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Counfounding Factors-SALT a)socioCultural Considerations:Drug abuse,Tobacco and alcohol use,AIDS b)Ageing of Population:Medical Care costs for elderly c)Technology in health Care:Diffusion in new Technology,the case of organ transplantation

### **UNIT-4**

# Physiological Effects of Alcohol, Drugs, and Tobacco on Women

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#### **Overview**

Based on human and animal studies, women are more sensitive to the consumption and long-term effects of alcohol and drugs than men. From absorption to metabolic processes, women display more difficulty in physically managing the consequences of use. In general, with higher levels of alcohol and drugs in the system for longer periods of time, women are also more susceptible to alcohol- and drug-related diseases and organ damage.

This chapter provides an overview of the physiological impact of alcohol and drugs on women, with particular emphasis on the significant physiological differences and consequences of substance use in women. It begins with a general exploration of how gender differences affect the way alcohol and drugs are metabolized in the body and then highlights several biopsychosocial and cultural factors that can influence health issues associated with drugs and alcohol. The chapter goes on to explore the physiological effects of alcohol, drugs (both licit and illicit), and tobacco on the female body. A summary of key research on the impact of these substance abuse has on women's HIV/AIDS status. Counselors can use the information presented in this chapter to educate their female clients about the negative effects substances can have on their physical health. A sample patient lecture is included that highlights the physiological effects of heavy alcohol use.

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### Physiological Effects and Consequences of Substance Abuse in Women

Alcohol and drugs can take a heavy toll on the human body. The same general statements can be made for both men and women about their long-term effects—for example, both genders incur liver problems resulting from alcohol abuse, respiratory impairment and lung cancer as a consequence of smoking, HIV/AIDS and hepatitis from injection drug use, and memory difficulties associated with the use of marijuana. Yet women have different physical responses to substances and greater susceptibility to health-related issues. Women differ from men in the severity of the problems that develop from use of alcohol and drugs and in the amount of time between initial use and the development of physiological problems (Greenfield 1996; Mucha et al. 2006). For example, a consequence of excessive alcohol use is liver damage (such as cirrhosis) that often begins earlier in women consuming less alcohol over a shorter period of time. By and large, women who have substance use disorders have poorer quality of life than men on health-related issues.

In addition, women who abuse substances have physiological consequences, health issues, and medical needs related to gynecology (Peters et al. 2003). Specifically, drugs and alcohol affect women's menstrual

cycles, causing increased cramping and heavier or lighter periods. Women sometimes use illicit drugs and alcohol as medication for cramping, body aches, and other discomforts associated with menstruation (<u>Stevens and Estrada 1999</u>). On the other hand, women who use heroin and methadone can experience amenorrhea (absence of menstrual periods; <u>Abs et al. 2000</u>), leading them to believe that they are unable to conceive and misreading early signs of pregnancy as withdrawal symptoms. Subsequently, they are unaware that they are pregnant. Women's substance use also poses risks to fetuses and nursing infants.

#### Limitations of Current Research on Gender Differences in Metabolism

In general, research on the unique physiological effects of alcohol and drugs in women is limited and sometimes inconclusive. Although the differences in the way women and men metabolize alcohol have been studied in some depth, research on differences in metabolism of illicit drugs is limited. For many years, much of the research on metabolism of substances either used male subjects exclusively or did not report on gender differences. Historically, women were omitted due to the potential risk of pregnancy and the possibility that hormonal changes across the menstrual cycle would wreak havoc on the drugs' effects and subsequent results.

Available research is typically based on small sample sizes and has not been replicated. Race and ethnic background can affect metabolism and the psychological effects of alcohol and illicit drugs, as can the psychopharmaceuticals sometimes used in treatment (Rouse et al. 1995), but their effects have not been studied. Similar to men, few women abuse only one substance. Polysubstance use complicates the ability to study and understand the physiological effects of specific drugs on women, while increasing the risk associated with synergistic effects when substances are combined. Significant gaps in knowledge exist regarding physiological effects across the continuum of a woman's life.

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### **Physiological Effects: Factors of Influence**

#### **Ethnicity and Culture**

The level of acculturation and cultural roles and expectations play a significant role in substance use patterns among women of color (<u>Caetano et al. 2008</u>). The prevalence of substance abuse among ethnic women typically coincides with higher levels of acculturation in the United States, thus leading to greater health issues. Literature suggests that women from ethnically diverse backgrounds who have substance use disorders possess greater risks for developing certain conditions and disorders, such as hypertension, high blood pressure, and HIV/AIDS (Centers for Disease Control [CDC] 2000*a*, *b*; <u>Steffens et al.</u> 2006; <u>Vernon 2007</u>). These health disparities arise from many sources, including difficulty in accessing affordable health care, delays in seeking treatment, limited socioeconomic resources, racism, and discrimination (<u>Gee 2002</u>; <u>Mays et al. 2007</u>; <u>Williams 2002</u>). In addition, mistrust of health care providers is a significant barrier to receiving appropriate screening, preventive care, timely interventions, and adequate treatment (<u>Alegria et al. 2002</u>). More recent studies have explored the role of gender in perceived discrimination and health, and some studies have noted differences in the type of stressors, reactions, and health consequences between men and women (<u>Finch et al. 2000</u>; <u>Flores et al. 2008</u>). For example, the Black Women's Health Study found that perceived experiences of racism were associated with an increased incidence of breast cancer (<u>Taylor et al. 2007</u>).

#### **Sexual Orientation**

Lesbian/bisexual women exhibit more prevalent use of alcohol, marijuana, prescription drugs, and tobacco than heterosexual women, and they are likely to consume alcohol more frequently and in greater

amounts (<u>Case et al. 2004</u>; <u>Cochran et al. 2001</u>, <u>2004</u>). Based on the Substance Abuse and Mental Health Services Administration's (SAMHSA's) 1996 National Household Survey on Drug Abuse, researchers compared patterns of use between homosexual and heterosexual women and found that lesbians have greater alcohol-related morbidity (<u>Cochran et al. 2001</u>). Likewise, they are less likely to have health insurance and to use preventive screenings, including mammograms and pelvic examinations. With less utilization of routine screenings, lesbians and bisexual women may not be afforded the benefit of early detection across disorders, including substance use disorders, breast cancer, and cardiovascular disease.

#### **Socioeconomic Status and Homelessness**

Overall, lower socioeconomic status is associated with higher mortality rates and greater risks for cervical cancer, coronary heart disease, HIV/ AIDS, and other health conditions and medical disorders (<u>Adler and Coriell 1997</u>). More than ethnicity, socioeconomic status heavily influences the health risks associated with substance abuse. Research suggests that when the socioeconomic conditions of ethnically diverse populations are similar to those of the White population, consequences of substance use appear comparable (<u>Jones-Webb et al. 1995</u>). Among women, alcohol and drug-related morbidity and mortality are disproportionately higher in individuals of lower socioeconomic status, which is associated with insufficient healthcare services, difficulties in accessing treatment, lack of appropriate nutrition, and inadequate prenatal care. Subsequently, impoverished women who abuse substances often experience greater health consequences and poorer health outcomes.

Similarly, homelessness is associated with higher mortality rates for all life-threatening disorders, including greater risks for infectious diseases. With greater high-risk sexual behaviors and repeated exposure to overcrowded shelters, homeless women who use injection drugs are more likely to be infected with HIV/AIDS and other infectious diseases, including airborne infections such as tuberculosis, thereby leading to greater health consequences (for review, see <u>Galea and Vlahov 2002</u>).

### **Developmental Issues and Aging**

Although little is known regarding the effect of alcohol and drugs on development across the lifespan, there is some evidence in alcohol-related research that there are different vulnerabilities at different ages for women. Even though developmental research on alcohol is not easily transferred to other drugs of abuse, it can give us a glimpse of the potential physiological issues associated with age and aging. For example, adolescent women are more likely than their male counterparts to experience cognitive impairment despite less alcohol consumption. Women of child-bearing age are more likely to experience infertility with heavier drinking (Tolstrup et al. 2003). Postmenopausal women are more likely to exhibit significant hormonal changes with heavy consumption of alcohol, leading to potentially higher risks for breast cancer, osteoporosis, and coronary heart disease (Weiderpass et al. 2001). Older women are more sensitive to alcohol and display a decrease in tolerance and alcohol metabolism (Center for Substance Abuse Treatment [CSAT] 1998d). While research has been more devoted to examining gender differences, limited data are available for other substances and less is known regarding the effect of these substances on development and aging.

### **Co-Occurring Disorders: A Bidirectional Influence**

According to SAMHSA's National Survey on Drug Use and Health (NSDUH) report (<u>Office of Applied</u> <u>Studies [OAS] 2004</u>), women with co-occurring mental and substance use disorders are likely to experience serious physical health problems. Co-occurring disorders have a bidirectional relationship and often a synergistic effect on one another. As much as substance abuse can increase the risk of, exacerbate, or cause medical conditions, medical disorders can also increase substance abuse as a means of self-medicating symptoms or mental distress associated with the disorder. Similar to men, women who have

mental disorders can have more difficulty adhering to health-related treatment recommendations, such as treatment attendance, diet restrictions, or medication compliance.

### **Physiological Effects of Alcohol**

#### **Gender Differences in Metabolism and Effects**

Alcohol is a leading cause of mortality and disability worldwide. According to the World Health Organization, alcohol is one of the five most significant risk factors for diseases, with more than 60 percent of alcohol-related diseases being chronic conditions, including cancer, cirrhosis of the liver, diabetes, and cardiovascular disease (<u>Chisholm et al. 2004</u>).

Alcohol's effects on women have been studied more than those of illicit drugs. Compared with men, women become more cognitively impaired by alcohol and are more susceptible to alcohol-related organ damage. Women develop damage at lower levels of consumption over a shorter period of time (for review, see <u>Antai-Otong 2006</u>). When men and women of the same weight consume equal amounts of alcohol, women have higher blood alcohol concentrations. Women have proportionately more body fat and a lower volume of body water compared with men of similar weight (<u>Romach and Sellers 1998</u>). As a result, women have a higher concentration of alcohol because there is less volume of water to dilute it.

In comparison with men, women, at least those younger than 50, have a lower first-pass metabolism of alcohol in the stomach and upper small intestine before it enters the bloodstream and reaches other body organs, including the liver. One researcher concluded that women's lack of a functional gastric protective barrier means that "for an alcoholic woman to drink alcohol is the same as taking the alcohol directly into a vein," contributing to her greater vulnerability to alcohol-related organ damage (Lieber 2000, p. 417).

These factors may be responsible for the increased severity, greater number, and faster rate of development of complications that women experience from alcohol abuse when compared with men, according to reviews of several studies (<u>Blum et al. 1998</u>; <u>Greenfield 1996</u>). Women develop alcohol abuse and dependence in less time than do men, a phenomenon known as telescoping (<u>Piazza et al. 1989</u>). At a rate of consumption of two to three standard drinks per day, women have a higher mortality rate than men who drink the same amount. Men do not experience an increased mortality risk until they consume four drinks daily (<u>Holman et al. 1996</u>).

Women develop other alcohol-related diseases at a lower total lifetime exposure than men, including such disorders as fatty liver, hypertension, obesity, anemia, malnutrition, gastrointestinal hemorrhage, and ulcers that require surgery (<u>Van Thiel et al. 1989</u>). Heavy alcohol use also increases the risk of hemorrhagic stroke, according to one study cited by <u>Nanchahal and colleagues (2000)</u>. Older women respond to alcohol somewhat differently than do younger women. They have even less body water, a heightened sensitivity to and decreased tolerance for alcohol, and a decrease in alcohol metabolism in the gastrointestinal tract (<u>CSAT 1998d</u>).

The following sections identify specific physiological effects related to alcohol use by women. These effects are not distinct from one another; rather, they interact in a synergistic way in the body.

#### Liver and Other Organ Damage

Females are more likely than their male counterparts to experience greater organ damage as a result of consuming similar amounts of alcohol. Compared with men, women develop alcohol-induced liver disease over a shorter period of time and after consuming less alcohol (<u>Gavaler and Arria 1995</u>). Women

are more likely than men to develop alcoholic hepatitis and to die from cirrhosis (<u>Hall 1995</u>). One researcher has theorized that women's faster alcohol elimination rate can endanger the liver by subjecting it to high, though transient, levels of acetaldehyde, a toxic byproduct of alcohol metabolism. This exposure may explain the higher liver cirrhosis rates among women (e.g., <u>Thomasson 2000</u>).

#### **Cardiac-Related Conditions**

According to current studies, women who drink exhibit a greater propensity to develop alcohol-induced cardiac damage. While light consumption (less than one drink per day) can serve as a protective factor for women who have a risk for coronary artery disease, studies suggest that protection is not evident for younger women, women who drink heavily, and women without risk factors associated with heart disease. Women who are dependent on alcohol or consume heavier amounts are more likely to die prematurely from cardiac-related conditions (Bradley et al. 1998*a*; Fernandez-Sola and Nicolas-Arfelis 2002; Hanna et al. 1992).

Heavy consumption (more than four drinks per day) is associated with increased blood pressure in both women and men (Bradley et al. 1998*a*). A major epidemiological study found that women between ages 30 and 64 who consumed 15–21 units of alcohol per week had an increased risk of hypertension compared with those who drank 14 or fewer units; those who drank 1–7 units per week had an overall decrease in 10-year risk of cardiovascular disease compared with those who drank more (Nanchahal et al. 2000). The female heart appears to experience a functional decline at a lower level of lifetime exposure to alcohol than does the male heart (Urbano-Marquez et al. 1995).

### What constitutes light, moderate, or heavy drinking?

The U.S. Department of Health and Human Services and U.S. Department of Agriculture's definition of moderate alcohol consumption (2005) varies by gender: In women, moderate drinking is considered to be no more than one drink per day, compared with no more than two drinks per day for men. These differences stem from gender differences in body composition and metabolism.

### **Reproductive Consequences**

Research into the adverse impact of alcohol consumption on fertility is growing. While numerous studies have shown a consistent relationship between heavy drinking and infertility (Eggert et al. 2004; Tolstrup et al. 2003), additional studies examining moderate consumption are more inconsistent. Nevertheless, findings suggest a need to educate and screen women for alcohol use while they are seeking infertility treatment (Chang et al. 2006). In addition, heavy drinking is associated with painful and/or irregular menstruation (Bradley et al. 1998a). The reproductive consequences associated with alcohol use disorders range from increased risk for miscarriage to impaired fetal growth and development (Mello et al. 1993).

There are considerable variations among women in their capacity to consume and metabolize alcohol. Early literature suggests that variations in alcohol metabolism among women may be linked to the different phases of the menstrual cycle, but more recent reviews suggest that there are no consistent effects of the menstrual cycle on the subjective experience of alcohol intake or alcohol metabolism (Terner and de Wit 2006). Studies reviewed by Romach and Sellers (1998) found that significant hormonal changes are reported in postmenopausal women who consume alcohol. Women taking hormone replacement therapy (HRT), now referred to as menopausal hormone therapy, and consuming 14 or more standard drinks weekly had significantly higher estradiol levels. These high levels are associated with a greater risk of breast cancer and coronary heart disease.

#### **Breast and Other Cancers**

Numerous studies have documented associations and suggested causal relationships between alcohol consumption and breast cancer risk (Key et al. 2006; Li et al. 2003; Zhang et al. 2007). A review of data from more than 50 epidemiological studies from around the world revealed that for each drink of alcohol consumed daily, women increased their risk of breast cancer by 7 percent (Hamajima et al. 2002). Postmenopausal women have an increased risk of breast cancer as well if they currently drink alcohol (Lenz et al. 2002; Onland-Moret et al. 2005). Women who drink alcohol have elevated estrogen and androgen levels, which are hypothesized to be contributors to the development of breast cancer in this population (Singletary and Gapstur 2001). In addition, postmenopausal women who are moderate alcohol drinkers (one to two drinks a day) and who are using menopausal hormone therapy have an increased risk of breast cancer, with even greater risk at higher rates of alcohol consumption (Dorgan et al. 2005).

While the risk for in situ and invasive cervical cancer and cancer of the vagina may be associated with other environmental factors including high-risk sexual behavior, human papilloma viruses, smoking, hormonal therapy, and dietary deficiency, <u>Weiderpass and colleagues (2001)</u> concluded, based on 30 years of retrospective data, that women who are alcohol dependent are at a higher risk for developing these cancers. Similarly, <u>Bagnardi et al. (2001)</u> conducted a meta-analysis of more than 200 studies whereby they found that alcohol significantly increased the risks for cancers of the oral cavity, pharynx, esophagus, larynx, stomach, colon, rectum, liver, and ovaries. Although further investigation is needed to explore the role of alcohol consumption on gastric cancer, preliminary findings suggest that the type of alcoholic beverage, namely medium-strength beer, creates an increased risk of gastric cancer (<u>Larsson et al. 2007</u>). Based on a multiethnic cohort study, the risk of endometrial cancer increases when postmenopausal women consume an average of two or more drinks per day (<u>Setiawan et al. 2008</u>). Additional risks are associated with tobacco use, particularly for cancers of the upper digestive and respiratory tract.

### Osteoporosis

According to <u>Bradley and colleagues (1998*a*)</u>, evidence suggests "decreased bone formation and abnormal vitamin D metabolism may predispose alcohol-dependent premenopausal women to osteoporosis" (p. 631). Heavy alcohol use clearly has been shown to harm bones and to increase the risk of osteoporosis by decreasing bone density. These effects are especially striking in young women, whose bones are developing, but chronic alcohol use in adulthood also harms bones (<u>Sampson 2002</u>). In addition, animal studies suggest that the damaging effects of early chronic alcohol exposure are not overcome even when alcohol use ceases (<u>Sampson 1998</u>). Tobacco use also may increase the risk of osteoporosis and fractures; people who drink are 75 percent more likely to smoke, and people who smoke are 86 percent more likely to drink (<u>Shiffman and Balabanis 1995</u>).Women in menopause who enter treatment need bone density assessment, nutritional guidelines, and medication consultations.

# **Neurological Effects**

Starting with adolescence, women appear to be more susceptible to the toxic effects of alcohol or its metabolites on the nervous system and more vulnerable to alcohol-induced brain damage than men (Bradley et al. 1998*a*; Hommer et al. 1996; Mann et al. 2005; Mumenthaler et al. 1999). Research supports that adult and adolescent women who are alcohol dependent experience greater declines in cognitive and motor function than men despite less alcohol consumption, shorter history of overall use, and

shorter duration of alcohol dependence (<u>Acker 1986; Flannery et al.</u> 2007; <u>Sullivan et al. 2002</u>).

In comparison with men who are alcohol dependent and female controls (women who are not dependent on alcohol), women who are alcohol dependent exhibit deterioration in planning, visuospatial ability, working memory, and psychomotor speed. They also show brain abnormalities and shrinkage after a shorter drinking history and lower peak consumption than do men. Studies demonstrate that in general, women with alcohol dependence disorders have significantly smaller volumes of gray and white matter, less hippocampal volume (memory), and greater peripheral neuropathy than either men who abused alcohol or women who did not abuse alcohol (Ammendola et al. 2000; Hommer et al. 2001; Romach and Sellers 1998; Schweinsburg et al. 2003).

Women appear to be at greater risk than men for Alzheimer's disease, although women's longer life spans may contribute to this higher risk (<u>Sohrabji 2002</u>). Heavy alcohol consumption is known to result in memory deficits and may increase the risk for Alzheimer's disease in both genders, but particularly in women, who appear to be more vulnerable than men to alcohol-induced brain damage (<u>Sohrabji 2002</u>).

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# **Physiological Effects of Licit and Illicit Drugs**

# **Gender Differences in Metabolism and Effects**

Research (Hernandez-Avila et al. 2004) supports the concept of an accelerated progression to treatment entry among women dependent on opioids, cannabis, or alcohol, and suggests the existence of a gender-based vulnerability to the adverse consequences of these disorders. No gender difference was noted for age at onset of regular use, but the women had used opioids, cannabis, and alcohol for fewer years before entering treatment. The severity of drug and alcohol dependence did not differ by gender, but women reported more severe psychiatric, medical, and employment complications than did men. In one substance abuse treatment study focused on urban outpatient clinics, women had more symptoms than men across substances (Patkar et al. 1999). They reported more cardiovascular, mood, nose and

throat, neurological, skin, and gastrointestinal symptoms than did men. In addition, there is evidence that women who use injection drugs are more susceptible to medical disorders and conditions (Zolopa et al. 1994). Similarly, women who use cocaine, heroin, or injection drugs have a heightened risk of developing herpes, pulmonary tuberculosis, and/or recurrent pneumonia (Thorpe et al. 2004).

To date, little is known regarding the consequences of specific drug use among women. Complicated by polysubstance use, studies are often unable to obtain adequate sample sizes of women who abuse only one drug. The following section highlights specific physiological effects of licit and illicit drugs that are unique to women. This is not a general primer on drugs, but rather a compendium of known physiological effects that are gender-specific.

### Cocaine, Amphetamine, and Methamphetamine

Hormonal changes across the menstrual cycle have the greatest effect on stimulant drugs, particularly cocaine and amphetamine. Literature highlights a consistent and greater mood-altering effect of stimulant use during the follicular phase of the cycle (for review, see <u>Terner and de Wit 2006</u>), and the fluctuations in progesterone levels may account, in part, for this sex difference (Evans 2007; Evans and Foltin 2006). More specifically, Evans and colleagues (2002) investigated whether cocaine effects vary as a function of menstrual cycle phase; they found that heart rate and ratings such as "good drug effect" were increased more during the follicular phase than the luteal phase. Conversely, injection drugs and/or crack cocaine appear to produce changes in the menstrual cycle, including the development of amenorrhea, degree of blood flow, and the intensity of cramps (<u>Stevens and Estrada 1999</u>). Overall, women who use cocaine report more positive subjective drug effects, including greater euphoria and desire to use, while physiological responses to the drug did not change (<u>McCance-Katz et al. 2005</u>).

Methamphetamine use has an array of possible adverse effects (for review, see <u>Winslow et al. 2007</u>), but data regarding specific gender differences are limited. Psychoactive effects of methylenedioxy- methamphetamine (ecstasy) have been found to be more intense in women than in men; women report experiencing a higher degree of perceptual changes, thought disturbances, and fear of the loss of control of their bodies. Acute adverse effects, such as

jaw clenching, dry mouth, and lack or loss of appetite, are more common among women (Liechti et al. 2001).

### Heroin and Other Opioids

Research is lacking that would allow definitive conclusions about gender similarities or differences in the following effects of heroin use: scarred and collapsed veins, bacterial infections of blood vessels and heart valves, abscesses, cellulitis, and liver or kidney disease (<u>National Institute on Drug Abuse [NIDA] 2000</u>).

Research suggests that there are no menstrual cycle differences in women's subjective experience or physiological reaction to opioids (Gear et al. 1996), but women using heroin or methadone do experience menstrual abnormalities, particularly amenorrhea or an irregular menstrual cycle (Abs et al. 2000; Santen et al. 1975; Smith et al. 1982). It can take up to a year for regular menstrual cycles to resume after drug use is stopped. Deficits in sexual desire and performance are also consequences of heroin use (Smith et al. 1982). These symptoms probably are related to the lower levels of luteinizing hormone, estradiol, and progesterone found in these women (Abs et al. 2000). Amenorrhea and other symptoms often make women believe they are permanently sterile, a fear that can be lessened with education. TIP 43 *Medication-Assisted Treatment for Opioid Addiction in Opioid Treatment Programs* (CSAT 2005*b*) provides more information.

# Marijuana

Studies on marijuana effects have not focused specifically on gender differences; therefore, little is known about how marijuana affects men and women differently. In studies evaluating hormonal changes and the physiological and psychological effects of marijuana use, findings suggest that the effects of marijuana do not vary markedly across the menstrual cycle (Block et al. 1991; Griffin et al. 1986; Lex et al. 1984).

Effects of marijuana on birth outcomes are discussed below.

# Prescription and Over-the-Counter Medications

Women are significantly more likely to use and abuse prescription medications, including anxiolytics (antianxiety medications) and narcotic analgesics (pain medications), than are men (<u>Simoni-Wastila 2000</u>). Little research is available, however, on the gender differences and differential physiological effects of abuse of prescription medications. Moreover, research into the influence of hormonal changes across the menstrual cycle on subjective, behavioral, and physiological effects is limited to benzodiazepines, and findings are minimal (<u>Bell et al. 2004; Kamimori et al. 2000</u>).

Over-the-counter (OTC) medications include cold remedies, antihistamines, sleep aids, and other legally obtained nonprescription medications. It is not uncommon for individuals with eating disorders, particularly those diagnosed with bulimia nervosa, to abuse laxatives, diuretics, emetics, and diet pills. Misuse of these medications can result in serious medical complications for those with eating disorders, who primarily are women (U.S. Department of <u>Health and Human Services, Office on Women's Health 2000</u>). Complications can involve the gastrointestinal, neuromuscular, and cardiac systems and can be lethal. Many prescription and OTC medications interact negatively with alcohol and drugs.

# **Gender Differences and OTC Drugs**

Across studies, prevalence rates comparing the use and misuse of OTC medications among men and women vary according to age and race/ethnicity. For individuals 65 years of age and older, women are more likely to use OTC drugs (Halon et al. 2001). NSDUH evaluated the misuse of OTC cough and cold medications among persons aged 12 to 25 (SAMHSA 2007) and found that women aged 12 to 17 were more likely than men to have misused OTC cough and cold medications in the past year, while men between 18 and 25 years of age were more likely to have misused these medications. Whites and Hispanics had higher rates of misuse than African Americans. Similar to men, women who had ever misused OTC cough and cold medications also had lifetime use of marijuana and inhalants. In evaluating prescription and OTC drug treatment admissions, women represented a larger proportion of prescription and OTC medication admissions (46 percent) than treatment admissions for all substances (30 percent; SAMHSA 2004).

"Every woman is different. No amount of drinking is 100 percent safe, 100 percent of the time, for every individual woman" (National Institute on Alcohol Abuse and Alcoholism [NIAAA] 2003).

# **Physiological Effects of Tobacco Use**

The health risks associated with nicotine use are considerable, particularly among women. In comparison with men, women who smoke show higher disease risk regardless of smoking level or intensity (Mucha et al. 2006). Currently, cancer is the second leading cause of death among women, with mortality rates higher for lung cancer than breast cancer. According to the Office of he Surgeon General (2001 *b*), women who smoke:

- Have an increased risk of peptic ulcers and Crohn's disease.
- Have an increased risk of estrogen deficiency; difficult, irregular or painful menstruation; and amenorrhea.
- Are more likely to be diagnosed with cancer, including cancer of the lung, bladder, cervix, pancreas, kidney, larynx, esophagus, liver, and colon.
- Have a higher risk for delayed conception and infertility.
- Are more likely to deliver premature and low-birth-weight infants.
- Have an increased risk for ischemic stroke, subarachnoid hemorrhage, peripheral vascular atherosclerosis, and an abdominal aortic aneurysm rupture.
- Are more likely to have premature decline in lung function, chronic obstructive pulmonary disease, and coronary heart disease.
- Have an increased risk of developing cataracts and macular degeneration.
- Reach menopause at a younger age.
- Have lower bone densities and an increased risk for hip fracture after menopause.

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# Effects of Alcohol, Drugs, and Tobacco Use on Pregnancy and Birth Outcomes

The use of alcohol, drugs, and tobacco can affect a pregnant woman in a variety of ways. Substance use can result in obstetric complications, miscarriage, or significant problems for the fetus. It is difficult to tease out individual effects of licit and illicit substances on fetal and infant development because women who abuse these substances typically abuse more than one, and the substance abuse can be accompanied by psychological distress, victimization, and poverty. A detailed discussion of alcohol- and drug-related problems in infants and children is beyond the scope of this TIP except insofar as these problems create additional demands and stressors for women as well as guilt and shame about the use of alcohol, drugs, and/or tobacco during pregnancy. This section highlights specific effects of alcohol and drugs during the course of pregnancy.

# **Alcohol Use and Birth Outcomes**

Above all other drugs, alcohol is the most common teratogen (any agent that interrupts development or causes malformation in an embryo or fetus) in pregnancy (<u>Randall 2001</u>). In utero, alcohol use is associated with an increased risk of spontaneous abortion and increased rates of prematurity and abruptio placentae (premature separation of the placenta from the uterus). A study found that women who consumed five or more drinks per week were three times as likely to deliver a stillborn baby compared with those who had fewer than one drink per week (<u>Kesmodel et al. 2002</u>).

Maternal alcohol use during pregnancy contributes to a wide range of effects on exposed offspring, known as fetal alcohol spectrum disorders (FASDs), and the most serious consequence is fetal alcohol syndrome (FAS). FAS is characterized by abnormal facial features, growth deficiencies, and central nervous system problems (Jones and Smith 1973). Symptoms can include hyperactivity and attention problems, learning and memory deficits, and problems with social and emotional development. Infants who show only some of these features were previously identified as having fetal alcohol effects (FAE). Since 1996, the term FAE has been replaced by alcoholrelated birth defects (ARBD), partial fetal alcohol syndrome (pFAS), and alcohol-related neurodevelopmental disorder (ARND; <u>Stratton et al. 1996</u>). Children with ARBD have problems with major and sensory organs, as well as structural abnormalities; children with ARND have central nervous system abnormalities (<u>Green 2007</u>). Despite alcohol-related birth defects being completely preventable, FASDs are the most common nonhereditary causes of mental retardation (CDC 2002).

Another risk factor associated with alcohol exposure in utero is the potential of substance use disorders. <u>Alati et al (2006)</u> found an association of early-onset of alcohol disorders among children exposed to alcohol prenatally; this association was more pronounced with early pregnancy exposure. While little is known about the prevalence of FASD among individuals with substance use disorders, this co-occurring condition is likely to further challenge recovery effects. For guidelines in identifying and referring persons with FAS, see <u>CDC (2005)</u>.

Women who drink during breastfeeding pass alcohol on to the baby. Although numerous studies of laboratory animals have demonstrated a variety of adverse outcomes in breastfed offspring during periods when their mothers are consuming alcohol, human data are limited. A review of empirical literature on women who drink while breastfeeding provides evidence that maternal alcohol consumption does not promote lactation and may affect infant sleep patterns. (for review, see <u>Giglia and Binns 2006</u>)

The SAMHSA FASD's Center for Excellence Web site provides information and resources about FASD and related information on legislation, treatment and training curricula, and community awareness (http://www.fascenter.samhsa.gov/).

# **Cocaine Use and Birth Outcomes**

According to reviews of several studies conducted during the late 1980s and early 1990s, there are a variety of adverse effects of cocaine use during pregnancy (Zuckerman et al. 1995; Burkett et al. 1994). Studies reported that cocaine-exposed infants had smaller head circumference; lower birth weight and length; irritability; poor interactive abilities; and an increased incidence of stillbirth, prematurity, and sudden infant death syndrome (SIDS; Bell and Lau 1995). Other studies dispute many previously reported severe effects of prenatal exposure of cocaine on the offspring. Frank and colleagues' review (2001) of the literature found that the most consistent effects were small size and less-than-optimal motor performance. Eyler and colleagues (2001) found no evidence of the previously reported devastating effects of prenatal cocaine exposure. Hurt and colleagues (1995) followed a cohort of cocaine-exposed

infants from birth to age 6; although they found lower weight and head circumference, they found no difference in developmental scores between cocaine-exposed and non–cocaine-exposed infants. However, other evidence suggests that children exposed to cocaine during the first trimester were smaller on all growth parameters at 7 and 10 years of age compared with children who were not exposed to cocaine (<u>Richardson et al. 2007</u>). This longitudinal analysis indicated that the disparity in growth between both groups did not converge over time.

# Advice to Clinicians: Substance Use and Birth Outcomes

- Counselors should be sensitive to female clients who are pregnant and help them manage the additional stresses, demands, and guilt that pregnancy can cause in a woman already struggling with a substance use disorder.
- Counselors can take the opportunity to educate their pregnant clients about how alcohol, tobacco, and cocaine affect the fetus in a variety of ways that are dose and timing dependent, which is an optimistic basis for encouraging pregnant women to remain abstinent during pregnancy and while breastfeeding.
- Pregnant women using opioids should enter methadone maintenance treatment, which protects the fetus from repeated episodes of withdrawal, eliminates the risks of infection from needles, and creates a mandatory link to prenatal care.

An extensive review by Frank and colleagues (2001) of all studies published in English from 1984 to 2000 (N = 74) that met rigorous methodological criteria (N = 36) concluded that many apparent adverse outcomes of cocaine use during pregnancy "can be explained ... by other factors, including prenatal exposure to tobacco, marijuana, or alcohol and the quality of the child's environment" (p. 1624). Other studies (Hurt et al. 2001; Kaltenbach 2000; Lewis et al. 2004*b*; Messinger et al. 2004) have supported this conclusion. Singer et al. (2004) reported that the quality of the caregiving environment was the strongest independent predictor of cognitive outcomes among children exposed to cocaine.

Nonetheless, the effects of cocaine on the fetus may be dose and timing dependent, and significant cocaine use during pregnancy, with or without

other drug use, is associated with negative consequences for the offspring and the mother (Thaithumyanon et al. 2005). Birth weight, length, and head circumference of infants with high exposure to cocaine differed from those with low or no exposure (Bateman and Chiriboga 2000). Heavily cocaineexposed infants were found to have more jitteriness and attention problems than infants with light or no exposure to cocaine and lower auditory comprehension than unexposed infants (Singer et al. 2000). Evidence suggests that subtle deficits exist in cognitive and attentional processes in cocaine-exposed preschool and 6-year-old children (Leech et al. 1999; Mayes et al. 1998). In addition, infants exposed to cocaine during pregnancy had more infections, including hepatitis and HIV/AIDS exposure (Bauer et al. 2005). Much is still unknown about the effects of prenatal cocaine exposure. However, cocaine use by a pregnant woman should be viewed as an indication of multiple medical and social risk factors (Eyler and Behnke 1999; Tronick and Beeghly 1999); her ability to access prenatal care, gain supportive and effective case management services, and obtain substance abuse treatment can make all the difference in outcome.

# **Opioid Use and Birth Outcomes**

Opioid use in pregnant women presents a difficult situation because of the many medical complications of opioid use, such as infections passed to the fetus by the use of contaminated needles. Obstetric complications in pregnant women who use opioids often are compounded by lack of prenatal care. Complications include spontaneous abortion, premature labor and delivery, premature rupture of membranes, preeclampsia (high blood pressure during pregnancy), abruptio placentae, and intrauterine death. The fetus is at risk for morbidity and mortality because of episodes of maternal withdrawal (Kaltenbach et al. 1998).

# Note to Clinicians

Since timely treatment for HIV/AIDS can virtually eliminate the chance of a pregnant woman passing the infection to her fetus, all women with substance use histories should have an HIV/AIDS evaluation at the first sign of any possible pregnancy.

Reviews of several studies recommend methadone maintenance treatment (MMT) as the only treatment for the management of opioid dependence

during pregnancy because, when methadone is provided within a treatment setting that includes comprehensive care, obstetric and fetal complications, including neonatal morbidity and mortality, can be reduced (Jarvis and Schnoll 1995; Kaltenbach et al. 1998). Effective MMT prevents the onset of withdrawal, reduces or eliminates drug craving, and blocks the euphoric effects of illicit self-administered opioids (Dole et al. 1966*a*, *b*; Kreek 1988). The use of methadone in pregnancy prevents erratic maternal opioid levels and protects the fetus from repeated episodes of withdrawal. Because needle use is eliminated, MMT reduces the risk of infectious diseases. The mandatory link to prenatal care, frequent contact with program staff, and elimination of the stress of obtaining opioids daily to feel "normal" are additional benefits from MMT (Burns et al. 2006).

Reviews of the literature note that studies consistently have found that fetuses exposed to opioids (i.e., heroin and methadone) have lower birth weights than unexposed fetuses and usually undergo neonatal abstinence syndrome (NAS) at birth. NAS is a generalized disorder characterized by signs and symptoms of central nervous system irritability, gastrointestinal dysfunction, respiratory distress, vomiting, and fever, among other symptoms. NAS can be more severe and prolonged with methadone exposure than heroin exposure, but with appropriate pharmacotherapy, NAS can be treated effectively (Kaltenbach 1994; Kaltenbach et al. 1998).

Although findings among studies are diverse, most suggest that methadoneexposed infants and children through age 2 function well within the normal range of development and that methadone-exposed children between ages 2 and 5 do not differ in cognitive function from a population that was not drug exposed and was of comparable socioeconomic and racial background (<u>Kaltenbach 1996</u>). Data suggest that such psychosocial factors as environment and parenting can have as much of an effect on development as prenatal exposure to opioids (<u>Johnson et al. 1987; Lifschitz et al. 1985</u>).

In more recent years, buprenorphine treatment has been examined as an alternative to maintenance therapy for opioid dependence during pregnancy. Nonetheless, research is limited and only two randomized, double-blind studies have been conducted comparing methadone with buprenorphine (Fischer et al. 2006; Jones et al. 2005; Kayembe-Kay's and Laclyde 2003; Raburn and Bogenschultz 2004). For additional information on maintenance therapies during pregnancy, see TIP 43 *Medication-Assisted Treatment for* 

*Opioid Addiction in Opioid Treatment Programs* (<u>CSAT 2005</u>*a*) and TIP 40 *Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction* (<u>CSAT 2004</u>*a*).

# **Marijuana Use and Birth Outcomes**

The limited research on the effects of prenatal exposure to marijuana shows somewhat inconsistent results (Bell and Lau 1995).

Longitudinal studies by <u>Day and colleagues (1992)</u> found marijuana to be associated with reduced length at birth, but it did not affect weight or head circumference. <u>Hurd et al. (2005)</u> found that exposed fetuses had significantly reduced body weight and length, even when the data were adjusted to account for maternal alcohol consumption and smoking. Children prenatally exposed to marijuana functioned above average on the Bayley Scale of Infant Development (BSID) at 9 months, but third-trimester marijuana use was associated with decreased BSID mental scores. Followup assessment of these children at age 10 found that prenatal marijuana exposure was associated with higher levels of behavior problems (<u>Goldschmidt et al.</u> <u>2000</u>). In a review of existing data, <u>Fried and Smith (2001)</u> reported that although global IQ is unaffected by prenatal marijuana exposure, aspects of executive function appear to be negatively associated with prenatal exposure in children beyond the toddler stage.

# **Amphetamine and Methamphetamine Use and Birth Outcomes**

Exposure to amphetamines in utero has been associated with both short- and long-term effects, including abnormal fetal growth, withdrawal symptoms after birth, and impaired neurological development in infancy and childhood (Wagner et al. 1998). Both animal and human studies have shown that fetal exposure to amphetamines increases the risk of reduced fetal growth, cardiac anomalies, and cleft lip and palate (Winslow et al. 2007). Unfortunately, knowledge of the effects of methamphetamine during pregnancy is limited. While there is evidence of increased rates of premature delivery, placental abruption, reduced fetal growth, and heart abnormalities, studies are confounded by other issues, including polysubstance abuse among participants and methodological issues in the research design. In one study, which took into account several confounding variables, findings suggest that methamphetamine exposure in utero is associated with decreased growth

(including lower birth weight) and smaller gestational age for exposed neonates (<u>Smith et al. 2006</u>).

# **Tobacco Use and Birth Outcomes**

Women who smoke tobacco increase their chances of ectopic pregnancy (development of a fetus outside the uterus), spontaneous abortion, premature rupture of membranes, abruptio placentae, placenta previa, preeclampsia, and preterm delivery. Infants born to women who smoke are more likely to have lower birth weights and have an increased risk of SIDS (<u>Office of the Surgeon General 2001*b*</u>; <u>Visscher et al. 2003</u>). Children of parents who smoke heavily can be affected adversely in their auditory, language, and cognitive performance; hyperactivity and attention deficit disorders are also common, according to the literature (<u>Bell and Lau 1995</u>). Studies have also drawn an association between maternal smoking during pregnancy and disruptive behavior earlier in development (<u>NIDA 2008; Wakschlag et al. 2006</u>).

Go to:

# Effects of Alcohol and Illicit Drugs on HIV/AIDS Status

People who inject drugs have a high prevalence of co-infection with tuberculosis, hepatitis, and HIV (<u>Cohn 2002</u>; <u>Martin et al. 2000</u>). Evidence suggests that women who inject drugs often incur added risk by injecting after men, who often procure the drugs and injection equipment (<u>Pugatch et al. 2000</u>). According to <u>CDC (2002</u>), 57 percent of HIV infections among women are attributable to use of injection drugs or intercourse with a person who injects drugs.

Some substances make women more vulnerable to STDs because of physiological changes. For example, women who abuse large amounts of alcohol tend to have drier mucous membranes, which results in abrasions and small tears that allow HIV easier access to the bloodstream during intercourse (Norris and Hughes 1996).

Douching increases vulnerability to HIV by removing protective bacteria (<u>Cottrell 2003; Funkhouser et al. 2002</u>).

Since timely treatment for HIV/AIDS can virtually eliminate the chance of a pregnant woman passing the infection to her fetus, all women with substance use histories should have an HIV/AIDS evaluation at the first sign of any possible pregnancy.

Although highly active antiretroviral therapy (HAART) has extended survival time, evidence suggests that the gains are not equal when comparing gender and status as a person who uses injection drugs. Poundstone and colleagues (2001) concluded that women who inject drugs do not benefit as much as men and women who do not use injectable drugs. CDC (1998) reports that antiretroviral drugs administered to pregnant women and their newborns have been shown to reduce greatly the risk of perinatal mother-to-child HIV/AIDS transmission. Aggressive combinations of drugs currently are recommended, but the specific regimens that can both treat a client's HIV/AIDS infection and reduce perinatal transmission depend on many factors. The ability to provide effective health care to women who are HIV positive can be influenced significantly by their use of substances and adherence to therapy (Lucas et al. 2006). Once women are in treatment, counselors need to ensure that they are provided with or referred for medical and prenatal care as soon as possible to prevent medical complications. For more detailed information regarding HIV/AIDS, refer to TIP 37 Substance Abuse Treatment for Persons with HIV/AIDS (CSAT 2000c).

# **HCV and Women**

The hepatitis C virus (HCV) is the primary cause of cirrhosis and liver cancer in United States. An estimated 4.1 million people in the United States are infected with HCV. Of these, 80 to 85 percent will develop chronic hepatitis C, but the rate is lower for women. In 2006, the rate of HCV in women was 0.25 cases per 100,000 (CDC 2008).

HCV can remain silent for many years; most people infected with chronic hepatitis C thus may not be aware that they are infected because they are not chronically ill (<u>Heintges and Wands 1997</u>). For some, the only sign of an infection is found in blood test results. A positive result can occur when the liver enzyme ALT is abnormally high. Women's ALT levels are naturally lower than men's, yet the cutoff number for abnormal liver tests is the same for both sexes. This can result in women being misdiagnosed as having a normal ALT level. If a woman's liver enzymes are on the high side of normal

or she has any risk factors for HCV, testing is recommended for HCV (<u>Porter</u> 2008).

Approximately 250,000 women are infected with HCV due to blood they received after a cesarean section prior to 1992 (<u>Porter 2008</u>). Since 1992, screening and regulations on U.S. blood supplies ensure that the recipient is free from risks of contracting any blood-borne illness. Currently, risk factors for contracting HCV are generally the same for men and women, yet women are at higher risk of contracting HCV from sexual contact with an HCV-positive partner, and women are more likely to be initiated into drug use or share equipment for injection drugs with a sexual partner. Below is a list of risk factors for acquiring HCV:

- Injection drug use (56 percent of HCV cases in men and women reported in 2006; <u>CDC 2008</u>).
- Sexual contact with HCV positive partner (0–3 percent for women in monogamous heterosexual relationships; the risk increases with multiple partners, the presence of a sexually transmitted disease, hepatitis B virus [HBV], or open sores, cuts, or wounds [Porter 2008]; 1–12 percent among female prostitutes [The C. Everett Koop Institute 2008]).
- Occupational exposure (1.5 percent of HCV cases reported in 2006; <u>CDC 2008</u>) through the use of razors, needles, nail files, a barber's scissors, tattooing equipment, or body piercing or acupuncture needles if these items are contaminated by blood from an infected person.
- Perinatal or vertical transmission (5 percent in children of mothers with HCV monoinfection; 18.7 percent rate in mothers with HIV/HCV co-infection; <u>Bell et al. 2004</u>).

Almost one out of four newly diagnosed cases of HIV in the United States is a woman, and approximately 20 percent of these newly diagnosed women with HIV are co-infected with HCV (<u>Orenstein and Tsogas 2001</u>). Among pregnant and nonpregnant women, HCV and HIV co-infection is significantly associated with injection drug use (<u>Nikolopoulou et al. 2005</u>). The rate of HIV/HCV co-infection may be as high as 50 to 90 percent for those who contracted HIV through injection drug use. HIV co-infection with HCV appears to raise the risk of mother-to-child transmission to 18.7 percent. The risk for transmission from a woman with HCV monoinfection to her infant is 5.4 percent (<u>Bell et al. 2004</u>).

# Prevention and intervention

Prevention strategies are gender neutral and include screening blood, plasma, organ, tissue, and sperm donors; effective infection control practices; identification, testing, and counseling of at-risk persons; and medical management of infected persons (Bell 2004).

Although this is by no means an overview of the disease or its treatment process, a review of interventions can prove beneficial when working with clients who are infected with HCV. Gender-specific guidelines for intervention are minimal.

Early medical intervention is helpful even though people infected with HCV infection often experience mild symptoms and subsequently do not seek treatment. Not everyone with hepatitis C needs medical treatment. Treatment is determined by HCV genotype, viral load, liver enzyme levels, and extent of liver damage. There are many elements to consider when undergoing treatment for chronic hepatitis C virus. Women are slightly more likely to respond favorably to HCV treatment; however, there are gender-specific issues that factor into the decision to start treatment.

# Issues of treatment specific to women

- Women should not get pregnant during and up to 6 months following HCV treatment; for those who are in treatment after childbirth, breastfeeding should be avoided.
- Autoimmune conditions occur more often in women than men. One of the HCV medications, interferon, can aggravate autoimmune diseases.
- Women have less hemoglobin (a component of red blood cells that carries oxygen to the cells) than men. Menstruating women have even lower hemoglobin levels because of monthly blood loss, which can sometimes cause anemia. HCV-positive women undergoing treatment should talk to their medical advisor about ribavirin (one of the treatment medications for HCV) and its connection to hemolytic

anemia—a type of anemia that causes red blood cells to burst before the body has a chance to use them. Women, especially menstruating women, are vulnerable to this kind of anemia and need to be monitored with regular blood tests during treatment.

In general, women are two times more likely than men to have depression. Depression is a common side effect of HCV treatment medications. Some providers recommend starting an antidepressant prior to starting treatment for HCV (Porter 2005).

Women are less likely to need HCV treatment because they tend to have less severe liver damage due to the virus (<u>Highleyman 2005</u>). Approximately 3 to 20 percent of clients with chronic HCV will develop cirrhosis over a 20- to 30-year period (<u>CDC 1998</u>). Alcoholic beverage consumption accelerates HCV-associated fibrosis and cirrhosis. A study by <u>Chen et al. (2007</u>) reveals that heavy alcohol use affects females more strongly than males, resulting in a higher mortality rate. This difference may be due to the more detrimental effect of alcohol on the progression of liver injury among women than among men with a similar level of alcohol use (<u>Becker et al. 1996</u>). Current guidelines strongly recommend that HCV patients be vaccinated for hepatitis A and B if they have not yet been exposed to these viruses, as these would radically worsen their liver disease.

Some ways addiction counselors can contribute to treatment are (for review, see <u>Sylvestre 2007</u>):

- Providing education and lifestyle guidelines.
- Distributing information on HCV in substance abuse treatment programs.
- Providing information on intervention programs such as the Healthy Liver Group. The Healthy Liver Group, launched in 2005, is an hourlong intervention comprising a 30-minute group educational session followed by an individualized meeting with the attending registered nurse to discuss laboratory results (<u>Hagedorn et al. 2007</u>).
- Teaching coping skil
- Is for side effects to clients undergoing medical therapy.

- Promoting self-care by urging clients to abstain from alcohol, to get vaccinated for hepatitis A and hepatitis B, and to inform themselves of HCV and its risk factors.
- Providing moral support and hope to clients of obtaining the best possible results by maintaining treatment.

Accessing screening and care on behalf of addicted clients with HCV can take persistence. Although the HCV antibody screening test is relatively inexpensive, the HCV viral test is not, but most county medical clinics and hospitals will provide it (Sylvestre 2007). Substance abuse treatment providers are more apt to spot the signs of depression or mania in those patients on medical therapy for HCV. Early detection and stabilization of any psychiatric side effect should not interrupt the progression of treatment. People with a substance use disorder can participate successfully in HCV therapy. For more information, see the planned TIP *Viral Hepatitis and Substance Use Disorders* (CSAT in development *j*).

# **Sociocultural aspects of HIV/AIDS**

South Africa is considered to be one of the countries worst affected by HIV/Aids in the world.

Certain sociocultural factors have been identified as responsible.

South Africa is considered to be one of the countries worst affected by HIV/Aids in the world. The reasons for this are complex; nevertheless, certain sociocultural factors have been identified as responsible for the rapid spread of the disease. These include the following:

- Gender inequality and male dominance
- Violence and sexual violence
- Political transition and the legacy of apartheid
- Stigma and discrimination
- Poverty
- Commercialisation of sex
- Lack of knowledge and misconceptions about HIV/Aids
- Cultural beliefs and practices

### Gender inequality and male dominance

South African culture is generally male-dominated, with women accorded a lower status than men are. Men are socialised to believe that women are inferior and should be under their control; women are socialised to over-respect men and act submissively towards them. The resulting unequal power relation between the sexes, particularly when negotiating sexual encounters, increases women's vulnerability to HIV infection and accelerates the epidemic.

Women's inferior status affords them little or no power to protect themselves by insisting on condom use or refusing sex.

Many women also lack economic power and feel they cannot risk losing their partners, and thus their source of financial support, by denying them sex or deciding to leave an abusive relationship.

Entrenched ideas about suitably "masculine" or "feminine" behaviour enforce gender inequality and sexual double standards, and lead to unsafe sexual practices. Abstinence and monogamy are often seen as unnatural for men, who try to prove themselves "manly" by frequent sexual encounters, and often the aggressive initiation of these.

Examples of other prevalent ideas which result in sexually unsafe behaviour include the following: sex on demand is part of the marriage "deal"; sexual violence is a sign of passion and affection; men have natural sexual urges that cannot be controlled in the face of women's powerful attractions; sex is necessary to maintain health and gender identity.

These views serve to justify men's sexual behaviour to some extent: men are given license to be sexually adventurous and aggressive, without taking responsibility for their actions.

Women's respectability is derived from the traditional roles of wife, home-maker and mother. Childbearing and satisfying her husband, sexually and otherwise, are key expectations for a wife - even if she is aware that her husband is unfaithful. Refusing a husband sex can result in rejection and violence.

The low status accorded to a woman without a male partner may be an additional reason for making women less likely to leave an abusive relationship. Too much knowledge about sex in women is seen as a sign of immorality, thus insisting on condom use may make women appear distastefully well-informed. Married women who request safer sex may be suspected of having extra-marital affairs or of accusing their husbands of being unfaithful.

#### Physical and sexual violence

Violence against women is a major problem in South Africa, and is linked to its male-dominated culture. Men often use violence in an attempt to maintain their status in society and prove that they are "real men" by keeping women under their control. Physically abusive relationships limit women's ability to negotiate safer sex: many men still do not want to use condoms, and some become violent if women insist on safer sex. Women may not even raise the issue of safer sex for fear of a violent response.

One result of apartheid-era violence by the state and the armed resistance movement is that violence came to be seen as a familiar, acceptable way of solving conflicts and wielding power. In addition to heterosexual relationships, violence pervades a wide range of social relations, including same-gender sexual relationships such as those between male prisoners.

South Africa, where a woman has about a one in three chance of being raped in her lifetime, has among the highest sexual violence statistics in the world – with obvious implications for the spread of HIV/Aids. The genital injuries that result from forced sex increase the likelihood of HIV infection; when virgins and children are raped, the trauma is more severe, and risk of infection even higher.

In cases of gang rape, exposure to multiple assailants further increases risk of transmission.

Increasing numbers of rapes of female children may represent men's attempts to seek sexual relations with young girls to avoid HIV infection or because of the belief that sex with a virgin will cure Aids.

Women with a history of being sexually abused are more likely to risk unsafe sex, have multiple partners, and trade sex for money. Men who are violent to their partners are also more likely to have sexually transmitted infections (STIs). These factors combine to put women who suffer sexual violence at very high risk of contracting HIV/Aids.

#### Political transition and the legacy of apartheid

The early years of the HIV/Aids epidemic in South Africa coincided with the end of the apartheid era, a period of complex political transition and societal instability. Leadership was distracted by the then more immediate concerns of the struggle towards democracy, with the result that crucial time was lost in the fight against Aids.

Elements of the apartheid regime - such as migrant labour, the homelands system, the Group Areas Act and forced removals - contributed to the widespread poverty, gender inequality, social instability and unsafe sexual practices that now continue to influence the spread of HIV/Aids.

The migrant labour system has been particularly important as a vehicle for HIV transmission. Labourers were prevented from settling where they worked in the urban areas, but maintained links with their families in rural parts, and moved between the two. This to-and-fro migration has been a major factor in the spread of HIV and other STIs (which, in turn, increase the risk of HIV infection). Migrant labour patterns persist because of uneven development and employment opportunities, both within the country and in neighbouring African states.

People separated for long periods tend to seek sex outside their stable relationships, which, in the single-sex hostels accommodating migrant labourers, has often been in the form of unsafe male-to-male sex, and making use of the sex-work industry that developed in the vicinity. Men frequently become HIV-infected at their place of work, and then carry the infection back home and pass it on to their wives and unborn children.

Another form of migration occurred when the former revolutionary cadres, such as umKhonto weSizwe, returned from the north of South Africa's borders in 1994 and were incorporated into the national defence force. Their return, from areas of high HIV prevalence, contributed to the rapid growth of the epidemic. Refugees from neighbouring African states also entered the country, often bringing new strains of the virus with them.

#### Stigma and discrimination

The stigma attached to HIV seriously hinders prevention efforts, and makes HIV-positive people wary to seek care and support for fear of discrimination. People who are infected may also be reluctant to adopt behaviour that might signal their HIV-positive status to others. For example, a married HIV-positive man may not use a condom to have sex with his wife; an HIV-positive mother may continue to breastfeed her baby. Many people might not want to get tested for fear of their community finding out.

Homosexuality is also stigmatised in South Africa. There is still significant denial of the existence of homosexuality in the black community and a history of poor government interventions focused on gay people. The violence often suffered by young homosexuals as a result of social stigma may cause them to hide their sexuality and not access information that could help protect them against HIV infection.

#### Poverty

High levels of unemployment and an inadequate welfare system have lead to widespread poverty, which renders people more vulnerable to contracting HIV because of the following factors:

- The daily struggle for survival overrides any concerns people living in poverty might have about contracting HIV.
- Strategies adopted by people made desperate by poverty, such as migration in search of work and "survival" sex-work, are particularly conducive to the spread of HIV/Aids.
- People living in deprived communities where death through violence or disease is commonplace tend to become fatalistic: the incentive to protect oneself against infection is low when HIV is only one of many threats to health and life. Poverty may also breed low levels of respect for self and others, and thus a lack of incentive to value and protect lives.
- Poverty is generally associated with low levels of formal education and literacy. Knowledge about HIV
  and how to prevent it, as well as access to information sources such as schools or clinics, is subsequently
  low in poor communities.

Ironically, socio-economic development and poverty relief can, in fact, sometimes drive the epidemic. This is particularly the case when development is linked to labour migration, rapid urbanisation, and cultural modernisation – all of which occur to a significant extent in South Africa. Thus, although poverty contributes to the spread of HIV/Aids, alleviating poverty can do likewise. For example, improved infrastructure such as new transport routes and improved access are seen as positive developmental goals. However, this often results in a larger migrant population, and facilitates the spread of Aids to previously inaccessible parts of the country.

#### Commercialisation of sex

A prominent aspect of South African culture that undoubtedly contributes to the HIV/Aids epidemic is that sexuality is frequently seen as a resource that can be used to gain economic benefits.

The country has seen the rapid development of a relatively affluent black middle class with a desire for material goods, and a sexual culture that associates sex with gifts. Men gain social prestige by showing off material possessions and being associated with several women.

Young women are often persuaded to have sex with "sugar daddies" – older, wealthier men – in exchange for money or gifts. Some girls enter the sex industry for similar reasons. Young women infected with HIV by sugar daddies then infect younger men, who in turn infect other young women and in time become HIV-positive older men themselves – and so the cycle continues. Older men also infect older women, usually their wives. Both younger and older women give birth to children, some of whom will be HIV-positive.

#### Lack of knowledge and misconceptions about HIV/Aids

It appears that the majority of South Africans have heard about Aids, and have a fairly good level of knowledge of the basic facts i.e. that the disease is spread sexually, and that condoms reduce risk. Nevertheless, there are still many people, especially those with low levels of formal education and who lack access to accurate, relevant information on HIV/Aids and sexuality, who are unaware of the risks.

Women in particular have high rates of illiteracy, and many girls do not complete basic education. Also, women may be unaware of risks because their time is taken up with tending the home, and they have limited links with the outside world.

Added to this is the problem that dangerous myths and misconceptions about HIV/Aids abound. These include believing that the virus can be contracted by sharing food, that infected people can be recognised by their symptoms, and, perhaps the most notorious of all, the belief that sex with a virgin can cure the disease. Beliefs

such as this give people a false sense of their level of risk, and contribute to confusion about how HIV is transmitted.

People who do possess some knowledge about HIV often do not protect themselves because they lack the skills, support or incentives to adopt safe behaviours. High levels of awareness among the youth, a population group particularly vulnerable and significant as regards the spread of HIV/Aids, have not led, in many cases, to sufficient behavioural change. Young people may lack the skills to negotiate abstinence or condom use, or be fearful or embarrassed to talk with their partner about sex. Lack of open discussion and guidance about sexuality is often lacking in the home, and many young people pick up misinformation from their peers instead.

#### **Cultural norms and practices**

Certain prevalent cultural norms and practices related to sexuality contribute to the risk of HIV infection, for example:

- Negative attitudes towards condoms, as well as difficulties negotiating and following through with their use. Men in southern Africa regularly do not want to use condoms, because of beliefs such that "flesh to flesh" sex is equated with masculinity and is necessary for male health. Condoms also have strong associations of unfaithfulness, lack of trust and love, and disease.
- Certain sexual practices, such as dry sex (where the vagina is expected to be small and dry), and unprotected anal sex, carry a high risk of HIV because they cause abrasions to the lining of the vagina or anus.
- In cultures where virginity is a condition for marriage, girls may protect their virginity by engaging in unprotected anal sex.
- The importance of fertility in African communities may hinder the practice of safer sex. Young women under pressure to prove their fertility prior to marriage may try to fall pregnant, and therefore do not use condoms or abstain from sex. Fathering many children is also seen as a sign of virile masculinity.
- Polygamy is practised in some parts of southern Africa. Even where traditional polygamy is no longer the norm, men tend to have more sexual partners and to use the services of sex workers. This is condoned by the widespread belief that males are biologically programmed to need sex with more than one woman.
- Urbanisation and migrant labour expose people to a variety of new cultural influences, with the result that traditional and modern values often co-exist. Certain traditional values that could serve to protect people from HIV infection, such as abstinence from sex before marriage, are being eroded by cultural modernisation.

# New and old technologies for organ replacement

The demand for organ transplantation has increased over time, increasingly exceeding the supply of organs. Whether and how new or old technologies separately or together could be applied to replacing organs will thus remain a question of importance.

About a decade ago, we considered, largely on theoretical grounds, how new and old technologies such as cloning, genetic engineering, tissue engineering, and cellular transplantation might be used to replace or improve the function of failing organs [1-4]. The severe shortage of human organs for transplantation, which slows the delivery of optimum therapy for some and prevents the delivery of optimum therapy for many more patients, motivated these considerations. With the passage of time and advances in medical care and technology, this shortage has become even worse and hence it would seem at least as appropriate

now as in the past to consider the dimensions of the problem and solutions with the potential to address to it.

#### Go to:

#### ANTICIPATING FUTURE DEMAND FOR ORGAN REPLACEMENT

The most thorough evaluation of demand for organ transplants and supply of organs for transplantation were published by Evans [5] 10 years ago. Although such thorough analysis has not been updated, one has the sense that the general conclusions reached then seem applicable today. As Table 1 shows, the aggregate demand for organ transplantation, as measured by the number of patients on waiting lists for transplantation, has certainly increased in the last decade (Table 1). But, this table considers only those individuals actually 'listed' for transplants and does not include those who might be listed but are not because providers have not considered transplantation as an a therapeutic option or have considered availability of organs too remote. Further, the aggregate increase in demand obscures more dramatic increases in the demand for some organs and decreases in demand for others. Thus, as Fig. 1, taken from the Annual Report of Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR) [6--], shows the demand for kidney transplants has nearly doubled in the last decade, whereas the demand for lung transplants has nearly halved. At the same time, as Fig. 1 shows, the number of organs available hence for the most part the number of transplants has not changed (except the availability of living donors) and the use of marginal donors has allowed more kidney transplant to be performed [7]. But, this approach neglects the changes in overall population. Adjustment for the 10% increase in the population of the USA in the last decade has had little impact on the demand but reveals that the number of transplants, adjusted for population, has decreased, except for kidney.



#### FIGURE 1

The demand for organ transplants and the supply of organs for transplantation. Demand for organ transplants is defined as the number of individuals on waiting lists (those on multiple waiting lists are counted once) in the USA. The supply of organs is defined as the number of transplants performed in the USA. Reproduced with permission from the Annual Report of the Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients [6••].

#### Table 1

The number of individuals waiting for organ transplants in the USA

2002	2007	2008	2009	2010	2011	2012

80790 97670 100775 105567 109375 112766 117040

Data are from UNOS and <u>http://optn.transplant.hrsa.gov</u>. Number waiting refers to number of individuals on waiting lists, individuals on more than one list are counted once.

Adjustment for population does not impact on the estimates of the current demand for transplantation and might not have served the analysis of prior demand because such adjustments are eclipsed by the improvements in medical and surgical practice that caused transplantation to evolve from a high-risk experiment to a routine procedure. On the other hand, we believe changes in population, demographics, and epidemiology of disease are central to any consideration of how technologies, the development, testing, approval, and routine application of which can span decades (as in the case of organ transplantation) will meet the needs of society. Indeed, some of our early considerations of this subject were remiss in considering only the existing supply and demand [8].

The PEW Research Center has published projections, which, if not particularly surprising, do help one imagine how demand might change over the next 20–30 years [9]. Not only is the population expected to expand during the next 3 decades, but also the demographic profile of the USA will change dramatically [9]. One important change will be in the numbers: the 'elderly', defined as those over age 65. In 2030, the elderly will comprise nearly 20% of the population, which will have swelled by nearly 100 million, versus about 12% today. If the next decades bring no other changes, the demand for organ transplantation, which we assume to be cumulative with age, will certainly increase. And, because the incidence and prevalence of heart failure and renal failure increase with age, the demand should increase still more.

Yet another demographic factor could change the demand of transplantation and the supply of organs profoundly. Immigration will account for most if not all of the growth of the population of the USA during the next 30 years [9]. Most immigrants will be Hispanic, some Asian. Immigration could well impact on the types of diseases people experience, the demand for organ transplants, and the frequency of organ donation. Changes in immigration law and extension of health benefits should also increase the demand.

On the other hand, one might hope that advances in medicine and surgery that bring new cures and improvements in care for diseases might in turn decrease the demand for organ transplants. Yet, experience in Europe and the USA suggests otherwise. Thus, greater appreciation of the importance of

controlling hypertension and hypercholesterolemia, and the availability of new drugs and devices have dramatically decreased the morbidity and mortality of cardiovascular disease in Europe and the USA [10], yet the number of patients listed for heart transplants has increased [11---]. Nor will changes in the epidemiology of disease likely decrease the demand. As mortality of cardiac disease in the USA decreased from approximately 300 per 100 000 population to approximately 150 per 100 000, the prevalence of diabetes and hypertension increased [12].

Discoveries and advances in molecular diagnosis, genomics, personalized medicine, etc., might increase still further the demand for organ transplantation. Transplantation of the kidney [13], liver [14,15], and pancreas [16] are occasionally performed in patients considered to be at high risk of developing lethal disease such as cancer. Although these procedures are rare today, the demand will only expand as the basic and clinical knowledge increases [17].

Go to:

### NEW AND OLD TECHNOLOGIES FOR REPLACING ORGAN FUNCTION

We previously considered how new and existing technologies might be applied separately and together toward the replacing of organ function [1,4,18]. Some of these technologies are listed in Table 2 and an example of how the technologies might be combined is illustrated in Fig. 2. Ten years ago, one might thoroughly review and critically discuss this subject in a communication such as this one; however, expansion of knowledge and technique makes that all but impossible today. Instead, we shall offer our perspective on a few key advances and unanswered questions.



#### FIGURE 2

Combining technologies for organ replacement. The figure illustrates a strategy proposed previously by the authors  $[\underline{1,4,18}]$ . The patient needing organ replacement is used either as a source of pluripotent stem cells or of mature cells that are made pluripotent by the nuclear transfer or other manipulation to generate induced pluripotent stem cells. The stem cells are transferred to a developing fetus, where the microenvironment coaxes the cells to become the primordium of the needed organ or a mature organ. The primordium or mature organ is harvested and transplanted into the human patient. Use of the primordium is preferred because it would acquire a vascular supply from the patient rather than from the animal; however, use of primordial might not be feasible for lung and perhaps for heart [18].

#### Table 2

Some technologies used for organ replacement

Technology	Supply	Feasibility now	Hurdles	Cost
Allotransplant	Limited	Yes	Supply and immunity	Moderate
ES cells	Unlimited	No	OF and immunity	Moderate or high
Cloning	Unlimited	No	OF and ? immunity	High
iPS cells	Unlimited	No	OF	High
Organogenesis	?	No	Size, maturation, and function	High
In-vivo organogenesis	?	No	Maturation and function	? Moderate

Technology	Supply	Feasibility now	Hurdles	Cost
Devices	Unlimited	Yes for heart	Toxicity and endurance	High
Xenotransplantation	Unlimited	Yes	Immunity	Low

Cloning, cloning by nuclear transfer; ES cells, embryonic stem cells; iPS cells, induced pluripotent stem cells; OF, organ formation.

One subject that has resonated with the scientists, physicians, and the public has been the potential use of stemcells to treat disease, including organ failure [19]. Some applications of stem cells have focused on repairing damaged organs such as the heart [20\*\*]. Others have focused on generating new tissues and organs. We shall consider only the later, and for the most part strategies in which stem cells are coaxed to differentiate into functioning tissue or an organ that can be transplanted into a patient.

Because tissues and organs contain numerous types of cells in more or less complex anatomic arrays, efforts to generate new tissues and organs usually involve the use of stem cells which can proliferate for many generations, perhaps indefinitely and differentiate into many different types of mature cells, that is, pluripotent stem cells [19,21]. Pluripotent stem cells were first isolated from the murine teratomas and after injection into the murine blastocysts were found to contribute to the formation of all tissues in the mosaic offspring [22,23]. The archetype of pluripotent stem cells is the embryonic stem cell [24]. Because embryonic stems are inevitably histoincompatible with those who would need treatment, effective use of these cells and especially of their differentiated progeny seemed to depend on the selection of least incompatible cells from a 'library' or engineering of histocompatibility [21]. Still, no matter how large a library of embryonic cells might be and despite the intensive efforts to engineer cells to make them less histoincompatible, one can no more assume embryonic stem cells can be selected or made histocompatible than one can assume bone marrow stem cells or donated organs can be selected or made histocompatible. Hence, the use of these cells for life-sustaining functions would probably require immunosuppression. Use of embryonic stem cells and their progeny is also hindered by the ethical concerns and by the observation in nearly every experimental system that after the transfer into histocompatible and even some histoincompatible individuals, the cells would generate teratomas and teratocarcinomas [25].

Transfer of nuclei into a zygote or blastocyst cell to bring about nuclear reprogramming can achieve better histocompatibility. Nuclear transfer can generate stem cells that are manifestly pluripotent and capable of generating intact animals, and capable of contributing to the germline [26]. Commonly referred to as 'reproductive cloning' when newly fashioned cells are used to generate whole animals and 'therapeutic cloning' when cells, tissues, or organs are to be produced [1,4,27], nuclear transfer could in principle be used to generate histocompatible cells for efforts to repair or replace failing organs. However, the progeny of stem cells generated by the nuclear transfer are not fully histocompatible with the source of the nucleus because the stem cells has the mitochondrial genome of the reprogramming cell, which encodes some minor histocompatibility antigens and the cells like embryonic stem cells, which generate teratomas [28]. And, if the 'reprogramming cell' derives from a human embryo, this approach provokes the same ethical concerns as the use of embryonic stem cells. Some efforts have been made to use

xenogeneic embryonic cells to reprogram mature cells, but the full promise of this approach is not yet clear.

Fortunately, the recent years have brought dramatic advances in the understanding and practice of nuclear reprogramming and with it those increasing hope that stem cells might be used to repair or replace failing organs. Nuclear reprogramming can now be accomplished by the expression of a definable set of genes in mature cells [29,30], yielding 'induced pluripotent stem cells' or 'iPS cells'. Expression of these genes is usually accomplished by the transfer of viral transforming genes [30,31••,32••]; however, fusion of donated oocytes with somatic cells [33], exposure to extracts from primitive cells [34], and defined substances might soon replace the need for gene transfer [35••].

Generation of pluripotent stem cells with such 'cloning factors' [18], a term we use to denote averting of gene transfer, is especially pertinent to tissue and organ replacement because with the exception of the fusion approach, the genome of the reprogrammed cells, both nuclear and mitochondrial, would derive fully from the donor of the mature cell, that is, the person to be treated. Hence, the stem cell should have no foreign genes. Further, generation of pluripotent stem cells in this way does not require use or destruction of a human embryo and hence avoids the most vexing ethical concerns. Still, induced pluripotent stem cells can form tumors [36] and hence, with full or near histocompatibility, this barrier remains.

Our commentary, to this point, has assumed that pluripotent stem cells containing no foreign DNA would be fully histocompatible with the individual from whom the DNA was obtained. However, some recent work has challenged this concept. Teratomas generated by the inoculation of induced pluripotent stem cells into the mice of the same strain were found to be immunogenic and indeed to be rejected in contrast to the teratomas formed from the embryonic stem cells [37...]. Needless to say, this observation seemed to indicate that induced pluripotent stem cells might not be immunologically superior to embryonic stem cells. However, this unexpected 'alloimmune' phenomenon has not been observed by all investigators and indeed it might be peculiar to the experimental system used [35...,38...]. From our perspective, we think the apparent immunogenicity of the induced pluripotent stem cells can be explained by the technical factors and that the key questions will not be immunogenicity, as immunosuppression, if needed, is obviously acceptable to allow organ replacement. Rather, the key questions to us are whether pluripotent stem cells will generate tumors, whether applications using those cells can be made efficient enough to impact on the problem of organ failure, and whether the cells will be able to generate organ replacements. We will consider this third question in the section that follows.