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<<NOTE TO USER: This is a large set of slides from which the presenter should select the most relevant ones to use in a specific presentation. These slides cover many facets of the problem. Present only those slides that apply most directly to the local situation in the region or replace them with your own slides and local data.>>

<<NOTE TO USER: This module presents several examples of risk factors that affect reproductive health. You can find more detailed information in other modules of the training package that deal with specific risk factors, such as lead, mercury, pesticides, persistent organic pollutants, endocrine disruptors, occupational exposures; or disease outcomes, such as developmental origins of disease, reproductive effects, neurodevelopmental effects, immune effects, respiratory effects, and others.>>

<<NOTE TO USER: For more information on reproductive health, please visit the website of the Department of Reproductive Health and Research at WHO:
www.who.int/reproductivehealth/en/>>

LEARNING OBJECTIVES

- ❖ Understanding the importance of preventing environmental exposures to protect reproductive health
- ❖ Understand various methods of prevention in public health, including in the occupational setting, for the consumer, and in personal matters

<<READ SLIDE.>>

Refs:

•WHO. Department of Reproductive Health and Research, Partner Brief. Geneva, Switzerland, *World Health Organization*, 2009. WHO/RHR/09.02. Available at whqlibdoc.who.int/hq/2009/WHO_RHR_09.02_eng.pdf – accessed 15 June 2011

•WHO. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference. New York, United States of America, *World Health Organization*, 1946.

OUTLINE

- ❖ The importance of implementing preventive measures
- ❖ Methods of prevention
 - A. Occupational
 - B. Consumer / Policies
 - C. Personal
- ❖ Tools available from WHO

<<READ SLIDE.>>

Refs:

- WHO. Department of Reproductive Health and Research. Geneva, Switzerland, World Health Organization, 2009. (WHO/RHR/09.02). Available at whqlibdoc.who.int/hq/2009/WHO_RHR_09.02_eng.pdf – accessed July 2010
- WHO. Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference. New York, USA, *World Health Organization*, 1946. Available at www.who.int/about/definition/en/print.html – accessed July 2010

METHODS OF PREVENTION

- A. Occupational
- B. Consumer/Policies
- C. Personal

Prevention is cost-effective and could have benefits that go well beyond health, and contribute to the overall health and well-being of communities



Environmental issues have been included in the United Nations Millennium Declaration as well as several high level initiatives. However, the importance of preventive methods in various sectors is not always fully appreciated. The following slides will describes preventive methods for different exposure situations.

Refs:

- UN Millennium Development Goals. Available at www.un.org/millenniumgoals/bkgd.shtml accessed 20 June 2010.
- WHO. Preventing disease through healthy environments. Geneva, Switzerland, *World Health Organization*, 2006.

Image: WHO, Prüss-Üstün, A. Preventing disease through healthy environments. Geneva, Switzerland, World Health Organization, 2006.

A. OCCUPATIONAL EXPOSURES

- ❖ Prime venue of toxic environmental exposures
- ❖ Scant research that characterizes reproductive hazards
- ❖ A big percentage of working men and women are of reproductive age



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The occupational setting is a prime venue for exposure to environmentally hazardous contaminants, including synthetic chemicals, organic compounds, and metals. Occupational health agencies use field studies, exposure assessments, and laboratory biomonitoring to study prioritized reproductive toxicants that may be present in the workplace. However, it is impossible to assess the toxicity of all occupationally relevant chemicals due to their sheer volume, complex exposure environments in the workplace, and individual susceptibility to effects.

<<NOTE TO USER: For more information regarding occupational exposures to environmental contaminants, please see the educational training module: "Occupational Health and Children's Risks," available at: www.who.int/ceh/capacity/occupational.pdf.>>

Refs:

•Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). Recommendations to U.S. EPA on Endocrine Disruptor Screening and Testing. Endocrine Disruptor Screening and Testing Advisory Committee. 1998. Available at www.epa.gov/scipoly/oscpendo/edsp/overview/finalrpt.htm - accessed 18 March 2010.

•Grajewski B et al. Occupational exposures and reproductive health: 2003 Teratology Society meeting symposium summary. *Birth Defects Res B Dev Reprod Toxicol*. 2005, 74:157–163.

The effect of shift work, and circadian rhythm disruption, on reproductive outcomes is poorly understood, although advances have been made in the development of metrics for measuring disruption of circadian rhythm in working populations. One such metric is the variability of 2-sulfoxymelatonin, the urinary metabolite of melatonin, which has been found to be correlated with travel by female flight attendants through multiple time zones

OCCUPATIONAL EXPOSURES AND REPRODUCTIVE HEALTH

Possible effects on future fathers

- ❖ Decreased sperm count
 - Estrogens, lead
- ❖ Decreased sexual drive
 - Chloroprene, stress
- ❖ Changes in genetic material (birth defects)
 - Radiation, pesticides

Possible effects on future mothers

- ❖ Menstrual disorders
 - Ionizing radiation, pesticides, fumonisins
- ❖ Reduced fertility
 - Arsenic, benzene, pesticides
- ❖ Changes in genetic material (birth defects, miscarriages)
 - Cadmium, mercury, pesticides

Future parents can be exposed at their workplaces to many occupational health risks that can affect their ability to have children or the health of their future children. Both men and women can be affected by reproductive occupational health risks.

Exposures to some chemicals or to stressful conditions may cause both male and female workers to experience a decrease in their desire or ability to have sex. For example, some chemicals may have depressant effects, such as certain solvents, and thus can suppress the libido (sex drive).

Occupational exposures can also cause menstrual problems, which may prevent ovulation from taking place.

Stress, working on shifts, or exposure to certain organic solvents can disrupt the normal menstrual cycle, which in turn can affect fertility. Another possible effect of exposure to certain occupational hazards is their ability to cause direct damage to the germ cells (sperm and eggs). Radiation and certain chemicals can cause decreased fertility or even sterility.

Occupational risks can reduce the number of sperm to a level below the minimal necessary for fertilization.

Certain occupational hazards can cause mutations in genetic material that can be passed on to future generations. Such hazards are called mutagens. Genetic mutations can result in birth defects, stillbirth or miscarriage, depending on the type of damage caused.

Refs:

•International Labour Organization (ILO). Male and female reproductive hazards in the workplace. ILO.

Available at actrav.ilo.org/actrav-english/telearn/osh/rep/prod.htm – accessed 10 June 2011

•US Navy Environmental Health Centre. Reproductive and developmental hazards: a guide for occupational health professionals. *US Navy Environmental Health Centre*, 2001, available at www-nehc.med.navy.mil/Downloads/Occmed/Reprodev2006.pdf - accessed 10 June 2011

MECHANISMS FOR PREVENTING OCCUPATIONAL EXPOSURES

Regulatory mechanisms:

- Encouraging "clean technologies"
- Implementing effective occupational exposure limits
 - For chemicals with threshold effects and carcinogenic endpoints
- Right-to-Know (US legal principle that individuals have the right to know the chemicals to which they may be exposed in their daily living)
- Industrial occupational regulations
 - Provisions of personal protective equipment (PPE) for workers

Individual mechanisms

- Nutritional supplementation
 - e.g. folate supplements for women
- Knowledge of workers' rights
- Worker education on adherence to safety guidelines and personal protective equipment

<<READ SLIDE>>

A study (Ormond et. al) found that although mothers exposed occupationally to endocrine disruptors faced an increased risk for fetal developmental disorders, folate supplementation during the first three months of pregnancy could significantly decrease the aforementioned risk. In the United States, the "Right to know" is the legal principle that individuals have the right to know the chemicals to which they may be exposed in their daily living. "Right to Know" US can address the community and the workplace "Right to Know".
Note: PPE is Personal Protective Equipment

Refs:

•Ormond G et al. Endocrine Disruptors in the Workplace, Hair Spray, Folate Supplementation, and Risk of Hypospadias: Case-Control Study. *Environ Health Perspect.* 2009, 117:303-307.
Hypospadias is one of the most common urogenital congenital anomalies affecting baby boys. Prevalence estimates in Europe range from 4 to 24 per 10,000 births, depending on definition, with higher rates reported from the United States. Relatively little is known about potential risk factors, but a role for endocrine-disrupting chemicals (EDCs) has been proposed. Our goal was to elucidate the risk of hypospadias associated with occupational exposure of the mother to endocrine-disruptor chemicals, use of folate supplementation during pregnancy, and vegetarianism. We designed a case-control study of 471 hypospadias cases referred to surgeons and 490 randomly selected birth controls, born 1 January 1997-30 September 1998 in southeast England. Telephone interviews of mothers elicited information on folate supplementation during pregnancy and vegetarianism. We used a job exposure matrix to classify occupational exposure. Results In multiple logistic regression analysis, there were increased risks for self-reported occupational exposure to hair spray [exposed vs. nonexposed, odds ratio (OR) = 2.39; 95% confidence interval (CI), 1.40-4.17] and phthalate exposure obtained by a job exposure matrix (OR = 3.12; 95% CI, 1.04-11.46). There was a significantly reduced risk of hypospadias associated with of folate use during the first 3 months of pregnancy (OR = 0.64; 95% CI, 0.44-0.93). Conclusions: Excess risks of hypospadias associated with occupational exposures to phthalates and hair spray suggest that antiandrogenic EDCs may play a role in hypospadias. Folate supplementation in early pregnancy may be protective.
•Damgård Nielsen G, Ovrebø S. Background, approaches and recent trends for setting health-based occupational exposure limits: A minireview. *Regul Toxicol Pharmacol.* 2008, 51(3): 253-269.
The setting of occupational exposure limits (OELs) are founded in occupational medicine and the predictive toxicological testing, resulting in exposure-response relationships. For compounds where a No-Observed-Adverse-Effect-Level (NOAEL) can be established, health-based OELs are set by dividing the NOAEL of the critical effect by an overall uncertainty factor. Possibly, the approach may also be used for carcinogens if the mechanism is epigenetic or the genetic effect is secondary to effect from reactions with proteins such as topoisomerase inhibitors, and mitotic and meiotic spindle poisons. Additionally, the NOAEL approach may also be used for compounds with weak genotoxic effect, playing no or only a minor role in the development of tumours. No health-based OEL can be set for direct-acting genotoxic compounds where the life-time risks may be estimated from the low-dose linear non-threshold extrapolation, allowing a politically based exposure level to be set. OELs are set by several agencies in the US and Europe, but also in-house in major chemical and pharmaceutical companies. The benchmark dose approach may in the future be used where it has advantage over the NOAEL approach. Also, more attention should be devoted to sensitive groups, toxicological mechanisms and interactions as most workplace exposures are mixtures.

RECOMMENDATIONS FOR INDUSTRY

- ❖ Increase screening of chemicals
 - Gap exists between the number of chemicals that are in commerce and the number that have been thoroughly tested
- ❖ Apply regulatory policies
 - Ensure worker protection via legislation
- ❖ Increase spectrum of population considered “exposed”
 - Not only women of childbearing age but also all working women, all working men, and all of their potential offspring
- ❖ New end points of reproductive health assessments
 - Female entry into menopause transition

Due in part to the ever increasing number of chemicals that are created every year, effective screening methods should be employed to gauge safety before they are used. High cost of screening assays is the prime reason for the gap that exists between existing chemicals and screened chemicals.

Because the transition to menopause marks the beginning of a series of important hormonal change, occupational health agencies have suggested using this female endpoint in worker health assessments. A standard definition of the start of the menopausal transition would also allow important comparisons across occupational health studies.

Ref:

•Lisabeth L, Harlow S, Qaqish B. A new statistical approach demonstrated menstrual patterns during the menopausal transition did not vary by age at menopause. *J Clin Epidemiol.* 2004. 57: 484–496

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