ADDICTIVE DISORDERS IN WOMEN

Sheila Specker, M.D.
Department of Psychiatry and Behavioral Sciences
University of Minnesota

DISCLOSURE

Minnesota Psychiatric Society CME
Sheila Specker, MD

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OBJECTIVES

The participant will be able to:

▪ Discuss the gender differences in development and course of substance use disorders
▪ Highlight neurobiologic aspects in addiction
▪ Describe substance use in pregnancy
▪ List medical and psychiatric problems in women with substance use disorders
▪ Identify specific needs of women in treatment and recovery

ADDICTIVE AND CO-OCCURRING PSYCHIATRIC DISORDERS IN WOMEN

▪ Epidemiology
▪ Neurobiology
▪ Pregnancy
▪ Co-occurring conditions
▪ Course and Treatment

BOTTOM LINE

▪ Women use drugs differently
▪ Women respond to drugs differently
▪ There are unique obstacles to effective treatment
Figure 1: The number of drug overdose deaths in 2021 was the highest annual number ever recorded.

Number of drug overdose deaths, 7-county metro vs. Greater PA, MI residents, 2011-2021

Alcohol Use Disorder among Women

Marijuana Use Disorder among Women: Significant Increase for 12-17 y.o.
ADDICTIVE DISORDERS IN WOMEN

Epidemiology

RATES OF ADDICTION (LIFETIME):*

<table>
<thead>
<tr>
<th></th>
<th>Women (%)</th>
<th>Men (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol abuse/depd.</td>
<td>4.4%</td>
<td>24%</td>
</tr>
<tr>
<td>Drug abuse/depd.</td>
<td>4.4%</td>
<td>7%</td>
</tr>
<tr>
<td>Alcohol depd.</td>
<td>8.4%</td>
<td>18%</td>
</tr>
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</table>

*Epidemiologic catchment area data 1994
**Nat. Longitudinal Alcoholic Epidemiological Survey (N=43,000, DSM-IV)

Epidemiology: Alcoholism Rates 2022 (WHO)

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>MALE</th>
<th>FEMALE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hungary</td>
<td>21.20%</td>
<td>7.20%</td>
<td>21.20%</td>
</tr>
<tr>
<td>Russia</td>
<td>20.90%</td>
<td>7.20%</td>
<td>20.90%</td>
</tr>
<tr>
<td>Belarus</td>
<td>18.80%</td>
<td>6.20%</td>
<td>18.80%</td>
</tr>
<tr>
<td>Latvia</td>
<td>16.00%</td>
<td>4.80%</td>
<td>15.50%</td>
</tr>
<tr>
<td>Estonia</td>
<td>13.90%</td>
<td>4.50%</td>
<td>13.90%</td>
</tr>
<tr>
<td>South Korea</td>
<td>13.90%</td>
<td>6.80%</td>
<td>13.90%</td>
</tr>
<tr>
<td>United States</td>
<td>13.90%</td>
<td>6.80%</td>
<td>13.90%</td>
</tr>
</tbody>
</table>

ADDICTIVE DISORDERS IN WOMEN

Epidemiology

- Adolescent girls begin alcohol/drug use slightly later than boys.
- Increase in heavy drinking in adolescent girls and college women, converge with male patterns
- Women more likely to obtain drugs via “licit” medical channels
- Smoking rates have fallen less in females
- Girls = boys on rates of smoking

*National Household survey; Harrison and Hoffman 1989; Opland, Winters, Stinchfield 1995
ADDICTIVE DISORDERS IN WOMEN

Trends

- Gender differences in drinking and alcohol related problems narrowing
- Both genders have earlier onset of drinking and problems
- Gender gap in binge drinking in high school students decreased from 23% (1975) to 12% (2001)

Genetic

- Clear evidence in men, less clear in women
- Twin study in 2000 female pairs* demonstrated importance of environment in modifying heredity:

<table>
<thead>
<tr>
<th></th>
<th>% variance of drinking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unmarried twins</td>
<td>60%</td>
</tr>
<tr>
<td>Married twins</td>
<td>31%</td>
</tr>
</tbody>
</table>

* Heath, et al 1989
Preclinical Studies

- Progesterone attenuates the drive for cocaine in rats
- Estrogen enhances drive and acquisition of cocaine self-administration

SEX DIFFERENCES IN VULNERABILITY TO DRUG ABUSE: PRECLINICAL

- Female rats compared to males:
  - More vulnerable to stimulant self-medication: acquisition, escalation, reinstatement
  - More vulnerable to reinstatement of cocaine-seeking behavior
  - Self-administered higher levels of cocaine
  - Maintained greater levels of ethanol intake
**Human Laboratory Study**

**Effect of Progesterone on Cocaine Craving, Physiology, Use**

- Inpatient trial with progesterone/placebo in men and women (N=38), cross-over, PC, Cocaine/placebo cocaine

- Women used more than men but had fewer treatments
- Women had more craving
- Higher progesterone levels associated with:
  - Decreased stimulation, decreased craving, decreased effects of last dose
  - Decreased BP elevation
- Men had more heart racing, more “high” in response to cocaine

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**Neuroimaging Evidence for Sex Differences in Stress and Reward Circuits in Cocaine Dependence** (Potenza et al., 2012)

- CD vs HC women
- CD vs HC men

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**Role of Neuroimaging/Neuromodulation**

- **Neuroimaging** has identified neural networks that support abstinence
- **Neuromodulation** can be used to target these networks and boost them to support abstinence
  - Non-invasive Transcranial direct current stimulation (tDCS)
Higher DLPFC-NAcc RSFC in long-term abstinence from alcohol

Lower DLPFC-NAcc RSFC associated with relapse
Sex-stratified Intervention Effect on Binary Relapse Outcome

Pregnancy and Substance Use

Challenges
- Conflicting interests: mother/ baby
- Recovery support for mother
- Infant effects of substance use: maximize long term recovery, minimize infant effects
- Social stigma, avoiding care
- Legal issues in pregnancy
Mandatory reporting

• Prior to July 2021:
  Any perinatal substance use must be reported except alcohol and cannabis

  Barrier to universal screening

  Decreased prenatal care
RESULT OF
CHANGES IN LAW
2021

-- Enhanced therapeutic relationship with patients using substances
-- Allows preparation time to arrange treatment
-- Prenatal care even without substance use treatment
-- More consistent care
-- Option to report
-- Requirement to report – if lost to follow up

The Data: Involuntary Commitment: not the solution?

-- Individuals subjected to involuntary treatment 2.2 x more likely to die from overdose compared to voluntary treatment
-- 34% patients reported relapsing to drug use the day they were released from civil commitment
-- Less than 20% patients received medication treatment during commitment
-- 7% followed up with addiction treatment after release

Messinger and Beletsky, Chau et al., Jain
GOALS IN PREGNANCY

- Establish rapport and trust
- Identify social, psychological, family issues
- Treat co-occurring psychiatric disorders
- Motivational approach for treatment/cessation
- Use opioid pharmacotherapies
- Easy access to care
- Team approach

WOMEN AND ADDICTION
Other Risk Factors for Alcohol Use/problems

- Motives
  - Stronger relationship in women alcoholics between distress and alcohol

- Behavioral
  - Men show greater impulsivity, under-control which are consistently associated with alcohol problems in men, less in women

- Antisocial
  - Associated with alcohol disorders in both genders

- Interpersonal
  - Strong similarities in drinking patterns in partners
ADDICTIVE DISORDERS IN WOMEN

Differences

Women with alcohol problems differ from men:

- Attribute onset of problem drinking to life stress
- Drink alone
- More likely to be separated/divorced
- Sexual abuse common (23 - 67%)
- More psychiatric symptoms and prior psychiatric treatments
- 20-40% of married women alcoholics report abuse in spouse

The Stress-Addiction Connection: Gender Differences

- Women greater craving to negative emotional cues compared to men
- Women endorse stress/interpersonal conflict as relapse precipitant
- Men more responsive to drug-related cues

Co-occurring Medical, Psychiatric Conditions
WOMEN AND ADDICTION

Women who drink excessively may be more prone to:

▪ Alcohol-induced depressive disorders

▪ Associate with others who drink excessively and thereby increase risk for domestic violence

▪ Increased risk for HIV exposure while intoxicated

WOMEN AND ADDICTION
Psychiatric Factors (cont.)

Traumatic events:

▪ 67% of alcohol women versus 28% of control women had been victim of sexual abuse during childhood.

▪ Higher rate in alcohol women than general psychiatric outpatients.

WOMEN AND ADDICTION
Domestic Violence

▪ Increased likelihood of violence by partner as consequence of substance use

▪ Domestic abuse may lead to higher rates of substance abuse in women who are victimized

▪ Link between physical/sexual abuse and greater use of cocaine, marijuana, alcohol among girls

▪ Increased prior suicidality in teenage girls with history of physical/sexual abuse
Stress-Addiction Connection

- Childhood adverse events strongly associated with SUD’s – particularly for women – ACES
- PTSD, mood/anxiety disorders strongly associated with SUD’s - 2-3 times more common in women

ADDICTIVE DISORDERS IN WOMEN

Physical

How are women using alcohol different from men?

- Single doses of alcohol produce higher BAC even corrected for weight (lower body water content in women, lower levels of alcohol dehydrogenase)
- Increased BAC variability in women (e.g. pre-menstrually)
- Less acute tolerance
- OCP’s may slow rate of alcohol clearance
- Women have a longer half-life for lipid soluble drugs (e.g. benzo’s)
ADDICTIVE DISORDERS IN WOMEN
Medical Effects of Alcohol

▪ Women develop adverse health effects more rapidly than men: fatty liver, cirrhosis, ulcer, hypertension, anemia, malnutrition, GI bleed
▪ Many effects on reproduction/sexual functioning: inhibits ovulation, obstetrical complications, FAS, irregular menses, early menopause, ↓ arousal
▪ Linkage to early cardiovascular mortality
▪ "Telescoping"

WOMEN AND ADDICTION
Psychiatric Comorbidity

▪ ECA data:
  – 65% of women alcoholics vs. 48% of men alcoholics had additional psychiatric diagnosis
  – Women alcoholics had four times the ratio of MDD than women in the general population

WOMEN AND ADDICTION
Psychological/Social

▪ Depression and anxiety are found more in women; antisocial personality trait disorder more in men.
▪ Prospective study: low self-esteem, impaired coping ability in high school predicted later problem drinking in girls.
▪ Longitudinal study: college women who drank to change feeling state predicted later drinking problems.
▪ Use influenced by male partners
WOMEN AND ADDICTION
Psychiatric Comorbidity (cont.)

▪ Depression preceded the alcoholic problem in two-thirds of alcoholic women.

▪ Depressive symptoms predicted higher alcohol consumption years later.

▪ Both depression and sexual dysfunction predicted chronicity of alcohol problems.

Course, Treatment, Outcomes

WOMEN AND ADDICTION
Course

▪ Women drink less than men but gender gap in binge drinking decreased from 23% in 1975 to 12% in 2001.

▪ Women start drinking later than men but have shorter times from use to dependence and treatment ("telescoping").

▪ Women drink to reach intoxication earlier than men.

▪ Women have higher severity of alcohol problems on treatment entry.

▪ Telescoping probably occurs with other drugs.

▪ Telescoping does not occur in younger women.
ADDICTIVE DISORDERS IN WOMEN
Course

Study: More rapid progression to treatment among opioid, cannabis or alcohol dependent women (N = 271)*

▪ No gender differences in age of onset of regular use
▪ Women: fewer years regular use opioid, cannabis, alcohol before entering treatment
▪ Women reported more severe psychiatric, medical and employment complications
▪ Same severity of drug and alcohol dependence

*Hernandez-Avila, Rounsaville, Kranzler. Drug and Alcohol Dependence, 74(3), 2004

ADDICTIVE DISORDERS IN WOMEN Course of Alcoholism

▪ Consequences differ
▪ Continuous versus episodic
▪ Higher socioeconomic women had later age of onset, older at treatment, less alcohol problems, drink less, lower rates of spouse alcoholism

Gomberg 1981, 1986; Smart 1979; Corrigan 1980; Ross 1989

Stress and Substance Use Disorders: Clinical Considerations

▪ Careful assessment/aggressive treatment of co-occurring stress sensitive disorders
▪ Importance of social support in mediating effects of stress
▪ Careful attention to environmental factors – ongoing stress/abuse
▪ Coping Skills/Stress Management Techniques
ADDICTIVE DISORDERS IN WOMEN Treatment Issues

▪ Good psychiatric history essential
▪ Attention to medical complications (e.g. STD’s)
▪ Special skills acquisition (e.g. assertiveness)
▪ Integration of 12 step and other treatment modalities (e.g. CBT)
▪ Individual therapy or all women’s groups
▪ Family therapy desirable

WOMEN AND ADDICTION Treatment

1. Attention to Hx abuse
2. Careful physical/psychiatric dxs
3. Evaluate, treat family members
4. Parenting education
5. Child care services
6. Skill building: assertiveness, etc.
7. Social role issues
8. Women role models

Medication Trials for Addiction: Gender Differences

Inconsistent results:
▪ Naltrexone associated with reduced craving for alcohol, more efficacious in women (Kiefer 2005)
▪ Naltrexone augments NRT in women smokers (Byars 2005)
▪ Pooled data: female gender associated with poorer outcome in med trials in cocaine use disorder
▪ Acamprosate US trial: not efficacious for women
ADDICTIVE DISORDERS IN WOMEN

Barriers to Treatment

▪ Parenting responsibilities (lack of child care)
▪ Economic dependency
▪ Stigma
▪ Few social supports
▪ Housing
▪ Legal system which equates drug misuse with child abuse/neglect
▪ Lack of insurance coverage

ADDICTIVE DISORDERS IN WOMEN

Outcome

▪ Gender as factor is understudied
▪ Most studies show similar outcome in women as compared to men when controlling for demographic and clinical variables (Vannicelli, 1986, McLellan et al 1986)
▪ Factors influencing outcome: supportive social network, number of life problems (Macdonald 1987)
▪ Higher mortality rates than men compared to expected (Lindberg & Agren 1988)

ADDICTIVE DISORDERS IN WOMEN

Relapse Dynamics

STUDY:
60 cocaine dependent women, recently abstinent, participated in a 90 day longitudinal study on relapse dynamics. The group was largely African-American (58%), single (58%), unemployed (83%) with mean age 32 years.

▪ Baseline structured psychiatric interview (SCID-I; SCID-II), Addiction Severity Index (ASI)
▪ At 30 and 90 days, Minnesota Relapse and Coping Skills Questionnaire, ASI
ADDICTIVE DISORDERS IN WOMEN
Relapse Dynamics

Antecedents to relapse:

<table>
<thead>
<tr>
<th>Relapse Factor</th>
<th>% Reporting</th>
<th>Most Important Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative emotional state</td>
<td>21%</td>
<td></td>
</tr>
<tr>
<td>Interpersonal conflict</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>Environmental</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>Craving</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>Situational</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Impulse</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Pressure to use</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Physical pain</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Positive emotional state</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

RELAPSE DYNAMICS IN COCAINE USING WOMEN

LINEAR INREPOLATION OF ESTIMATED SURVIVAL FUNCTIONS

ADDICTIVE DISORDERS IN WOMEN
Conclusions

- Women have a more severe course of addiction
- High rates of psychiatric co-morbidity are found
- Coping skills are essential in preventing relapse
- Broader treatment services are needed
Thank you

References

- Epidemiologic catchment area data 1984
- Nat. Longitudinal Alcohol Epidemiological Survey (N=43,000, DSM-IV)
- National Household survey; Harrison and Hoffman 1989; Opland, Winters, Stinchfield 1995
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- Helzer, Pryzbeck 1988 (ECA-data)
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