

Physical & Psychological Harms of Psychotropic Substance Abuse on Women

Seminar organized by HKCSS

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? Gender Difference in Addictive Disorders

- Traditionally, most of researches and treatment programs primarily designed for male patients
- The first version of Michigan Alcohol Screening Test contained a question about the subject's wife. Later it was changed to 'spouse'
- Recent research has identified male-female differences in the way addictions develop and in treatment needs

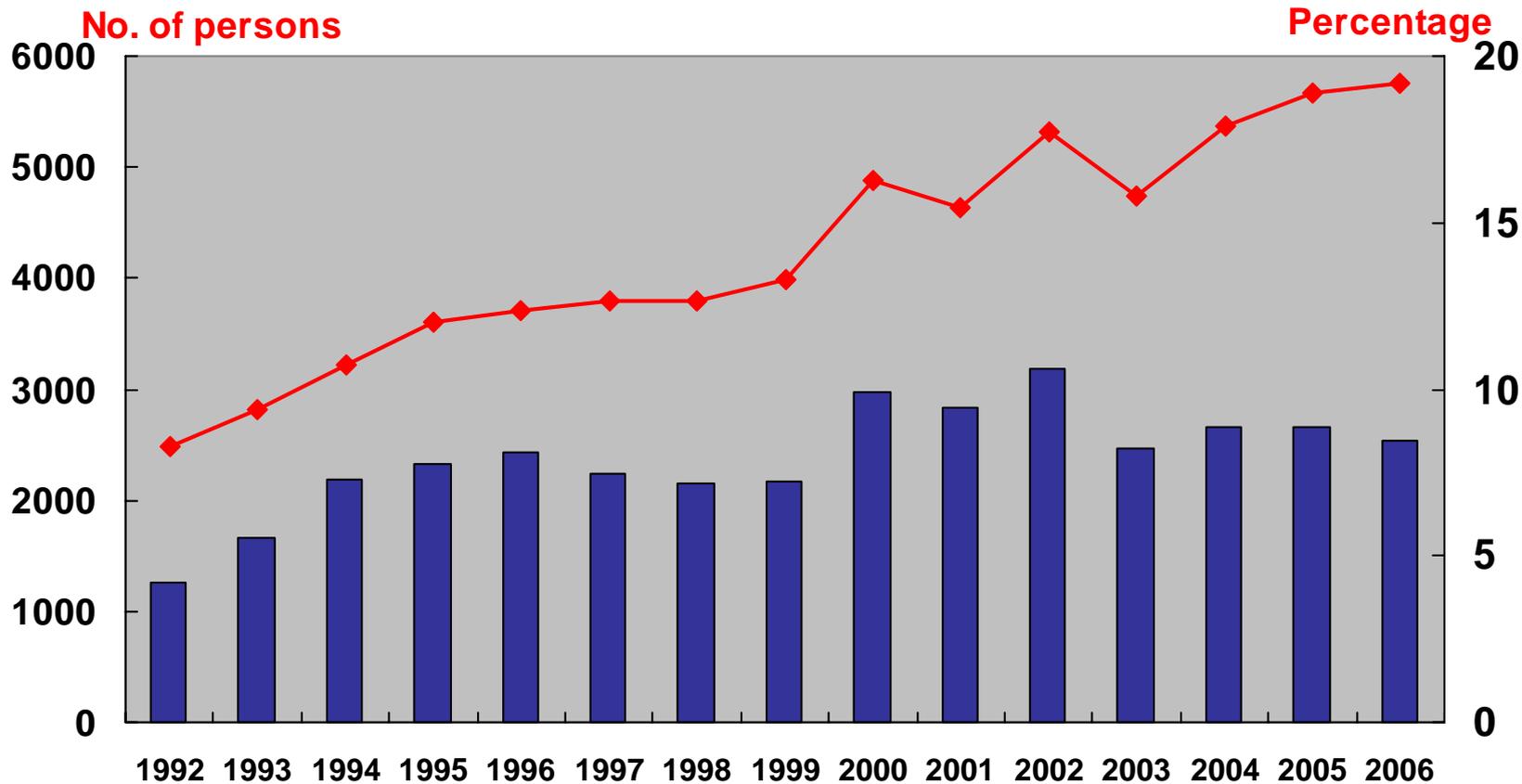
Gender Difference: Epidemiology in USA

- The prevalence of drug abuse / dependence in men is around 2 times more than female
- Women ages 45-54 reported a higher lifetime prevalence of drug dependence than men (3.8% vs 2.1%)
- Higher prevalence of prescription drug dependence in women while men have higher rates of dependence on illicit drugs
- For alcohol problems, women ages 21-34 reported the highest problem rates
- For smoking, falling rate in men is greater than women so their difference is progressively smaller (27% vs 23%)

Gender Difference: Epidemiology in USA

- Prominent risk factor is a history of physical and/or sexual abuse (Simpson 2002)
- ECA study in early 1980s: those women who have history of sexual assault found to have 3X increase of alcohol abuse/ dependence and 4X increase of drug abuse/ dependence
- The influence of male 'significant others' who are likely to introduce women to abuse drugs and to supply drugs to them (Amaro 1995)
- High rates of alcohol & drug abuse among lesbian women (McKirnan 1989) and in criminal justice system (CASA 1996)

Female drug abusers in HK CRDA



■ Female

◆ % of female drug abusers among all reported individuals in that year

CRDA 03 & 06: Marital Status

	2003 Male	2003 Female	2006 Male	2006 Female
Never married	59.1%	54.7%	58.9%	66.8%
Married / cohabiting (partner took drug)	30.2 (6.6%)	29.3 (42.5%)	30.7 (8.1%)	21.8 (38.3%)
Widowed	0.9	2.2	1.1	3.0
Divorced/ separated	9.7	13.8	9.3	8.5

Gender Difference: Pharmacology

- For same amount of alcohol, women reach higher blood alcohol levels (20-30% more) than men because
 1. Women have less body water
 2. Men have higher levels of enzyme (ADH) in gastric mucosa leading increased metabolism in the stomach and less absorption into the bloodstream
- Women have greater variability in blood alcohol concentration and reduced acute tolerance to alcohol → more intense and less predictable reactions
- Lipid-soluble drugs such as diazepam and oxazepam will have longer half-lives in women
- Variations in women's plasma levels according to menstrual cycle phases have also been reported (Zilberman 2004)

Gender Difference: Health Effects

- Chronic alcohol complications develop more rapidly in women: liver cirrhosis, hypertension, anemia, malnutrition, GI bleeding, peptic ulcer, peripheral myopathy and cardiomyopathy
- HIV & STD are linked with drug abuse in women (CASA, 1996) injection, sex with drug-abusing partner, prostitution

Gender Difference: Reproductive Functioning

- Chronic drinking → inhibition of ovulation, infertility, suppress both sexual & orgasmic function (alcohol is not aphrodisiac)
- Cocaine abuse → inhibit of sexual desire and orgasm, menstrual alterations, hyperprolactinemia
- Heroin: suppress sexual desire and ovulation

Gender Difference: Fetal Effects

- USA: 23% pregnant women use alcohol, 12% smoke & 4.4 % abuse drugs
- Fetal alcohol syndrome (FAS): 1-3 infants for every 1000 births in USA
- Triad features: mental retardation, growth retardation, facial abnormalities
- Women took 6 or more units /d during pregnancy is at high risk
- Fetal alcohol effects (FAE) for those drink less: miscarriage, low birthweight, birth defects, behavioural abnormalities (Warren 2001)

Gender Difference: Fetal Effects

- Smoking: miscarriage, low birthweight, sudden infant death syndrome
- Cocaine: women believe cocaine facilitates a quick and less painful delivery, but actually it produces obstetric complications as well as birth defects
- Heroin: neonatal opiate withdrawal
- Continued drug abuse in a new mother affects maternal-infant bonding, parenting, and child care

Gender Difference: Genetic Influence

- All studies showed that alcohol/drug dependence are affected by a combination of genetic and environmental factors
- Some evidence showed genetic influences are stronger for men while environmental factors are more evident to female (Zilberman 2004)

Gender Difference: Co-morbid Mental Disorders

- Female has higher rates in general
- Female has more: depression, anxiety, PTSD, eating disorder
- Male has more: antisocial personality disorder, pathological gambling, residual attention deficit disorder
- Alcohol abuse/dependence & depression: primary depression in 66% women and only 22% in men (EAC study)

Gender Difference: Sociocultural Factors

- Intense stigma linked to female alcohol or drug abuser: they are indecent & promiscuous
- They are more likely to be victims of sexual assault and rape
- Stigma also makes them reluctant to seek help and hide their problems till very late

Gender Difference: Clinical Features

- Start substance use later (A)
- Disease progresses more rapidly (AC)
- Use significantly less than males (ACO)
- 'Significant other' more likely to be substance abuser (ACO)
- Higher rates of comorbid psychiatric disorders (AC)
- Higher rates of comorbid prescription drug dependence (A)
- More likely to make suicide attempts (A)
- More likely to have a history of physical & sexual abuse (ACO)
- More often date the onset of pathological alcohol/drug use to a specific stressful event (AC)
- More likely to report previous psychiatric treatment (A)
- Higher mortality rate (A)

A: alcohol , C: cocaine, O: other drugs

Gender Difference: Treatment

- Psychiatric assessment for comorbid disorders
- Assessment of prescription drug abuse / dependence
- Comprehensive physical examination esp signs of pregnancy
- Attention to past history & present risk of physical and sexual assault
- Attention to guilt, shame & self-esteem issues
- Assessment & treatment of sexual dysfunction
- Evaluation & treatment of significant others and children
- Need for access to health care (including obstetric care)
- Psychoeducation on substance use in pregnancy
- Child-care services for women in treatment
- Parenting education and assistance
- Avoidance of iatrogenic (therapy-induced) drug dependence
- Special attention to the needs of lesbian women & those in prison

Gender Difference: Unsolved Treatment & Prevention Issues

- Whether women-only programs are superior to mixed programs is still not well established
- In USA, women abuse alcohol or drug during pregnancy have been charged with 'prenatal child abuse ' or 'delivery of controlled substances to a minor'.
? whether it is a preventive measure or deterrent to pregnant abusers to seek help

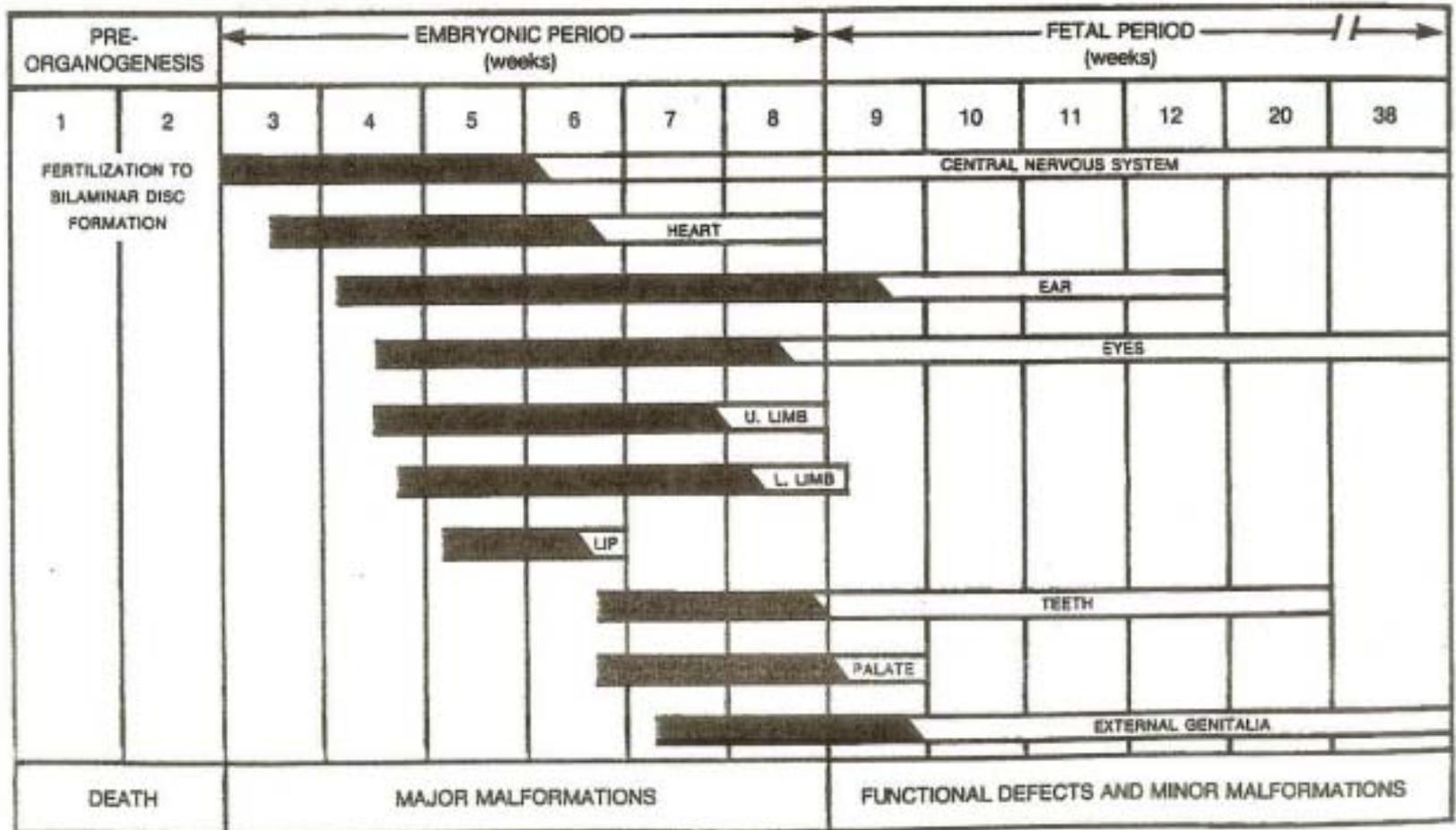
Signs of Substance Abuse in Pregnant Women



Dependent Factors

- Type & form of drug used
- Timing of exposure during gestation (most organ development occurs in first trimester)
- Frequency of exposure
- Actions of individual drug on placental blood flow and fetal tissues

SUSCEPTIBILITY TO TERATOGENESIS FOR ORGAN SYSTEMS
 (SOLID BAR DENOTES HIGHLY SENSITIVE PERIODS)



SA in Pregnant Women: Maternal Signs

- Increased spotting / vaginal bleeding
- Sexually transmitted diseases
- Anemia
- Subacute bacterial endocarditis (SBE)
- Seizures
- Poor venous access

SA in Pregnant Women: Pregnancy & Placental Signs

- Spontaneous abortion
- Premature rupture of membranes
- Precipitous labour (rapid expulsion of fetus)
- Premature labour (<37 weeks)
- Placental insufficiency
- Abruptio placentae (premature detachment of a normally situated placenta)

SA in Pregnant Women: Fetal Signs

- Intrauterine growth retardation
- Low birth weight
- Meconium (first intestinal discharges of newborn) staining
- Stillbirth
- Fetal tachycardia
- Abnormal fetal heart monitoring
- Hyper or hypoactive fetus
- Breech presentation

SA in Pregnant Women: Behavioural signs

- Late registration for prenatal care
- Poor compliance
- Reluctant to give urine specimen
- Mood swings
- Agitation, anxiety, defensiveness about the topic of substance abuse

Factors Affect Fetal Drug Exposure: Maternal Factors

Drug absorption

- GI absorption (\downarrow GI motility, delayed GI emptying, \downarrow gastric acid secretion, \uparrow mucous secretion)
- Pulmonary absorption due to \uparrow alveolar ventilation
- Intramuscular absorption due to \uparrow venous pressure in lower limbs

Drug distribution

- Increased intra & extravascular volume
- Large accumulation of body fat
- Decreased drug binding to plasma proteins \rightarrow higher effective concentration
- Hemodynamic changes

Factors Affect Fetal Drug Exposure: Maternal Factors

Drug metabolism \uparrow (\downarrow albumin binding \rightarrow
 \uparrow free drug concentration)

Drug excretion

- \uparrow renal excretion due to \uparrow renal plasma flow, \uparrow GFR, \downarrow albumin binding
- \uparrow pulmonary excretion due to \uparrow respiratory rate, \uparrow tidal volume & \uparrow minute volume

Factors Affect Fetal Drug Exposure: Placental Factors

Diffusability of substances across the placenta is determined by

- Size of the substance
- Lipid solubility of the substance
- Protein binding of the drug in plasma
- Degree of ionization of the drug molecule
- Morphology & stage of development of the placental membranes

Uterine & umbilical blood flow rates

Factors Affect Fetal Drug Exposure: Fetal Factors

Fetal distribution

- 55% of umbilical venous blood passes through ductus venosus so bypassing liver & lung metabolism → ↑ drug distribution to upper portions of the body

Delayed maturation of metabolic enzymes that inactivate drugs

Decreased renal excretion

- ↓ fetal renal plasma flow
- ↓ fetal glomerular filtration

Adverse Effects of Individual Substance

Alcohol Effects on Fetus

- First described by Lemoine in France in 1968
- Fetal alcohol syndrome (FAS) was labelled by Jones in 1973
- Milder syndrome called Fetal alcohol effects (FAE)
- Maternal daily consumption 4-6 drinks → 1/3 FAS, 1/3 FAE & 1/3 normal
- Mechanism: uncertain
- Fetal alcohol withdrawal is not well understood
- 2-4 fold ↑ risk of miscarriage

Fetal Alcohol Syndrome

- 3 main features: growth retardation, mental retardation (account for 1.7/1000 live birth) & special facial features
- Facial features: microcephaly, short palpebral fissures, low nasal bridge with short nose, flat maxillary area, indistinct philtrum, thin upper lip
- Other long-term deficits: 75-80% attention deficit disorder, fine & gross motor deficits, impaired reaction time, problems in visual perception, poor socialization & adaptive skills

Cigarette Smoking in Women

- Those on contraceptive pills, smokers have 10X risk of stroke or heart disease
- Affect hormonal regulation, smokers are 25% lower in terms of chance of pregnancy
- Smokers would have menopause 2-3 years earlier. 4X more non-smoker to start menopause before age 40
- Higher risk to have cervical cancer

Cigarette Smoking on Pregnancy

Mechanism

- Nicotine ↓ oxygen & nutrient delivery to fetus by vasoconstriction
- CO further ↓ oxygen-carrying capacity of blood

Complications of pregnancy

- Vaginal bleeding
- Spontaneous abortion (10X ↑)
- Stillbirths
- Prematurity (account for 14% of all birth <37 wks)

Cigarette Smoking on Fetus & Child Development

Fetal effects

- Growth retardation (\downarrow 200g, \downarrow 1.3cm)
- Congenital anomalies

Child development

- \uparrow 2.5X risk for sudden infant death syndrome
- \uparrow neonatal apnea (first 28 days after birth)
- \uparrow 2X risk for respiratory disease (bronchitis etc)
- \uparrow 2X risk of visual problems
- Developmental & intellectual delays
- Behavioural disorders (impulsive, rebellious)
- Mental disorders (anxiety, depression)
- Drug abuse & smoking

Cocaine

Mechanism: ↑ catecholamines →
vasoconstriction & ↑ uterine contractility

Complications of pregnancy

- Premature birth (25%)
- Abruptio placentae & stillbirth (8%)
- Fetal injury due to maternal convulsions, arrhythmias, and stroke

Cocaine

Fetal effects

- Growth retardation
- Congenital urinary malformations
- Structural CNS damage
- Neurobehavioural abnormalities (selective language delay, impaired attention span)
- Irritability & vigorous sucking after birth:
? withdrawal or ? toxicity (slow elimination)

Opiates

Pregnancy complications due to opiate dependence

- Toxemia of pregnancy / preeclampsia (hypertension + edema/proteinuria)
- Meconium-stained amniotic fluid
- Intrauterine growth retardation
- Premature birth

Pregnancy complications due to acute stop of opiates

- Abruptio placentae & stillbirth
- Spontaneous abortion
- Premature labour
- Fetal meconium passage /aspiration

Opiates

Fetal effects

- Low birthweight
- Microcephaly
- ↑ incidence of sudden infant death syndrome
- Respiratory distress syndrome in the premature
- ↑ incidence of breech presentation

Opiates

Child development

- Fine motor coordination deficit
- Delayed mental, motor, speech development at 18 months of age
- Attention deficit hyperactivity disorder
- Sleep disturbances
- Abnormal muscle tone
- Difficulties with social adjustment

Opiates

Neonatal withdrawal syndrome

- 60-90% of those with chronic exposure, if untreated → 3-5% mortality
- General features: irritability, high-pitched cries, sweating, fever, yawning, sneezing, running nose & eyes, poor sleep
- GI symptoms: diarrhea, vomiting, poor feeding
- CNS symptoms: tremors, twitching, rigidity, convulsion

Benzodiazepines

- Not considered as teratogenic for normal therapeutic dosage
- For high dose use during first trimester, some reports indicated it is associated with cleft lip & palate
- Neonatal withdrawal syndrome: hypotonia, hypothermia, irritability, poor feeding

Barbiturates

- Some studies indicated that it is associated with microcephaly, growth retardation, heart anomalies, cleft lip & palate
- Neonatal respiratory depression
- Neonatal withdrawal: hyperactivity, rigidity, poor feeding, seizures

Cannabis

- Teratogenic to animals but no evidence in humans
- CO → ↓ fetal oxygenation & fetal growth retardation
- ↑ Meconium staining
- Longer duration of labour
- Visual response abnormalities

LSD

- ↑ risk for spontaneous abortion
- Previous studies reported it was associated with fetal anomalies but recent studies found no such association

Phencyclidine (PCP)

- May have teratogenic effects on facial development
- Use during first 6 weeks of pregnancy may cause cerebellar malformations
- Behavioural disturbances: attention deficits, sudden outbursts of agitation, labile mood

Organic Solvents

- Significant adverse effect on fetal growth & neurologic development
- Some described a 'fetal solvent syndrome' similar to FAS

Breast Feeding

- Most of illicit drugs will pass into breast milk
- Mothers continue drug abuse should not breast-feed their babies