



## TOXIC INDIA ---TREAT THE PATIENT AND NOT THE POISON

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### ARTICLE INFO

#### Article History:

Received 27<sup>th</sup> September, 2017

Received in revised form

26<sup>th</sup> October, 2017

Accepted 19<sup>th</sup> November, 2017

Published online 30<sup>th</sup> December, 2017

#### Key Words:

phocomalia,  
"Flipper babies",  
Viviparous,  
Thalidomide.

### ABSTRACT

The subtle effect of Thalidomide tragedy resulting in phocomelia, apoda etc in the offspring led to untold miseries. The drug Thalidomide caused an estimated 10,000 birth defects and thousands of fetal deaths worldwide. The affected babies typically suffered from phocomelia, a failure of the limbs to develop. These unfortunate babies were cruelly referred to as "Flipper babies". This drug formerly used as a sedative, but withdrawn in the early 1960's after it was found to cause congenital malformation or absence of limbs in children whose mothers took the drug during early pregnancy. Thalidomide is a sedative that used to be prescribed to treat anxiety, tension, gastritis and insomnia. It was also used to relieve morning sickness in pregnant women. There are similar good number of cases of fetal deaths, still births, teratogenics etc. The young ones of mothers exposed to toxic agents like pesticides, radiation, heavy metal etc. Can we save innocent lives growing in the wombs of the mother from becoming the victims of hostile environment that cannot avoid. This was the question that was prompted me to choose the topic of my research. Women working in metal industries smelter and other industries where heavy metals are used always run the risk of impact of heavy metals on the fetuses. Doing research with human subjects is illegal and unethical. So I have to go non-human material which stimulates human being. Viviparous is common among most mammals but not many provide long gestation period. There are two major challenges, designing a drug that could potentially target the multiple pathways involved and developing models that would help rapid screening of potential drugs. Most drugs in the pipeline have failed in clinical trials. To study the long term effects of the toxicants on the fetal development. Rats have 21, rabbits 30, dog has 60 days gestation period. Where as gestation period is long as in case of sheep, horses, monkeys, elephants, they are not available because of cost procurement and maintenance. So in this situation scorpion comes handy, cheap, available, viable and reliable, with viviparous and long gestation period. All scorpions have a long gestation period. It goes from several months to a year and a half, depending on species. The young scorpions develop as an embryo in the mother's uterus. During this time, the embryo gets food from his mother. Hence scorpion was chosen as a medical research model. It is not enough, that we discover that the pollutant affects the mother and the fetus. In several ways but not to overcome these effects in more important to live in the toxic circumstances without toxic impact.

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Citation: Raghavendra Rao, M.V., Sireesha Bala, A., Sateesh Babu, Arja, Samir Fatteh, Jitendra Kumar Naik, Anusha.C.Pawar and Jattavatu Madhavi, 2017. "Toxic India ---treat the patient and not the poison", *International Journal of Development Research*, 7, (12), 17985-17988.

### INTRODUCTION

Heavy metals are believed to exert their influence on the activity of the enzymes playing a vital role in the biochemical transactions of a living system. Embryonic development is characterized by growth and formation of new tissues.

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The alterations in the activity of enzymes and/or embryonic tissues would invariably influence the developmental processes in viviparous animals as embryonic nourishment is provided by the maternal sources. Shift in the metabolism of either the maternal tissues or the embryos owing to changes in the enzyme activity influenced by heavy metals can be reflected in the form of deviations from the normal development. Heavy metals define as any metallic chemical element that has a high density and is poisonous at lower

concentration. Heavy metals include arsenic, lead, copper and mercury which mainly effects reproductive system and especially toxic to growing fetus. The soluble compounds of lead is poisonous .lead may access into body through inhalation, by ingestion or by absorption through skin and mucous membrane (www./cdc.gov/mmwr/pdf/wil/mm6133.pdf). When women encountered to lead during pregnancy can cause a miscarriage, premature birth Low birth weight and it effects development of fatuous brain and growth of new born baby also retarded. Lead poses health risks for everyone, but young children and unborn baby more porn to lead toxicity which contributes to effect development of growing children and their behavior and learning ability (Altmann *et al.*, 1993). Copper in metallic form is not poisonous but some of its salts are poisonous such as blue vitriol and sub acetate. Copper is a powerful inhibitor of enzyme. Sources of copper are common in the diet, particularly in vegetarian diets, and can be found in the water due to copper plumbing (Sinkovic *et al.*, 2008). Many multiple vitamins contain relatively high doses of copper. The hormone estrogen promotes the retention of copper and this is why women are particularly vulnerable to the problem of copper toxicity. Copper toxicity may leads to poor fertility rate 5.

Occupational exposure is often cited as a risk factor for female fertility, as well as for early pregnancy loss and pre-term delivery. Miscarriage an abrupt end of a pregnancy at a stage where the embryo or fetus is not capable of surviving independently (Franchitto *et al.*, 2008), is the most common adverse pregnancy outcome with aggravating emotional consequences for affected individuals and families. Miscarriage is a critical indicator of embryo toxicity. It is an important outcome for the study of embryo toxic effects of chemicals including environmental contaminants and drugs (Kalumbi *et al.*, 2005; Goldstein *et al.*, 2001) and a vital end point to track the progress of reproductive health programs and their impact on maternal health.

Pregnant women and their fetuses are more vulnerable to adverse effects from the exposure of environmental toxic substances (Kumar, 2011; Vahter , 2009). Meanwhile, exposure to environmental contaminants during pregnancy may extend negative impacts in early childhood and in later life (Zheng *et al.*, 2014) Although the placenta may act as a selective transporter that prevents the passage of potentially toxic substances to the developing fetus, some environmental contaminants can freely or partially cross the placental barrier (Quansah *et al.*, 2015). Particularly, arsenic, cadmium and lead are well-known environmental heavy metals, and they could extend the health risk to the fetus even at a low level through trans-placental circulation (Gluckman *et al.*, 2008; Needham *et al.*, 2011; Caserta *et al.*, 2013).The toxicological effects of heavy metals could alter the physiological changes during pregnancy, the critical phase of fetal cell division and differentiation (Chen *et al.*, 2014; Al-Saleh *et al.*, 2014) As an example, prenatal cadmium exposure could impair steroid genesis that leads to suboptimal fetal growth and development (Gundacker, 2012). Lead exposure could interfere with calcium deposition in the bone, resulting in decreased fetal bone growth (Stasenko *et al.*, 2010) Arsenic exposure during pregnancy may also contribute to placental insufficiencies, which could lead to intra-uterine growth retardation through inducing oxidative stress (Potula *et al.*, 2005)

However, heavy metals at higher concentrations prove hazardous affecting life and life processes. Man has always has been exposed to heavy metals through natural concentration in soil and water. Metals leached from eating- utensils and vessels used for cooking increased the risk. The emergence of industrial age and large scale mining brought occupational hazards caused by various toxic metals. Metallic constituents of pesticides and therapeutic egeents are additional sources of hazardous exposure. The burning of fossil fuel containing heavy metals and the addition of tetra ethyl lead to gasoline have now become the major sources oheavy metal poisoning, adding to environmental pollution (Klassen, 1985). With the increased use of chemicals in modern technology, the concentration of the metal is increasing in the environment.

Heavy metals are known to affect reproduction and development of animals. Long term oral administration of cadmium caused reproductive failures of fetal growth retardation in rats (Pond, 1975). Exposure of fish to sub lethal levels of zinc decreased the growth rates and markedly reduced reproductive potentials (Crandall, 1962). Survival of developing fertilized eggs and their hatchability decreased with increasing concentration of mercury and selenium in the rainbow trout *Salmo gairdnerii* (Klaver, 1983). Copper sulphate proved more toxic than zinc sulphate to both the adults and juveniles were more susceptible than the adults to both metals (Rao and Jayasree,(1987).

Exposure of jetuses and striped dolphin in mercury resulted in higher mercury in suckling stges than the fetal stage (Itano, 1984). Administration of cadmium to laboratory rats induced fetal growth retardation (Ahokas, 1980), (Verschure, 1976), found chromosomal aberration and increased aneuploidy in methyl mercury exposed workers. Heavy metals, finding entry in to an organism induces biochemical and metabolic changes. Exposure of Chenna punctatus to chromium resulted in hyperglycaemia and hyper lactemia (Sastry, 1984). Administration of cadmium to the teleost, *Puntius conluonus* produced hyperglycaemia, promoted glycogenolysis and raised myocardial glycogeentration (Gill, 1981). Kulkarni and Utkal (Kulkarni *et al.*, 1983) studying the effect of coppersulphate on the biochemical composition of viviparous bengalensis, found marked decrease in the haemolymph glucose and tissue glycogen levels (Arillo, 1982) studied the effect of chromium,cadmium and nickel on biochemical constituents of the rainbow trout *Salmo gairdnerii*. *Rana cynoflictis* exposed to mercury and cadmium exhibited alterations of glycogen content in tissues (Dudgall, 1986) Mercury and cadmium produced marked depletion in rainbow trout, of glycogen content of both liver and muscle (Lowe-Jinde, 1984). Administration of Mercury to Caspian sea gammarids reduced glycogen content of tissues and glucose concentration of haemolymph (Garanina, 1984). Gluconeogenesis and glycogenolysis were induced by mercury in fish, *Channa punctatus* (Sastry, 1982) The fresh water mussel *Peerresia rugosa* subjected to mercuric chloride revealed changes in the levels of glycogen (Ravider Reddy, 1985) Blood level was elevated in a seven month old girl when she was exposed to mercury vapour (Moutinho, 1981). Amjnul Islam and Roy (Aminul, 1983) reported that that the decline in the protein content in the insect *Crysocorisstelli* exposed to cadmium chloride was due to the effect of the metal which is an enzyme inhibitor known to block m RNA synthesis at the level of transcription. Administration of cadmium to *Daphnia magna* produced significant reduction in protein, mRNA and DNA

(Knowles, 1987). Exposure of *Channa punctatus* to sub lethal concentration of mercury decreased the uptake of glycine. (Sastry, 1982) Heavy metals like mercury, cadmium and lead inhibit the amino acid transport (Sastry, 1982). Heavy metal poisoning is treated often with antidotes which detoxify through the mechanism of chelation and revert the toxic effects. Dimercaprol (2,3-dimercapto propanol, British anti Lewisite-BAL is an antidote used to treat mercury and lead poisoning.

### Major advances and discoveries-

The most common heavy metal chelators prescribed by the medical profession are EDTA, DMPS, and DMSA. These chelators are life-saving drugs in cases of acute metal poisoning. Of these, the DMSA and DMPS especially carry risks of harm, and should only be used as a last resort. DMPS, an oral medication for arsenic, cadmium, and mercury toxicity. Succimer (DMSA), an oral medication for mild-to-moderate lead, arsenic and mercury toxicity. It was suggested that dimercaprol can be used to revert the biochemical lesions induced by heavy metals and achieve safety not only to the maternal animal but also to the fetus during the gestation period.

### History and mechanisms

The subtle effect of Thalidomide tragedy resulting in phocomelia, apoda etc in the offspring led to untold miseries. The drug Thalidomide caused an estimated 10,000 birth defects and thousands of fetal deaths worldwide. The affected babies typically suffered from phocomelia, a failure of the limbs to develop. These unfortunate babies were cruelly referred to as "Flipper babies". This drug formerly used as a sedative, but was withdrawn in the early 1960's after it was found to cause congenital malformation or absence of limbs in children whose mothers took the drug during early pregnancy. Thalidomide is a sedative that used to be prescribed to treat anxiety, tension, gastritis and insomnia. It was also used to relieve morning sickness in pregnant women. There are similar good number of cases of fetal deaths, still births, teratogenesis etc. The young ones of mothers exposed to toxic agents like pesticides, radiation, heavy metal etc. Can we save innocent lives growing in the wombs of the mother from becoming the victims of hostile environment that cannot avoid. This was the question that was prompted me to choose the topic of my research. Women working in metal industries smelter and other industries where heavy metals are used always run the risk of impact of heavy metals on the fetuses. Doing research with human subjects is illegal and unethical. So I have to go non-human material which stimulates human being. Viviparity is common among most mammals but not many provide long gestation period.

### Significant gap in research-

There are two major challenges, designing a drug that could potentially target the multiple pathways involved and developing models that would help rapid screening of potential drugs. Most drugs in the pipeline have failed in clinical trials.

### Current Debate

To study the long term effects of the toxic agents on the fetal development. Rats have 21, rabbits 30, dog has 60 days

gestation period. Whereas gestation period is long as in case of sheep, horses, monkeys, elephants, they are not available because of cost procurement and maintenance. So in this situation scorpion comes handy, cheap, available, viable and reliable, with viviparity and long gestation period. All scorpions have a long gestation period. It goes from several months to a year and a half, depending on species. The young scorpions develop as an embryo in the mother's uterus. During this time, the embryo gets food from his mother. Hence scorpion was chosen as a medical research model. It is not enough, that we discover that the pollutant affects the mother and the fetus. In several ways but not to overcome these effects in more important to live in the toxic circumstances without toxic impact.

### Ideas Where Research Go Next

It is found in my research, by administering the chelating agents like Dimercaprol (BAL) to the heavy metal exposed mothers the adverse effects of Mercury and Lead on both mother and the fetus could be elevated. Extrapolating to humans, it is possible to protect the fetus of industrial workers by monitoring the heavy metal load periodically and administering the appropriate dose of antidote. Of course, much work on these lines is needed before we can carry it over. If I am permitted to suggest, I may say that there is enormous scope for us in the medical field to contribute to science and human welfare by taking research of this type and doing collaborative work with other professors of different universities.

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