Approach to the Patient with Alcohol or Drug Dependency

Alcohol and drug dependency is prevalent in the United States. There are approximately 14 million alcohol abusers, tens of millions who have tried cocaine or marijuana, approximately a million have tried anabolic steroids, and there are over 700,000 heroin addicts. Three percent to 16% of pre-employment drug screening tests produce positive results. Furthermore, patients with chronic pain syndromes are at risk for addiction to prescription narcotics. Most drugs produce tolerance with continued use, causing the abuser to gradually increase the dose. Tolerance is often but not invariably accompanied by physical dependence, which is an adaptive state that manifests itself by intense physical disturbances when drug use is suspended, or by psychic dependence, a condition in which the agent produces satisfaction or a psychic drive that requires periodic drug use for its maintenance. If drug discontinuation affects neural systems, the withdrawal syndrome will be physiologically violent (e.g., seizures), whereas withdrawal from psychic dependence may produce depression and drug craving. Many classes of agents with different physiologic and psychological effects produce drug dependency.

Ethanol

Clinical Features and Diagnosis

The risk of alcoholism involves a genetic component that is highly sensitive to environmental factors, with a lifetime risk of 20% to 25% for men and 5% for women. Symptoms of intoxication include somnolence, dysarthria, ataxia, nystagmus, and impaired judgment. The alcohol dependence syndrome has several features: narrowing of the drinking pattern such that there is little variability from day to day; an awareness of the compulsion to drink; tolerance to the intoxicating effects of ethanol; physical dependence; early drinking to relieve “morning after” symptoms; the inability of negative consequences (e.g., family, social, professional,
health) to deter drinking; and rapid reinstatement of the syndrome with recurrent drinking (Table 22-1). These issues should be raised with the patient and the family members. The CAGE test is a simple, nonthreatening series of four questions that has 93% sensitivity and 76% specificity with two or more positive responses. There is no biochemical test to quantitate drinking behavior; however, elevations in mean corpuscular volume, uric acid, triglycerides, and $\gamma$-glutamyl transpeptidase may support the suspicions of the family or clinician, and newer tests such as carbohydrate-deficient transferrin and acetaldehyde-protein adducts show some promise as useful screening tests. Within 6 to 12 hours of ingestion, alcohol can be detected by analysis of breath, blood, or urine. In general, ethanol is cleared at a rate of 100 mg per kg per hour, but this may vary up to threefold according to individual metabolism.

Principles of Management

Ethanol detoxification, with intensive counseling, behavior modification, and support group enrollment, may be undertaken on an outpatient basis in the absence of major medical illness or withdrawal symptoms; otherwise, hospitalization should be considered. In the 1 to 2 days of abstinence, tremor and tachycardia occur, which may progress to hallucinations in 10% to 20% of cases. Seizures and delirium tremens, which is characterized by hallucinations and severe sympathetic overactivity (e.g., tachycardia, fever, dilated pupils, hypertension, diaphoresis), develop later in a minority of patients. Benzodiazepines and barbiturates are effective in preventing ethanol withdrawal symptoms. The response to detoxification programs depends on the underlying support system. Those with stable support have abstinence rates of 60% for up to 18 months, compared with 30% for unemployed individuals in lower socioeconomic strata. Monitoring alcohol consumption with carbohydrate-deficient transferrin may be useful. The use of medications to maintain sobriety has provided mixed results. Serotonin-reuptake inhibitors
(e.g., fluoxetine, zimeldine) have been somewhat effective, as have opiate antagonists (e.g., naltrexone). Alcohol-sensitizing drugs (e.g., disulfiram) inhibit aldehyde dehydrogenase, leading to nausea, tachycardia, flushing, and hypotension as a result of acetaldehyde accumulation. However, the largest controlled trial showed no difference in abstinence rates with disulfiram and placebo (~20%) and the drug is associated with hepatotoxicity. Other drugs, including the 5-HT₃ receptor antagonist, ondansetron and other opioid antagonists (eg nalmefene).

Sedative-Hypnotics

Clinical Features and Diagnosis

Barbiturates and benzodiazepines are used for sedation, muscle relaxation, seizure control, anxiety, and panic disorders. High doses produce emotional lability, dysarthria, ataxia, and rarely, delirium, disorientation, and altered perception, all of which may be increased by concurrent ethanol use. Dependence on barbiturates occurs in 1 month, whereas benzodiazepine dependence requires about 20 weeks of use. Users of benzodiazepines develop tolerance to the sedative effects of the drugs but not to their anxiolytic effects. Barbiturates and benzodiazepines are reliably detected with urine drug screening tests for several days after the last use (Table 22-2).

Principles of Management

Abrupt withdrawal from barbiturates and benzodiazepines produces tremor, dysphoria, insomnia, hyperreflexia, anxiety, and, rarely, seizures. Barbiturate withdrawal may be as dangerous as delirium tremens. Seizures may occur in patients who are dependent on benzodiazepines if they are administered flumazenil, a benzodiazepine antagonist. Safe withdrawal is accomplished by gradual dose reductions of 10% per day.

Opiates
Clinical Features and Diagnosis

Heroin is the choice of most narcotic addicts, but prescription drugs such as codeine, methadone, meperidine, and oxycodone are also widely abused. Fentanyl is abused most frequently by medical personnel and carries a significant risk of overdose due to its potency. Methylphenyltetrahydropyridine is a synthetic derivative of meperidine that caused an outbreak of toxic parkinsonism in the 1970s by destroying substantia nigra neurons in users. No tolerance to the miotic or constipating effects of opiates develops, so these manifestations may provide clues to narcotic abuse. Urine tests for opiates may produce positive results for 2 to 5 days after the last use. Although ingestion of large quantities of poppy seeds can give a false-positive result, the cough suppressant dextromethorphan usually does not give a positive test result. Fentanyl is difficult to detect in the blood of users because it is highly potent at very low doses.

Principles of Management

Fully developed symptoms of opiate withdrawal result from overactivity of the sympathetic nervous system and include lacrimation, rhinorrhea, dilated pupils, piloerection, diaphoresis, yawning, hypertension, tachycardia, and fever. In contrast, hallucinations, tremor, and delirium are not typical of opiate withdrawal and suggest other drug use. Withdrawal symptoms can be blocked by clonidine, which inhibits the activity of neurons in the locus caeruleus that are hyperactive secondary to the suspension of opiates. Methadone may be used to wean the patient from shorter-acting opiates. Relapse may be prevented by chronic use of methadone or oral naltrexone, but this drug is potentially hepatotoxic. Newer drugs under study include levomethadyl acetate and buprenorphine, a partial opioid agonist.

Cocaine and Other Stimulants

Clinical Features and Diagnosis
Cocaine may be taken nasally, intravenously, or in its base form (freebase, crack) by smoking it. It induces tolerance, but only relatively mild withdrawal. Nonetheless, it has the highest abuse potential of drugs in current use. Amphetamines are active orally or intravenously and include many active derivatives (e.g. methamphetamine or “crystal”, and MDMA or “ecstasy”). The sympathetic effects of cocaine and amphetamines include pupillary dilation, tachycardia, hypertension, cardiac arrhythmias, myocardial infarction, aortic dissection, myocarditis, intestinal ischemia, disseminated intravascular coagulation, rhabdomyolysis, ulcer perforation, and seizures. Use during pregnancy causes microcephaly, growth retardation, intrauterine cerebral infarction, and cerebral hemorrhage in the fetus. Amphetamines can produce hallucinations and delirium. If taken intravenously, they can cause necrotizing angiitis as well as carrying the risk of acquiring Hepatitis B and C and HIV. Cocaine metabolites can be detected on drug screening for up to 48 hours after use. The detection of amphetamines is complicated by cross-reactions with over-the-counter sympathomimetics (e.g., ephedrine, pseudoephedrine).

Principles of Management
Withdrawal from stimulants produces depression, fatigue, disturbed sleep with increased dreaming, and intense drug craving. Treatment is usually performed on an outpatient basis and consists of complete abstinence, which is documented by mandatory urine testing. Cocaine craving is treated by intensive counseling as well as tricyclic antidepressants, imipramine and desipramine, which may reduce dysphoria and improve sobriety. Extinction therapy, in which the user watches videotapes of cocaine use or handles drug paraphernalia without using the drug, has been used for some patients. Acupuncture, phenytoin, and amantadine have had some reported success.

Cannabis
The active ingredient of marijuana, 9-tetrahydrocannabinol, causes euphoria, relaxation, subjective intensification of perception, altered sense of time, and impaired psychomotor function, as well as vasodilation (tachycardia, conjunctival injection) and appetite stimulation. Five percent of episodes of cannabis use result in anxiety attacks or paranoia. Prolonged use may cause an “amotivational” syndrome of passivity, preoccupation with drug use, decreased drive, and memory loss. Cannabis withdrawal produces restlessness, insomnia, and nausea. Urine tests may produce positive results for up to 30 days after the last use of the drug. Treatment is based on counseling and should include suspicion of other illicit drug use.

**Phencyclidine**

Phencyclidine (PCP or angel dust) may be taken by any route, including smoking. It produces euphoria at low doses and sympathetic activation, hyperactivity, and hallucinations at higher doses. The hallucinations are frequently auditory, thus producing behavior that mimics paranoid schizophrenia. Physical findings of drug use include vertical and horizontal nystagmus, sympathetic overactivity, numbness, increased pain thresholds, ataxia, and dysarthria. PCP may be detected on urine testing for up to 8 days after use; however, false-positive results occur with over-the-counter decongestants. Ketamine, a veterinary and pediatric anesthesia drug, has similar pharmacology and clinical profile.

**Hallucinogens**

Lysergic acid diethylamide (LSD) and hallucinogenic amphetamines are sympathomimetics and produce hypertension, pupillary dilation, tachycardia, hyperreflexia, and disordered perception. Users may experience loss of control, flashbacks (i.e., re-experiencing of drug-induced perceptions), and “bad trips” (i.e., terrifying hallucinations). Tolerance develops after three to
four doses, but there is little physical dependence or craving. Screening urine tests are not widely available for detection of LSD.

Other drugs

Inhalants including solvents (eg toluene, benzene), nitrous oxide, and trichloroethylene are frequently the first drugs if abuse for children. They produce acute effects similar to alcohol but have been associated with sudden death and significant long-term neurologic, hepatic, and renal toxicity. Flunitrazepam (rohypnol) and gamma-hydroxybutarate, along with ketamine and MDMA have been used by teens and young adults at rave parties and been associated with date rape. They are all CNS depressants, can be taken orally and are odorless, colorless, and tasteless.

Tobacco

Clinical Features

Tobacco is highly addictive because the nicotine is absorbed through the oral mucosa and lungs. Nicotine produces manifestations of increased sympathetic activity (e.g., tachycardia, mental arousal) and muscle relaxation. Tolerance to nicotine occurs rapidly (within hours) and a withdrawal syndrome that consists of restlessness, irritability, anxiety, impatience, and impaired concentration is common. Tobacco may also increase metabolism of imipramine, lidocaine, oxazepam, propranolol, and theophylline.

Principles of Management

To reduce the severity of tobacco withdrawal, several nicotine delivery systems have been developed, including the use of nicotine polacrilex in nicotine gum, transdermal nicotine patches, nasal sprays and inhalers. When used in conjunction with counseling, these agents demonstrate efficacy superior to that seen with placebos. Nicotine preparations should be used cautiously in patients with angina, cardiac arrhythmias, or a recent myocardial infarction.
Anabolic Steroids

Clinical Features and Diagnosis

Anabolic steroids are used usually in 4 to 12 week cycles by athletes to augment training, especially in power sports such as weightlifting and football. Several drugs, often including recombinant growth hormone, are often used together in a practice referred to as stacking. Six percent of male and 1% of female high school students admit to steroid use. Hepatic complications of anabolic steroid abuse include reversible elevations in liver chemistry values, jaundice, liver cell hyperplasia, hepatic adenoma, hepatocellular carcinoma, angiosarcoma, and fatal peliosis hepatis. Other adverse effects include increases in low-density lipoproteins, with concurrent decreases in high-density lipoproteins, prostate hypertrophy, prostate carcinoma, testicular atrophy, decreased sperm counts, gynecomastia, premature epiphyseal closure in adolescents, irreversible masculinization in women, mood changes, psychosis, and aggressive behavior.

Principles of Management

Anabolic steroid abuse may be suspected by prominent muscular development in a patient as well as by development of adverse side effects. Needle tracks may be visible on the thighs or buttocks. Anabolic steroid use may be detected by gas chromatography-mass spectrometry and by measurement of serum gonadotropins. Testosterone is found by detecting increased ratios of testosterone to epitestosterone in urine. Treatment of a patient who abuses steroids involves strict suspension of drug use. No significant withdrawal syndrome occurs after discontinuation of anabolic steroids.
TABLE 22-1  Change to table 55-4

TABLE 22-2  Guidelines for Screening Tests for Drug Abuse—update table 55-8

Duration of positive urine screening tests

Ethanol: 6–12 hours
Barbiturates and benzodiazepines: several days
Opiates: 2–5 days
Cocaine: 2–4 days
Amphetamines: 2–4 days
Marijuana: 30 days
Phencyclidine: 8 days

Sources of false-positive urine screening tests

Barbiturates and benzodiazepines: ibuprofen
Opiates: poppy seeds (morphine), dextromethorphan
Amphetamines: ephedrine, phenylpropanolamine, pseudoephedrine, other sympathomimetics
Marijuana: ibuprofen, naproxen, fenoprofen, passive smoke inhalation

Sources of false-negative urine screening tests

Adulteration of sample with acids, bases, benzalkonium chloride (e.g., Visine), soap
Dilution of urine (including with diuretics)
Short time elapsed after use
Ibuprofen may interfere with confirmation testing (gas chromatography-mass spectrometry)

for marijuana

Screening tests not available [AU/ED: 1]
Lysergic acid diethylamide (LSD)
Mescaline
Psilocybin
Designer drugs