

# Environmental Pollution and Unborn Child

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## Introduction

We pay price for every good thing in life so are we paying price for all scientific breakthrough and their applications for the betterment of mankind in the form of environmental exhaustion and degradation. Pollution, the fall out of industrialization and globalization, affects all living beings. Pollutants become part of the ecological cycle and circulate in the environment from soil, water and air to vegetation, to animals, to humans and even to the fetus.

For the developing pregnancy, the environment includes anything fetus is exposed of as well as any thing that may alter conditions within the womb<sup>1</sup>. Altered metabolism and physiological adjustments during pregnancy e.g. increased tidal volume, expanded blood volume, increased body fat, hypoalbuminemia and progesterone-induced hypomotility of the gut may facilitate the bioavailability of various pollutants in the pregnant woman which can then be passed onto the growing fetus<sup>2</sup>. Functional, anatomical, physiological, metabolic and developmental immaturity renders the fetus more vulnerable to harmful effects of the pollutants than mother herself.

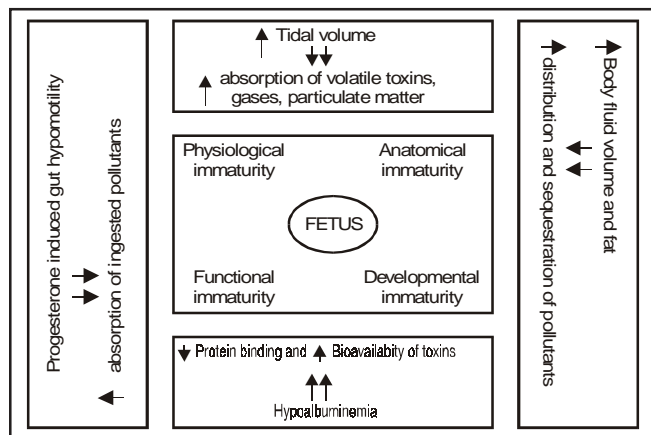


Fig. 1 : Physiological changes during pregnancy make a woman and her fetus more susceptible to pollution damage. (Adapted from Environmental pollution and human health by Prof. Satish Kumar Bhargava.

Several reports have conclusively proved deleterious effects of many industrial wastes, toxins and metals on the reproductive performance of both man and woman. From oligozoospermia to infertility in man, pollutants have been found to affect menstrual rhythm and ovulation and may cause abortion, intrauterine growth retardation, structural defects, stillbirths and neonatal deaths. "Yusho Disease" of newborn is a classical example of modern industrial disease<sup>3</sup>. There is infant growing concern of fetal well-being and environmental pollution. Unfortunately there is paucity of data on the effects of pollutants on the placental histology, fetoplacental blood flow, embryogenesis and fetal physiology, metabolism and

homeostasis. Similarly there are no specific guidelines/recommendations on safety levels of pollutants for pregnant women which are safe for growing fetus.

## Mechanism of Fetal Damage<sup>4</sup> :

The exposure to the pollutants may be of two types : (i) Concurrent exposure; (2) Non-concurrent exposure.

1. **Concurrent exposure** : It means that the mother is exposed to the pollutants during pregnancy, from conception till confinement, which may also affect the fetus in-utero. The exposure to the child may even continue during infancy via breastmilk. Concurrent exposure can take place either at home (indoor pollution), at workplace or the residence may itself be in the occupational premises. The another form of concurrent exposure could be paraoccupational, where other family members bring home the pollutants from their work place and the pregnant mother is exposed to these pollutants passively. The fetus can be protected if pregnant women is kept away/removed from the polluted environment.

2. **Non-concurrent exposure** : In this form of exposure either parent was exposed to some pollutants before conception but not thereafter, till the end of pregnancy. The ovum or sperm might have been damaged before conception which may cause infertility, abortion, IUGR or stillbirth. The mother might have been exposed to some pollutant during her childhood or adolescent age which was deposited in the tissues. This pollutant may be mobilized during pregnancy and may be transported to the fetus via blood. The classic example of non-concurrent exposure is lead, to which mother was exposed as a child and the latter got deposited in her bones at the time of mineralisation. During pregnancy when calcium is chelated from the maternal bones, lead also gets chelated and affects the fetus in-utero. Hence pollutants can affect fetus several years after exposure of the mother.

## Pathways of Fetal Exposure to Environmental Pollution

Two possible routes are proposed for fetal exposure to environmental Pollution (2) : (i) dependent on placental circulation, (ii) independent of placental circulation :

**Placental Dependent** : The fetus remain confined in a cosy, sterile and well protected fluid filled sac inside the uterus. For a pollutant to reach to the fetus, it must enter the mother's blood first and then cross the placenta to enter circulation. For example carbon monoxide present in the vehicle exhaust and cigarette smoke is inhaled by the mother, enters her blood and is then transported to the fetus via placental circulation.

**Placental Independent** : Some pollutants need not enter the mother's blood stream and placental circulation to reach the fetus. They may exert direct effect on the fetus like ionizing radiations, hyperthermia, electromagnetic field etc.

## Stages of Fetal Development and Deleterious effects of Pollutants<sup>2</sup>:

Most structural development of the fetus occurs during early pregnancy, within 3 months after conception. The embryonic stage of exposure determines the fetal structural malformation.

**Pre Embryonic Phase :** It extends from conception till 17 days. During this phase implantation, blastocyst formation and gastrulation take place. If an insult occurs at this time it can result in death/abortion. However few embryos can survive into normal fetuses, through multiplication of some totipotent cells, still left after the damage.

**Embryonic Phase :** It extends from 18-55 days after conception. This is the period during which organogenesis occurs e.g. heart forms during 3 to 9 weeks, limbs, during 3 to 6 weeks, eyes, during 4 to 7 weeks, teeth, during 6 to 9 weeks and external genitalia develops during 7 to 9 weeks<sup>5</sup>. The growing fetus is most sensitive to the environmental insult during this period because the rapidly dividing cell lines are more susceptible to damage and once this damage occurs it is due to are bioaccumulative substances. These toxins do not readily breakdown, they persist and build up in the tissues of animals and humans.

Mercury is an element occurring naturally in earth's crust but it does pose a health risk. It is produced by coal burning combustion of medical waste in incinerators e.g. thermometer, antiseptics and CT scan films. So far burning of fossil fuel is the largest source of mercury in the atmosphere. Mercury when reacts with water produces its most toxic form methyl mercury. In pregnant woman, both mercury and methyl mercury move freely across placenta contaminating mother and fetus together. Once mercury is in the body, it moves into all tissues, concentrating in brain, liver and kidneys due to its bioaccumulative tendencies and concentration within these organs can easily reach dangerous levels. CNS is the major target organ, though neurological sequelae may take years to manifest. In Minamata Bay, Japan, there was accidental exposure of fishes to methyl Mercury. Six percent of the children born over 10 years period in this area has cerebral palsy and mental retardation. Other features of fetal Minamata syndrome<sup>3</sup> are CNS tumors, deafness, blindness and irritability.

PCB and dioxin together form a group known as Polychlorinated aromatic hydrocarbon (PCAH). These are formed as a by product during manufacture and incineration of most of chlorinated products like PVC and other plastic used in hospital e.g. blood bags, i.v. sets, tubes, vinyl surgical gloves, enema bags etc. These substances are also bioaccumulative substances. Environmental exposure to PCAH may interfere with sexual maturation and thus in long term may adversely affect human reproduction<sup>12</sup>. Studies have shown that prenatal exposure to these compounds produces long lasting cognitive and behavioural damage but there is some evidence of recovery also<sup>13</sup>. In utero exposure to these agents caused a symptom complex called "Yusho Disease" in a Japanese community that used cooking oil contaminated with PCB. The fetal PCB syndrome consists of transient dark brown skin pigmentation, growth retardation, dental and skull deformities, exophthalmos, facial edema and delayed skeletal age. PBB at high exposure rates cause adverse pregnancy outcome including low birth weight and delayed neuropsychological development<sup>3</sup>.

## Pesticide and Insecticide

It has been seen that exposure to indoor pesticides are associated

with significant reduction in fetal growth and head circumference in mothers having low paraoxonase-1 enzyme activity levels<sup>14</sup>. Another recent study has shown that chlorpyrifor, propoxur and diazinon when used during pregnancy may impair fetal growth<sup>15</sup>. DDT has also been seen to affect pregnancy outcome adversely in the form of high risk of eclampsia, preterm birth, cleft palate & lip and intrauterine deaths. However contrary to earlier belief the association of smoking with heart and limb defects is not straight forward and smoking did not seem to increase neural tube defects<sup>8</sup>.

## Indoor Smoke Pollution :

Pregnant women are exposed to pollution not only outdoor but also indoor. Source of this indoor smoke is mainly the use of unvented gas stoves, chulhas, burning cowdung cakes, wood, kerosene, coal and cooking use of mosquito repellents, lighting agarbattis and scented sticks. In one Indian study it was found that level of COHb in the women exposed to different cooking fuel (biomas, kerosene, LPG) was statistically not different<sup>9</sup>. It was mainly because kitchens had poor ventilation and so even LPG use (which is supposed to be smoke free fuel) was associated with high COHb levels. Fetus has higher affinity for carbon monoxide. It has been seen in animal studies that it takes longer (twice) to normalize blood COHb levels in fetus than mother after exposure to CO. Hence poor indoor air quality can affect fetal growth and can lead to low birth weight baby.

## Automobile Exhaust :

Automobile exhaust produces carbon dioxide, carbon monoxide, lead, sulphur dioxide etc. Recent studies have shown that pregnant women breathing high levels of carbon monoxide are more likely to have low birth weight babies and it also increases the risk for ventricular septal defects in dose response fashion with increasing second month carbon monoxide exposure. It is also seen that exposure of pregnant woman to ozone is associated with increased risk for aortic artery and valve defects, pulmonary artery and valve anomalies and conotruncal defects<sup>10</sup>. Lead is another pollutant, which poses a major health risk. It is released in traffic fumes and household coal combustion. Maternal lead levels may also increase if some other family member is being occupationally exposed to lead. Blood levels of lead are determined by bone resorption rather than dietary absorption. In late pregnancy cortical bone is resorbed and if mother has high levels of lead in her bones due to childhood lead exposure, it may lead to higher lead levels in the maternal blood and in the fetus<sup>11</sup> even if mother is not exposed to lead during this pregnancy. Fetal lead toxicity leads to IUGR, preterm labour, congenital malformation, mental retardation and neonatal death. Significant association has also been found between impaired semen parameter and elevated lead levels in male partners<sup>5</sup>.

## Industrial wastes :

The main health hazards in industrial wastes include Mercury, Polychlorinated (PCB) and polybrominated biphenyls (PBB), Dioxins and DDT. These toxins pose a major health risk irreparable. Each organ and system has a particular susceptible period during its early differentiation. The precise time of maximum susceptibility varies from organ to organ.

**Fetal phase :** It extends from 56 days till birth. This period of fetal growth is characterized by hyperplasia and hypertrophy. During this phase the effects of various pollutants are mainly on

the growth and functional loss rather than structural abnormalities because the process of differentiation has already been completed.

## Effect of Specific Pollutants

**Tobacco Smoking :** Tobacco smoke produces both nicotine and carbon monoxide. Nicotine readily crosses placenta with fetal concentration generally 15% higher than maternal levels. Nicotine, which is a powerful vasoconstrictor, has effect on uterine arteries and fetoplacental blood flow. Nicotine may also compromise the fetal blood flow by constricting the umbilical arteries. Reduced fetal circulation can decrease both nutrients and oxygen supply to the fetus and in the process can affect the growth of the fetus. Moreover, carbon monoxide which in an asphyxiant, forms carboxy Hb in both mother as well as in the fetus and further compromises the oxygenation of the fetal tissues.

Nicotine causes increased spontaneous abortion in first trimester, increased premature delivery rates and decreased birth weight. Researches show that not only active but passive smoking during pregnancy may adversely affect the fetal growth.

There is also association between smoking and decreased female fertility especially with a relationship to primary tubal infertility. Smoking appears to have adverse effects along a continuum of preimplantation and implantation including gamete production and function, ovulation and cyclicality, fertilization, early embryonic cleavage, embryo transport and implantation. In males, clear evidence is there that smoking results in fewer and less motile sperms as well as lower proportion of normally shaped sperms<sup>6</sup>. Beside the increased rate of low birth weight and small for date babies, there are two other major toxic consequences of smoking :-

- (i) Intellectual impairment and
- (ii) Increased rate of infantile cancer, primarily leukemia, lymphoma and cerebral tumors are increased in children born to women who smoke during pregnancy<sup>7</sup>. Recently California birth defect monitoring programme studies have shown that smoking raises the risk for oral clefts and the hazard is even more in babies who carry a cleft susceptibility gene named transforming growth factor  $\alpha$  gene (TG F- $\alpha$ ) A<sub>2</sub> form.

Men and women working in the floriculture are exposed to 127 different herbicides. A study conducted in Bogota on floriculture workers revealed serious consequences of the herbicide exposure (Table 1). This study recruited 8867 workers of which 33% were male and 67% female with mean ages of 29.2 & 27 years respectively. The mean length of time worked in the floriculture was about 3 yrs. The total number of pregnancies included in the

**Table 1 : Rtes and odds ratios (OR) for various adverse pregnancy outcomes before and after work in floriculture (95% CI=95% confidence interval)**

Pregnancy outcome	Female workers Prevalence rates (%)			Wives of male workers Prevalence rates (%)				
	Before	After	Or	95%CI	Before	After	Or	95%CI
Induced abortion	1.46	2.84	1.98**	1.47-2.67	0.29	1.06	3.63**	1.15-8.70
Spontaneous Abortion	3.55	7.50	2.20**	1.8202.66	1.85	3.27	1.79**	1.16-2.77
Premature baby	6.20	10.95	1.86**	1.59-2.17	2.91	7.61	2.75**	2.01-3.76
Stillbirth	1.37	1.34	0.99	0.66-1.48	1.01	0.89	0.87	0.42-1.83

\*P=0.05-0.01 \*\*P=<0.01

analysis were 13984; pregnancies of female employee and wives of male workers were 10481 and 3503 respectively<sup>2</sup>.

## Ionizing and Radiation :

It is a well known fact that maternal exposure to high dose ionizing radiation is teratogenic to human fetus. At 2-4 weeks of age, the embryo is sensitive to lethality of ionizing radiation. During 4-8 wks, the fetus is growth retarded and sustains mental retardation, microcephaly, cataract and microphthalmia. At 9-10 wks, it retains CNS sensitivity and is retarded. In late fetal stage, at (12-16 wks) the fetus can sustain cellular damage but is not grossly deformed<sup>16</sup>.

## Electromagnetic Radiations :

These radiations are generated by sources as diverse as video display, power lines, microwave oven & cellular phones. One study showed that females with history of subfertility, having renataluse of electric blankets was associated with more than four fold increase in risk of CUTA (congenital urinary tract anomalies)<sup>17</sup>. Risk was greater if exposure occurred during first trimester. Risk also appeared to increase with increasing duration of electric blanket use. But studies also suggest that no clear-cut association is seen between using electric bed, heating devices and neural tube defects/oral clefts<sup>19</sup>.

Although neurotic disturbances, depression and anxiety disorders are seen in population living in vicinity of overhead high voltage transmission lines<sup>18</sup> yet the recent study suggest that no clear association is seen living within 150-300 feet of high voltage power line and increased risk for birth defects<sup>19</sup>.

Regarding the use of cellular phones during pregnancy and its effect on fetus no conclusive study is available. Some studies done in nonpregnant adults show that there is no association between use of cell phone to uveal melanoma, brain tumor, skin cancer, meningioma. Till now no such studies have been carried out to look for the effect of cellphone use on fetus and thus, caution is advised for the use of mobile phones by pregnant women until some conclusive studies disprove the possibility of any harmful effect of cell phone use on fetus.

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### Conference News

**Medicon 2005 - 80th National Conference of IMA** will be held on 27 to 29 December 2005, at *Venue* : Chennai Trade Centre, Mount Poonamallee Road, Nandambakkam, Chennai-600089. *For details* Contact Organizing Secretary **Dr. T. Sadagopan**, Usha Nursing Home, 23/2 Filter Bed Road, Vellore-632001, Tamil Nadu. Telephone : 0416-2224878; 2223222, Mobile : 98430-34878 and 94433-74878. *Scientific Committee Convenor*. **Dr. S. Chandrasekharan**, No.4, Jambulingam Street, Nungambakkam Chennai-600034, Tel : 044-28275832, 28312946 Mobile : 9840015023 E-mail : schan2004@rediffmail.com. Please offer your scientific faculty participation.

**5th International Symposium on Diabetes** will be held at Mumbai, India, on 21st and 22nd January 2006; *Theme* 'Emerging Treatments in Diabetes and Complications' International Faculty includes Prof. Robert Rizza, Prof. K.S. Nair Prof. William Young Jr. *For details*, please contact **Dr. Shashank R. Joshi**, Joshi Clinic, 12 Golden Palace, Turner Road, Bandra (N), Mumbai 400050, India. Email : mayoiiid\_5@yahoo.com.in

**7th World Congress of Nephrology** will be held at Rio de Janeiro, Brazil for April 21-25, 2007. *For further information* contact website : [www.wcn2007.org](http://www.wcn2007.org)

### Literature Review

Compiled by **Dr. P.D. Gulati**

**Safety and success of kidney transplantation and concomitant immunosuppression in HIV-positive patients.** *Anil Kumar MS, Sierka DR, Damask AM et al. Kidney International, 67;1622-1629, 2005.*

Human immunodeficiency virus-associated nephropathy (HIVAN) has become the third leading cause of end-stage renal disease (ESRD) in African Americans, and is expected to grow exponentially. High active antiretroviral therapy (HAART) has significantly prolonged the survival of patients with HIV infection. Despite the growing number of HIV-positive dialysis patients with prolonged life expectancy, kidney transplantation with immunosuppression has been declined because it is considered a waste of scarce donor kidney due to potential increase in morbidity and mortality. The effect of immunosuppression on HIV infection. Forty (40) HIV-positive dialysis patients received kidney transplantation between February 2001 and January 2004. Patient inclusion criteria were maintenance of HAART, plasma HIV-1 RNA of <400 copies/mL, absolute CD4 counts of 200 cells/ $\mu$ L or more. Immunosuppression was basiliximab induction and maintenance with cyclosporine, sirolimus, and steroids. HAART was continued post-transplant. Acute rejections were diagnosed by biopsy and treated with methylprednisolone. Surveillance biopsies were completed at 1,6,12 and 24 months, and evaluated for subclinical acute rejection, chronic allograft nephropathy, and HIVAN.

One and 2-year actuarial patient survival was 85% and 82%, respectively, and graft survival was 75% and 71%, respectively. Plasma HIV-1 RNA remained undetectable, and CD4 counts remained in excess of 400 cells per  $\mu$ L with no evidence of AIDS for up to 2 years. Conclusion. One-and 2-year graft survival is comparable to other high-risk populations receiving kidney transplantation. One-and 2-year patient survival is higher than HIV patients maintained on dialysis. Immunosuppression does not adversely affect HIV recipients maintained on HAART in the short

term. This study shows that kidney transplantation in HIV positive patients who have plasma HIV-1 RNA of <400 copies/ml on HAART is safe and is associated with survivals better than on dialysis. However monitoring of combined immunosuppression and HAART due to major drug interactions is challenging. In those receiving protease inhibitors, very low doses of cyclosporine and sirolimus are needed.

**Helicobacter pylori Stool Antigen Test.** E. Mahir Gulcan, Aydin Varol, Tufan Kutlu, et al. *Ind. Jr. Paed.* 2005;72,675.

*Helicobacter pylori* (*H.pylori*) infection is usually acquired in early childhood. Invasive techniques used for diagnosis of *H.pylori* infection require endoscopic examination which is expensive and inconvenient and may cause complications. The aim of this study was to evaluate the performance of a new noninvasive diagnostic method, stool antigen test for *H.pylori* in untreated children with recurrent abdominal pain. Eighty children (35 female, 45 male) who have undergone upper gastrointestinal endoscopy due to recurrent abdominal pain were included in the study. The *H.pylori* stool antigen test (HpSA) is based on a sandwich enzyme immunoassay with antigen detection. HpSA sensitivity, specificity, and positive and negative predictive values were determined with reference to the results of both histology and rapid urease test as a gold standard (*H. pylori* status). While 49 of the 80 children (61%) tested were positive for *H.pylori* according to the results of both histology and rapid urease test, 28 children had negative *H.pylori* status. Among those 49 children, 48 were found to be positive by HpSA. Of 28 patients with negative *H.pylori* status, 28 were *H.pylori*-negative also in the stool test. The sensitivity, specificity, and positive and negative predictive values of HpSA were found to be 98%, 100%, 100% and 96.5%, respectively. These findings have demonstrated that HpSA as a relatively simple inexpensive and time saving noninvasive test is a reliable method for detection of *H.pylori* infections in children.