thought flow, an enhancement in motor activity, and a decreased drowsiness and fatigue. Accompanying these psychological changes are increases in heart rate and blood pressure, along with GI irritability. Fatal overdosage from caffeine would require about 10 g (70–100 cups of coffee).

11.7.3. Epidemiology and Pattern of Misuse

Not counting beverages, 16 million Americans have used O/C stimulants. Two-thirds of the users are male, but all races and socioeconomic groups are represented. There is an increased level of use among students and employed males.

The drugs containing caffeine as their major ingredient are No Doz (which has 100 mg per tablet), Efed II (ephedrine 25 mg, phenylpropanolamine 50 mg, and caffeine 125 mg), and Vivarin (which has 200 mg per tablet).[25] Other drugs are Come Back, Enerjets, Tirend, and Chaser for hangover.[26]

11.7.4. Emergency Situations

The most frequent emergencies include panic reactions and medical problems. There is no evidence that these substances are physiologically addicting, no evidence of flashbacks, and no information to indicate that they produce psychoses. The one exception to psychosis could be Efed II, as it contains the stimulant phenylpropanolamine.[27] Of course, in high enough doses, these changes can produce an organic brain syndrome, but this is extremely rare.

11.7.4.1. Panic (See Section 1.6.1 and 5.2.1)

11.7.4.1.1. Clinical Picture

Stimulants can produce an increased blood pressure, a rapid heart rate, and palpitations, which may be perceived by the individual as a heart attack.

11.7.4.1.2. Treatment

The treatment is exactly the same as that for any panic reaction (see Sections 5.2.1 and 7.2.1):

1. Carry out a rapid physical examination, including an EKG to rule out physical pathology.
2. Draw blood (10 ml) or collect urine (50 cc) for a toxicologic screen.
3. Center treatment on gentle reassurance.

11.7.4.1.3. Medical Problems

The major medical disorders seen with stimulants include exacerbation of preexisting heart disease or hypertension and precipitation of pain in individuals with ulcers. Treatment is symptomatic.

11.8. WEIGHT CONTROL PRODUCTS (See also Section 11.7 and Chapters 5 and 12)

11.8.1. General Comments

These substances are of limited, if any, value in weight control. As is true of the prescription CNS stimulants, any weight reduction that occurs tends to be temporary. Most O/C weight control products contain either a relatively weak sympathomimetic-type drug (phenylpropanolamine), a local anesthetic (benzocaine), or a bulk producer (methylcellulose).

11.8.2. Pharmacology

Phenylpropanolamine is a sympathomimetic or adrenalinelike agent similar to amphetamine, which produces an adrenaline-type response along with weak CNS stimulation. In the suggested dosages, it is of questionable efficacy in decreasing appetite. The drug is associated with nervousness, restlessness, insomnia, headaches, palpitations, and increased blood pressure.

Benzocaine is a local anesthetic that is included in some weight control products in an attempt to decrease hunger. There is no evidence that this drug is effective in decreasing appetite.

Methylcellulose produces bulk and thus a feeling of fullness in the stomach. However, this substance is no more effective than a low-calorie, high-residue diet, and it does have the danger of producing esophageal obstruction.

11.8.3. Epidemiology and Pattern of Misuse

There is very little, if any, evidence available on the patterns of misuse of weight control substances. One would estimate the most frequent users to be young to middle-aged women.

11.8.4. Emergency Situations

There are now adequate data to show that in high enough doses phenylpropanolamine can produce emergency situations similar to those outlined under the CNS stimulants (Section 5.2). Case reports indicate that the O/C stimulantlike weight-reducing products are capable of producing psychoses almost identical to the CNS stimulant psychosis described in Section 5.2.4.[27,28] In addition, syndromes of depression and mania-like states and/or mania have also been noted after chronic misuse.[29,30] The clinical characteristics, diagnostic procedures, and treatments are identical to those described in Section 5.2.4.

Methylcellulose can produce esophageal obstruction, especially in individuals who already have esophageal or gastric disease. This should be treated symptomatically.

11.9. ABUSE OF SOME PRESCRIPTION DRUGS

11.9.1. Antiparkinsonian Drugs

Probably the most commonly abused of the prescription drugs not yet described in this text are the antiparkinsonian agents. These include drugs used to treat Parkinson's disease itself and those prescribed for the relief of the Parkinsonian side effects of antipsychotic drugs. The most widely prescribed of these agents are trihexphenidyl (Artane) and benztropine (Cogentin), as well as biperiden (Akineton) and procyclidine (Kemadrin). The potential misuse of these substances reflects their wide level of prescription (they are among the 10 most prescribed drugs in the United States).[31] A dose of 10–15 mg of trihexphenidyl has been reported by patients to be associated with an increased sense of well-being (i.e., euphoria), as well as increased social interactions and a transient feeling of the relief of depression.[32,33]

The mode of action is probably related to changes in the cholinergic nervous system that may tie in with the euphoria.[34–36] Evidence of the

potential misuse of these substances was first presented in 1960, when a patient deliberately increased the trihexphenidyl dose from 8 mg per day to 30 mg, with subsequent interference in functioning. Four additional cases were presented in 1974 as part of a description of individuals with toxic reactions, and cases of misuse, particularly of trihexphenidyl and benztropine, have consistently surfaced over the last decade.

11.9.1.1. Clinical Picture

The emergency problems associated with these drugs are fairly typical of the anticholinergic syndrome. The onset of symptoms varies from a few minutes, as seen in an overdose, to the more gradual evolution of signs of confusion and physical pathology in an elderly patient consuming close to the "normal" doses. Agitation and anxiety may be accompanied by a very rapid heart rate and other anticholinergic signs, such as dry mouth, difficulty swallowing, abdominal distension, urinary retention, blurred vision and sensitivity to light, and a rash covering the face and the upper neck. There may also be an elevation of blood pressure. The patient usually presents in a state of agitation and may evidence varying degrees of an OBS. The signs of confusion, along with the stigmata of an anticholinergic crisis (e.g., dry mouth and warm dry skin), usually establish the diagnosis.[37,38] However, a toxicologic screen (10 ml of blood or 50 ml of urine) may be useful. As with any patient with unstable vital signs and a level of organic impairment, it is necessary to establish baseline levels of functioning and to rule out other physical causes, such as infections, trauma, and tumors.

11.9.1.2. Treatment

Therapy for the toxic reaction involves general support; symptomatic treatment of physiological reactions, such as the elevated body temperature; and a direct attack on the anticholinergic syndrome. The factors to consider are listed below, but their order of importance may change with specific clinical situations.

1. Attention must be paid to the maintenance of an adequate airway, adequate circulation, and the control of any traumatic lesions or bleeding. This treatment is described in greater depth in Sections 2.2.3 and 6.2.3.
2. A rapid physical exam and careful monitoring of vital signs must be carried out.
3. Because these drugs are usually taken orally, if a toxic overdose has occurred saline gastric lavage might be beneficial. The procedure should be continued until a clear return from the stomach is noted.

However, if the patient is comatose or semicomatose, lavage may be done safely only with an inflated cuff on a tracheal tube.

4. Relatively normal body temperature must be maintained by using a hypothermic blanket or alcohol/ice soaks, if necessary.[37,38]
5. The anticholinergic syndrome is best treated directly by the antidote physostigmine, given by slow IV injection of 1–4 mg (0.5–1.0 mg/kg for children).[38] The dose can be repeated in 15 minutes if the patient does not respond; and once improvement is noted, it may be repeated every 1–3 hours until the symptoms abate. With this regimen, one can expect improvement in the mental status and the physiological symptoms, although there is no reversal in pupillary dilatation until the anticholinergic drugs wear off.
6. It is wise to avoid all other drugs, if possible. However, if the patient is exceptionally excitable, one might use diazepam (Valium) in doses of 5–20 mg given orally or IM, or chlordiazepoxide (Librium) in doses of 10–25 mg orally. The dose may be repeated in an hour, if necessary.

11.9.2. Other Prescription Drugs

The misuse of other psychotropic medications probably occurs in the context of "pill testing" among young people trying to experience the effects of the substances found in the medicine cabinet. In one series of individuals treated for antipsychotic drug misuse (e.g., of haloperidol, or Haldol), the symptoms usually occurred within hours and tended to encompass prominent Parkinsonian side effects, such as muscle spasms and grinding teeth, along with feelings of unreality.[1] The treatment generally consists of the IM administration of antiparkinsonian drugs such as diphenhydramine (Benadryl—50 mg for an adult), which generally results in a rapid clearing of the clinical picture.

An additional related but fairly unusual problem can occur in those individuals seeking out and self-administering diuretics for any of a variety of reasons, frequently in an attempt to lose weight.[39] The problems are primarily those of electrolyte and acid–base imbalance.

11.10. GENERAL CONCLUSIONS

The misuse of O/C drugs, whether done deliberately or inadvertently, can result in toxic reactions characterized by panic, OBS, or medical complications. These substances must be considered whenever an individual presents to an emergency room with a fairly rapid evolution of an OBS. In evaluating all patients, it is important to gather an adequate history of O/C drug preparations, being especially wary regarding older or more debilitated individuals.

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CHAPTER 12

The Xanthines (Caffeine) and Nicotine

12.1. GENERAL COMMENTS

This chapter deals with the most culturally accepted legal drugs. As might be expected, these relatively mild (per usual dose) and highly attractive psychoactive substances have the widest use in our society. Despite the relatively benign effects that can be expected at low doses, the high prevalence of use results in frequent morbidity and (for tobacco) even a high level of mortality. These substances are discussed here because of the interaction between their use and various psychiatric disorders, as well as because of medical complaints that can be seen in emergency settings. The chapter first deals with the xanthines, including caffeine, and then goes on to a discussion of nicotine.

12.2. XANTHINES (CAFFEINE)

12.2.1. General Comments

Coffee, tea, and, to a lesser extent, colas and cocoa all contain these related psychoactive substances. The use of xanthines can probably be traced back to prehistoric humans, who appear to have recognized that caffeine-containing substances can yield stimulation and an elevation in mood, as well as an enhanced capacity to work.[1] The modern use of caffeine originated in the New World and the Orient and first reached Europe via Venice in the early 1600s. Probably because of the relatively mild apparent side effects and attractive psychoactive properties, by 1700 these substances were widely used on the European continent and in England.[2]

12.2.1.1. Pharmacology

The three substances discussed in this section are caffeine (found in coffee, tea, cocoa, and chocolate); theobromine (found primarily in chocolate); and theophylline (found in all of these beverages and, because

of its relatively high potency, also marketed as an antiasthmatic agent). Most xanthine-containing beverages also have significant amounts of oils (perhaps related to some of the gastric irritability caused by coffee); tannin (perhaps related to the constipating properties of tea); and a variety of other substances. Thus, it is difficult to be certain of the specific etiology of the symptoms associated with the use of coffee and tea.[3–5]

The probable level of xanthines in the most popular beverages and some over-the-counter as well as prescription drugs has been established.[6] The interested reader is advised to review Chapter 11 on the over-the-counter medications, some of which contain caffeine. Among the beverages, the highest level of caffeine is in brewed coffee (90–120 mg), with less caffeine in instant coffee and tea (about 70 mg) and still less in colas (20 mg). There are very low levels of caffeine but high levels of theobromine (a less potent relative of caffeine) in chocolate.[1,2,7]

The xanthines (also known as *xanthine derivatives* and *methyl xanthines*) are closely related alkaloids that are derived from plants.[1] They are readily absorbed from the gastrointestinal tract and are metabolized mostly in the liver, with 1% excreted unchanged in the urine and a plasma half-life of 3–3.5 hours.[1,8] The modes of action are relatively complex but probably involve an interaction with beta-adrenergic receptors and perhaps a competition with the endogenous ligands of benzodiazepine receptor sites.[3,9] The interested reader is referred to Chapter 2 on CNS depressants for a more in-depth discussion of these endogenous psychoactive substances, probably purines.

12.2.1.2. Predominant Effects

The effects of caffeine (and other xanthines) are dose-related, more mild (and frequently beneficial) results coming from low doses and more troublesome effects from higher doses.[10] In the cardiovascular system, caffeine tends to increase cardiac contractility and to decrease vascular resistance at lower doses, but it increases resistance at higher levels.[1,3,5] In a similar dose–response relationship, lower levels of caffeine appear to decrease the heart rate secondary to vagal stimulation, but higher doses result in an increased pulse and can even cause arrhythmias.[1] The effects on the respiratory system include an increase in breathing rate, secondary to direct stimulatory effects in the medulla, and a beneficial effect of the relaxation of smooth muscle in the bronchi, which, in the case of theophylline, can be helpful in asthma.[1,3]

The caffeinelike substances also have important effects on the kidneys and the gastrointestinal system. Increased production of urine is a predictable finding, occurring, in part, through a direct effect of the substances on the renal tubules in a manner similar to those noted for the thiazide

diuretics.[1,3] Gastrointestinal problems are related to the increase in gastric acid secretion, perhaps through a direct effect on the gastrointestinal system, as well as indirectly, through the release of peripheral catecholamines.[1,11] Diarrhea and GI pain may be related to the direct effect of caffeinelike substances that stimulate the phasic contraction of gut muscle, as well as to a direct irritation of the mucosa and the enhancement of gastric acid secretion.[3] Although the usual effect of caffeine is an *increase* in esophageal sphincter pressure, individuals with preexisting impaired sphincter strength can experience "heartburn" after caffeinated beverage ingestion, perhaps because of increased gastric secretions.[11]

Additional organ-system effects include an increase in the capacity for skeletal muscle work, with a subsequent increase in muscle tension.[1] The endocrine effects can include a reactive hypoglycemia (perhaps secondary to catecholamine release).[2] As is true of most psychoactive substances, caffeine interacts with the actions and the metabolism of other substances, antagonizing the actions of the benzodiazepines, perhaps through a direct effect on relevant receptors, and increasing the metabolism of other substances via a possible induction of microsomal enzyme systems in the liver.[9,12] Although the caffeinelike substances may antagonize the effects of opiates, they do not have a marked antagonism for the depressant effects of ethanol.[13]

Actions on the CNS are probably important in the attractiveness of these drugs. There is what appears to be a direct stimulation of the cortex, with a decrease in drowsiness and an increased flow of thought with doses as low as 80 mg of caffeine.[1,3] As already mentioned, caffeine appears to have a direct stimulatory effect in the brain stem on the respiratory, vagal, and vasomotor centers.[2] Through a combination of both central and peripheral actions, increasing doses of caffeine result in insomnia, restlessness, tremor, and anxiety. The interference with sleep involves a decrease in the deeper sleep levels, a possible shift of the rapid-eye-movement (REM) type of sleep to later in the evening, and a fragmentation of the usual sleep pattern.[1,8] The resulting effects on behavior are discussed in greater depth below.[13–15]

12.2.1.3. Tolerance and Dependence

As was discussed in Chapter 2, tolerance is a complex phenomenon involving changes in metabolism, CNS responses, and behavioral mechanisms. Dependence is also related to the pharmacological results of chronic exposure of the nervous tissues to the substance, but it has behavioral components as well. Thus, almost by definition, most attractive psychoactive substances produce tolerance and dependence, and the xanthines, especially caffeine, are no exception.[1,8] Rapid cessation of chronic

use results in a subtle but annoying pattern of discomfort that has been characterized as withdrawal and that is discussed further below.[16,17]

12.2.1.4. Epidemiology

The use of caffeinated beverages is almost ubiquitous in Western societies, as these substances, even more than nicotine, are the most popular psychotropic drugs ingested in North America.[10] It has been estimated that in the 1970s the per capita consumption in the United States was 14.3 pounds of coffee per year per adult; the resulting average was at least 200 mg of caffeine per day, 90% of which was taken as coffee.[1,8]

The use of caffeine in the form of colas begins in childhood, and the use of brewed beverages, including coffee and tea, begins in the early teens.[18] Although most caffeine consumers drink two to three cups of coffee a day or the equivalent, between one-quarter and one-third ingest 500–600 mg of caffeine daily.[18] The pattern of consumption appears to be higher in males, Caucasians, those with lower education, and those with lower levels of religious beliefs, and it tends to increase with age.[3] There also appears to be a direct correlation between the level of caffeine used and the use of benzodiazepines and other antianxiety medications.[19]

Most individuals appear to ingest caffeinated beverages both for their taste and for their ability to combat feelings of fatigue and lethargy.[10] As may be true of most of the substances described in this text, the desire to tolerate the side effects and to seek out the active effects of the drug appears to be familial and may be genetically influenced.[20]

12.2.2. Emergency Problems

12.2.2.1. Panic Reactions

12.2.2.1.1. The Clinical Picture

Caffeinated beverages (as well as the prescribed xanthines, like theophilline) can induce a classical panic picture.[21] With caffeine doses in excess of 500–600 mg per day, the symptoms of "caffeinism" resemble those of panic attacks and must be included in the differential diagnosis of all high-anxiety-level problems seen in medical settings.[10,19]

12.2.2.1.2. Treatment

As the half-life of many of the caffeinated substances is between three and four hours,[1] and as the symptoms are relatively mild, treatment involves observation, education, and waiting several hours until the symptoms dissipate. Antianxiety medications are rarely required.

12.2.2.2. Flashbacks

Probably because of the relatively mild effects of caffeine and the short half-life, flashbacks are not seen.

12.2.2.3. Toxic Reactions

12.2.2.3.1. Clinical Picture

An overdose of caffeine tends to be relatively mild, and death is exceptionally rare. Very high doses of caffeine, either through excessive coffee drinking or (more likely) through the ingestion of over-the-counter and prescription substances containing caffeine, result in a clinical pattern consistent with the pharmacological effects of the drugs (see also Sections 11.7 and 11.8). Most patients present with hyperstimulation, high levels of anxiety, dizziness, a buzzing in the ears, and feelings of derealization, but these can progress to visual hallucinations and confusion.[22,23] The cardiovascular effects can result in high blood pressure, tachycardia, and possible extrasystoles, as well as an increased respiratory rate.[1,22] At least one case of death has been reported after the ingestion of between 6 and 12 gm of caffeine (along with other substances), with resulting pulmonary edema, enlarged liver, probable arrhythmias, and a dilated gastrointestinal tract.[7]

12.2.2.3.2. Treatment

The treatment is symptomatic. Care should be given to adequate respirations, control of body temperature, control of convulsions, and control of hypertension.

12.2.2.4. Psychosis

Psychotic pictures are rarely observed as a direct effect of the caffeinated beverages. However, these substances may exacerbate preexisting psychotic disorders, and there are anecdotal reports of relatively rare psychotic syndromes resulting from caffeine itself.

12.2.2.4.1. The Clinical Picture

A possible clinical worsening of schizophrenia-type disorders after caffeine ingestion has been described by a number of investigators.[3,8] These may be related to the direct CNS effects of these substances or, perhaps, to an antagonism of the effects of antipsychotic medications, as precipitation of these substances in solution has been observed *in vitro*.[12] Even mild stimulants like the xanthines have been noted to increase the symptoms of clinically significant mania.[10]

Thus, it appears that caffeine-type substances can worsen most psychiatric disorders, ranging from psychoses through depression to, as expected, the anxiety-type syndromes.[19,22] Despite this observation, between 15% and 20% of psychiatric patients consume 500–750 mg of caffeine per day.[8,19] These figures underscore the necessity of taking a careful history of caffeine intake by all psychiatric patients (in whom caffeine may exacerbate symptoms) as well as by general medical and psychiatric patients (for whom caffeinism should be considered part of the differential diagnosis of anxiety).

12.2.2.4.2. Treatment

Treatment involves the recognition of caffeinated beverages as possible exacerbating and causative factors in all psychiatric disorders. Decreasing and then stopping caffeine intake can be expected to result in improvement in a matter of hours to days.

12.2.2.5. Organic Brain Syndrome

12.2.2.5.1. Clinical Picture

It is unlikely that caffeine is a major cause of clinically significant confusion. However, in high doses (perhaps in excess of 500–600 mg a day), it has been reported that caffeine can induce periods of agitated confusion (i.e., delirium) and that these substances should be considered a part of the differential diagnosis in all such clinical pictures.[10]

12.2.2.5.2. Treatment

As is true of all of the caffeine problems, treatment involves stopping the substances in the expectation of relatively rapid improvement.

12.2.2.6. Withdrawal

12.2.2.6.1. Clinical Picture

The withdrawal symptoms seen after the chronic intake of a relatively mild substance like caffeine are probably a mixture of direct pharmacological and behavioral effects. No matter what the etiology, the rapid cessation of heavy caffeine intake has been associated with a variety of mild but disturbing symptoms.[16,17] Most patients complain of headache along with increased levels of muscle tension, irritability, anxiety, and fatigue; these symptoms begin within a matter of hours.[3,5,24–26]

12.2.2.6.2. Treatment

The importance of the recognition of these symptoms is to rule out caffeine withdrawal whenever the clinician is dealing with patients with muscle tension, anxiety, or related symptoms. As is true with most relatively mild withdrawal syndromes, treatment involves reassurance and the passage of time.

12.2.2.7. Medical Problems

The series of medical complaints that can be associated with a chronic and relatively high intake of xanthines are predictable based on the drugs' physical and psychological effects. However, these difficulties may be more than just "mild," as animal models have demonstrated that modest to high intake of caffeine can result in decreased longevity and impaired general physical condition in rodents.[27]

1. High levels of xanthines can result in increased blood pressure, tachycardia, and arrhythmias.[3] These substances should be considered a part of the differential diagnosis of all such problems.
2. Another relatively frequent problem involves gastrointestinal upset, including pain (seen in perhaps 20% of heavy coffee drinkers); diarrhea (also seen in 20%); and even peptic ulcers, as well as exacerbation of esophagitis with associated heartburn.[3,11]
3. Neuromuscular problems can include a feeling of restlessness in the legs and arms as well as persistent tremor.[2,3]
4. Both direct and indirect effects on the CNS can result in insomnia (reported by 40% of regular heavy users); headache (reported by 20%–25%); and anxiety and agitation as described above.[3,28]
5. More serious and life-threatening problems can also occur. There is a possible weak (but potentially significant) association between caffeine and bladder cancer and with pancreatic cancer.[29]
6. The long-held belief that caffeine is relatively safe in pregnancy has been challenged by the observation of teratogenic effects in animals, and this substance has been taken off the "generally recognized as safe" list by the Food and Drug Administration.[30,31]

12.3. NICOTINE

12.3.1. General Comments

Nicotine ingestion is an ancient and widespread practice. Prior to the Europeans' discovery of the New World, nicotine was used by North

American natives, usually through tobacco smoking, chewing, or salves. The goal was to achieve a transcendental experience, often as part of a ceremony of offerings to the gods and of warding off evil. It is possible that the older forms of tobacco were more potent and may have contained high concentrations of psychoactive substances.[32] Tobacco ingestion came to the Old World following the explorations of Columbus in the 1490s and soon spread throughout Europe and thence to Africa and Asia over the next 50–100 years.[33]

Nicotine can be thought of as causing a prototype dependency process.[34] It resembles all of the other substances abused in that people begin feeling that they can stop at any time; they ingest the substance despite knowledge of its serious dangers; they tend to titrate their dose; most deny problems even after these are obvious to those around them; there is a high rate of relapse once use ceases; and genetic factors may influence the risk for abuse.[17,35] The widespread use despite known dangers probably reflects nicotine's low cost, its high level of social acceptance, and the relatively mild immediate side effects.[17]

12.3.1.1. Pharmacology

In Western cultures, nicotine is primarily ingested through smoking or chewing tobaccos. In the predominant mode of administration, smoking, almost 4,000 substances are inhaled, including nitrogen oxides, ammonia, and aldehydes (e.g., acetaldehyde), with the specifics depending on the temperature of burning. A smaller number of substances are ingested with chewing or intranasal administration through snuff.[1,39] The three major components of *Nicotinia tobacum* (named after Jean Nicot, who promoted nicotine for its medicinal values) are tars, carbon monoxide (CO), and nicotine. The tars, or total particulate matter (TPM), are measured through collection by a Cambridge filter after the subtraction of moisture and nicotine, and they contain possible cancer-causing polycyclic aromatic hydrocarbons, which also induce liver enzymes. These cause changes in the metabolism of other body substances.[40] The CO causes a decreased ability of the blood to carry oxygen and thus an increase in red blood cell number (polycythemia), and it is probably a major "culprit" in the generation of heart disease, perhaps through the promotion of atherosclerosis.[39,40] The prominent psychoactive component of tobacco ingestion, however, is nicotine, and unless otherwise specified, this chapter deals primarily with this substance.

Nicotine is probably the major (although not the only) reinforcer of tobacco ingestion and as such is also probably the rate-limiting substance in tobacco intake. Most smokers and chewers modify their use based on the

nicotine content (although there is not a perfect correlation).[41,42] This alkaloid is one of the few naturally occurring liquids of its class and is rapidly absorbed through the lungs or the digestive tract; thus, a puff of smoke results in measurable nicotine levels in the brain within seconds.[1,43]

The average cigarette contains between 1.5 and 2.5 mg of nicotine, with perhaps slightly lower levels for filter cigarettes, although these "low-tar" products may have heightened levels of CO.[39] Snuff contains 4.5–6.5 mg of nicotine, and nicotine gums contain between 2 and 4 mg.[45] After ingestion, peak plasma concentrations are found in the range of 25–50 ng/ml, with a half-life of disappearance from the plasma of 30–60 minutes.[46]

12.3.1.2. Predominant Effects

This substance has potent effects on many body systems.[46] In the *digestive* tract, there is a decrease in the strength of stomach contractions (perhaps related to appetite suppression), but intake can also result in nausea and vomiting through a direct effect on the medulla.[41,46] Effects on the *respiratory* system include local irritation, the deposit of potential cancer-causing substances, and a decrease in ciliary motion.[46] Acute effects on the *cardiovascular* system include an increase in heart rate (perhaps related to a release of epinephrine), an increase in blood pressure, cutaneous vasoconstriction, an increase in the strength of heart contractions, and an elevation in platelet adherence.[39,41,47] The *endocrine* system reacts to nicotine with a release of epinephrine and norepinephrine, both from the adrenals and from the adrenergic axons, along with an increase in growth hormone, cortisol, and antidiuretic hormone.[39,46,47] Direct effects on the *brain* through unknown mechanisms (perhaps a nicotine receptor) include a generalized stimulating EEG pattern with low-voltage fast waves predominating, while in the periphery there is a decrease in muscle tone and deep tendon reflexes (perhaps related to direct effects on the spinal cord).[41,46,48]

As is true of so many psychoactive substances, nicotine interacts with other drugs. The clinical observation of an increase in smoking with increased coffee intake has been substantiated experimentally, although the specific mechanism is unknown.[15] Similarly, the interaction between alcohol intake and smoking has been observed in adolescents and in adults, leading some authors to speculate that drinkers may turn to tobacco to antagonize some of the CNS-depressant properties of ethanol.[49] Tobacco smoke, probably through the effects of nicotine, also induces intestinal microsomal enzymes, with resulting interactions (usually enhancement of the rate of metabolism) with anticoagulants, phenacetin, propranolol, and caffeine.[33,46]

12.3.1.3. Epidemiology and Natural History

The percentage of smokers in most Western cultures increased after World War I, reaching a peak in the mid-1960s, when it was estimated that 52% of American males and 32% of American females were regular smokers, consuming 600 billion cigarettes per year.[46,50] In 1964, an Advisory Commission to the Surgeon General of the United States reported that tobacco intake was a major health hazard, after which time per capita consumption began to drop, with a marked decrease during the early 1970s.[51] By 1975, the percentage of regular smokers among males had decreased to 39%, although females showed only a slight drop, to 29%.[50,52] Parallel findings in adolescents (age 12–18) showed a modest decrease among boys, from 15% smokers in 1968 to 11% in 1979, but a reverse trend among girls, with an increase from 8% to 13% over the same years.[33,52]

Smoking usually begins in early adolescence, and most young people experiment by age 12 or 13.[53] The characteristics of smokers parallel those of ingesters of other substances—indeed, few young people begin using marijuana or other substances of potential abuse unless they are smokers. Thus, the chance of smoking tobacco in youth increases with increasing signs of adjustment problems (e.g., academic failure), increased evidence of risk-taking, and increased characteristics of extraversion.[41]

Once they have begun, the majority of smokers (anywhere from one-half to two-thirds) say that they want to stop.[54] Whether it is a true desire to stop or just an attempt to tell investigators what the subjects think they want to hear, these findings still reflect the recognition by most smokers that tobacco is socially undesirable and dangerous to health.[54] Thus, it is not surprising that the natural history of smoking is one of frequent attempts to abstain, but (unfortunately) there is as high a rate of relapse with tobacco intake as there is with illicit drugs.[41]

12.3.1.4. Tolerance and Dependence

Tolerance to nicotine is real and is probably a combination of behavioral and metabolic effects, as well as pharmacodynamic changes.[46,55] Tolerance does not develop uniformly to all aspects of nicotine's actions (e.g., the most prominent changes occur for nausea, dizziness, and vomiting), and some aspects of tolerance begin to disappear within several days of abstinence, whereas others may be relatively long-lasting.[46,55] As is discussed further below, both psychological and physiological withdrawal symptoms are prominent and may be in part responsible for the difficulty that smokers have in stopping.[46,56]

12.3.2. Emergency Problems

Although usually seen as a benign substance, nicotine and the associated chemicals taken in through tobacco are responsible for a great amount of morbidity and mortality.

12.3.2.1. Panic Reactions

With the exception of the toxic reactions described below, it is unlikely that nicotine intake results in a full-blown panic in individuals not so predisposed. However, for a person under stress or with preexisting anxiety disorders, the increased blood-pressure and heart-rate changes caused by nicotine could precipitate attacks.[39,41,47] Treatment is symptomatic, and it includes reassurance and informing the patient that his tobacco intake is exacerbating his existing problems.

12.3.2.2. Flashbacks

Flashbacks are not a problem known to exist with nicotine.

12.3.2.3. Toxic Reactions

12.3.2.3.1. Clinical Picture

A fatal overdose of nicotine in adults can occur with 60 mg (as might be seen with an ingestion of some insecticides). Lesser amounts (even from tobacco) are dangerous for children. The symptoms can include nausea, salivation, abdominal pain, diarrhea, vomiting, headache, dizziness, decreased heart rate, and weakness in the more mild reaction.[44] In higher doses, these problems are followed by feelings of faintness, a precipitous drop in the blood pressure, a decrease in respirations, convulsions and even death from respiratory failure.[44]

12.3.2.3.2. Treatment

The treatment of nicotine overdose is symptomatic. In addition to general support of the respirations and the blood pressure, as well as the administration of oxygen, a number of maneuvers can be used to try to rid the body of the substance. Gastric lavage can be useful, as emptying is often delayed, and a slurry of activated charcoal can also help.[44] The excretion of nicotine is probably enhanced by acidifying the urine through the use of ammonium chloride (500 mg orally every three to four hours).[57]

12.3.2.4. Psychosis

No known clinically significant psychotic state has been reported with nicotine in modern times. This topic is of historical value, however, in light of the possibility that in ancient times more potent tobacco forms may have been used by North American natives to achieve transcendental states along with visual hallucinations.[32]

12.3.2.5. Organic Brain Syndrome

With the exception of the toxic reaction described above, nicotine is not expected to precipitate an OBS. However, a number of states of confusion are associated with the chronic effects of this substance through the destruction of the lung architecture, as is seen in chronic obstructive lung disease, or emphysema.

12.3.2.6. Withdrawal

12.3.2.6.1. The Clinical Picture

There is little doubt in the mind of any smoker that sudden cessation or attempts to "cut down" cause a withdrawal syndrome. The actual symptoms tend to be disturbing but relatively mild, and the intensity varies greatly between people.[46] It has been hypothesized that most heavy smokers get to the point where they continue to administer nicotine to avoid withdrawal symptoms rather than actually to enjoy the substance itself.[41,57]

The symptoms tend to begin within hours of stopping intake, increasing over the first half day. The discomfort is often worse in the evening.[41,46,56] The specific problems include a decrease in heart rate; an EEG slowing, with a decreased arousal pattern; nicotine craving; restlessness; a feeling of dullness or drowsiness; and an inability to concentrate.[41,56] Smokers also complain of irritability and feelings of hostility, headache, and sleep problems, which are accompanied by an increase in rapid-eye-movement (REM) latency and total REM time.[56] Constipation and/or diarrhea may occur early, and there may also be a significant weight gain, frequently 5 kgm or more.[56] In some individuals, these changes can be observed for 30 days or longer, but the psychological symptoms of craving may still exist for many months after that.[56]

Nicotine withdrawal has an interesting associated phenomenon not seen with most other drugs. It appears that tapering off may result in even more intense symptoms of craving than precipitous stopping. When tapering off, the symptoms last over a longer period of time, and thus, tapering off may be inferior to "cold turkey" stopping and may be associated with a higher level of relapse.[56]

12.3.2.6.2. Treatment

Most tobacco users attempt to stop on their own (perhaps up to 95% of people who quit successfully do so without external help). Treatment of the withdrawal symptoms may be an important part of "rehabilitation" and may require general supports; counseling (so the smoker knows he is not going through it alone); and perhaps the administration of nicotine gum in decreasing quantities over three weeks or more.[58] These approaches are described in greater depth below in the discussion of the treatment and prevention of smoking.

12.3.2.7. Medical Problems

With the possible exception of alcohol, tobacco intake has the highest cost to society of any abused substance. It has been estimated that 12% or more of deaths annually are related to smoking and that tobacco intake increases the mortality rate threefold while also significantly enhancing morbidity.[59,60] Public health costs resulting directly from tobacco substances probably total $8.2 billion per year, or 8% of the health care costs of the United States in 1976.[61] If indirect costs (e.g., lost work time) are included, the total costs climb to over $27 billion annually. The highest level of morbidity and mortality is seen with cigarette smoking. The level is probably lower for cigars and even less for pipe, chewing, and snuff.[46]

1. There is little doubt that tobacco substances, especially through smoking, are associated with a significantly elevated rate of cancer, especially of the lung, the oral cavity, the pharynx, the larynx, and the esophagus.[39,59,62]

2. High levels of morbidity and mortality are also associated with both cerebrovascular and cardiovascular problems, including strokes, heart attacks, and angina.[39,63] Although low-tar cigarettes appear to lower the level of cancer risk, these have little beneficial effect on the increased risk for heart disease.

3. An area of concern is the effect of nicotine and other tobacco substances on the developing fetus and the neonate. Many of these substances (especially nicotine) easily cross the placenta to the baby and are also found in breast milk. An increase in the heart rate of the fetus of a smoking mother can be seen for 90 minutes after a cigarette has been smoked.[64,65] Mothers who smoke heavily have almost a two-fold increased risk of spontaneous abortion, are likely to deliver babies who are small for their gestational age, and have offspring with over a two-fold increased risk of congenital abnormalities, including patent ductus arteriosis, tetralogy of Fallot, and cleft palate and lips.[65–67] Although fewer data are available, the children of mothers who smoke heavily may demonstrate a higher risk of

symptoms of hyperactivity in childhood and adolescence and may demonstrate higher risks of cancer later in life.[64,65] Smoking is also associated with abnormal sperm forms and evidence of chromosomal damage in lymphocytes.[68]

4. The problems in the respiratory system do not stop with cancer. There is evidence of acute effects of tobacco smoke in decreased ciliary action, which may help explain the increased risk of bronchitis and other infections in smokers.[59] Once these problems persist, chronic obstructive lung disease can be expected.[59,69] Although the discussion of associated morbidity may be bad news for the smoker, the good news is that abstinence for 5–10 years returns the risk for most of these problems to normal levels.[46]

12.3.3. Treatment and Prevention

Treatment involves a blending of efforts to alleviate withdrawal symptoms and then teaching new behaviors. Because they will probably continue to inhale, it may do little good to advise cigarette smokers to switch to a pipe or a cigar.[70] Because the length of physiological withdrawal may go on for 30 days or more and because psychological craving may even last much longer, the relatively bleak outcome reported in some programs may be improved through the use of nicotine gum (2–4 mg per stick), to be taken in decreasing amounts over several weeks to several months.[35,70,71]

Most "rehabilitation" programs center on behavioral approaches. All can be expected to result in some fairly rapid level of improvement (if abstinence is used as the measure), but it is unlikely that this level will be maintained for any period of time unless the patient is given "refresher" courses. One type of behavioral modification involves self-control strategies. Here, the smoker is asked to keep reminding himself why he wants to stop and to smoke in the least pleasurable way possible. For instance, he can be told never to smoke after meals, always to smoke away from people (alone), or to begin using his least preferred brand.[71]

Other behavioral approaches center on aversive conditioning, coupling an unpleasant event with the nicotine intake. The use of mild electric shocks to the hands while smoking does not appear to be as effective as aversions more directly related to the smoking itself. Many programs use a forced consumption of two to three times the usual amount, having stale and warm smoke blown in the smoker's face, or the enforced rapid intake of one cigarette after another. As a result of these types of approaches, as many as 50% of smokers may maintain abstinence after six months if they complete the entire original program.[35] As is true with all forms of behavior modification, the results are probably enhanced when the patient has a warm relationship with the counselor.[71]

Considering the relatively wide use of tobacco substances and its high price to society, as well as the difficulty many users have in stopping, it is worthwhile to discuss briefly the apparent success of prevention strategies. This may be a lesson of importance for prevention of abuse of other substances, as few areas of public health can boast the changes in national patterns of a deleterious problem that have been described above in the sections on epidemiology and natural history of smoking. No one is certain why consumption in the Western countries (especially the United States) has decreased. It may be because the approach to prevention has involved a combination of factors, including increasing the price of tobacco products through taxation, extensive public education, and antismoking campaigns targeted at youth. Health problems may have decreased through the development of less harmful cigarettes that filter out some of the tars and nicotine.[62,72]

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CHAPTER 13

Multidrug Misuse

13.1. INTRODUCTION

13.1.1. General Comments

The format of this chapter differs slightly from the rest of the text; it places the emphasis on the major types of drug interactions. Because the focus is on the relationship between types of drugs of misuse, careful reading will give you an opportunity to review much of the material already presented, that is, the general lessons given in this text about the prediction of drug interactions.

Few members of our society take only one drug. There is a strong correlation between the misuse of heroin and alcohol problems; abusers of stimulants frequently also misuse depressants; and alcoholics are at higher risk for the abuse of both other depressants and stimulants. However, as I observe the treatment programs available in most communities, I'm struck by the almost complete absence of "polydrug" or "multidrug" programs; that is, the multiple drug abuser must convince treatment personnel that his major problem includes alcohol or opiates before he will be admitted. With that in mind, I hope that clinicians working with methadone maintenance programs and those interested in alcoholism treatment will read this chapter carefully and go back and review the information presented on specific classes of drugs (e.g., CNS depressants and CNS stimulants) in order to find the best way to meet the needs of the patients entering their programs.

13.1.2. Problems of Definition and Classification

Investigators distinguish between *polydrug* and *multidrug* use. The former, by convention, indicates the use of more than one psychoactive substance, *not including opiates,* whereas multidrug use involves two psychoactive substances other than alcohol, nicotine, caffeine, or prescribed medications.[1] Although most polydrug clinics exclude individuals

who have difficulties related to opiates,[1] the recognition that many people who primarily use multiple drugs may also casually use opiates leads me to use the less restrictive *multidrug* term here.

The abuse of multiple drugs can be further classified from a variety of clinical perspectives, none of which has been proved to be better than the others.

1. First, it is possible to divide users by the *type of drug* taken:
   a. Those who regularly abuse *narcotics* who can be subdivided into:
      i. Those who use only narcotics.
      ii. Those who use narcotics and alcohol, as well as other psychoactive substances when available.
      iii. Those who use other drugs only during methadone maintenance or when narcotics are unavailable.
   b. Those who primarily abuse *alcohol* and occasionally turn to other drugs of misuse.
   c. Users of *hallucinogens*, *stimulants*, and/or *depressants*, with or without alcohol, who do not take narcotics.
2. Another, somewhat overlapping subdivision, is based on *drug patterns*[2,3]:
   a. Those who are dependent on one drug and use other drugs only when they are easily available.
   b. Those who are dependent on one drug and use other drugs only when the primary substance is not available.
   c. The people who prefer one drug but take others to decrease the side effects of the first.
   d. Those who abuse different drugs at different times of the day, for example, stimulants in the morning, antianxiety drugs during the day, and hypnotics at night.
   e. Last, those who have no drug preference but take whatever is available.
3. Of course, within any of these patterns, one must also consider:
   a. The influence of prior psychiatric disorders (primary versus secondary drug abuse as described for alcohol in Section 3.1.2.3).[4,5] Men and women with the antisocial personality (see Section 3.1.2.3.1) are likely to misuse multiple substances, but they are best labeled primary antisocial personalities and secondary multidrug abusers. Similarly, primary alcoholics may begin "treating" their lethargy or depression with stimulants and their anxiety with depressants, such as the benzodiazepines, in which instance they should best be labeled primary alcoholics (their first appearing major disorder) and secondary polydrug

abusers. As has been discussed in depth elsewhere, the proper assignment of primary and secondary labels is essential if the clinician wishes to predict the probable course and to select the most effective treatment.

b. The frequency and amount of drug misuse.
c. Whether drugs are taken intravenously or orally (as the former often yields higher risk of problems).
d. Whether the person is a middle-class individual usually obtaining substances from a physician or is more actively involved in a street culture.

In summary, I prefer to distinguish carefully between the primary and secondary misuse of multiple substances, placing primary alcoholics, primary antisocial personalities, and primary opiate abusers in a category separate from multidrug abusers. The treatment and prognosis for individuals who evidence different patterns of multiple drug misuse or who have different psychiatric or social backgrounds may vary markedly. Thus, all of these considerations must be taken into account.

13.1.3. The Natural History of Multidrug Misuse

The ages of first use and misuse and the pattern of drug intake vary among groups. For example, a person with an antisocial personality[4] utilizes drugs as part of a larger antisocial picture—drugs are almost "incidental" to his life pattern.[5] One recent long-term follow-up of a group of inner-city youth demonstrated that the antecedent lifestyles and stresses are probably different for antisocial personalities and alcoholics, implying that the same might be true of multidrug abusers versus antisocial personalities.[6] When substance abuse and the delinquency coexist, it is most often the case that the delinquency antedated the drug use pattern, a fact indicating the probability that the patient may demonstrate an antisocial personality.[7]

Also, natural histories differ with the immediate environment, as exemplified by the ubiquitous availability of most drugs of abuse in urban ghettos versus middle-class suburbs. In addition, the changing views of society might be expected to have a great impact on use and abuse patterns, as seen regarding marijuana.

With these caveats in mind, it is still possible to make some generalizations about likely patterns of misuse. In Western society, youth begin drug experiences with caffeine, nicotine, and alcohol. If they go on to use other substances, the next drug is likely to be marijuana, followed in frequency by one of the hallucinogens, depressants, or stimulants, usually taken on an experimental basis, ingested orally, and with few serious consequences. Individuals who go on to heavier intake may graduate to intravenous drug use, with a progression to opiates.[7–9]

This patterning of misuse has been viewed by some investigators as an age-related clustering of drugs that does not represent a continuum or a "stepping-stone" from one particular drug to another.[8] Other researchers, however, have outlined a sequential pattern of misuse, from nonuse to beer or wine, progressing to cigarettes and/or hard liquor, and then to marijuana, which may presage the use of other drugs.[9] These studies have indicated that it is rare for an individual to proceed directly to marijuana use without a prior use of beer or cigarettes. Marijuana, in turn, is seen as a step on the road to the use of other substances. One could suggest that once an individual has crossed the barrier against the use of any substance, especially any illegal substance (remembering that alcohol is usually illegal at age 18 or under), it becomes easier to take a second and third drug.[10] This progression does not prove that one drug caused the use of the other.

13.1.4. Pharmacology

13.1.4.1. General Comments

The effects of a drug may be either increased or decreased through interactions with other drugs:

1. The effect of a drug is *decreased* when it is administered to an individual who, while *not* taking any other drug at the same time, has developed cross-tolerance to a similar drug. This can occur through metabolic tolerance (usually reflecting the increased production of the relevant metabolic enzymes in the liver) or pharmacodynamic mechanisms (where the effect of the substance on brain cells has been decreased). Thus, higher levels of the substance are needed to generate the expected clinical effects. A relevant example is the need for higher levels of anesthetics, hypnotics, antianxiety drugs, or analgesics in alcoholics.

2. The results are the opposite, however, when two drugs with similar effects are administered *concomitantly*. Here, both drugs must compete for the same enzyme systems, both in the liver and at the target cell, the latter usually occurring in the brain. The effect is *potentiation*, where, for example, the amount of depression of brain activity that results from the conjoint administration of two depressant drugs or a depressant and an analgesic is more than would be expected from the actions of either drug alone. The effect can be an unexpected lethal overdose for the individual who has had too much to drink and decides that a few extra sleeping pills will help him rest through the night.

13.1.4.2. Some Specific Examples

Thus, the clinician should think twice before administering more than one drug to a patient. Because of the opposing effects, specific drug–drug in-

teractions are somewhat unpredictable, underlining the dangers in multidrug misuse. However, it is possible to make some generalizations about particular types of drug combinations.

13.1.4.2.1. Depressants–Depressants

If the drugs are not used at the same time, one would expect a decreased potency of the second depressant when administered to an individual who has already developed tolerance to the first. If, however, the two depressants (e.g., alcohol and sleeping pills) are given at the same time, potentiation of respiratory depression develops, with resulting morbidity and even mortality.[11] In one clinical example, a lethal overdose of barbiturates might require blood levels of 1.0–1.5 mg/100 ml (1.5 mg/dl) if taken alone, but in the presence of 100 mg/dl of ethanol, the lethal barbiturate blood level may be as low as 0.5 mg/dl.[11]

13.1.4.2.2. Depressants–Opiates

Even though these drugs do not have true cross-tolerance, one frequently sees a decreased efficacy in one drug when administered to an individual who has developed tolerance to the second class. Of greater clinical importance, however, is the fact that both opiates and depressants have depressing effects on the central nervous system, and thus, each potentiates the actions of the other in overdose, increasing the likelihood of death.

13.1.4.2.3. Depressants–Stimulants

The concomitant use of these drugs usually decreases the level of the side effects encountered with one drug alone. For example, the depressant-drug abuser or the alcoholic may seek out stimulants to help him feel less sleepy from abusing his favorite drug, or the CNS-stimulant abuser may use alcohol or other depressants to help him feel less anxious and demonstrate less tremor while taking his preferred drug. The dangers rest with the unpredictability of the reaction, as the CNS and metabolic systems attempt to maintain equilibrium or homeostasis in the presence of multiple drugs with opposite effects.

13.1.4.2.4. Hallucinogens–Stimulants

The similarities in the clinical action and the chemical structure of these two classes of drugs frequently lead to a potentiation of side effects. This possibility militates against the use of stimulants in the treatment of a hallucinogen-related toxic reaction (see Section 8.2.3.2), as clinical symptoms may worsen, not improve.

13.1.4.2.5. Hallucinogens–Atropinic Drugs

The same generalizations hold here as for the hallucinogen–stimulant interaction. This makes it unwise to use antipsychotic medications, with their anticholinergic side effects, in treating patients with a hallucinogen-induced toxic reaction.

13.1.4.2.6. Marijuana–Other Drugs

Marijuana has been shown to potentiate the CNS-depressing effect of alcohol,[12] and it may increase the likelihood of a flashback from hallucinogen-type drugs. Although these relationships require more research, it is unwise to take marijuana concomitantly with other substances, especially alcohol, because of the resulting motor incoordination and CNS depression, a problem with great implications for driving abilities.[13,14]

13.1.5. Epidemiology and Patterns of Abuse

Although the extent of multiple drug misuse is not known, it appears to be a rather common phenomenon among drug abusers. There is also anecdotal evidence that multiple substance misuse has increased over the years.[3,15,16] This is not surprising, because as many as 90% of young people report the use of alcohol, almost 60% have used marijuana, and almost 20% report the use of amphetamines, barbiturates, or LSD.[17] Perhaps the most common association is the almost universal use of alcohol and subsequent drunkenness in patients reporting multidrug or opiate problems.

Over one-half of the people presenting to a polydrug clinic report the use of three or more substances.[18,19] Certain individuals appear to be at especially high risk for multidrug misuse, including those with a history of psychiatric problems[19]; those "denied" access to their favorite drug (for example, subjects in methadone maintenance programs)[20]; and those who deliberately use the more "exotic" substances, such as phencyclidine (PCP)[21] (see Chapter 9). A fourth special group live in high-stress situations while separated from their families, such as the young soldiers using drugs, 70% of whom, according to one survey, persistently administer multiple substances.[22]

In general, multidrug users tend to be young and from middle-class backgrounds, and they often show some evidence of preexisting life maladjustment, sometimes severe enough to be labeled a personality disorder.[23]

13.1.6. Establishing a Diagnosis

It is important to remember that substance abuse is a relatively common phenomenon in our society and must be considered in the differential

diagnosis of a wide variety of medical and psychological problems. To review briefly, in evaluating an individual who, by past history, fits the criteria for the antisocial personality, one must note the likelihood that he or she is abusing multiple drugs. This is also probable for those on methadone maintenance programs and those living in high-stress situations. On another level, any individual presenting to the emergency room with a drug overdose must be evaluated for the *possibility* of multiple drug misuse, particularly any person who does not show the usual response to emergency room interventions.

13.2. EMERGENCY ROOM SITUATIONS

The most important clinical pictures seen with multiple drugs include toxic reactions (usually overdoses), drug withdrawal pictures, psychoses, and organic brain syndromes. The discussion given here is brief, as, once multiple-drug problems are indicated, treatment involves combining those procedures used for each substance alone.

13.2.1. Panic Reactions (See Section 1.6.1)

The clinical picture, course, and treatment for panic reactions resemble those seen for any one of the substances, including marijuana, the hallucinogens, the stimulants, and the atropinic drugs. The treatment is as outlined in the specific drug chapters. Good examples are given in Sections 5.2.1, 7.2.1, and 14.2.

13.2.2. Flashbacks

Flashbacks are seen with the hallucinogens or marijuana, and the clinical course and treatment for recurrences after the use of these drugs in combination with others is the same as outlined in Sections 6.2.3.2 and 7.2.3.2 for the individual drugs.

13.2.3. Toxic Reactions (See Sections 1.6.3 and 14.4)

13.2.3.1. The Clinical Picture

Toxic reactions, of great clinical significance, most often result from the concomitant administration of two depressant-type drugs or of opiates along with depressants.

13.2.3.1.1. Multiple Depressants (See Sections 2.2.3 and 4.2.3)

Multiple-depressant overdosage is complex because the depth of respiratory depression and the length of severe toxicity are difficult to

predict. However, the clinical manifestations are those described for the CNS depressants and for alcohol.

13.2.3.1.2. Depressants–Opiates (See Sections 2.2.3 and 6.2.3)

The concomitant administration of opiates and depressants results in unpredictable vital signs, reflexes, and pupillary reactions, along with fluctuation between stupor and semialertness.[2] The specific symptoms are combinations of those reported for the CNS depressants and the opiates.

13.2.3.2. Treatment

13.2.3.2.1. Multiple Depressants

For mixed-depressant toxic reactions, the treatment is outlined in Section 2.2.3, including acute life-preserving steps and the use of general life supports, relying on the body to detoxify the substances. Dialysis or diuresis should be reserved for extremely toxic cases. The major unique caveat is the unpredictability of the length of drug effects when multiple depressants are involved.

13.2.3.2.2. Depressants–Opiates

In the instance of combined opiate and CNS-depressant overdose, acute emergency procedures (e.g., airway and cardiac status) are again followed. Naloxone (Narcan) is administered at doses of 0.4 mg IM or IV, with repeat doses given every 5 minutes for the first 15 minutes and every several hours thereafter, as needed, for control of the respiratory depression and the degree of stupor. General supports are then continued until the body is able to destroy the drugs. These procedures are outlined in Sections 2.2.3 and 6.2.3.

13.2.3.2.3. Other Combinations

The treatment of other drug combinations is symptomatic in nature and follows the procedures outlined in the relevant drug chapters. It is worthwhile to note the importance of physostigmine when atropinic drugs (e.g., the antiparkinsonian drugs, such as benztropine [Cogentin]) are involved (Section 11.2.4.2).

13.2.4. Psychoses (See Section 1.6.4)

The drug-induced psychoses seen with stimulants (Section 5.2.4) and CNS depressants (Sections 2.2.4 and 4.2.4) are evanescent pictures, disappearing with general supportive care. Little, if any, information is available

on the psychosis produced by the multiple administration of these substances.

13.2.5. Organic Brain Syndrome (See Section 1.6.5)

Any drug in high enough doses can cause confusion and disorientation, the hallmarks of an organic brain syndrome. In drug combinations, one can expect this clinical picture to be evanescent and should follow the general treatment plans outlined in the individual chapters. However, it is wise to remember that with multiple drugs, the course is unpredictable, and it is probable that the patient will be impaired for a longer time than would be expected for either drug alone.

13.2.6. Withdrawal from Multiple Drugs (See Section 1.6.6)

The most common multiple-drug withdrawal pictures are those seen following the concomitant abuse of multiple depressants, depressants and stimulants, or multiple addictions to opiates and depressant drugs.

13.2.6.1. Clinical Picture

13.2.6.1.1. Multiple Depressants

The depressant withdrawal syndrome, described in Section 2.2.6, is similar for all CNS-depressant drugs; however, a higher incidence of convulsions is seen with hypnotics or antianxiety drugs than with alcohol. The latency of onset and the length of the acute withdrawal syndrome roughly parallel the half-life of the drugs, ranging from relatively short periods of time for alcohol to much longer withdrawals for drugs such as chlordiazepoxide (Librium) and phenobarbital. It is probably safest to treat withdrawal from the longer-acting drug most aggressively, assuming that the second depressant will be adequately "taken care of" through this approach, but keeping an open eye for any unusual symptoms.

13.2.6.1.2. Depressants–Stimulants (See Sections 2.2.6 and 5.2.6)

The withdrawal from depressants and stimulants more closely follows the CNS-depressant withdrawal paradigm but probably includes greater levels of sadness, paranoia, and lethargy than would be expected with depressants alone.

13.2.6.1.3. Depressants–Opiates

The individual withdrawing from depressants and opiates usually demonstrates an opiate-type withdrawal syndrome (Section 6.2.6) along

with heightened levels of insomnia and anxiety and a depressant-related risk for convulsions and confusion (see Sections 2.2.6 and 4.2.6).

13.2.6.1.4. Other Combinations

Withdrawal reactions for other classes of drugs either have not been proved to exist or have low levels of clinical significance. Therefore, multiple withdrawal syndromes for drugs other than depressants, stimulants, and opiates will not be discussed here.

13.2.6.2. Treatment

13.2.6.2.1. Multiple Depressants

Adequate therapy for physical addiction to multiple depressants follows the guidelines outlined in Section 2.2.6, with the added caveat that the time course of withdrawal is unpredictable.

1. Thus, it is unwise to decrease the level of administered CNS depressant at a rate faster than 10% a day, taking special care to reinstitute the last day's dose if there are increasing signs of serious withdrawal.
2. It is usually possible to carry out a smooth withdrawal from multiple CNS depressants by administering only one of those depressant drugs to the point where the symptoms are markedly decreased on Day 1.

13.2.6.2.2. Depressants–Stimulants

In the case of multiple addiction to depressants and stimulants, it is the depressant withdrawal syndrome that produces the greatest amount of discomfort and is the most life-threatening (Section 2.2.6). Thus, although there may be an intensification of some of the symptoms, it is best to proceed with the mode of treatment for depressant withdrawal.

13.2.6.2.3. Depressants–Opiates

1. In the case of addiction to CNS depressants and to opiates, it is advisable to administer both an opiate and a CNS depressant, as outlined in Sections 2.2.6 and 6.2.6, until the withdrawal symptoms have been abolished.
2. Most authors then recommend stabilization with the opiate (Section 6.2.6), while the depressant is withdrawn at 10% a day (Section 2.2.6).
3. After the depressant withdrawal is completed, opiate withdrawal can then proceed (Section 6.2.6).[2,24,25]

13.2.7. Medical Problems

The concomitant administration of two substances over an extended period of time does, in all likelihood, increase the risk of the development of

medical consequences. However, the specific problems depend on the specific drugs involved, as well as the individual's age, preexisting medical disorders, and concomitant nutritional status and experience of stress. When treating a patient misusing multiple drugs, the clinician should review the sections on medical problems in each of the relevant chapters.

One special problem is seen in those individuals whose drug abuse has occurred secondary to attempts at controlling pain, usually by misusing depressants or analgesics on a doctor's prescription. Pain syndromes that are unresponsive to the usual measures (frequently back pain and chronic headache) are very difficult to treat and not at all well understood. It is important to gather a history of any addiction and of concomitant medical complaints in evaluating any drug misuser. Following withdrawal, these identified individuals can be included as part of a polydrug or individual drug program, but they will probably also require additional care, such as that offered in specialized pain clinics.[26,27]

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CHAPTER 14

Emergency Problems: A Rapid Overview

14.1. INTRODUCTION

14.1.1. Comments

If you have come to this section of the book after reading (or at least skimming) Chapters 1 through 13, you should be ready to use this chapter as a review. If you are here because you feel that an overview of emergency problems is the most important task for you, I bid you welcome and hope that you will have a chance to go back and review the other topics in greater depth. This single chapter *cannot* review each topic in depth, and it is hoped, for instance, that you will *not* approach the toxic reaction or overdose patient without also looking at the material in the relevant subsections of the chapters on CNS depressants, opiates, and so on (e.g., see Sections 2.2.3 and 6.2.3).

The goal of this chapter is to teach some general guidelines for drug emergencies. The material is presented from a perspective different from that in the rest of the text. I have approached the problem from the standpoint of *patient symptoms*, assuming a situation in which you do not know the specific drug involved. The chapter is divided into topic areas similar to those already presented, with emergent situations ranging from panic to medical problems.

14.1.2. Some General Rules

1. By common sense, first address life-threatening problems, then gather a more substantial history and carry out other patient-care procedures, and finally, plan disposition and future treatment.[1,2] The first priority is to support respirations, maintain adequate blood pressure, aggressively treat convulsions, and establish an intravenous (IV) line.[3]

2. Avoid giving additional medications whenever possible.[1] The administration of additional drugs to an individual with a drug-related prob-

lem can result in unpredictable drug–drug interactions, made all the worse by the high level of arousal usually demonstrated by the patient. However, when there is good reason for administering medications, it is important that they be given in doses adequate to produce clinical effects.

3. It is always important to establish a complete history by gathering information from the patient *and an additional resource person,* usually a spouse. For a patient who is stuporous or out of contact with reality, the patient's belongings might contain the names of individuals able to provide accurate information.

4. Your general *attitude* and demeanor can be important, especially if you are dealing with a panicked, confused, or psychotic patient. While carrying out your evaluations, it is important that you first clearly identify who you are, that you use the patient's name when you directly address him or her, and that you consistently behave in a self-assured and (as much as possible) calm manner.[3] Reassurance can be provided through both verbal and nonverbal support, the latter including frequent eye contact.

5. Finally, it is important to review briefly how to determine the relevant drug-problem category (see Section 1.6). *First,* any patient who has taken enough of a drug to show a serious compromise in vital signs should be regarded as having a toxic reaction. In the midst of this, he may demonstrate hallucinations or delusions or may show high levels of confusion, but all of these can be expected to return to normal once the toxic reaction has been adequately treated.

Second, patients with basically stable vital signs but showing symptoms of withdrawal are labeled as drug withdrawal *even* if they show confusion and/or signs of a psychosis, as these can occur as part of withdrawal.

Third, any patient with basically stable vital signs and no obvious withdrawal, but with clinically significant levels of confusion, is regarded as having an organic brain syndrome. In the midst of this, he may demonstrate hallucinations or delusions, but these will be expected to return to normal once the OBS is adequately treated.

Fourth, an individual with stable vital signs and no clinically significant confusion or withdrawal, but shows hallucinations and/or delusions without insight, would be regarded as having a psychosis.

Thus, as is true in medicine in general, it is not only the specific signs or symptoms that are used to arrive at a diagnosis, but also the constellation or grouping of symptoms along with their time course.[4]

14.1.3. An Overview of Relevant Laboratory Tests

There is no perfect laboratory panel that should be covered for each drug emergency patient. You are best advised to follow the general rule of allowing your medical knowledge and common sense to dictate which of

the specific tests must be ordered—always making an effort to avoid unnecessary costs on the one hand, but trying to be certain that the patient's condition is adequately evaluated on the other.

Table 1.5 lists a variety of blood chemistries and blood counts that are important in many drug-related situations. In addition, you should consider a urinalysis (you will be collecting urine for a toxicologic screen anyway) to look for evidence of kidney damage or infections; a screening for the hepatitis-related Australia antigen for patients who have misused drugs IV; a chest X ray for all patients who have not received one in the last six months; a pap smear for women who have not had one in the last six months; a baseline electrocardiogram (EKG) for patients over the age of 35 and/or those who have any evidence of heart disease; a serology evaluation for syphilis; and a possible culture for gonorrhea for patients who have a history of sexual promiscuity or prostitution. A word of warning is needed regarding Table 1.5, however, because the normal values for most blood tests differ among laboratories, and the reader is encouraged to check with his own facility.[5]

A toxicologic screen on blood and/or urine should be considered in all relevant patients. Some representative toxic levels are shown in Table 14.1. Take care in interpreting negative results, however, as signs of withdrawal, OBS, psychosis, and so on may persist for up to two weeks or longer after blood and urine levels return to zero by most techniques.

14.1.4. An Introduction to Specific Emergency Problems[6,7]

Table 14.2 gives some helpful symptoms and signs that can be used in making an educated guess as to which drug was taken and the future course of problems. I must emphasize that this table allows you to establish only a *guesstimate*. The chart has not been tested in controlled investigations and therefore can be used as nothing more than a guideline.

Table 14.1
A Brief List of Relevant Blood Toxicologies

Drug	Toxic blood level	Units
Bromide	10–20	mEq/l
Chlordiazepoxide (Librium)	0.6–2.0	mg/dl
Diazepam (Valium)	0.5	mg/dl
Ethchlorvynol (Placidyl)	1.5–10.0	mg/dl
Glutethimide (Doriden)	1.0–3.0	mg/dl
Meperidine (Demerol)	100–500	μg/dl
Meprobamate (Miltown, Equanil)	5.0–10.0	mg/dl
Morphine	0.1–0.5	mg/dl
Oxazepam (Serax)	0.5–1.5	mg/dl
Phenobarbital	3–10	mg/dl

For example, if an individual comes to you with decreased respiration and pinpoint pupils, one of the first things to be considered is a toxic opiate overdose. A second example is an individual who comes with an elevated temperature; warm, dry skin; and fixed, dilated pupils: this is probably a toxic reaction involving an atropinelike anticholinergic drug.

I will now proceed with a discussion of each of the major emergency-room situations, first giving a definition, than making some generalizations about the drug state and reviewing some of the drugs that might be involved. The reader is encouraged to return to the chapters dealing with specific drugs for more in-depth discussions.

14.2. PANIC REACTIONS (See Section 1.6.1)

14.2.1. Clinical Picture

The panic reaction is identified by a patient's presenting with a high level of anxiety, usually expressing fears that he is losing control, is going crazy, is having a heart attack, or has done damage to his body. He may give a drug history and is able to maintain contact with reality in a highly structured environment. The history usually demonstrates that the patient is a naive user and that other individuals have taken the same amount of drug with no serious effects. This state is usually a benign, self-limited, emotional overreaction to the usual drug effects.[8]

14.2.2. Differential Diagnosis

Panic reactions most frequently occur with drugs that stimulate the user and change the level of consciousness: *hallucinogens, cannabis,* or *stimulants.* It is important to rule out physical disease (e.g., a genuine heart attack or a hyperthyroid state) and to consider possible psychiatric pictures, such as anxiety neurosis, obsessive neurosis, or phobic neurosis.[4]

14.2.3. Treatment

The cornerstone of treatment is reassurance, education about the drug effects, and time.

1. Carry out a quick physical examination.
2. Gather a history of recent events.
3. Give reassurance, talk to the patient as frequently as possible, and help him to orient to time, place, and person. It is best to place the patient in a quiet room, with friends or relatives available to help "talk him down."

Table 14.2
A Rough Guide to Symptoms in Drug Reactions

Symptom or sign	Reaction type	Possible drugs
Vital signs		
Blood pressure		
Increase	Toxic	Stimulants or LSD
Decrease	Withdrawal	Depressants
Pulse		
Increase	Toxic	Stimulants
	Withdrawal	Depressants
Body temperature		
Irregular	Toxic	Solvents or stimulants
Increase	Toxic	Atropine-type, stimulants, or LSD
Decrease	Withdrawal	Opiates or depressants
Respirations		
Decrease	Toxic	Opiates or depressants
Head		
Eyes		
Pupils		
Pinpoint	Toxic	Opiates
Dilated, reactive	Toxic	Hallucinogens, withdrawal, opiates
Dilated, sluggish	Toxic	Glutethimide or stimulants
Dilated, unreactive	Toxic	Atropine-type
Sclera		
Injected (bloodshot)	Toxic	Marijuana or solvents
Nystagmus	Toxic	Depressants
Tearing	Withdrawal	Opiates
Nose		
Runny (rhinorrhea)	Withdrawal	Opiates
Dry	Toxic	Atropine-type
Ulcers in membranes or septum	Chronic use	Cocaine
Skin		
Warm, dry	Toxic	Atropine-type
Warm, moist	Toxic	Stimulants
Needle marks	Chronic use	Opiates, stimulants, or depressants
Gooseflesh	Toxic	LSD
	Withdrawal	Opiates
Rash over mouth or nose	Toxic	Solvents
Speech		
Slow, not slurred	Toxic	Opiates
Slow, slurred	Toxic	Depressants
Rapid	Toxic	Stimulants

(*Continued*)

Table 14.2
A Rough Guide to Symptoms in Drug Reactions (Cont.)

Symptom or sign	Reaction type	Possible drugs
Hands		
Fine tremor	Toxic	Stimulants or hallucinogens
	Withdrawal	Opiates
Coarse tremor	Withdrawal	Depressants
Neurologic		
Reflexes		
Increased	Toxic	Stimulants
Decreased	Toxic	Depressants
Convulsions	Toxic	Stimulants, codeine, propoxyphene, methaqualone
Lungs		
Pulmonary edema	Toxic	Opiates or depressants

4. For those individuals showing lability in vital signs, bed rest is important, with carefully monitored blood pressure and pulse.
5. Avoid additional medication, but where needed, I would suggest a benzodiazepine (e.g., diazepam [Valium] at doses of 15–30 mg) given either orally or, if absolutely necessary, intramuscularly. These doses can be repeated every 1–2 hours as needed, the dose being kept as low as possible.
6. In the midst of a panic, some patients not only may be frightened but may demonstrate violence (e.g., with PCP; see Chapter 9). There are a number of general guidelines that you can follow in approaching a patient who has recently demonstrated either verbal or physical violence or who is threatening to do so.[3]
   a. Do not approach a violent patient alone; it is much better to use a number of individuals who carefully approach the patient at one time in as nonthreatening a manner as possible.
   b. Avoid any aggressive actions (e.g., sudden moves toward the patient) unless there is an immediate possibility of serious injury to the patient or to those around him. When approaching the individual, be sure that he knows who you are, reassure him that you will not harm him, and inform him of each movement you are about to make and its purpose.
   c. When making physical contact to control the patient, try to limit all movements to those that do not represent possible direct physical harm to him. Thus, you should use defensive manipulations such as holding the patient's arms and legs and rolling him in a blanket if needed.

d. Do *not* approach an armed and aggressive patient. Under these circumstances, it is usually best to call the hospital security or the police. More thorough discussions of approaching and working with violent patients are offered elsewhere.[3,9]

14.3. FLASHBACKS (See Section 1.6.2)

14.3.1. Clinical Picture

This drug-induced state involves a recurrence of feelings of intoxication some time after the initial drug effects have worn off. This is a benign, self-limited condition that rarely, if ever, represents a serious physical threat.

14.3.2. Differential Diagnosis

Flashbacks are seen primarily with *marijuana* and the *hallucinogens.* However, it is also important to take time to rule out the possibility of underlying psychiatric disorders, especially schizophrenia or affective disorder,[4] or an organic brain syndrome.

14.3.3. Treatment

The approach to this condition is straightforward reassurance and education.[8] If the person does not respond to reassurance, he may be administered an antianxiety drug such as diazepam (Valium) in doses of 10–20 mg orally, repeated as needed.[8]

14.4. TOXIC REACTIONS (See Section 1.6.3)

14.4.1. Clinical Picture

In this instance, the individual has ingested more than the usual amount of a substance and presents with an overdose. To allow for generalizations, I have, somewhat arbitrarily, distinguished in this text among a *toxic overdose,* with unstable vital signs predominating; a *psychosis,* with hallucinations and delusions in an alert individual; and an *organic brain syndrome,* where the major symptomatology is confusion and disorientation. However, the high level of overlap between these syndromes must be noted.

14.4.2. Differential Diagnosis

The serious overdoses are most likely to be seen with drugs that depress the CNS, such as *opiates, PCP,* and *depressants.* Because the treatments for

the toxic reactions of these drugs differ slightly, it is important to identify the drug involved.

There are no major psychiatric syndromes that mimic the overdose, with the possible exception of a catatonialike stupor seen with serious depression,[4] but medical disorders that can cause coma (e.g., hypoglycemia or severe electrolyte abnormalities) must be considered.

14.4.3. Treatment

The definitive treatment of shocklike states is complex and requires precise knowledge that is beyond the scope of this text. Briefly, it is necessary to address acute life supports and then to provide general patient care, allowing the body to metabolize the drug ingested.

14.4.3.1. Acute Life-Saving Measures (See References 10–18)

1. Establish the vital signs.
2. Assure adequate ventilation. This procedure includes:
   a. Straightening the head.
   b. Removing any obstructions from the throat.
   c. Carrying out artificial respiration, if necessary.
   d. Doing tracheal intubation, if necessary (use an inflatable cuff tube, if at all possible, to allow for safer gastric lavage).
   e. Establishing the patient on a respirator, if necessary. Use 10–12 respirations per minute, avoiding oxygen, as this may decrease spontaneous respirations.
   f. Maintaining an adequate circulatory state. Very briefly:
      i. If the heart is stopped, use external chest massage and administer intracardiac adrenaline.
      ii. If there is evidence of cardiac fibrillation, use a defibrillator.
      iii. If inadequate circulation is evident, an intravenous drip of 50 ml of sodium bicarbonate (3.75 gm) should be used to treat the acidic state.
3. Carry out a quick physical examination to rule out serious bleeding, life-threatening trauma, and so on.
4. Start an IV:
   a. Use a large-gauge needle.
   b. Use restraints, if necessary, to make sure that the needle will stay in place.
   c. Use a slow IV drip until the need for intravenous fluids has been established.[10]
5. Aggressively control convulsions, protecting the patient from aspiration by placing him on his side with (if possible) his head

slightly extended over the side of the table. Maintain ventilation, be certain that an adequate IV line has been started, and loosen clothes. In most instances a single seizure or a limited number of seizures will occur, but repeated convulsions (i.e., status epilepticus) require aggressive treatment with IV diazepam (e.g., slow infusion of 10 mg, which can be repeated in 20 minutes if necessary) or (less preferred) phenytoin, 600–1000 mg IV, given in 100-mg boluses, or even with general anesthesia.[3] The proper control of convulsions is not covered in detail here, and the reader is referred to general medical texts and emergency manuals.[12]

6. Draw blood for chemical analysis:
   a. 10 cc, at a minimum, is needed for a toxicologic screen.
   b. 30–40 cc is necessary for the usual blood count, electrolytes, blood sugar, and BUN.
7. If there is any chance that the individual is hypoglycemic, administer 50 cc of 50% glucose IV.
8. An EKG or rhythm strip is especially important because of the cardiac irregularities that may be seen with nonbarbiturate hypnotics.[11–13]
9. For recent ingestions, induce vomiting or carry out gastric lavage[3,11]:
   a. Do not do this until the heart rate is stable, to avoid inducing a clinically significant vagal response and subsequent cardiovascular problems.
   b. For the awake and cooperative patient, emesis can be induced with syrup of ipecac, which is given as 10–30 mg orally and repeated once in 15–30 minutes if vomiting does not occur. Some patients require one glass of fluids (e.g., water or saline) to distend their stomachs slightly to allow them to vomit. Take care not to give ipecac and activated charcoal at the same time, as the latter will block the effects of ipecac.
   c. If the patient is not awake and cooperative or if emesis does not work, carry out gastric lavage. For sleepy or comatose patients, lavage only after tracheal intubation. Use an inflatable cuff to prevent aspiration.
   d. Gastric lavage should be carried out only on individuals who have taken drugs orally within the last 4–6 or, at most, 12 hours. The longer period of time is especially important with PCP, as this drug may be recycled and excreted in the stomach for more than 6 hours after the actual ingestion. Lavage should *not* be carried after individuals have also ingested corrosives, kerosene, strychnine, or mineral oil.

e. For adults, a nasogastric tube is usually used, and the patient is placed on his or her left side with the head slightly over the edge of the table.
f. After evacuating the stomach, administer an isotonic saline lavage until the returned fluid looks clear. It is preferable to use small amounts of fluid so as to not distend the stomach and increase the passage of the drug into the upper intestine. Lavage may be repeated 10–12 times, and it is best to save the washings for drug analyses.
g. Consider administering activated charcoal or castor oil (60 ml) to help stop absorption. The castor oil is especially important for lipid-soluble substances such as glutethimide (Doriden).

10. Collect urine if possible—this may require catheterizing the bladder. Send 50 ml of the urine for a toxicologic screen.[6]
11. If the patient's blood pressure has not responded, you may use plasma expanders or pressors as for any shocklike state, taking care to titrate the needed dose and being aware of any potentially life-threatening drug interactions.
12. If there is a chance that the overdose includes an opiate, administer a test dose of naloxone (Narcan)[14] in doses of 0.4–0.8 mg (1–2 ml) IM or IV, as discussed earlier (Section 6.2.3.2). However, it is important to beware of precipitating a severe opiate withdrawal syndrome—this would usually be treated with reassurance and readministration of a mild analgesic, such as propoxyphene (Darvon), or with methadone (Section 6.2.6.2).
13. If the overdose appears to involve an atropinelike (anticholinergic) drug as indicated by a rapid heart rate, dry skin and mouth, a rash, and so on, consider giving physostigmine, 1–4 mg, by slow IV injection.

14.4.3.2. Subacute Treatment

1. Establish the vital signs every 15 minutes for at least the first 4 hours; then monitor carefully (perhaps every 2–4 hours) over the next 24–48 hours, even if the patient's condition is improved. Many of the substances (e.g., the fat-soluble hypnotics like glutethimide [Doriden] or ethchlorvynol [Placidyl]) clear from the plasma temporarily and are then rereleased from fat stores, causing severe reintoxication after the patient has apparently improved. Also, for opiate overdoses, the antagonists are active only for a relatively short period after administration.
2. Carry out a thorough physical examination, with special emphasis on the status and changes in neurologic signs.[10,13]

3. Gather an intensive history from the patient and a resource person, such as the spouse.
4. Establish a flow sheet to monitor vital signs, medications, fluid intake, fluid output, and so on.[10]
5. Establish a baseline weight that can be used as a guide to fluid balance.[11]
6. Dialysis or diuresis is rarely needed[15]:
   a. If you choose to carry out diuresis, you may use furosemide (Lasix) in doses of 40–100 mg, administered regularly to maintain a urinary output of approximately 250 ml per hour. Of course, it is very important to replace electrolytes and fluids.[11]
   b. Diuresis can also be carried out through the careful administration of enough intravenous fluids to maintain a urinary output in excess of 200 ml/hr using half-normal saline with potassium supplementation (Section 2.2.3.2).
   c. Dialysis is effective for almost all nonbarbiturate sedatives.[11] If available, hemodialysis is preferable to peritoneal dialysis, as the former tends to be more efficient and has less chance of decreasing respiration.

      The indications for dialysis include severe intoxication with markedly abnormal vital signs; report of the probable ingestion of a highly lethal dose of the drug; blood levels of the drug in the lethal dose range; impaired excretion or metabolism of the drugs due to liver or kidney damage; progressive clinical deterioration; prolonged coma; and underlying lung disease. Once again, it is important to emphasize that most overdose patients will recover completely without dialysis or diuresis.
7. Avoid administering any medications unless absolutely necessary.
8. If the patient is comatose, take the steps necessary for adequate care, including careful management of electrolytes and fluids, eye care, frequent turning of the patient, and careful tracheal toilet.

14.5. PSYCHOSIS (See Section 1.6.4)

14.5.1. Clinical Picture

Psychosis is a loss of contact with reality, which, as discussed in this text, occurs in the midst of a clear sensorium. The patient usually presents with hallucinations (most frequently auditory) and/or delusions (usually persecutory). Although clinically very dramatic, this is usually a self-limited problem, running its course within a matter of days to a week for most drugs (exceptions are STP and PCP).

14.5.2. Differential Diagnosis

Any psychiatric disorder capable of producing a psychotic picture, especially schizophrenia, mania, an organic brain syndrome, or depression, must be considered a part of the differential diagnosis.[4] The drugs most frequently involved in psychoses are *alcohol,* the other *CNS depressants, stimulants,* and (as part of a toxic reaction) perhaps *PCP.*

14.5.3. Treatment

The major goal is to protect the patient from harming himself or others, or from carrying out acts that would be embarrassing or would cause later difficulties. At the same time, it is important to review the problems adequately, so as to rule out other serious medical and psychiatric disorders. The patient presenting with a hallucinating/delusional state, therefore, usually requires hospitalization until the delusions clear.

14.6. ORGANIC BRAIN SYNDROME (See Section 1.6.5)

14.6.1. Clinical Picture

The organic state can be caused by high doses of any drug and consists of confusion and disorientation along with decreased general mental functioning. This reaction may be accompanied by illusions (misinterpretations of real stimuli, such as shadows or machinery sounds), hallucinations (usually visual or tactile), or delusions.

14.6.2. Differential Diagnosis

Any drug can cause an organic brain syndrome, but in clinical practice, this problem is most likely to be seen with *CNS depressants, atropine-type drugs, solvents, stimulants,* and *phencyclidine* (PCP).[19,20]

Whenever organicity is observed, it is important to consider the possibility of acute or chronic brain damage, trauma, vitamin deficiency, or serious medical problems that might disrupt electrolytes. If these medical disorders are overlooked, a life-threatening condition can ensue.

14.6.3. Treatment

The treatment consists of general life supports. Because this problem is either a minor toxic reaction or the early stage of a serious overdose, the treatment is identical to that outlined above for the relevant toxic reaction. Although most organicities disappear within a matter of hours to days,

some secondary OBS pictures caused by vitamin deficiencies or traumas can take many months to clear (see Section 4.2.5).

14.7. DRUG WITHDRAWAL STATES (See Section 1.6.6)

14.7.1. Clinical Picture

A sudden cessation or a rapid decrease in the intake of any of the drugs capable of producing physical dependence can result in the withdrawal state. This, simplistically, is manifested by anxiety, a heightened drive to obtain the drug, a flulike symptom, and physiological symptoms that are usually in the direction opposite to those expected with intoxication.

Withdrawal from drugs is rarely life-threatening (with the possible exception of the CNS depressants) unless the patient is allowed to go through it in a seriously impaired physical state.

14.7.2. Differential Diagnosis

It is important to determine whether the withdrawal state is related to *stimulants*, *depressants*, or *opiate analgesics*, as the specific treatments differ greatly. It is also necessary to rule out the physiological disorders that can result in a flulike syndrome and to implement proper medical treatment.

14.7.3. Treatment

In addition to recognizing and treating all concomitant medical disorders, offer reassurance, rest, and good nutrition.

1. Carry out a good physical examination, taking special care to rule out infections, hepatitis, subdural hematomas, heart failure, and electrolyte abnormalities. A patient entering withdrawal with impaired physical functioning has a markedly increased chance of dying during the withdrawal. Also, if any physiological abnormality is overlooked at the inception of withdrawal, it may be difficult, as the abstinence syndrome progresses, to tell whether abnormal vital signs are a response to the withdrawal or represent other physical pathology.[21,22]

2. Specific treatment of the withdrawal depends on a recognition of the fact that the symptoms have developed because the drug of addiction has been stopped *too quickly*. Therefore, the basic paradigm of treatment is giving enough of the drug of addiction (or one to which the individual has cross-tolerance) to greatly diminish the withdrawal symptoms on Day 1. This drug is then decreased by 10%–20% of the initial day's dosage each day over the subsequent 5–10 days.

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CHAPTER 15

Rehabilitation

15.1. INTRODUCTION

This chapter serves as an introduction to the concept of rehabilitation for alcoholism and drug abuse rather than a definitive discussion of all aspects of care. It can be read for general knowledge, for guidelines to the appropriate referral of patients, as a framework for the critical evaluation of programs, or as a basis for the development of your own treatment efforts. I will first present a series of general rules that (with modifications) fit rehabilitation for all substance misusers. These are followed by a discussion of guidelines specifically tailored to particular drug approaches.

15.1.1. Some General Rules

The same basic guidelines apply to all types of rehabilitation efforts with substance misusers. Each is given only briefly below, and most are discussed in more detail in the subsections on alcohol and drug rehabilitation (Sections 15.2 and 15.3).

15.1.1.1. Justify Your Actions

Our patients, coming to see us in the midst of crises, may be prepared to "do almost anything" to make things improve. All substance-abuse problems tend to fluctuate naturally in intensity, with the result that one can see improvement with time alone.[1] There is also a considerable rate of "spontaneous remission" with no intervention at all. The key questions to be addressed in judging any treatment are "Did the improvement occur *because* of the treatment?" and "Were the therapeutic efforts those with the greatest chance of success?"[2] The therapist must constantly justify his actions, both in a financial cost–benefit framework and in a manner that considers patient

and staff time, physical or emotional dangers to the patient, and the trauma of separation from job and family.

15.1.1.2. Know the Natural Course of the Disorder

It is only through knowledge of the probable course of drug misuse that one can make adequate treatment plans.[3,4] The usual course of alcoholism is discussed in Chapter 3.

15.1.1.3. Guard against the Overzealous Acceptance of New Treatments

Most treatment efforts "make sense" in some theoretical framework; and most patients improve, and many get "well," no matter what treatment is used. This improvement can be the result of the fluctuating nature of the disorder and of spontaneous remission. Therefore, demand good, controlled investigations before accepting newer treatment approaches as valid.

15.1.1.4. Keep It Simple

In evaluating treatment efforts or accepting new therapies, a sensible approach is to stay with the least costly, least potentially harmful, and simplest maneuvers until there are good data to justify more complex procedures.

15.1.1.5. Apply Objective Diagnostic Criteria

It is not enough to accept a patient into a program because he or she appears at the door of a treatment center. In order to apply knowledge of the natural course and to predict future problems, as well as to justify treatment efforts, standard diagnostic criteria must be applied to each patient.[5] An individual may, however, be labeled "ill but undiagnosed" and given a tenuous set of working diagnoses; may be given a "probable" diagnosis and treated as if he or she had a definite disorder but with extra care taken to reevaluate the label at a future date; or may be given a definite diagnosis. Of course, all patients must be evaluated for major preexisting psychiatric disorders requiring treatment or affecting the prognosis (e.g., primary affective disorder or primary antisocial personality, as described in Section 3.1.2.3).

15.1.1.6. Establish Realistic Goals

In substance misuse, we rarely achieve "dramatic cures." I attempt to maximize the chances for recovery, to encourage abstinence at an earlier age than might have been achieved with no therapeutic intervention, to offer good medical care, to help the people close to the patient better under-

stand what is going on, and to educate patients so that they can make their own decisions about treatment goals. Although health care practitioners can and must offer their best efforts, the patient's motivation and level of "readiness" for recovery have a great impact on outcome.

Different therapeutic interventions have different goals. For instance, a detoxification facility established in a skid row area attempts to offer the best possible medical care and general supports. However, although the treatment personnel will try to encourage abstinence, the 10% rate of probable abstention 12 months later for skid row alcoholics does not justify this as the primary goal of treatment. On the other hand, an alcoholic rehabilitation program established in industry or with married and working patients does focus on rehabilitation as two-thirds of the patients are likely to be dry a year later, and most abstinent alcoholics will be functioning as well as their nonalcoholic peers.[2,5,6]

15.1.1.7. Know the Goals of Your Patients

In establishing patient goals, it is important to understand the patient's reasons for entering treatment: Was it to detox only? To meet a crisis? Or actually, to aim at long-term abstinence?

15.1.1.8. Make a Long-Term Commitment

Because there is no "magic cure" in these areas, recovery is usually a long-term process that requires some counseling and therapeutic relation for at least six months to a year.

15.1.1.9. Use All Available Resources

The patient's substance-abuse problem does not occur in a vacuum. Part of the therapeutic effort should be directed at encouraging the family and, if appropriate, the employer to increase his or her level of understanding of the problem; to be available to help you whenever necessary; to make realistic plans for themselves as they relate to the patient; and, in specific instances, to function as "ancillary therapists," helping to carry out your treatment efforts in the home or job setting.

15.1.1.10. When Appropriate, Notify All Involved Physicians and Pharmacists

When dealing with a substance misuser who is obtaining drugs from physicians or pharmacists, it is my *bias* to make all possible efforts to cut off the patient's supply. This must be done with tact, understanding, and empathy for the ego of the prescribing physician or the dispensing pharmacist

involved and with the patient's permission, to avoid infringing his legal rights.

15.1.1.11. Do Not Take Final Responsibility on the Patient's Actions

Although I do everything within my power to help, in the final analysis the decision to achieve and maintain abstinence is the patient's responsibility. If I do not follow this rule and the patient stops only to please me, he will soon find an excuse to get angry with me and return to alcohol and/or drugs.

15.1.2. A "General" Substance-Abuse Treatment Program

If we recognize that there are patients in need, that money is available for care, and that there is a great deal of pressure to "do something now," it is possible to establish a rehabilitation program that will *probably* do the most good with the least harm. I emphasize the probable nature of my recommendations, as adequately controlled investigations have rarely been carried out to test even the most basic assumptions in rehabilitation. The *usual* rehabilitation program would[2]:

1. Attempt to accomplish three basic goals:
   a. Maximize physical and mental health as patients will find it difficult to achieve abstinence if chronic medical problems have not been adequately treated.
   b. Enhance motivation toward abstinence through educating the patient and his family about the usual course of the disorder, employing appropriate medications to stop the patient from returning to substance misuse on the spur of the moment (e.g., disulfiram [Antabuse] for alcoholics and opiate antagonists like noroxymorphone [Naltrexone] for drug addicts), and using such behavior modification approaches as aversive conditioning.
   c. Help the patient to rebuild a life without the substance through vocational and avocational counseling, family counseling, helping him develop a substance-free peer group, showing him how to use free time, and so on.
2. Whenever possible, use outpatient rehabilitation over inpatient, as the former costs less and teaches the patient how to adjust to a life without the substance while he is functioning in the "real world."[7] Candidates for inpatient rehabilitation include patients who have not responded to outpatient counseling, those with medical or psychiatric problems serious enough to warrant hospitalization, and those patients whose lives are in such chaos that it is difficult or impossible to deal with them on an outpatient basis.

3. If inpatient rehabilitation is used, keep it as short as possible (usually less than two to three weeks), as longer inpatient care and other more intensive interventions have not been demonstrated to be more effective than short-term care for the average patient if the shorter course is followed by 6- to 12-month aftercare.[1,8–11]
4. Avoid using most medications in the treatment of substance misuse after withdrawal is completed. Possible exceptions are disulfiram (see Section 15.2.4.1.5) for alcoholism and methadone for opiate abuse.
5. Use group more than individual counseling, as the former costs less and is probably equally effective.
6. Use self-help groups such as Alcoholics Anonymous, as they can be quite helpful while costing nothing. They offer the patient a model that may be important in his achieving and maintaining recovery.
7. Recognize that there is no evidence that specialized and expensive forms of psychotherapy (e.g., gestalt or transactional analysis) are any more effective than general "day-to-day" life counseling for the substance misuser.
8. Maintain continued contact with the patient for at least 6–12 months. All efforts should be used to decrease attrition; for example, letters noting your desire to continue to help and/or phone calls should be used to try and get patients to come back after they have missed even just one aftercare or outpatient counseling session.[12]
9. Use nondegreed (paraprofessional) counseling staff supervised by people with more formal training in counseling, as there is little evidence that treatment must be carried out by individuals with advanced degrees in order to be successful.

15.2. A SPECIAL CASE: ALCOHOLISM

Because alcohol is the most common substance of abuse, I will use it as the prototype for my discussion of all other types of rehabilitation. I assume that you have already reviewed Chapter 3 and recognize that the average alcoholic is a middle-class man or woman with a family, who comes into your office with general complaints and is unlikely to appear in a state of intoxication or withdrawal. The diagnosis is made by recognizing that one in five patients are alcoholic and through observing the pattern of medical problems (e.g., mild hypertension; cancers of the esophagus, stomach, or head and neck; or impotence) and the pattern of psychological problems (e.g., depression, anxiety, or insomnia) most closely associated with alcoholism. Diagnosis will be aided by carefully observing the pattern of laboratory results, especially mild elevations in the mean corpuscular volume, uric acid, triglycerides, and gamma glutamyl transferase.[6] With

be carried out in either an inpatient or an outpatient mode, with inpatient care preferred for individuals who demonstrate any type of serious medical difficulties and those who have had withdrawal seizures in the past, as well as for elderly or debilitated patients (see Section 4.2.6). Finally, rehabilitation in either an inpatient or an outpatient mode must be followed up with extended aftercare for 6–12 months for all patients.

15.2.1. Confrontation of the Alcoholic

The pattern of laboratory tests, physical findings, history of life problems, and information gathered from family members may help you to recognize the alcoholic. Once this is accomplished, the next step is confronting the patient in an attempt to help him or her recognize the problem and to act on that recognition.

The patient is responsible for his or her actions; your responsibility is to do all that is possible to raise his level of motivation. Whether your efforts "take" or not may be beyond your control.

A first step in confrontation is to utilize the patient's area of concern and to demonstrate to him how alcohol ties in. For instance, you can confront an individual coming in complaining of just "not feeling well" or of insomnia, impotence, high blood pressure, and so on by telling him that he has good reason for concern. You might then go on to share the relevant laboratory tests and physical findings, and to state, "There is one way I have of pulling all of these findings together. I believe you have reached a point in life where alcohol is causing more trouble than it's worth."

Next, you might teach him about the difficulties he can expect in the future unless he stops drinking. It may not be necessary at this point to use the term *alcoholism;* rather, in this initial confrontation, alcohol-related life problems can be the focus.

Next, discuss the probable future course of the alcohol-related problems and explore possible avenues for treatment. If he accepts help, determine if detoxification is required, and either begin counseling or refer him to an adequate alcohol-treatment facility (either outpatient or inpatient) or use Alcoholics Anonymous.

Many patients will not respond to your initial confrontation with glee. Most individuals recognize somewhere deep inside that they are having alcohol-related problems, but they have been aggressively denying it both to themselves and others. The individual who refuses to respond to your first confrontation might best be told that you understand his disagreement but that you need to evaluate some things further and that he should return to you in several weeks (you hope that in the interim, he will decrease his level of denial and be more likely to cooperate). If he refuses to come back or continues to deny problems at the next visit, I do all I can to "leave the door open," telling him that I am willing to continue to treat him for general

problems and will do all I can to maximize his level of functioning despite his alcohol-related difficulties. I will warn him, however, that I will not be able to treat his medical and psychological problems adequately until he stops drinking. I thus hope that he will see me as a reasonable and caring physician and that he will return to me as his alcohol problems escalate. To try to maximize the chance that he will come back, I generally arrange with the patient for a "checkup" at least every three months.

Some patients respond to the initial (or 17th) confrontation by admitting that alcohol might be a problem and that they should "cut down." As is apparent in the natural history of alcoholism outlined in Chapter 3, cutting down is not usually a problem: it is staying cut down that becomes so difficult. I do all I can to dissuade the patient from this path, but if he resists, I set up a meeting with the patient and his or her significant other (e.g., usually the spouse). Here, I continue to try to discourage "controlled drinking," pointing out that it is not likely to work for any period of time, but I will yield if the patient insists. Next, I establish a regimen that, if followed, will stop the patient from ever becoming intoxicated. For instance, the patient's intake of alcohol should be limited to two drinks per 24 hours; a drink is defined as 12 oz of beer, 4 oz of nonfortified wine, or 1½ oz of 80-proof beverage. Twenty-four hours is also defined as a magical clock that begins from the time he takes his first sip of a beverage. Almost inevitably, drinking escalates, problems occur, and I hope that the patient will come back to me for help.

It can be seen that confrontation is rarely a "one-shot" phenomenon. Rather, my attempts to increase motivation frequently involve multiple contacts with the patient (always keeping the responsibility for his behavior with him and not me), outreach to the family, and various stages of general support, until the patient finally decides not to drink. Once the patient has agreed to abstinence, I then evaluate the need for detoxification (see Section 4.2.6) and enter him in either an outpatient or an inpatient rehabilitation program. Attempts to rehabilitate alcoholics consist of long-term contact aimed at enhancing motivation and increasing the ease of readjustment to life without alcohol.

15.2.2. Enhancing Motivation

These maneuvers are used during confrontation and on through rehabilitation in either the outpatient or the inpatient mode. The steps in this area include:

1. Educating the patient and his family about the natural course of alcoholism and the problems they can expect in the future.

2. Emphasizing the patient's responsibility for his own actions. For example, the family should never protect the patient from the actions of his drinking by putting him to bed when he is drunk (they should let him fall

asleep in front of the television set and go up to bed themselves) or rescuing him from jail (he should spend the evening in jail if necessary). In your interactions any "Yes, but . . ." should be met with "You can make decisions about what you wish to do and the consequences you wish to accept."

3. Motivating the patient toward abstinence can be enhanced through the use of drugs that make it difficult for the patient to return to drinking on the spur of the moment (e.g., Antabuse, as described below in Section 15.2.4.1.5). Motivation is also helped through establishing a conditioned reflex that causes the smell or taste of an alcoholic beverage to precipitate nausea or vomiting (as described below in Section 15.2.4.1.4).

15.2.3. Helping Patients to Readjust to a Life without Alcohol

By the time you have established a diagnosis, the average alcoholic has been having serious life problems for 10–20 years or more. Once he has entered rehabilitation, he has recognized (on some level) that alcohol is causing more troubles than it is worth and has agreed to stop drinking. However, because alcohol has been such a central part of his life for so long, there are many life situations that decrease his chance of continued abstinence. These must be carefully addressed.

Alcohol treatment programs utilize group counseling for the patient and for the family, vocational rehabilitation for the patient, sessions that center on the proper use of free time, and the establishment of a peer group who are abstinent.[6,15] They also do everything else they can to enhance a smooth readjustment to life without alcohol. These programs may be begun in an inpatient setting, but the day-to-day emphasis on group counseling should continue for many months in an outpatient or aftercare mode, so that the patient can receive support and counseling while he is actually attempting to function in his real-life situation.

15.2.4. Treatment Programs

15.2.4.1. Inpatient Treatment

If patients fulfill the criteria for inpatient rehabilitation outlined in Section 15.1.2, you will choose either to hospitalize them yourself or to refer them to an established program. Either way, there is no single best way to treat the alcoholic. Rather, because of the general helping nature of rehabilitation, most patients are offered programs with multiple components aimed at enhancing motivation and increasing the ease of readjustment to a life without drinking.

Selection of an inpatient or an outpatient treatment mode is based on the preferences of the patient or client and his family, financial considerations, and your prior experiences. Although there are no absolute indications for hospitalization after detoxification, patients with serious medical

or emotional problems, or those who face severe crises, will probably function best in a structured environment. Also many health-care deliverers feel that a short "time-out" from life stresses is an important part of treating the average alcoholic.

There are no data to support hospitalization of more than two or three weeks for the *average* patient.[9,10,15,16] Of course, common sense dictates that individuals with severe medical problems or persistent organic brain syndromes and those with very unstable life situations might require longer care. It is important, however, to recognize the potential dangers associated with inpatient care, which include risks of treatment-center-acquired infections, physical or emotional harm by patients or staff, loss of income or loss of job, embarrassment among peers, and family dissolution through separation at a time of crisis. In addition, the patient is treated in an artificial environment where the lessons learned may not readily generalize to everyday living.[7,15] Although inpatient care is a potentially important part of the rehabilitation spectrum, final decisions should depend on a calculated balance between the negative and the positive aspects of any program.

15.2.4.1.1. The Facility

Good alcoholic detoxification and rehabilitation can be carried out in an established alcoholic program or on a general medical ward,[17] the latter being especially important when you are dealing with a patient who has serious medical problems or who refuses care from anyone other than his primary physician. In such instances, the primary treatment is medical, but the counselor can work with the treatment staff to carry out adequate detoxification, if needed, and to enhance the patient's receptivity to rehabilitation.

In a similar manner, the relatively rare patients with primary affective disorder and secondary alcoholism (see Section 3.1.2.3.) are best treated by a psychiatrist. If these patients have active suicidal ideation, care should be given in a psychiatric facility, where suicide precautions can be observed. After detoxification, active pharmacological treatment of the affective disorder can be carried out. For patients presenting with depressions who have no histories of manias, this usually entails the same treatment given any patient with unipolar affective disorders, usually tricyclic antidepressants. Patients who have both manias and depressions respond best to lithium. The reader is referred to some excellent reviews of the proper use of medications in primary affective disorder.[18,19] The data to date, however, do *not* justify the routine use of antidepressants or lithium in the average primary alcoholic.

The very rare secondary alcoholic with process schizophrenia[18] will require relatively high doses of antipsychotic medications such as chlor-

these points in mind, this section reviews general treatment philosophy, confrontation, and rehabilitation.

In order to maximize the resources available to reach the maximal number of patients, I emphasize outpatient rehabilitation. This costs 5 to 10 times less than inpatient care and may be just as effective.[7]

Even within inpatient approaches, the types of intervention offered should follow the general rules offered in Section 15.1.2, as the most direct and least complex schemes may even be superior to the more costly.[8] Figure 15.1 gives a *simplified* flow of patient problems. The diagnosis is established from the history given by the patient and his family as well as from the physical examination and the laboratory tests. Once you decide that the patient is an alcoholic, you next face the decision about detoxification, remembering that your missing potentially important withdrawal signs may cause the patient to lose faith and drop out of treatment. Detoxification can

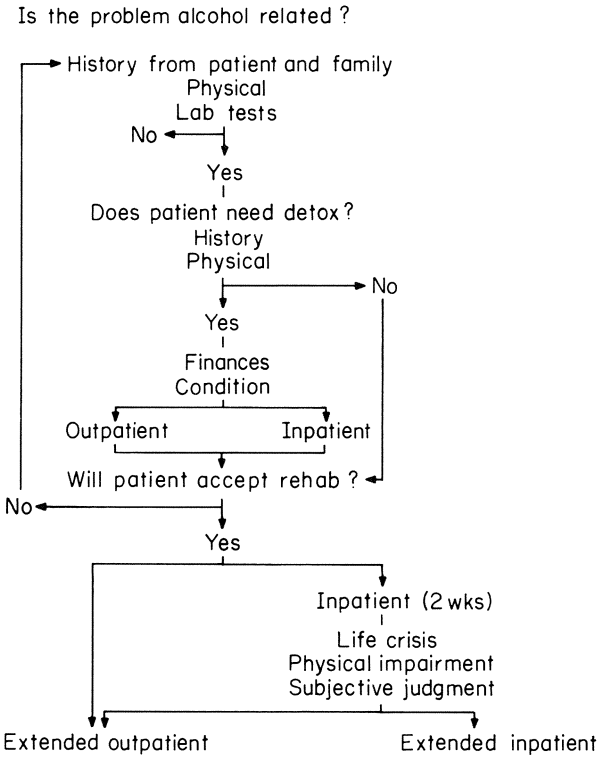

Figure 15.1. Discussions in alcoholism treatment. From Schuckit, M. A. Treatment of alcoholism in office and outpatient settings. In J. H. Mendelson & N. K. Mello (Eds.), *Diagnosis and Treatment of Alcoholism*. New York: McGraw-Hill, copyright © 1979. Reprinted with permission of the McGraw-Hill Book Company.

promazine (Thorazine). The clinician must take special care not to misdiagnose alcoholic psychosis as schizophrenia (see Section 4.2.4).

For patients without serious medical or psychiatric problems, the specific facility can be chosen with other considerations in mind. As it is the characteristics of the patient rather than of the treatment program that best predict outcome, a particular facility can be chosen considering the eventual financial cost, convenience to the patient, and other patient-care–related issues. Usually, a treatment program established in a freestanding facility located near a hospital can offer many of the same benefits as a hospital-based inpatient program and may (because of decreased overhead) be carried out with less cost.

15.2.4.1.2. The Daily Schedule

Rehabilitation includes offering good education, counseling for the patient *and his family,* and a long-term commitment to help with life adjustment. The usual inpatient schedule offers daily educational lectures and/or films, along with daily counseling and "rap" sessions, and, in some centers, behavior modification therapy. Most programs favor a busy daily schedule.

15.2.4.1.3. Counseling or Psychotherapy

The patient usually meets daily with a counselor in a group setting to clarify life adjustment issues and to set the stage for outpatient follow-up visits. The family should be included in some sessions to help them deal with the life problems and to increase their level of understanding of alcoholism.

Therapy generally centers on the "here and now" of the patient's life, giving him a chance to discuss his adjustment to a life without alcohol and to the stresses of job, friends, and family. The focus is on the reactions of those around him and on how to handle the situations in which he is most likely to return to drinking.[20] In addition, lecture/discussion sessions can emphasize the dangers of alcohol and help the patient to understand the course and effects of his disease. Along with other forms of therapy, patients should be encouraged to take part in Alcoholics Anonymous (AA).

Comparisons of group and individual psychotherapy for alcoholism reveal that group therapy is as effective.[20,21] Some authors may feel that group therapy has specific *advantages,* such as allowing the patient to share his feelings with a number of other people and teaching him social skills.[22] However, there is little hard evidence to back up this belief. The group session is an excellent place to begin an interdisciplinary approach,[23] with the psychiatrist or psychologist being used primarily to supervise other therapists.

15.2.4.1.4. Behavioral Approaches

Many alcoholism treatment programs use some form of behavioral approach in dealing with their patients. This may include the offering of supports like biofeedback to help with anxiety and sleep problems, teaching the patient how to relax and handle stress. Another behaviorally oriented intervention, assertiveness training, is based on the premise that in the midst of their alcoholism (or perhaps because of some original problem existing before the alcoholism began), most patients do not learn how to express their desires and frustrations.[24] The training sessions usually involve education about recognizing situations in which resentment occurs and practicing a variety of methods for handling them.

Some programs utilize behavioral approaches as a core resource in the treatment of alcoholism. The behavioral modification procedures are usually added to the regular education and counseling as previously described.[15,21] Most often, this treatment involves attempts to "teach" the patient *not* to drink through coupling the sight, scent, or taste of alcohol with an unpleasant event, such as vomiting or receiving a mild electric shock to the skin.[25] Chemical aversion treatments, aimed at inducing vomiting in the presence of alcohol, usually utilize such substances as emetine or apomorphine and are generally felt to be more effective than electrical aversion. These treatments are usually offered in hospitals that have special experience with them, and controlled studies indicate that the approach is as effective as any other in dealing with alcoholism. Although it is possible that a specific type of patient responds preferentially to behavioral interventions, there are no data to help us choose those individuals.

One modification of the electrical aversion treatment attempts to teach alcoholics how to drink in a moderate, controlled manner. This approach may have some potential, but at present, there are *no* data to justify its use in any clinical setting.[25,26] Use outside the experimental laboratory must await clear demonstration that the assets of such a treatment outweigh the liabilities.

15.2.4.1.5. Medications

1. It is important to remember that any treatment (especially medications), when given as part of uncontrolled clinical evaluations, can appear effective; but in reality, it may be no better than placebo.[27] Therefore, with the possible exception of disulfiram (Antabuse) and vitamins, I tend to use *no* medications in treating the detoxified alcoholic.

2. Sleeping pills and antianxiety drugs, even though the patient may demand them, have *no place* in alcoholic *rehabilitation* (after withdrawal is

completed). These drugs have dangers of addiction, adverse reactions with other depressant drugs such as alcohol, and, for most hypnotics, the potential for overdosage.

I use a special approach in dealing with complaints of insomnia and/or anxiety in alcoholics. First, I let them know that I understand the intensity of their discomfort and that I will try to help them. Second, I tell them that many of their problems are a physiological response to the long-term self-administration of a brain-depressing drug and that these physical changes will persist for up to six months, although at decreasing intensity. Third, I emphasize that sleeping pills or antianxiety drugs might help them for a week or two but will then make their problems worse, and that we will inevitably have to face the day when their bodies must adjust to living without CNS-depressing medications.

To help them deal with their sleep difficulties, I prescribe a regimen of going to bed at the same time every night (reading or watching television, if needed) and awakening at the same time every morning, even if they have had only 15 minutes of good sleep. This regimen is coupled with a rule against caffeinated beverages after noon and against naps during the day. All of these combine to force the patient's sleep cycle into a more normal pattern after several days. Problems with anxiety are handled with similar types of explanation and a search, carried out jointly with the patient, to find nonmedicinal avenues for release of tension. Possibilities range from church work, to developing a hobby, to learning to play a musical instrument, to yoga, to physical exercise, and so on.

3. Disulfiram (Antabuse) is a promising drug for the treatment of the alcoholic, but this substance has dangers and cannot be given to patients with serious medical disorders.[28] Although Antabuse does not decrease the "drive" to drink, the patient's knowledge of a possible severe physical reaction following drinking while on Antabuse is associated with an improved recovery rate.[15,28–30] The drug is given orally, usually at a daily dose of 250 mg, over an extended period of time, perhaps up to a year.

Disulfiram works by causing a nonreversible destruction of aldehyde dehydrogenase, the enzyme responsible for the metabolism of acetaldehyde, the first major breakdown product of ethanol (see Section 3.2). As a result, after drinking, acetaldehyde builds up in the blood. The intensity of the disulfiram–ethanol reaction depends on the blood-alcohol level (thus, the amount and the rapidity of drinking), as well as on some as yet not-well-understood individual characteristics of patients.

In the midst of a reaction, the most frequent symptoms include facial flushing, palpitations and a rapid heart rate, difficulty breathing, a possibly serious drop in blood pressure, and nausea and vomiting. The most usual reaction begins within minutes to a half hour after drinking and may last

30–60 minutes. Once it has begun, no specific mode of treatment is available, and most authors advocate general supportive care, antihistamines (to block the effects of acetaldehyde-mediated histamine release), vitamin C (to enhance acetaldehyde oxidation), and possibly 4-methylpyrazole (to stop the production of acetaldehyde) in doses of 7 mg/kg IV.[30,31] Although a relatively healthy individual is likely to tolerate the ethanol–disulfiram interaction well, it could be quite dangerous for individuals with a history of serious heart disease, stroke, serious hypertension, or diabetes. Disulfiram should not be prescribed for those individuals.

As is true of all treatments of alcoholism, the efficacy of this approach is difficult to prove. Controlled studies comparing disulfiram prescription with no drug prescription show a higher rate of abstinence with disulfiram. However, other studies comparing disulfiram with a placebo have not shown a convincing superiority of the active drug. Thus, the clinician is placed in a dilemma, because if a placebo is prescribed to all alcoholic patients, eventually no one will believe that he is getting the active drug, and any placebo effect (i.e., fear of a reaction when he drinks) will be lost.

Another difficulty with disulfiram is the need to take the drug daily. Investigators are currently working on the development of a long-lasting implant, but present methods have not been successful in maintaining adequate blood levels of the drug.[32] Finally, Antabuse is *not* an effective agent for aversive conditioning, because the time lag between the ingestion of alcohol and the reaction is often up to 30 minutes, and the intensity of the reaction is unpredictable.

15.2.4.2. Outpatient Programs

Although you may be offering alcoholic rehabilitation yourself, there are also a variety of outpatient programs available for referral. These range from private care, to clinics, to the outpatient extensions of inpatient programs. One valuable information resource is the National Council on Alcoholism (NCA) (usually listed in the telephone book), which in most urban areas will act as a referral source. Many communities also have state- or county-operated evaluation centers that can be reached through government-run health services.

In addition, many alcoholics have life crisis problems or vocational rehabilitation needs. Referral to a social service agency, a visiting nurses' association, or state vocational rehabilitation offices can be most helpful.

As is discussed in more detail elsewhere,[6] the same general approach applies both to patients who have never been hospitalized and to those beginning an aftercare program. The patient is counseled about day-to-day life adjustments and is helped to deal with crisis situations. After a period of

time, life adjustment tends to stabilize, and the patient incorporates enough of the messages being presented by the counselor to stop formal treatment.

Usually, counseling is begun at a frequency of once a week, but then it is slowly decreased, so that by the end of a year the patient is seen about once a month. If problems with drinking or life adjustment occur, the frequency of meeting can be increased to meet the acute need.

For the *secondary alcoholic* (see Section 3.1.2.3) who does not require inpatient care, referral to a mental health specialist should be considered. If the diagnosis is primary affective disorder, but the patient is *not* felt to be severely incapacitated or suicidal (if suicidal he should be hospitalized), outpatient treatment with antidepressants is possible. In such instances, the patient should be referred either to a psychiatric clinic or to a psychiatrist for evaluation, in addition to his alcoholic rehabilitation.

In delivering care to the secondary alcoholic with a primary *antisocial personality,* it is necessary to recognize the high rates of concomitant drug abuse and the elevated risk of the commission of serious crimes by these individuals.[33,34] There is no highly effective treatment known, but some authors favor heavily structured group sessions following a therapeutic community model. Outpatient referral to an experienced health specialist is advisable, as there is no evidence that inpatient care is routinely justified.

Some individuals are not ready to return to their day-to-day life after inpatient treatment. If the problem is either a chronic medical problem or psychiatric impairment, a nursing home or halfway house should be considered. For those with more serious problems, a nursing home is probably required, but whenever possible, this should be integrated with continued outpatient treatment and AA.

These nursing or halfway settings usually offer continued group meetings, supervision of medications, and help in dealing with emotional problems and crises. As is true with any of the modes of treatment, it is important that the clinician carefully evaluate each individual program before actual referral.[35]

15.2.4.3. The Role of Alcoholics Anonymous

Alcoholics Anonymous is an excellent resource for treatment.[36] This group, composed of individuals who are themselves recovering alcoholics (many of whom have been "dry" for years), establishes a milieu where help is available 24 hours a day, seven days a week.[6] At meetings, members share their own recovery experiences, demonstrating to the patient that he is not alone and that a better lifestyle is possible. AA also offers additional help in the form of groups that discuss the special problems of the children of alcoholics (Alateen) and of their spouses (Alanon). Each AA group has

its own personality, and the patient might experiment with different groups before choosing the one in which he is most comfortable.

AA can be used as a referral resource where no other outpatient service is either available or acceptable to the patient. It can also be utilized as an adjunct to outpatient or inpatient treatment efforts.

15.2.4.4. An Overview

In summary, alcoholic rehabilitation consists of a series of general helping maneuvers aimed at increasing and maintaining the highest level of motivation toward abstinence, helping the individual to reestablish a lifestyle without alcohol (and giving outreach to the family), and maximizing physical and mental functioning. Inpatient rehabilitation has not been shown to be essential, although individuals with specific needs may be best reached in the more sheltered setting.

Whether in an inpatient or an outpatient mode, most patients are offered group counseling sessions centering on day-to-day living and covering such problems as reestablishing meaningful relationships with the spouse and other family members; handling oneself at parties and with friends when alcohol is offered; reestablishing free-time activities and peer groups free of ethanol; adjusting job or avocational activities so that they are consistent with abstinence; and so on. Much of this work can be done by the average clinician with the help of AA and the judicious use of disulfiram.

Thus, therapy involves a commonsense approach to group counseling, long-term follow-up, working with the patient and the family together, and avoiding most medications. There is no place in alcoholic rehabilitation for antianxiety drugs or hypnotics.

15.3. A SPECIAL CASE: OPIATES

The opiate abuser differs from the alcoholic in that the former tends to be younger and to have more antisocial problems, comes from different referral sources (e.g., jail or probation), and more often abuses ancillary drugs. The high level of crime associated with the illicit use of opiates has helped motivate the development of a "maintenance" program that is purported to result in lowered levels of antisocial activities,[37] but that does not deal with the basic addiction. Even with these differences, however, the same general rules for rehabilitation apply to the opiate abuser and the alcoholic. These "basics" include detoxification; the need to reach out to the family; the need to carefully evaluate efforts; establishing patient goals and a program of counseling giving drug education; and making a long-term commitment to the patient. I will therefore concentrate on specific aspects of rehabilitation of the opiate abuser that have not already been covered.

The best predictors of the outcome of any form of opiate treatment are similar to those discussed for alcohol. Men and women entering care with a job or a legitimate source of income, relatively good health, a stable address, and lower levels of legal problems are much more likely to complete treatment and to be found to be abstinent several years later.[38] Such individuals are likely to show lower levels of drug abuse, lower arrest rates, and increased psychological functioning.[39,40] The worst prognosis is to be expected for those who have supported their "habit" almost solely by criminal activities.[39]

15.3.1. Methadone and Methadyl Acetate Maintenance

Methadone and methadyl acetate maintenance can be given only in licensed clinics established to ensure adequate care and to minimize the flow of methadone into illegal channels.[41]

15.3.1.1. Goals

Methadone does not "cure" opiate addiction. The program substitutes legal access to a longer-acting drug (e.g., methadone) for the addiction to a shorter-acting drug such as heroin. Methadone maintenance is used to help the addict to develop a lifestyle free of street drugs in order to improve functioning within the family and job, to decrease police problems, and to improve health.[40–42]

Methadone should be given only as part of a holistic patient approach, incorporating all the other aspects of rehabilitation thus far described.[43] In this therapy, it is hoped that, if the addict receives a drug legally (orally, to avoid the "rush" felt with IV drugs), at little or no cost, he will not return to the costs and problems inherent in street drugs. At the same time, methadone is felt to decrease drug craving and to (at least partially) block the "high" experienced with heroin.

15.3.1.2. Treatment Program

Methadone is a long-acting opiate that shares almost all the physiological properties of heroin, including addiction, sedation, respiratory depression, and effects on heart and muscle. The addict who has been carefully screened to rule out prior psychiatric disorders may be maintained on a relatively *low* (30–40 mg a day) or higher dose (100–120 mg a day) methadone schedule, the former giving fewer side effects but not the same degree of hypothetical "blockade" against the effects of heroin.[44] Although the results are not definite, there is some evidence that the use of higher doses of methadone may result in higher levels of retention in treat-

ment and in consequent lower levels of arrest, readdiction to street drugs, and criminal behavior.[45]

The drug is administered in an oral liquid given once a day at the program center, with weekend doses taken by the patient at home. An approach similar to methadone maintenance utilizes a longer-acting methadone congener, methadyl acetate.[46] The dosage is usually 20–30 mg, given three times a week in the beginning, then increased to 80 mg three times a week, if necessary. Available evidence indicates that the results are similar to those with methadone.

After the period of maintenance (usually six months to a year, or longer), the clinician should work closely with the patient to regulate the rate of drug decrease.[47] Most studies suggest that the dose be lowered as slowly as 3% a week.[48]

Methadone-type drugs have been taken by some individuals for over 10 years and are *felt* by clinicians to be relatively safe and effective.[42,45,49] However, the dangers associated with these drugs include the relatively benign side effect of constipation (seen in 17%),[50] the danger of addicting the fetus when the drug is given during pregnancy, a potentially serious depression,[51,52] and the possibility that the drug will find its way into illegal channels. Another special problem (seen in as many as one-quarter of methadone maintenance patients) is abuse of alcohol, especially for those individuals who abused alcohol before using the opiates, or who took alcohol concomitantly with their opiate abuse.[53] These problems are discussed in greater depth in Section 6.1.2.1.2.

As is true of almost all treatments of drugs of abuse, there are few carefully controlled studies demonstrating that methadone maintenance is definitely superior to other modes of care or placebo. Although most studies demonstrate that good outcome correlates significantly with the length of time in treatment (with maintenance for three months or less hardly being superior to detoxification alone),[54] a recent investigation sheds some light on efficacy. The authors compared individuals enrolled in two similar methadone-maintenance clinics, one of which was phased out because of fiscal constraints and the other of which continued.[45,55] After a rather thorough two-year follow-up, readdiction to heroin was observed in 55% of the men and women whose program was closed, but in only one-third of those being seen in the continuing program, with similar figures of 75% versus approximately 40% for arrests, 45%–65% versus 20%–40% for signs of alcohol abuse, and 40%–60% versus 30% for a history of selling drugs on the street during the subsequent two years. Although no differences between groups were noted on the incidence of committing crimes against property, employment rates, or history of having been on welfare during the two-year follow-up, the results do point out the probable importance of methadone maintenance to the opiate abuser.

15.3.2. Opiate Antagonists

These drugs occupy opiate receptors in the brain and block the effects of heroin and other opiates.[43] Concomitant administration of the antagonist with heroin may stop the development of physical dependence but does not block the drug hunger (psychological dependence).[50]

15.3.2.1. Goals

The use of antagonists is not limited to rehabilitation. They help in the treatment of opiate toxic reactions and can be used to test addicts who say that they are drug-free (the antagonist will precipitate withdrawal if opiates have been abused).[43] In rehabilitation, however, these drugs are administered over an extended period so that the patient receives no "high" if he takes opiates.

15.3.2.2. Specific Antagonists

There are a variety of opiate antagonists, most of which are themselves addicting. These drugs include the following:

1. *Cyclazocine* was the first antagonist tested in the early to mid-1960s.[56] Doses of 4 mg by mouth per day are effective in blocking up to 15 mg of heroin for 24 hours. However, the blockade is not complete, and most patients complain of cyclazocine side effects of sleepiness and a drunken feeling. A decrease in respirations may also be noted. Thus, this drug has not been widely used.[43,57]

2. *Naloxone* (Narcan) is an excellent narcotic antagonist that has no known morphinelike (agonistic) properties. Unfortunately, it is not well absorbed orally, and its action lasts no more than two to three hours, so that up to 3 gm per day may be needed to block 15 mg of heroin for a 24-hour period.[56,57]

3. *Nalorphine* (Nalline) is primarily used to test addiction to opiates. It is administered in a dose of 2–5 mg in a dark room; if the individual is addicted, pupillary dilatation is seen within 15 minutes to half an hour, whereas if no addiction is present, pupillary constriction is seen.[43,57] If no reaction at all is noted, 5 mg and then 7 mg can be given at half-hour intervals.[57] This drug is not usually used as a rehabilitative agent.

4. *Noroxymorphone* (Naltrexone) is a widely used narcotic antagonist that can be given orally, has a length of action of approximately 24 hours, and *has few side effects.*[58,59] Fifty mg per day is effective in blocking 15 mg of heroin for 24 hours, and higher doses (125–150 mg) of noroxymorphone are capable of blocking 25 mg of IV heroin for 72 hours.[56,60] This drug is free of agonistic properties, and there are no known withdrawal symptoms

when the medication is stopped. The side effects tend to be relatively mild gastrointestinal distress, anxiety, and insomnia, all of which tend to disappear over a period of days.

Patients to be started on this antagonist should be free of opiates for a minimum of five days, must be given a thorough physical examination, and should be challenged with 0.8 mg of naloxone to be certain that they will be able to tolerate the longer-acting antagonist. Following this procedure, a test dose of 10 mg of noroxymorphone can be given, with the expectation that any withdrawal signs will develop within one-half to two hours. Over the next 10 days, the daily dose should be increased to 100 mg on Mondays and Wednesdays and 150 mg on Fridays.[60]

Of course, treatment with an antagonist alone is inadequate. Patients will benefit best when they develop a close rapport with treatment personnel and may also gain from behavioral techniques that help them to learn how to handle anxiety and to cope with life situations.[56,60] However, for unknown reasons, most addicts are reluctant to begin and stay with narcotic antagonist treatment; only 60% or so completed the six days of noroxymorphone induction in one study.[60] Of the 153 remaining patients, 30 dropped out within two days of completing the induction, one-third had dropped by one month and one-half by two months, and slightly fewer than 10% were left at the end of six months. Although this rate of dropout is greater than that observed with methadone maintenance in similar patients, those who do remain in treatment with antagonists are less likely than methadone patients to take other drugs—in one study, 10% versus 30%.

In summary, narcotic antagonists are not uniformly successful. Although theoretically they are very helpful, and although noroxymorphone has many assets (e.g., no agonistic effects, low levels of side effects, ease of oral administration, and ability to be administered three times a week), it is probable that fewer addicts stay in treatment with antagonists than remain in methadone maintenance treatment approaches.

15.3.3. Other Drugs Used in Treatment

Any disorder with a natural history that includes periods of improvement with a relatively high rate of spontaneous remission runs the danger of having a variety of touted but ineffective treatments. Uncontrolled experiments have extolled such misleading cures as carbon dioxide inhalation and LSD.[48] I will mention only a few of the more promising approaches here.

1. *Propoxyphene* (Darvon) has cross-tolerance with other opiates and has been used as a method of detoxification from opiate addiction. Because of the belief that this drug has less appeal on the street and lower side effects

than some other medications, short-term "maintenance" with this medication (approximately three weeks) has been used but has not been shown to be uniquely effective.[61]

2. *Propranolol* (Inderal) in doses of from 5 to 120 mg per day has been administered in an attempt to block the immediate "rush" or "high" seen with heroin.[62] Uncontrolled studies indicate a decrease in drug craving, but better-controlled evaluations are necessary before this drug is used in general settings.

3. *Heroin* itself has been administered as part of a maintenance program.[63] The rationale here is similar to that offered for methadone; that is, it is used to decrease the necessity for getting the drug on the street and to cut down on the medical complications from adulterated drugs and contaminated needles. It has been used primarily in Britain, where the magnitude of opiate problems is very small compared with that in the United States (it is estimated that there were only 500 addicts in Britain when heroin maintenance was begun). After it became legal to prescribe heroin, the number of addicts doubled, necessitating the establishment of clinics similar to methadone maintenance programs. It is now uncommon to find a drug clinic in Britain that prescribes heroin and only heroin, as most are turning toward methadone maintenance.

15.3.4. Drug-Free Programs

Most inpatient treatment models offered to the opiate abuser utilize modifications of the therapeutic community (TC), as first proposed by M. Jones.[64] This is an exception to the general rule of short-term inpatient rehabilitation, as it lasts up to a year while the addict is taken out of the street culture and given a new view of life within the group. In this structure, group members, including ex-addict leaders, constantly confront each behavior in an attempt to help the participants gain insight and find a new and more successful lifestyle for coping with problems. Most large cities in the United States have programs run on the Synanon or Day Top models.[64] Unfortunately, very little controlled evaluation has been carried out regarding this approach.

It is difficult to compare results from TCs and methadone maintenance, as the patients in the former tend to be young and Caucasian, whereas those in the latter tend to be older and are more often minority-group members.[65] However, individuals assigned to methadone maintenance are more likely to appear at the clinic for actual care (29% versus 18% for TCs in one series) and may be 50% more likely to stay in treatment for one year.[65] As is true in other treatment approaches, the best prognosis in TCs is for those who are employed; who have higher levels of school completion, less intense involvement with heroin, and lower levels of jail records; and who

stay in treatment for two or more months.[65–69] The most usual retention rate in a TC is approximately 50% or less at 12 months.[65]

15.3.5. The Medical Abuser

The middle-class individual primarily abusing prescription opiates may be more similar to the alcoholic in general life outlook and history than to the street abusers of opiates. There is little good information on the best rehabilitation mode for this population, and the final program should be tailored to the specific patient, perhaps using the same approach applied to alcohol. Some of the patients will have chronic pain problems that must be addressed as part of their rehabilitation.

15.4. A SPECIAL CASE: HALLUCINOGENS, STIMULANTS, DEPRESSANTS, AND MULTIDRUG MISUSE

It is rarely necessary to establish specific rehabilitation efforts for individuals who are "casual" users of marijuana or hallucinogens. However, serious consequences can occur when hallucinogens are used regularly or in high doses and when stimulants or depressants are regularly ingested. Because there is a high level of correlation between the heavy misuse of any one of these substances and the use of multiple drugs, I will present a discussion that is aimed primarily at the multidrug misuser but that can also be applied to those individuals involved with only one type of substance.

After establishing the diagnosis, carrying out detoxification, if necessary, and ruling out the possibility of any major preexisting psychiatric disorder, the next step is to determine the answers to the following questions:

1. Is the individual primarily abusing street drugs or taking medications prescribed by a physician?
2. Is there a primary or preferred drug of misuse?
3. Under what circumstances does the individual misuse multiple drugs?
4. Is the client a member of a street subculture of drug users or a middle-class, blue-collar or white-collar working individual?

In a program dealing primarily with street users, the middle-class individual may be referred to a more appropriate program. This type of flexibility is of great importance in giving the patient an adequate and comfortable milieu. The actual treatment protocol chosen will resemble either the efforts described for alcoholism or, for the person more heavily involved in the street culture, those described under the drug-free program for opiates. Each individual client's needs, of course, must be considered in designing patient rehabilitation plans.

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