REPRODUCTIVE ISSUES AND WORK

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Potential workplace issues and normal pregnancy

FIRST TRIMESTER:
• Fatigue
• Morning sickness (nausea + vomiting)

SECOND TRIMESTER:
• Increased physical bulk: Loss of balance
• Reduced effective arm reach: Affecting desk work
• Lower back pain: Aggravated by standing, bending and stooping
• Dizziness and fainting: Aggravated by heat and prolonged standing
• Increase in rate of breathing and tidal volume could increased absorption of chemicals

THIRD TRIMESTER:
• Fatigue and insomnia
• Constipation and haemorrhoids
• Varicose veins
• Bladder problems
Work related health effects and reproduction

- Complex
- Insufficient or inadequate data—especially re chemical exposures
- Absence of evidence doesn’t equal no effect
- Not just pregnancy but when trying to get pregnant and when breastfeeding
- Male reproductive health effects important & overlooked
Some landmarks

• Explosion in number of synthetic chemicals after world war 2-millions & tens of thousands in regular use-reproductive toxicity usually not documented/studied

• Widespread entry of women into the workforce

• Thalidomide late 50s-stimulated research into teratogens

• Dibromochloropropane (DBCP) a nematocide- in late 70s caused infertility in exposed male workers

• Toxic waste issues-e.g. children with severe neurological problems due to maternal consumption of methyl mercury contaminated fish from Minamata Bay (Japan).
It’s complicated

- Infertility -15-20% (affluent countries)-6%+ of children conceived by artificial fertilisation
- Up to 75% of fertilisations are lost (usually early & unrecognised)
- 10-20% of recognised pregnancies terminate spontaneously
- Preterm delivery (< 37 weeks)- 5-6% in western countries
- Intrauterine growth retardation (birth weight < 10th percentile for gestational age) - 3-5%
- Congenital malformations - 3-5% of births – cause known in 1/3

Hunters Diseases of Occupation Tenth Edition

Identifying causal relationships to occupational/environmental factors difficult with above background “noise”
Many potential adverse outcomes

• Menstrual disorders and other hormonal issues
• Reduced libido, male performance problems, poor semen quality
• Infertility
• Spontaneous abortion
• Stillbirth or infant death
• Low birth weight
• Congenital malformations
• Cognitive changes/ reduced IQ
• Developmental delays
• Childhood cancer
Occupational exposures and risk of infertility

Men (substantial evidence for)
• Lead
• OC and sexual hormones
• Carbon disulphide
• PCBs
• DBCP
• Ionising radiation
• Radiant heat

Female
• Ionising radiation
Occupational risks and children’s health

OCCUPATIONAL EXPOSURE DURING PREGNANCY

Occupational hazards

Chemical risks
- cancer drugs, ethylene-glycol ethers, CO, pesticides, solvents, carbon disulfide, lead, mercury

Physical agents
- radiation (X-rays and gamma rays), noise

Biological agents
- cytomegalovirus, hepatitis B virus, HIV, rubella, toxoplasmosis, varicella-zoster virus

Strenuous physical labour
- prolonged standing, heavy lifting, twisting movements of the torso

Health effects

- Birth defects
- Low birth weight and premature birth
- Complications of pregnancy
- Miscarriage
- Developmental disorders
- Childhood cancer
- Genotoxicity
Most common work exposures in pregnancy

• Radiation
• Organic solvents
• Lead

Causes of malformations

- Unknown: 65%
- Genetic: 5%
- Mutations: 15-20%
- Chromosomal abnormalities: 5%
- Maternal conditions e.g. Diabetes: 4%
- Maternal infections e.g. Rubella: 3%
- Mechanical e.g. Uterine malformation: 1-2%
- Chemicals, drugs, radiation: <1%
- Preconception exposures (excluding mutagens and infections): <1%

Hunters Diseases of Occupation
Terminology

TERATOGEN
An agent or factor which causes abnormal development of the developing foetus - Four manifestations of abnormal development
• Death
• Malformation
• Growth retardation
• Functional Defect

FOETOTOXIN
An agent or factor which poisons the developing foetus (in a similar fashion to what would happen to an adult)
Teratogens

- Therapeutic drugs (e.g. anticonvulsants, retinoic acid, warfarin)
- Recreational drugs (e.g. ethanol, cigarettes)
- Intrauterine infections (e.g. toxoplasmosis, rubella, varicella)
- Heavy metals (e.g. lead, mercury)
- Radiation
- Organic solvents
- Maternal conditions (e.g. type 1 Diabetes Mellitus, phenylketonuria)
- Procedures (e.g. CVS/amniocentesis, D&C, ICSI)
- Other (e.g. hypotension, hyperthermia)
Tetratogens and male reproduction

Although animal studies raised concern about paternal exposure, currently there is no evidence of birth defects from paternal exposures in humans. Nevertheless, to minimize possible risks, it is reasonable to delay conception or, as some drug manufacturer’s recommend, to avoid semen vagina contact by using condoms in cases of paternal exposure to drugs for which teratogenic potential has been well assessed or suspected for maternal exposure and to wait at least 3 months after the end of paternal radio and/or chemotherapy.

De Santis et al Paternal exposure and counselling: experience of a tetratology counselling service Reproductive Toxicology (26) 2008 42-46
Teratogen exposure-not just what but when
Schematic illustration of the sensitive or critical periods in human development. Red denotes highly sensitive periods; yellow indicates stages that are less sensitive to teratogens.

Childhood cancer

- Increasing incidence
- **Transplacental carcinogenesis proven in humans** - maternal diethylstilbestrol (DES) and clear cell carcinoma of the vagina after puberty in some children
- No parental occupation consistently linked with childhood malignancies
- Possible increased risk of leukemia and nervous system cancers following parental exposure to organic solvents, paints and pesticides
Chemical Hazards

Chemicals enter body by three routes

- **Inhalation**- via lungs.
- **Dermal**- via skin.
- **Ingestion**- via gut following eating
Lead

- Lead causes reduced sperm counts, decreased sperm mobility & viability and more frequent spontaneous abortions & still births
- Neurotoxicity well documented from industrial revolution.
- 1882 Turner and Gibson- correlation between childhood neurocognitive deficits and lead exposure.
- From 1980s, numerous studies demonstrated correlation between pregnant women’s Pb levels and long-term neurocognitive deficits in offspring.
Mercury and other metals

• Organic Hg severely disrupts developing foetal brain (e.g. Minamata Bay - ingestion of contaminated fish and shellfish)

• No consistent evidence to implicate inorganic or metallic Hg as a human teratogen

• Nickel, Arsenic, Manganese and Cadmium – associated with reproductive toxicity in some studies but limited evidence
Anaesthetic gases

• Old studies suggested higher risk of spontaneous abortions (very high exposures by modern standards)
• Animal studies reassuring when exposure was low level (similar to modern operating theatres with closed anaesthetic systems and efficient exhaust ventilation i.e. scavenging systems)
• More risk in dental and veterinary environments where controls can be lacking
• Nitrous oxide is teratogenic in rats at high exposures and some limited human evidence for increased miscarriage risk at high doses
Certain Pharmaceuticals

• Anti-neoplastic agents (studies show increased risk of spontaneous abortions in nurses handling these drugs & biologically plausible)

• Certain immunosuppressive, antiviral and anti-inflammatory drugs display reproductive toxicity in rodents

• If strict control is not possible pregnant women should not handle antineoplastic drugs other than facilitating oral administration.
Reactive chemicals used to sterilise

• High exposure to very reactive chemicals used to sterilise objects/surfaces (e.g. ethylene oxide, formaldehyde & glutaldehyde) associated with increased risk of foetal loss in some studies

• Exposures in pregnancy needs to be well controlled
Pesticides

• Large diverse group of chemicals
• People at most risk involved in manufacture/ handling concentrate e.g. diluting prior to use
• Skin absorption important as well as inhalation when spraying
• Some have weak hormonal activity and concern about endocrine disruption to foetal development
• Bio-persistent organochlorines such as DDT and DDE may cause intrauterine growth retardation & miscarriages
Chemicals and endocrine disruption

• Concern not limited to one class of chemicals e.g. pesticides, metals, additives or contaminants in food, pharmaceutical compounds, plasticizers
• Concern not just confined to female hormonal effect e.g. thyroid gland
• Most public concern about endocrine disruption & effects on male foetus (hypospadias-penile abnormality, undescended testicles), on male fertility and hormone dependent cancers (breast, prostate) in later life?
Organic solvents-animal studies

• Many organic solvents are teratogenic and embryotoxic in laboratory animals: hydrocephaly, exencephaly,
• Skeletal defects, cardiovascular abnormalities
• Neurodevelopmental deficits
Organic solvents-human data

• Very strong evidence they are teratogenic in very high doses (evidence from solvent abusers).
• Conflicting data if levels exposed to in the workplace have a deleterious effect – if so the effect would appear small
• Exposures should be strictly controlled in pregnancy
Biological agents - Infections

• Most not work related
• Infectious diseases - Rubella, Toxoplasmosis, hepatitis B, HIV, Herpes simplex, TB, Syphilis, Varicella (chicken pox), Typhoid, Coxiella burnetti (Q-fever) parvovirus B19, ovine chlamydiosis (chlamydophila abortus formerly psittaci).
• Q fever, ovine chlamydiosis and parvovirus B 19 (school teachers, child care workers) can be work related
TORCH
Infections most commonly associated with congenital anomalies

• Toxoplasmosis
• Other (syphilis, varicella zoster, parvovirus B19)+ Zika
• Rubella
• Cytomegalovirus (CMV)
• Herpes

SELDOM WORK RELATED
Zika

• Can be work related-pregnant women or their male partners travelling to affected countries
• Congenital anomalies- some severe
• Microcephaly
• Risk of congenital abnormalities in all trimesters of pregnancy (Source Australian government Department of Health)
• More research needed to further define situation
Physical agents

- Movements and postures
- Heat and cold
- Manual handling
- Shocks and vibrations
- Noise
- Radiation (ionising and non-ionising)
- Compressed air and diving
- Underground mining work
Radiation

• Non ionising radiation is safe
• Ionising radiation-complex issue
Ionising radiation

- Direct evidence of harmful effects is derived from nuclear catastrophes (Hiroshima; Nagasaki; Chernobyl) & animal experimentation.
- Microcephaly
- Loss of 20–30 IQ points reduced per 1 Gy
- Birth defects above 1 Gy
- Growth retardation
- Childhood cancer (leukemia)
Ionising radiation

- Negligible < 50 mGy or less
- Deterministic effects have thresholds greater than 100–200 mGy (radiation therapy)
- Crucial time to avoid radiation exposure is from the 8th to the 15th week of gestation
Radiation in the workplace

• Prospective (long term) studies are lacking


• Increased risk for spontaneous abortion among female vets exposed to five or more x-ray films per week (RR = 1.81, 95% CI: 1.01–3.24) Am J Epidemiol 1990;132: 96–106.

• Foetal ear sensitive to noise induced damage from 20\textsuperscript{th} week
• Noise attenuated by uterus and amniotic fluid (less so for low frequencies where resonance could reinforce sound pressure wave)
• Pregnant women should avoid very loud noise exposure (>110dB over 8 hours) and particularly low frequency noise
• In some studies high noise exposure associated with miscarriages preterm birth and intrauterine growth retardation but lots of potential confounders in studies
Working conditions

- Facilities (including rest rooms)
- Mental and physical fatigue, working hours
- Stress (including post-natal depression)
- Passive smoking
- Temperature
- Working alone
- Working at height
- Travelling
- Violence/harassment
- Personal protective equipment
- Nutrition
Strenuous physical work

• Exercise safe in healthy well nourished pregnant women

• Long standing medical view that premature birth & intrauterine growth retardation associated with very strenuous work

• Preterm birth might be associated with heavy physical work, prolonged standing and long working hours (confounders make it difficult to judge)

• Prudent to have rest periods & avoid prolonged strenuous work, awkward postures and prolonged standing particularly in 3rd trimester and with history of previous pregnancy failures or a complicated pregnancy
Mental Strain

• Severe emotional stress related to unexpected loss of a child associated with an 8 fold increased risk of neural tube malformation if event occurred in 1st trimester

• No data re less severe psychological stressors - can infer that stressful events if sufficiently severe could put pregnancy and foetus at risk
Shift work

• Inconsistent results across studies
• Several studies indicate shift work related increases risk of spontaneous abortion, preterm birth & foetal growth retardation
• Most convincing evidence is working fixed night shift being associated with risk of spontaneous abortion
Breast feeding

Harmful chemicals can be in breast milk-some examples

• Lead, mercury & other heavy metals
• Organic solvents and volatile organic chemicals (such as dioxane, perchloroethylene, and bromochloroethane)
• Chemicals from smoke, fires, or tobacco
• Some radioactive chemicals used in hospitals for radiation therapy (such as Iodine-131)
• PCBs, PBBs, DDT, lindane, phthalates
Universities and research environments

• Diverse range of small scale activities
• On the leading (potentially bleeding) edge
• Assume some personnel in child producing/child bearing age group & some pregnant
• Risk assessment must always consider the above
ALARA PRINCIPLE IN PREGNANCY

As Low As Reasonably Achievable
Determining Interventions

Risk Assessment in Men and Women

- High concern
- Moderate concern
- Low concern
- No concern

Available options in order of preference:

1. Reduce exposure
2. Transfer job
3. Temporary leave
4. Quit work

1. Reduce exposure
2. Transfer job
3. Temporary leave

1. Reduce exposure
1. Reassure the person
Hierarchy of control of workplace hazards

• Elimination
• Substitution-less hazardous substance/process
• Enclosure
• Ventilation (dilution & extraction)/wet methods
• Administrative controls e.g. task/workstation redesign, job rotation, information provision/training
• Biological monitoring/medical surveillance/environmental & personal monitoring
• Personal Protective Equipment-PPE
Acknowledgements

• Hunter’s Diseases of Occupation Tenth Edition
• Occupational Risks and Children’s Health WHO updated 2009
• Paul M Occupational Reproductive Hazards Lancet 1997 349:1385-88
• Paul M et al Occupational and Environmental Reproductive Hazards A Guide for Clinicians published by Williams& Wilkins
• Presentation to 2015 ANZSOM annual scientific meeting by Assoc Prof Michael Gabbett, Clinical Geneticist, Genetic Health Queensland