

## CHAPTER I

# Substance Abuse across the Lifespan in Women

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In the last decades, a considerable body of knowledge regarding differential gender issues in substance abuse has evolved. Researchers have focused on topics such as prevention, treatment, harm reduction, and public policies across genders. This chapter aims to review and summarize how a woman's life cycle stage influences her substance use and risk for developing abuse or dependence.

### EPIDEMIOLOGY

In 2005, the Monitoring the Future survey, that evaluates substance use of 14- to 18-year-old students enrolled in 8th to 12th grades, found that, when data from the five grades were pooled, male students presented higher rates of heavy drinking and illicit drug use than female students. However, this did not hold true among the 8th graders in the last years. Also, at 10th grade, girls presented higher last-30-days prevalence rates of drinking. As for cigarette smoking, similar rates have been observed across genders, but at 8th grade girls presented higher 30-day prevalence rates of use than boys. It was observed that gender differences (with boys presenting higher rates of use) emerged as students grow older, whereas for younger students (8th grade) a pattern of gender convergence or higher rates of use for girls was evidenced at least for some drugs (Johnston, O'Malley, Bachman, & Schulenberg, 2007).

Combined data from the 2002, 2003, and 2004 National Surveys on Drug Use and Health (NSDUH) conducted annually in the United States also provides evidence for gender convergence among youths ages 12–17 for misuse of psychoactive prescription medications. Past year rates for girls were 9.9% (8.2% for boys; Colliver, Kroutil, Dai, & Gfroerer, 2006).

In the general population, alcohol dependence or abuse is more frequent for men than for women. However, among men and women ages 12 or older that are heavy drinkers (e.g., those drinking five or more drinks on the same occasion on each of five or more days in the 30-day period prior to the survey), similar rates of past year alcohol dependence or

abuse were found (Substance Abuse and Mental Health Services Administration [SAMHSA], 2007a).

Younger women are a matter of particular concern given their increased likelihood of smoking while pregnant compared to older pregnant women. Roughly one-quarter of pregnant women ages 15–17 and 18–25 reported past-month smoking compared to 10% of those ages 26–44 (SAMHSA, 2007b). Recent data from NSDUH conducted from 2004 to 2006 estimate that annually almost 10% of women of childbearing age (18–49 years) needed treatment for a substance-use problem. Of these, 85% did not receive or perceive their need for treatment. The most frequently cited reasons for not receiving treatment were not being ready to stop using substances (36%), lack of funding (34%), and social stigma (29%; SAMHSA, 2007c).

### **ADOLESCENCE: DEPRESSION, TRAUMA, AND EATING DISORDERS**

Several studies point out that psychological factors play a distinct role in substance use and abuse across genders. The seminal Oakland Growth Study identified that for girls, but not for boys, feelings of low self-esteem and coping difficulties at junior high and high school levels predicted future problem drinking (Jones, 1968, 1971). In the following decade, Fillmore, Bacon, and Hyman (1979) conducted a 27-year follow-up study of drinking among college students in the United States, reporting considerable gender differences in predictive factors for future problem drinking. For college women, drinking to relieve shyness, to get high, and to get along better on dates were all predictors of future problem drinking, whereas for men, the best predictor of future problem drinking was having “incipient problems.” In a U.S. national survey published in 1997, 1,099 women were asked about sexual experiences occurring before age 18, and it was found that those women who reported childhood sexual abuse were significantly more likely to report recent alcohol use, intoxication, drinking-related problems, and alcohol dependence symptoms; lifetime use of prescribed psychoactive drugs and illicit drugs; depression and anxiety; pain that prevented intercourse; and consensual sexual intercourse before age 15, suggesting that women’s experience of sexual abuse in childhood may be an important risk factor for later substance abuse, psychopathology, and sexual dysfunction (Wilsnack, Vogeltanz, Klassen, & Harris, 1997). More recently, the National Center on Addiction and Substance Abuse ([CASA]; 2003) released a comprehensive study of girls and young women in the United States confirming that feelings of depression, hopelessness, sadness, and suicidal ideation are a great deal more frequent in high school girls than boys and these same feelings are significantly associated with a heightened risk for not only drinking but also for other drug use for girls.

These findings suggest that prevention strategies at high school and college levels should focus on those girls and young women who display emotional distress and those who drink to enhance self-esteem and ability to function. Providers of health and mental services for girls and young women can play an important role in prevention by helping them avoid self-medicating with alcohol or drugs of abuse.

Drinking also influences young women’s aggressive behavior differently from men. Results from the National Longitudinal Survey of Youth of 808 drinkers ages 17–21 in 1994, 1996, and 1998 revealed a stronger relationship between heavy episodic drinking and fights after drinking for females than for males. Particularly, those young women who dropped out of high school were significantly more likely to fight after drinking compared with college students (Wells, Speechley, Koval, & Graham, 2007).

Reasons for substance-use initiation differ in young females and males. Substance use is often perceived by young women as a coping mechanism in dealing with shyness, anxiety, and/or depression. Curiosity is the main reason for substance use initiation for boys. Also, more girls now are focused on body image and thinness, and cigarette smoking and stimulants use may be one strategy in accomplishing these ideals. Standard treatment and prevention strategies may be difficult to apply in these young women, requiring additional effort and gender-specific content in helping them maintain a good relationship with their bodies (Blume, Zilberman, & Tavares, 2005).

## ADULTHOOD

### Menstrual Cycle and Fertility

Many of the effects of substance use on women's sexuality and fertility, as well as use of substances in the perinatal period, have been elucidated. The relationship between drinking and the menstrual cycle was reviewed by Mumenthaler, Taylor, O'Hara, and Yesavage (1999). They concluded that the menstrual cycle is unlikely to have a significant influence over alcohol pharmacokinetics. Conversely, although at low levels alcohol seems to have little effect on female sex hormones, there is evidence that acute alcohol intoxication is associated with increased plasma levels of testosterone in women. This is due to an increased rate of conversion of androstenedione to testosterone in the liver caused by alcohol even in healthy women who drink episodically (Sarkola, Fukunaga, Makisala, & Peter Eriksson, 2000). This may be the basis for a variety of fertility problems such as ovulation inhibition, decreased gonadal mass, infertility, and other sexual dysfunctions often observed in women who drink heavily (Blume & Zilberman, 2004). In men, alcohol intoxication produces a transient reduction in testosterone levels (Frias, Torres, Miranda, Ruiz, & Ortega, 2002).

The effects of drinking on sexuality involve a complex interaction of socially determined expectations and pharmacological effects. A commonly held societal belief is that women who are drinking crave sex and become promiscuous. This stereotype encourages men to seek sexual intercourse with women who show intoxication. A 1981 national survey of 917 women showed that a large proportion of women drinkers reported that drinking lessens their sexual inhibitions and helps them feel close to others, 22% reported feeling more sexually assertive, but only 8% reported becoming less selective in partner choice. However, 60% reported having been the target of other drinkers' sexual aggression. Women who were heavier drinkers had higher rates of sexual dysfunction such as lack of sexual interest, difficulties reaching orgasm, and vaginismus (Klassen & Wilsnack, 1986).

Another interesting finding is the dissociation observed in women between subjective feelings of sexual arousal and physiological responses after drinking. Physiological measures demonstrate that alcohol consumption actually reduces sexual arousal in women, although they subjectively reported feeling more aroused (Wilson & Lawson, 1976). The same dissociation was observed regarding their ability to reach orgasm, which was depressed by alcohol in a dose-response relationship (Malatesta, Pollack, Crotty, & Peacock, 1982).

Likewise, some women rely on the use of drugs for their presumed aphrodisiac properties. The literature, instead, reveals that, apart from the subjective effects, substance use negatively affects the sexual response (Johnson, Phelps, & Cottler, 2004). For instance, although the acute effect of cocaine is as a stimulant, its chronic use causes sexual dysfunction mainly due to hyperprolactinemia, but is also linked to increased levels of luteinizing hormone (Mello & Mendelson, 1997). Cocaine use is associated with negative effects over the men-

strual cycle, producing amenorrhea, luteal phase dysfunction, galactorrhea, and infertility (Mendelson, Sholar, Siegel, & Mello, 2001).

Opioids at high doses inhibit the hypothalamus–pituitary–gonadal axis and increase prolactin levels that, in turn, interfere with sexual response and fertility (Cofrancesco et al., 2006). Cigarette smoking has been associated with a number of menstrual abnormalities, fertility problems, and early menopause in women, related to nicotine inhibitory effect over luteinizing hormone and prolactin release (Fuxe, Andersson, Eneroth, Härfstrand, & Agnati, 1989). Acute cannabis use during the luteal phase of the menstrual cycle is also associated with decreased prolactin and luteinizing hormone levels, whereas chronic cannabis use does not alter hormone levels (Block, Farinpour, & Schlechte, 1991), suggesting that cannabis effects on women's hormones may not be persistent.

### **Pregnancy and Breastfeeding**

Substance use during the perinatal period poses significant risks for women and their offspring. Antenatal alcohol exposure has a broad range of adverse effects on placental development and function including placental dysfunction, decreased size, impaired blood flow and nutrient transport, endocrine changes, increased rates of stillbirth and abruption, umbilical cord vasoconstriction, and low birth weight (Burd, Roberts, Olson, & Odendaal, 2007). Fetal alcohol syndrome (FAS) is one of the most common developmental disabilities in the United States. FAS occurs at a rate of 0.5–2.0 per 1000 live births, making it one of the three most frequent causes of birth defects associated with mental retardation. The syndrome includes prenatal and postnatal growth retardation and central nervous system abnormalities. A characteristic facial dysmorphism, composed of short palpebral fissures, epicanthic folds, and maxillary hypoplasia, may be present. Other signs may include birth defects such as microcephaly, altered palmar creases, and heart abnormalities. The full-blown FAS is seen in the offspring of approximately one third of women who are alcoholics drinking the equivalent of 10 standard drinks daily, but other fetal alcohol effects such as spontaneous abortion, reduced birth weight, and behavior changes have been associated with lower levels of alcohol intake (Warren et al., 2001). Binge drinking is an important risk factor, but studies of genetic associations have focused on the alcohol dehydrogenase 1B gene, suggesting a protective effect for genotypes containing ADH1B2 or ADH1B3, associated with faster alcohol metabolism, while the ADH1B1 homozygous genotype would be involved with slower metabolism and FAS susceptibility (Green & Stoler, 2007). There are controversial data regarding potential adverse effects of low to moderate alcohol levels during pregnancy. A recent systematic review observed no conclusive evidence regarding the matter but observed that methodological weaknesses in the studies reviewed precluded assumptions about the safety of light drinking during pregnancy. In addition, countries vary broadly in definitions of low-risk drinking (Henderson, Gray, & Brocklehurst, 2007). Therefore, the recommendation for women who are pregnant or attempting to become pregnant is to refrain from drinking.

There is a need for more data on drinking patterns during the breastfeeding period. Results from the 1993–1994 Food and Drug Administration Infant Feeding Practices Study I, a longitudinal study of infant–mother pairs that included 772 breastfeeding women and 776 controls, found no significant differences in self-reported alcohol consumption at 3 months postpartum among breastfeeding and non-breastfeeding women (approximately 38%). However, data about levels of infant exposure and consequences are lacking for the most part (Breslow, Falk, Fein, & Grummer-Strawn, 2007). A study uncovered a significant (albeit relatively small) difference in motor development at one year of age between infants breastfed by mothers who drank during lactation and infants of mothers who were abstinent (Little,

Anderson, Ervin, Worthington-Roberts, & Clarren, 1989). This finding was not replicated in a more recent study conducted by the same group of investigators (Little, Northstone, Golding, & ALSPAC Study Team, 2002).

Data from pregnant women participating in the four-site Maternal Lifestyle Study estimated that 5–10% of pregnant women in North America use cocaine during pregnancy (Lester et al., 2001). Only 2% of these women reported cocaine use only. Hence, it is difficult to isolate the specific pharmacological effects of cocaine on pregnancy and offspring due to polydrug use. Perinatal complications associated with cocaine use include sexually transmitted diseases, abruptio placentae, meconium staining, premature rupture of membranes, and low birth weight (Bauer et al., 2002).

A recent review highlighted findings about the effects of prenatal cocaine exposure on offspring's mental health. These effects tend to be nonpersistent and are largely mediated by psychosocial factors, such as malnutrition, increased maternal age, and other drug use including alcohol and tobacco, in such a way that most associations between child development and intrauterine cocaine exposure disappear when psychosocial factors are taken into account (Williams & Ross, 2007). However, longer follow-up studies are still needed, as cognitive demands tend to be higher in adolescence. For instance, recent studies in children and adolescents with in utero cocaine exposure uncovered reduced cerebral blood flow (Rao et al., 2007) and slower growth rate (Richardson, Goldschmidt, & Larkby, 2007), even when psychosocial factors are taken into account. Unlike antenatal cocaine exposure, there is a lack of information regarding recommendations for breastfeeding mothers who were cocaine users, although case studies record detection of cocaine in breast milk in levels that could lead to symptoms such as seizures, tachycardia, and irritability in the newborn (Sarkar, Djulul, & Koren, 2005).

Being highly lipophilic, tetrahydrocannabinol may be sequestered in fat tissue for weeks in chronic users. Hence, even if the user quits cannabis use after finding out about pregnancy, tetrahydrocannabinol will still be slowly released from fat tissue into the bloodstream, freely crossing the placental barrier and exerting its potentially deleterious effects on pregnancy and offspring. These effects are caused by cannabis-induced decreased uteroplacental perfusion, preterm delivery, and intrauterine growth retardation with low birth weight. Regarding regular antenatal exposure to cannabis, data support a subtle neurodevelopmental effect upon later functioning that includes specific cognitive deficits, particularly in visuospatial working memory (Smith, Fried, Hogan, & Cameron, 2006), and also hyperactivity, impulsivity, attention deficit, depressive symptomatology, and substance use disorders (Sundram, 2006). Environmental factors and use of other substances may have additive effects with cannabis use during pregnancy and in many cases may be even stronger factors in determining perinatal morbidity. Antenatal cannabis exposure effects tend to increase with heavier use. There is no study evaluating the impact of cannabis exposure in early as opposed to late pregnancy, and the literature lacks data about potential effects of cannabis use during breastfeeding.

Intravenous opiate use during pregnancy is associated with problems linked to injection risks, such as HIV and hepatitis and increased neonatal morbidity associated with various environmental factors, such as lack of prenatal care, poverty, and malnutrition (Bauer et al., 2002). Prenatal opiate exposure in the last trimester of pregnancy elicits a well-described neonatal withdrawal syndrome (NWS) affecting central nervous, autonomic, and gastrointestinal systems, characterized by weight loss, feeding difficulties, sleep abnormalities, and seizures. Although methadone maintenance is the treatment of choice for pregnant women who are opioid dependent in the United States, most neonates who are methadone exposed develop NWS of enough severity to require treatment (Chiriboga, 2003). In a sample of pregnant women who were opioid maintained, the largest proportion of neonates requir-

ing treatment for NWS was found in the morphine-maintained group (82%), followed by the methadone-maintained group (60%). The smallest percentage of clinically significant NWS was found among women who were buprenorphine maintained (21%; Ebner et al., 2007). Maternal and neonate factors that may affect vulnerability to NWS in infants born to mothers who are methadone maintained are not completely understood. Population data show that 27% of babies born to pregnant women who are methadone maintained present NWS. These mothers had more previous pregnancies and were more likely to be heavy cigarette smokers (Burns & Mattick, 2007). Available evidence indicates that the administration of opiates to the neonate with significant NWS appears to reduce time to regain birth weight but may increase the duration of hospital stay. This approach seems to be more effective than the use of sedatives, clonidine, or benzodiazepines (Osborn, Jeffery, & Cole, 2005). Maternal methadone dose does not predict the need for neonate treatment. A study comparing breastfeeding women who were methadone maintained and women who were formula feeding showed that fewer breastfed neonates required additional pharmacotherapy for NWS (Jansson et al., 2008). Hence breastfeeding has been suggested as an appropriate treatment strategy for managing the symptoms of withdrawal in infants who were methadone exposed. Women still unstable in their recoveries or prone to relapse and those infected with HIV should not breastfeed. Hepatitis C per se is not a contraindication, unless nipples are cracked or bleeding (Jansson, Velez, & Harrow, 2004). Methadone stabilization at the lowest possible dose, adjusted for the increased body mass, is the recommended treatment for pregnant women with opiate dependence in the United States. Comparatively little data exist on buprenorphine treatment during pregnancy. Most data on buprenorphine comes from European countries (Auriacombe, Fatséas, Dubernet, Daulouède, & Tignol, 2004). A recent prospective study of 259 pregnant women maintained on methadone or high-dose buprenorphine showed that approximately 12% had premature delivery and 70% of neonates displayed a NWS with similar perinatal outcome for women and their infants across groups (Lejeune, Simmat-Durand, Gourarier, & Aubisson, 2006). Similar to what happens with cocaine, the mental, motor, and behavioral consequences of prenatal opiate exposure on infants up to age 3, as measured by the Maternal Lifestyle Study, were associated mostly with low birth weight and reflect environmental risks such as lack of adequate prenatal care, malnutrition, cigarette smoking, and polydrug use, rather than with direct effects of opiates (Messinger et al., 2004).

Nicotine use is the most important preventable risk factor for an unsuccessful pregnancy outcome, even surpassing poverty in many countries (Cnattingius, 2004). Exposure to tobacco constituents can affect placental development directly (by negatively influencing cytotrophoblast proliferation and differentiation) or indirectly by reducing blood flow (Zdravkovic, Genbacev, McMaster, & Fisher, 2005). Various effects of tobacco on pregnancy are derived from oxytocin stimulation and include still birth, preterm birth, placental abruption, fetal growth restriction with low birth weight and height, obstetric complications (such as spontaneous abortions, ectopic pregnancies, and placenta previa) and neonatal mortality (Cnattingius, 2004). Maternal smoking, either prenatal or after birth, is currently the most frequent and preventable risk factor for sudden infant death syndrome, and this relationship appears to be dose dependent. This is possibly due to arousal impairments in association with changes in control of autonomic cardiac function (Horne, Franco, Adamson, Grosswasser, & Kahn, 2004). Long-term physical and behavioral consequences of prenatal exposure to maternal smoking have also been reported, such as impaired lung function and delinquency, independent of other confounding variables (Zilberman & Blume, 2004). Regarding breastfeeding, there is evidence that, given its clear benefits in counterbalancing morbidity in neonates of smoking mothers and the potential additive effects of pre- and postnatal mater-

nal smoking and second-hand paternal smoking, breast milk nutrition should be encouraged for infants born to parents who smoke (Dorea, 2007).

Women who use substances that become pregnant suffer severe disapproval for exposing their future babies to drugs. There is evidence, however, that many women stop using drugs during this period. For example, from 1993–1999, the odds of quitting smoking during pregnancy raised 51% (Colman & Joyce, 2003). Among those who do not quit, the quantity and frequency of drug use are often considerably reduced, demonstrating that these women are indeed concerned about their offspring (Bottorff et al., 2006). A nonjudgmental approach is essential in attracting more pregnant women to treatment. Preliminary evidence suggests good results for therapeutic interventions for this population (Windsor, 2003). The additional challenge is to help them remain abstinence in the postpartum period. A particular cause for concern is the fact that most women who quit smoking during pregnancy eventually return to using tobacco within 6 months after delivery (Solomon et al., 2007).

## AGING: MENOPAUSE

Over the next two decades, a huge increase in the rates of drinking among older women is expected due to the gender convergence of prevalence rates of alcohol use in adolescents observed in recent cohorts. At this stage of the life cycle, women are confronted with additional challenges, biological and social in nature, including menopause, motor limitations, osteoporosis, retirement, and “empty nest.” Vulnerability to alcohol is augmented in older women, although there is limited evidence that drinking of one standard drink per day might confer some protection against heart disease and osteoporosis. Heavy drinking, however, increases osteoporosis risk, and there is evidence that bone damage provoked by early heavy drinking may be irreversible (Sampson, 2002). Additionally, drinking has been linked to increased rates of breast cancer (Key et al., 2006; MacMahon, 2006). Furthermore, the risk of combined effects of alcohol with prescription drugs should not be overlooked. Alcohol also increases risks for trauma, hypertension, cardiac arrhythmias, gastrointestinal problems, neurocognitive deficits, and depressive/anxiety symptomatology (Register, Cline, & Shively, 2002). Many older women who drink alcoholic beverages also take medications that may interact negatively with alcohol. Age-related changes in the absorption, distribution, and metabolism of alcohol and medications may partly explain these negative interactions (Epstein, Fischer-Elber, & Al-Otaiba, 2007). Some medications have disulfiram-like reactions when taken together with alcohol. Additionally alcohol may interfere with the effectiveness of some medications. Practitioners and patients need to be aware of these potential risks of combined alcohol and medication use. Approximately 10% of older women misuse prescribed medications (Johnell, Fastbom, Rosén, & Leimanis, 2007). Substance abuse in older women is usually a consequence of social isolation and psychiatric comorbidity. Particular attention should be given to the abusive potential of sedative and opioid medications among older people (Simoni-Wastila & Yang, 2006).

There have been findings from epidemiological studies suggesting that light-to-moderate drinking is associated with reduced risk of atherosclerosis (by altering cholesterol metabolism and reducing blood clotting and platelet function). This may be the basis for its protective effect for cardiovascular and Alzheimer’s diseases. Moderate drinking is also associated with increased bone mineral density and consequent decreased fracture risk in older women. The problem is to safely define the limits of light-to-moderate drinking given great individual vulnerability to alcohol particularly among women (Mancinelli, Binetti, & Ceccanti, 2006).

Only recently specific treatment programming for this age bracket has attracted atten-

tion. In designing treatment strategies, cognitive limitations and social isolation need to be taken into consideration. Support groups are particularly helpful, and themes such as widowhood and role loss should be addressed (Epstein et al., 2007).

### KEY POINTS

- A pattern of gender convergence or higher rates of substance use has been evidenced among younger women at least for some drugs (including cigarette smoking and prescribed medications).
- Emotional problems and psychiatric comorbidity are more prevalent in women compared to men and are important risk factors for substance use in women.
- Women are particularly vulnerable to the physical effects of different substances, being at greater risk of developing health-related problems.
- Substance use among women poses particular programming and treatment issues given women's specificities in different phase of their life cycle such as fertility, pregnancy, breastfeeding, menopause, and aging.
- There is a critical need for the development of prevention strategies aimed at retarding substance-use initiation among girls. Also, media campaigns designed to reduce the stigma attached to substance use among women are required to alert and help women with substance-use problems.

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