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ENDOCRINE OUR LIFE LINE

ENVIRONMENTAL FACTORS AND FEMALE INFERTILITY

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"Human health is directly proportional to environmental health"

"Human activities inversely proportional to environmental health"!!

Infertility- A revenge of environment?

OVERVIEW
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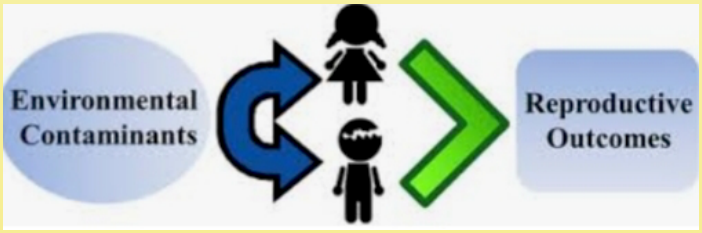
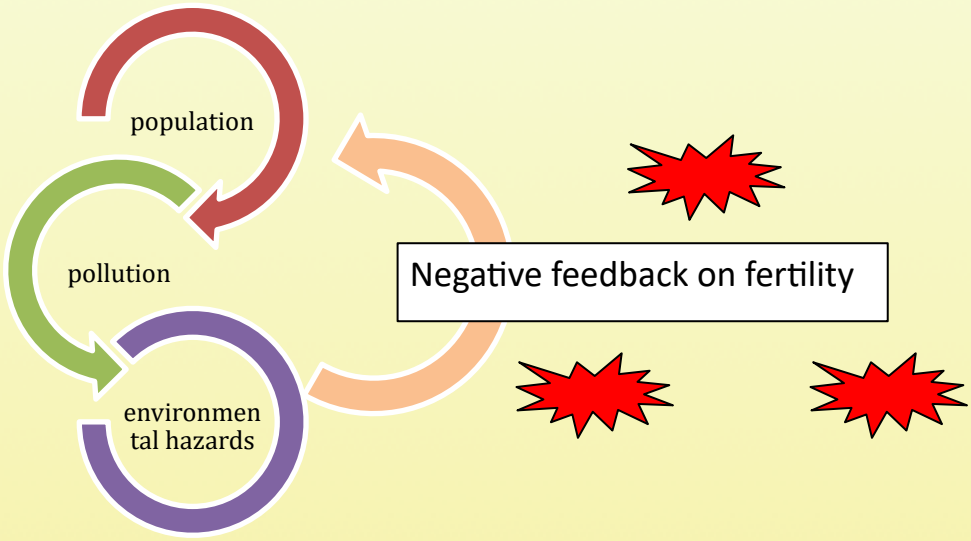


Introduction

Increasing population leading to increased demands from the mother earth results in detrimental effects on environmental health in turn affects not only the human health but also all earthly inhabitants. With thousands of synthetic chemicals thronging on human environment, there is growing scientific evidence over last decade focusing on the environmental pollutants and effects on human body. There are different mechanisms by which these factors exert their effects; Reproductive system is not exempted. United States National Survey of Family Growth found that the rate of "impaired fecundity" (difficulty conceiving or carrying a child to term) rose significantly between 1982 and 1995[1].

Further issues pertaining to reproductive health are at risk of being transmitted to next generation. Is this a revenge of environment on the growing population?

Figure.1: Negative feedback of environmental hazards



Visible and invisible Environmental hazards

Over the decades human body in addition to internal milieu like sedentary lifestyle and junk foods has to face a tremendous change in external environment**.** Environmental hazards are broadly classified into visible and invisible hazards; visible ones are the heaped garbage, blocked drainages, stained water, fogged air, noisy and dust trodden surrounds while invisible ones are organic solvents, heavy metals, pesticides and endocrine disrupting chemicals.

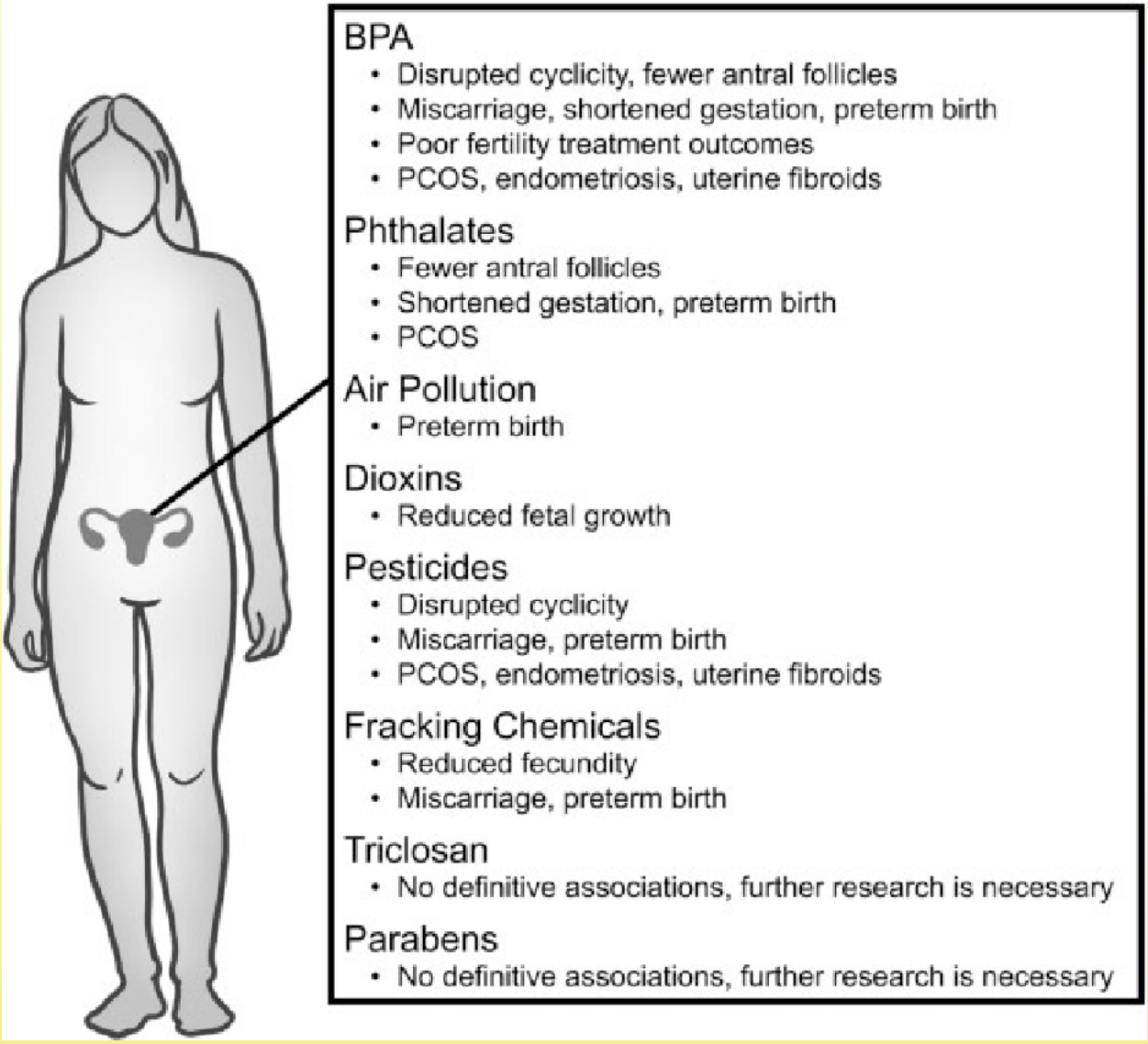
Environmental agents and Impact on Fertility

Human knowingly or unknowingly exposed to these visible as well as invisible foe from womb, rather some culminates in a cumulative effect. Some of the exposed substances along with the agents and their impact are listed in Table.1[2]. Some of these agents have been shown to affect the female conceptus of the exposed women leading to early puberty, obesity, masculinization Reproductive tract malformations, reduced fertility and faster fertility loss with ageing. A diagrammatic representation of these agents has been attempted in Figure.2[3]

Table.1: Impact of Exposure to Toxins on female reproduction

Exposure	Agents	Impact on women
dry cleaning fluid	Perchloroethylene	Prolonged time to pregnancy Miscarriage (conflicting data)
inks, coatings, gasoline, cosmetics, glues	Toluene	Reduced fecundity Miscarriage
plasticizers added to plastics like polyvinyl chloride; also widely used in cosmetics	Phthalates	Decreased fecundity, Miscarriage, Pregnancy complications like preeclampsia
monomer used to make polycarbonate plastic and various resins	Bisphenol A	Meiotic aneuploidy (observed only in mice; no human studies)
resins for particle board, plywood, insulation, cosmetics, labs, rubber production, dyes	Formaldehyde	Menstrual irregularities, Miscarriages, reduced fecundity
electronics, deicing, inks, dyes, varnish, paint, printing, cosmetics, photography, some pesticides	Glycol ethers (primarily short-chain)	Miscarriage; infertility
Solvent mixtures	Benzene, chloroform, acetic acid, methanol	Infertility, Reduced Fecundity, miscarriage, menstrual disorders, lowered LH
paint, batteries, electronics, ceramics, jewelry, printing, ammunition, PVC plastic	Lead	Miscarriage
pesticides, wood preservatives, dioxins, PCBs, fumigants	Chlorinated hydrocarbons	Spontaneous miscarriage; Infertility, time to pregnancy, Endometriosis, Disrupted oocyte development and decreased blastocyte formation (animal study)
Cigarette smoke	Nicotine, Formaldehyde, cyanide, arsenic	Infertility, reduced fecundity, pregnancy loss

Figure.2 Impact of Environmental Toxins on female reproduction



Mechanism – proofs and hypothesis

Different mechanisms have been proposed like epigenetics, oxidative stress, transcription factors, endocrine disrupting other signaling pathways and so on. Environmental pollutants like DDT, DDE, ketone, heptachlor, PCBs, dioxin, and breakdown products of detergents can mimic the hormone estrogen and hence adversely affect reproductive physiology. Many of these compounds are disseminated through air pollution and then deposited into soil and water, entering into the food chain.

Time taken for pregnancy (TTP) was found to be longer in couples where the female partner was exposed to such Endocrine disrupting chemicals (EDC).

The Environment and Reproductive Health (EARTH) Study of 2018, a large-scale prospective cohort study over 20 years, examining the impact of environment, diet and lifestyle on human reproduction has studied 131 foods, beverages as well as supplements, cosmetics and daily personal use items. Analyzed urinary biomarkers of > 40 chemicals, including phthalates and di-isononyl cyclohexane-1,2-dicarboxylate metabolites, phenols (e.g. bisphenol A, triclosan, parabens), and pesticides (metabolites of organophosphates, pyrethroids, 2,4-dichlorophenoxyacetic acid and N, N-diethyl-m-toluamide); blood samples for heavy metals and metalloids, semen, hair and various biological samples right from preconceptional sample to men and women till primary teeth of their children born. The authors made about 130 publications in scientific journals and has proposed that higher urinary concentrations of some phthalate were associated with decreased oocyte yields, lower clinical pregnancy and live birth rates even with assisted reproduction. Soy intake has been associated with modification of association with bisphenol A (BPA) and IVF outcomes[4].

A systematic review on the Impact of air pollution on fertility including animal and human studies in 2014 has shown that high concentrations of nitrogen dioxide (NO2) and particulate matter with diameter between 2.5 (PM 2.5) and 10 μm (PM10) had a detrimental effect on live birth. Increased miscarriages were noticed. Further air filters in Assisted reproduction alleviates the effects. Sulphur di oxides (SO2) have also shown to decrease live birth rates but results were not statistically significant[5].

Another systematic review of Fertility sterility 2016 on outdoor air pollution and human Infertility have identified four components of traffic pollution that could contribute to impair human fertility viz. particulate matter (2.5-10 μm), Nitrogen dioxide, Sulphur dioxide (the main source being the combustion of fossil fuels in heating, power generation) and carbon monoxide (CO) from motor vehicles and cigarette smoke. Sulphur dioxide and its metabolite causes a decrease in DNA synthesis, and has been found to induce chromosomal aberrations in in-vitro studies. Carbon monoxide with its ability to unite directly with hemoglobin in red blood cells, forms carboxyhemoglobin, which is more stable than oxyhemoglobin and prevents red blood cells from absorbing oxygen resulting increased miscarriages too along with the respiratory and cardiovascular effects[6].

Last but not the least, we have witnessed increased incidence of abortion, IUGR, still births and increased perinatal mortality amongst women in Bhopal, India, who were exposed to the industrial methyl isocyanate (MIC) gas leak.

Conclusion

There is no doubt that a deviation of normalcy has happened over few decades in the female fertility and environmental impact. Threshold of exposure, creation of the scenario in animal experiments, physiological variation from individual to individual, Body burden survey and estimation of the quantity of synthetic hazards pertaining to rising health issues has been a challenging task. Yet the keen interest of the authors concerned has kept the matter weighed with resultant changing pattern of clinical practice by reproductive medicine consultants. Routine incorporation of antioxidants or supplements right from the first visit has not been a rare sight. Still there is a questionable role of remedial care and primary prevention in combating environmental hazards is yet to be coined out.

AREHNA" a European Union project for Awareness Rising about environment and health of Non expert advisors

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