Chapter 1 Introduction

Use of illicit substances contributes to significant morbidity and mortality worldwide. In the USA, drug use is a leading cause of preventable death and contributes to the incidence and morbidity of other mental health and physical health conditions. Healthcare providers are well aware that use of illicit substances is associated with environmental and social harms; it is not unusual for a person with an addiction to be unemployed, homeless, impoverished, or associated with illegal activities. These social morbidities also contribute to poor physical health by influencing such things as sanitation, medication compliance, and risky behaviors. Most of the current criteria to diagnose both substance abuse (four) and substance dependence (seven) disorders have little to do with the amount of substance used but rather the non-medical harm associated with its use (American Psychiatric Association 2000). Simply put, drug addiction is a complex illness that impacts mental, physical, and environmental health.

Recent advances in addiction research have indicated that a pathophysiological basis for disease exists for many illicit substances: addiction is not simply a behavior of compulsive consumption of a substance. The association of use of various illicit substances with various mental health conditions has been firmly established; however, the association between illicit substance use and physical health conditions is less known. The influence of illicit substance use on comorbid conditions is important and often under-recognized by the treatment provider. Associations of illicit substances with medical health conditions – whether epidemiological or causative in nature – play important roles in how patients interact with the healthcare system and how providers interact with patients who use illicit substances. Comorbidity among people with psychiatric conditions – including medical conditions and substance use and abuse – is recognized as a significant challenge for mental healthcare providers and even more of a challenge for generalist healthcare providers.

Nonetheless, it is becoming increasing clear that treatments that attend to patients' comorbid conditions need to be developed, and that generalist healthcare providers ought to assess and treat addiction disorders within the confines of generalist settings. In fact, recent principles of effective treatment published by the US National Institutes of Health, National Institute on Drug Abuse indicate that addictive disorders should be assessed and treated in the presence of comorbid mental health and physical health conditions (National Institute on Drug Abuse 2009).

It is challenging to encourage generalist providers to attend to addictive disorders. Perhaps generalist physician treatment of addictive disorders will be aided by the current attention to the quality of medical care. The US Preventative Services Task Force recommends routine screening for alcohol use and brief counseling interventions. In addition, a recently published report from the Institute of Medicine (IOM), *Improving the Quality of*

Health Care for Mental and Substance-Use Conditions, addresses this issue (Institute of Medicine 2005). This report was the product of an IOM consensus process in which experts in a range of disciplines impacting the broad fields of mental health and addiction medicine reviewed the literature and developed an agenda for changing the approach to the treatment and prevention of these conditions. An underlying theme of the IOM is that only by addressing substance use and mental health problems can one achieve optimal benefit for patients in medical care. Integration of mental health, physical health, and substance abuse services promotes optimal benefits to the provider and the patient (Gordon *et al.* 2007).

One of the most important recommendations of the IOM report pertains to the delivery of coordinated care by providers of primary care, mental health, and substance use treatment. The basis of this recommendation lies in the "crossing the quality chasm" rules, which endorse "shared knowledge and the free flow of information" and "cooperation among clinicians." Specifically, coordination models can be straightforward (e.g., formal agreements among providers of mental healthcare, substance use care, and primary care) or moving incrementally towards more complex arrangements (e.g., case management among systems, collocation of services, clinically integrated practices of all of these healthcare providers) (Institute of Medicine 2001). Evidence suggests that the more complex arrangements yield improved patient outcomes. Other recommendations addressed to all clinicians – including primary care physicians – included the need to screen all mental health patients for alcohol and drug use problems given the high comorbidity of these conditions and the need to maintain a patient-centered approach to the care of the patient with alcohol and drug problems.

Recent work from the Program of Research to Integrate Substance Use Issues into Mainstream Healthcare (PRISM) has revealed the impact of substance use on disparate medical conditions including diabetes mellitus, hypertension, low back pain, sleep, depression, lung cancer, chronic obstructive pulmonary disease, and osteoporosis (Howard *et al.* 2004; McFadden *et al.* 2005; Mehra *et al.* 2006; Stein *et al.* 2004; Sullivan *et al.* 2005). The increasing attention to the impact of substance use disorders on patients' medical outcomes will continue to drive efforts to engage all physicians in identifying and treating these disorders.

This book examines the epidemiological associations between physical illness and drugs of abuse. Drugs of abuse impart significant morbidity and mortality on people worldwide; in the USA, they are the ninth leading cause of preventable deaths (Mokdad *et al.* 2004). A number of reviews have examined the comorbid or co-occurring disorders of drug use and mental health disorders, but no review has systematically examined the epidemiological associations between various drugs of abuse and physical illness. Furthermore, leading textbooks in addiction medicine and internal medicine (Graham & Schultz 1998; Kasper *et al.* 2005) do not adequately review the physical morbidity associated with drugs of abuse. Recently, three textbooks have been published that highlight some physical health problems associated with alcohol and other drugs of abuse (Brick 2008; Frances *et al.* 2005; Rastegar & Fingerhood 2005). However, no systematic, comprehensive review of the recent peer-reviewed literature relating the physical diseases associated with drugs of abuse has been completed.

Therefore, the purpose of this book is to examine the relationships between drugs of abuse and physical illness. Secondary purposes are to critically review the current literature regarding these associations and to suggest future research in this field. Finally, we hope to promote practitioners' awareness, identification, and engagement of physical illnesses that afflict patients who abuse drugs.

Unfortunately, the literature regarding the associations of substance use disorders with medical illness is vast and often specific to a certain illicit drug or medical disease process. The approach in this book is to examine – comprehensively and critically – the recent evidence of causal and correlative association of substance use/abuse and physical illness. This approach will thus provide a resource for clinicians, investigators, and policy makers.

The scope of this book is narrower than that of medical literature of the same topic. First, we excluded from our evaluation of the literature associations based on the route of administration. The association of illicit substance use and increased incidence of infections by hepatitis viruses, human immunodeficiency virus (HIV), and sexual transmitted disease (STD) pathogens are well known; it is less clear whether the actual drug of abuse is the linking factor to the disease process. For instance, hepatitis and HIV are associated with intravenous drug use (particularly heroin/opioid injection), but it is likely that the intravenous administration of the illicit drug is the comorbid link, not the drug itself.

Second, we examined the identified peer-reviewed literature in PubMed (www.PubMed.gov) from January 1, 1988 through December 2008. Certainly, studies prior to 1988 examined co-occurring or comorbid medical illnesses. Recent reviews (Brick 2008; Frances *et al.* 2005; Graham & Schultz 1998; Rastegar & Fingerhood 2005) have noted many of them. However, our intention was to examine the latest literature. In addition, the decision to examine recent literature reflected curiosity as to whether recent studies were examining associations of substance use and medical comorbidities, and a desire to assess the quality of these studies and to examine where gaps in knowledge are occurring. Finally, the decision to examine recent literature greatly reduced the number of studies the authors needed to critically examine.

Third, the scope of this book is limited by an examination of associations of medical illnesses with only a few illicit substances. Patients around the world abuse an unknown number of illicit substances. We decided to limit our examination of the literature to four broad classes of illicit substances: cocaine, marijuana, opioids, and common hallucinogens and stimulants. These substances are more likely to affect several organ systems, have been studied intensely, have known mental health comorbid associations, and are relatively common around the world.

The book is divided into chapters by drug of abuse and subsections examining the associations between the drug and each physical illness domain. The published relationships for each of the drugs are examined with respect to each physical disease (e.g., infectious, neoplastic, musculoskeletal, etc.).

The addiction literature is rife with misleading terms and inaccuracies in diagnostic and treatment terminology. Definitions should be clear, without ambiguity. One of the most important advances in addiction medicine over the last few years is to simplify and specify terms in addiction medicine. Therefore, before embarking on examination of the literature, the following definitions will be used.

Addiction: a chronic, relapsing disease characterized by compulsive drug seeking and abuse in spite of known adverse consequences, and by functional, sometimes long-lasting changes in the brain.

Comorbidity: the occurrence of two disorders or illnesses in the same person, either at the same time (co-occurring comorbid conditions) or with a time difference between the initial occurrence of one and the initial occurrence of the other (sequentially comorbid conditions).

Mental disorder: a mental condition marked primarily by sufficient disorganization of personality, mind, and emotions to seriously impair the normal psychological or behavioral functioning of the individual.

Physical health disorder: a disease, not otherwise a mental disorder, that impairs the health of an individual and is a diagnosable illness.

Substance use: use of illicit substances that are generally not intended for use and not prescribed by a healthcare provider. Substance use may or may not meet diagnostic criteria for either substance abuse or substance dependence.

Substance abuse: defined by harmful consequences of repeated use but does not include the compulsive use, tolerance, or withdrawal, which can be signs of addiction, or substance dependence. Defined by the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (DSM-IV).

Substance dependence: defined by criteria of DSM-IV, which may include consequences of use, compulsion to use, tolerance, and withdrawal.

The need to develop treatments that take comorbidity into account is increasingly recognized. Identifying, managing, and treating comorbid medical illness among people with psychiatric conditions – including the comorbid conditions of substance use, abuse, and dependence – is a significant challenge for clinicians, researchers, and policy makers. Substance use occurs in many patients with psychiatric disorders, and comorbidity with mental health disorders is the rule rather than the exception among some people, such as the elderly, chronically ill, or homeless patients. Comorbidity impacts the course of mental health problems and leads to exacerbations of symptoms and increased healthcare utilization. Those with mental health disorders and another comorbid condition also experience barriers to treatment.

Providers should recognize that substance use and physical health conditions also co-occur. While it is difficult to disentangle the overlapping symptoms of drug use with physical health (and mental health) disorders, an awareness of co-occurrence and association of substance use with physical conditions may prompt providers to recognize and treat these conditions. While the harm of physical health conditions and substance use is not necessarily additive, the morbidity of both types of condition contributes to deleterious outcomes and treatment responses to both. Awareness is the first step in addressing substance use and physical health comorbidity.

Chapter 2 Methods

Similar to the methods described by Leucht *et al.* (2007), we conducted a detailed search of an electronic PubMed database to identify all articles that indicated a relationship between an illicit drug of abuse and physical illnesses. The search identified key words (and words within titles and abstracts) associated with major categories of illicit drugs of abuse (1) marijuana, (2) cocaine, (3) opioids, (4) hallucinogens, stimulants, benzodiazepines, and barbiturates and combined each with major categories of physical illness. These key words included such terms as "crack" for cocaine and "heroin" for opioids.

A broad search strategy was conducted to ensure that all physical illnesses that corresponded to an illicit drug were identified. The Medical Subject Headings (MeSH) terms for each drug of abuse were combined with the approximately 23 MeSH terms for the general disease categories of physical diseases. To obtain the latest results, the search was limited to January 1, 1988 to December 1, 2008 (approximately the last 20 years). The search was limited to peer-reviewed literature regarding human studies and in the English language. It was not restricted to only population-based or controlled studies in order to identify as many potential studies as possible that indicated even limited associations between drugs of abuse and physical illness.

The MeSH terms were included for the major categories of physical illness:

1. Infectious disease (including bacterial, mycotic, parasitic, and viral infections)
2. Neoplastic disease
3. Musculoskeletal disease
4. Digestive system disease
5. Stomatognathic disease
6. Respiratory system disease
7. Otorhinolaryngological disease
8. Nervous system disease
9. Ocular disease
10. Male urological, renal, and genital disease
11. Female urological and gynecological disease, and neonatal, congenital, and pregnancy disease
12. Cardiovascular disease
13. Dermatological disease
14. Nutritional and metabolic disease
15. Endocrine system disease
16. Immune system disease

17. Environmental disease
18. Other pathological conditions (if any).

Because the focus of the search and subsequent review of the literature were on human epidemiological associations, "animal associations" associated with illicit substances of abuse were not included in the search.

The first search was made in February 2008, and an update search was completed on December 1, 2008. After the initial search strategy, all the abstracts were read. Potentially relevant articles were then reviewed for more detailed inspection. At the beginning of each section, the number of abstracts initially reviewed in each search strategy is noted for each drug of abuse. After this initial search, known review articles, books, and book chapters were also used to supplement the search findings and identify studies that were not found in the initial search strategy. In addition, references within the identified articles were examined for additional sources of associations between the drug of abuse and physical illness, but all mentioned and summarized articles were still restricted to the time frame of the primary search (1988 to 2008).

All authors contributed to the content of every chapter, but specific authors had primary responsibility for specific chapters and led the writing for that chapter. As such, there were some deviations from secondary search strategies. The drafts of all chapters were sent for external peer review for comment on completeness and narrative (see the Acknowledgements).

Each chapter summarizes the literature in the searched time frame for a specific drug of abuse or groups of drugs of abuse. Each chapter commences with a general description of the drug of abuse. Each subsequent subsection then examines associations of that drug of abuse with the major categories of physical illness. At the end of each chapter, a summary section examines research implications and a table indicates the evidence of association between drugs of abuse and each category of physical illness, and any research implications. The quality of the literature for many associations was not strong, and many associations were "case reports" or "limited subject" descriptions of evidence. A general summary at the end of each chapter considers the quality of the literature when possible and summarizes the strengths of the associations.

It is important to note that this review is not all-inclusive of the evidence of association of drugs of abuse with the major categories of physical illness because it summarizes the recent (1988 to 2008) literature. It may be that associations have been found prior to 1988; if this is a prominent association it is often indicated but the findings are not summarized as the literature was outside the search time frame. In addition, drugs of abuse are often inhaled, injected, or otherwise administered, and the administration route may be associated with physical findings and major clinical diseases. A classic example is the strong association of injected drug use with hepatitis C virus (HCV) infection. Often, it is unclear whether the association reflects the intravenous route of administration or is specifically with the hepatitis virus. Because of this quandary, we chose not to select and summarize literature regarding associations between route of administration and illness.

Chapter 3

Results: cocaine

Introduction

Cocaine is a powerful, addictive drug that has been used as a stimulant for centuries. The drug can be smoked, snorted, and injected intravenously, subcutaneously, or intramuscularly. Abused by over six million Americans in 2006, most of the users are between the ages of 12 and 60. At the beginning of the twentieth century, cocaine was a component of throat lozenges and tonic waters, and it was frequently used as an anesthetic. The Harrison Act of 1914 outlawed the use of cocaine and opiates, and the 1970 Controlled Substance Act in the USA further restricted use. (Das 1993; Warner 1993). However, its availability and addictive properties have made cocaine a highly abused drug in the USA.

The consequences of using cocaine vary among its users. Psychoses, violent behavior, cardiovascular and nervous system events, and altered pregnancy outcomes have all been described in the literature. This chapter reviews the epidemiological research included in the PubMed database and published between 1988 and 2008 that explores the relationship between cocaine and various health conditions. Each of the following subsections provides a synopsis of the research, followed by a commentary on the research and tables highlighting the major findings. Where appropriate, suggestions are made for additional research that might strengthen or clarify the role of cocaine in adverse health outcomes. Since research may overlap several topics, articles are cross-referenced where appropriate and may be described in several subsections.

While the review of the epidemiological literature primarily addresses the effect of cocaine use that might influence or cause altered physiology in the body systems, this introductory subsection provides some background information about cocaine that might provide insight into how cocaine might influence body function.

Cocaine HCl is a white crystalline powder derived from the coca plant (*Erythroxylum coca*) that is native to the Andes Mountains. The powder can be snorted, sniffed, or dissolved in water and injected. Crack cocaine is an inexpensive alkaloid of cocaine that is smoked, and it may be found as off-white chips, chunks, or rocks.

Cocaine binds to the dopamine transporters on presynaptic neurons and interferes with the transporter's ability to reabsorb dopamine into the presynaptic neuron. This results in an accumulation of dopamine in the synapse and a prolonged dopamine effect on the target organ. Over time, with prolonged exposure, the dopamine receptors are downregulated and signal transduction is altered. This leads to a decrease in dopamine signaling, which may contribute to addiction by affecting the brain reward system, reinforcing the need for additional cocaine use.

Besides interaction with dopamine transporters, cocaine also affects the serotonergic system by inhibiting reuptake of various members of the serotonin (5-hydroxytryptamine,

5-HT) family, resulting in an increase of some 5-HT receptors. Norepinephrine reuptake is also blocked by cocaine, resulting in stimulation of the sympathetic nervous system and subsequent sympathetic nervous system responses (e.g., elevation of blood pressure, increased heart rate). Cocaine's influence includes affecting the dopaminergic, serotonergic, and adrenergic pathways throughout the body. Some recent laboratory research has shown that cocaine can inhibit sigma receptors and serotonergic and adrenergic transmitters on placental tissue. The effect of this action on fetal development is an area of ongoing study.

Other receptors may also be affected by cocaine, including sigma receptors (where cocaine is a ligand) and the glutamate *N*-methyl D-aspartate (NMDA) receptors. Sigma receptor stimulation can lead to increased muscle activity and tachycardia. Seizure activity may be enhanced by cocaine stimulation of sigma receptors. Cocaine may also stimulate endothelial cells to release endothelin-1, which is a strong vasoconstrictor and can cause vasospasm, thus contributing to cardiovascular effects of cocaine.

Once in the plasma, only approximately 1% of cocaine is excreted unchanged in the urine. While most of the drug is metabolized in the liver to benzoylecgonine, other urinary metabolites include ecgonine methyl ester and ecgonine. Urine metabolites can be found within hours and as long as 10 days after heavy cocaine use. Since cocaine can be detected in the hair of users, hair samples have been used in diagnostic tests for cocaine exposure.

The physiological effects of cocaine can be experienced in 10 to 30 minutes if cocaine is inhaled or injected, or in 5 to 10 minutes after smoking. The half-life of cocaine in the plasma is approximately 50 minutes.

The action of cocaine is dose dependent. In low to moderate doses, cocaine can cause vasoconstriction and an increase in heart rate and blood pressure. Cocaine use is associated with cardiac arrhythmias, which can lead to cardiac arrest or seizures and respiratory arrest. An increased risk of cerebro- and cardiovascular incidents is possible. The behavioral effects on the central nervous system (CNS) include increased arousal, increased performance on tasks of vigilance, and alertness. Cocaine can increase self-confidence, sense of well-being, energy, and euphoria. A decreased appetite may also be seen in cocaine users.

In high doses, cocaine may lead to enhanced euphoria, arousal, and restlessness. Involuntary motor activity may also occur. Paranoia and increased irritability can increase the risk of violent behavior. Seizures may also occur. In a "cocaine crash", or withdrawal, the individual may experience depression, fatigue, jumpiness, and fearfulness.

Cocaine can interact with other drugs taken concurrently, including alcohol and nicotine. Cocaine and alcohol form cocaethylene in the liver. The effects of cocaethylene are similar to the pharmacological effects of cocaine, particularly in blocking dopamine uptake, and often results in a greater euphoria than that seen with cocaine use alone. Cocaethylene appears to be less effective in blocking norepinephrine and 5-HT transporters. Nicotine increases the dopamine levels in the CNS; consequently, the combination of nicotine and cocaine can result in increased euphoria. Nicotine appears to affect dopaminergic neurons associated with motor and cognitive function, and also has a role in motivational aspects of drug abuse.

Crack use results in consequences similar to cocaine, but because it is often smoked, there is a quicker onset and more intense response than with powdered cocaine. Crack users may have a greater likelihood of psychotic responses, hyperactivity, and violence.

Use of cocaine in any form can stimulate muscle activity, resulting in increased heat production (pyrogenic effect). Because increased dopamine and norepinephrine levels will cause increased vasoconstriction, this can lead to ischemic muscle damage, which increases the risk of rhabdomyolysis and its consequences.

Cocaine withdrawal is generally mild but may result in dysphoria, depression, sleepiness, and fatigue. Bradycardia may also occur. Unlike other drugs of abuse, cocaine causes a "crash", and patients in cocaine withdrawal "sleep off" the withdrawal effects.

Besides use as a psychological/physiological stimulant, cocaine has been used as a local anesthetic, primarily in eye and ear–nose–throat surgery. Cocaine blocks nerve action potentials and inhibits local norepinephrine uptake in the central and peripheral nervous systems. It is seldom used in the USA because of the availability of safer local anesthetics. However, cocaine is still used as a local anesthetic in some areas of the world.

Short- and long-term effects of cocaine use have been described in the literature. The following sections discuss the epidemiological research that describes the role of cocaine use in a number of body functions.

Infections

In a review of epidemiological studies published between 1988 and 2008, a search of PubMed found five articles on bacterial infections, one article on mycoses, nine articles on viral disease other than HIV, and two articles on parasitic infections. These articles are described in the following subsections. Additional discussion of infections and cocaine use may be found in other relevant subsections (e.g., genital, cardiovascular, respiratory).

Bacterial infections

Gittelman *et al.* (1991) studied individuals with rhinosinusitis in order to determine the risk of toxic shock syndrome in individuals with *Staphylococcus aureus* infections. Nasal cultures were taken from 140 patients with rhinosinusitis: 35% were identified as *S. aureus* carriers; 30% of those scheduled for surgery were *S. aureus* carriers; and 40% of those tested had isolates of the toxic strain of *S. aureus*. A statistically higher incidence of *S. aureus* was found in cocaine users, as well as those using topical decongestants and steroid nasal sprays. The authors suggested that identifying those patients at risk for toxic shock syndrome associated with the toxic strain of *S. aureus* will guide practice to prevent infection complications after rhinoplastic surgery.

In a second article exploring risk of infections, Murphy *et al.* (2001) examined soft-tissue abscesses in a case–control study. The injection drug users (IDU) studied included 151 with abscesses requiring incision and drainage, and 267 IDU without abscesses or bacterial infections in the previous year. The cases and controls were matched for age, sex, and race. The major risk factor identified was subcutaneous or intramuscular injection of abused drugs (but not intravenous injection). Those who injected heroin and cocaine (speedball) may be at risk for ischemic soft-tissue injury. Alcohol cleansing of the skin was a protective measure preventing development of abscesses. Those who were seropositive for HIV or T-lymphotropic virus type II did not have an increased risk of abscess formation.

Two articles explored notification of individuals testing positive for syphilis. In a descriptive study, Gunn *et al.* (1995) reviewed case reports of individuals with primary and secondary syphilis associated with inner-city epidemics in 1990 to 1992. Thirty percent of the cases were illegal drug users. The drug users, particularly crack cocaine users, were also associated with prostitution, had 4.2 sex partners/person, and only 1.5 named sex partners/person. Only 26% of the sex partners received treatment for syphilis. The results suggested that a greater increase in screening of high-risk groups and partner identification through social networks is needed to control syphilis epidemics.

The second article (Ross *et al.* 2006) looked at notification of syphilis in individuals in a jail-based syphilis notification database and an Arrestee Drug Abuse Monitoring (ADAM) program from 1991 to 1998. The data were compared with the ADAM database and from a large county database. Three racial/ethnic groups were studied: African American, Hispanic, and non-Hispanic. The findings showed a significant association between cocaine use and syphilis in African Americans, but not in other groups. Linear regression analysis linked cocaine use and syphilis (58% of the variance). In the African American group, the association was stronger in males than females when only the ADAM and jail notification databases were considered. The researchers suggested that crack cocaine use and increased syphilis rates were related and that there was a close association between drug abuse and some STDs.

Two articles describe bacterial infections in cocaine users. The first (Oh *et al.* 2005) described an intravenous cocaine user who developed tricuspid valve endocarditis after licking needles prior to injecting the cocaine. He apparently licked the needles in order to determine the strength of the cocaine. Three anerobes were found: *Actinomyces odontolytica*, *Veillonella* species, and *Prevotella melaninogenica,* all oral anaerobes.

Another case of bacterial infection was described by Dettmeyer *et al.* (2004). A 17-year-old female died after developing mixed bacterial infections and infarctions following splenic infarct, thought to be related to cocaine use. Microabscesses were found in the heart, meninges, and kidneys. Petechial hemorrhages were also found in various organs.

A recent study by Swaminathan *et al.* (2007) looked at the benefit of two-step testing for tuberculosis (TB) infection in drug users. A two-step TB test involves tuberculin (purified protein derivative) skin testing twice, one week apart. If both tests are negative, the individual is unlikely to have the disease. If only one test is done and is negative, an asymptomatic individual may still have latent TB. By giving a second TB test, the second test, if positive, will identify those individuals whose immune systems did not respond to the antigen initially. The "booster phenomenon" occurs when the second test is positive since the first TB test stimulates "forgetful" immune recognition. The study comprised 619 drug users in a methadone treatment program. A positive tuberculin skin test was found in 174 (28%) at the first test. After the second test (booster), 24 of 445 (5%) additional drug users had a positive test. The older age of some subjects was associated with the booster phenomenon (adjusted odds ratio [AOR] 2.38/decade; 95% confidence interval [CI] 1.34–4.22). A history of using crack cocaine also increased the odds of a booster effect (AOR 2.61; 95% CI 1.10–6.18). Prior work as a home health aide was also associated with the booster phenomenon (AOR 4.23; 95% CI 1.39–12.86). The use of the two-step test for TB increased the proportion of individuals identified with latent TB from 22 to 25%. The researchers suggested using the two-step TB test for screening drug users for better identification of persons with TB.

Table 3.1 summarizes these data for bacterial infections.

Mycoses

A case report by Jaffey *et al.* (1990) found a *Conidiobolus* infection in a crack cocaine user. This fungus infection is rare in humans and rarely disseminates except in immunocompromised individuals. In the case study described, the fungal infection caused endocarditis and also infected the lungs, kidneys, skeletal muscle, and brain. Rhabdomyolysis also occurred, with a plasma creatine kinase (CK; also known as creatinine phosphokinase) of 1.2×10^6 U/L (normal 25–200 U/L). No mention was made concerning the HIV status of the individual (Table 3.2).