

Mercury level in Maternal and cord blood of 3rd trimester pregnant Egyptian females

A thesis

Submitted in fulfillment of the requirements of Master Degree in
Obstetrics and Gynecology

Presented by

Nahed Gamal Shawky

M.B.B.Ch : Mansoura University, 2005

Resident of Obstetrics and Gynecology (Port Said General Hospital)

Under supervision of

Prof. Mahmoud Ali Ahmed El-Shourbagy

Professor of Obstetrics and Gynecology

Faculty of Medicine, Ain Sham University

Prof. Hesham Mahmoud Mohammed Harb

Professor of Obstetrics and Gynecology

Faculty of Medicine, Ain Sham University

Dr. Tamer Ahmed El-Refai

Lecturer in Obstetrics and Gynecology

Faculty of Medicine, Ain Sham University

Ain Shams University

Faculty of Medicine

2012

ACKNOWLEDGEMENT

First of all, thanks merciful God who helped me finish this work

I would like to express my deep appreciation to **Prof. Mahmoud Ali Ahmed El-Shourbagy**; Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Sham University, for his invaluable help, advice and expertise throughout the whole work.

I would like to express my deepest gratitude to **Prof. Hesham Mahmoud Mohammed Harb**; Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Sham University, for his follow up and scientific refinement throughout this work.

I also would like to express my sincere thanks to **Dr/ Tamer Ahmed El-Refaei**; lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Sham University, for his guidance, and support throughout the work

I am also grateful to **Prof. Mostafa Khalil**; the head of laboratories at Faculty, of Science Ain Shams University, for his cooperation and generous help

I am much obliged to the **volunteer patients** who accepted to participate in the study.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

INTRODUCTION	1
AIM OF THE WORK	4
REVIEW OF LITERATURE	
History of mercury	5
Sources and forms of environmental mercury	6
Mercury biogeochemical cycling.....	8
Human exposure to mercury species.....	9
Toxicokinetics.....	16
Health effects of mercury exposure.....	20
▪ Neurological effect.....	21
▪ Cardiovascular effects.....	25
▪ Respiratory effects.....	29
▪ Gastrointestinal effects.....	30
▪ Haematological effects	31
▪ Hepatic effects	32
▪ Renal effects	32
▪ Immunotoxic effects	34
▪ Endocrinal effects.....	36
▪ Dermatologic effects.....	38
▪ Neoplastic effects	39
▪ Male reproductive effects.....	41
▪ Genotoxicity	41

Maternal and fetal effects.....	44
• Birth Outcomes and Infant Growth.....	49
• Neurodevelopmental outcomes	52
• Cardiovascular.....	60
• Immunological	61
SUBJECTS AND METHODS	64
RESULTS	72
DISCUSSION	94
SUMMARY	104
CONCLUSION AND RECOMMENDATIONS	107
REFERENCES	108
APPENDIX	
ARABIC SUMMARY	

LIST OF TABLES

Table I:	Mercury levels in selected commercial fish and shellfish.....	10
Table 1:	Demographic characteristics of pregnant women.....	72
Table 2:	Anthropometric measurements of pregnant women.....	73
Table 3:	Distribution of gravidity, parity and abortion among studied women.....	74
Table 4:	Fish consumption during pregnancy.....	75
Table 5:	Frequency of urinary and gastrointestinal complaints among studied women.....	76
Table 6:	Urianalysis of the enrolled women.....	77
Table 7:	Complete Blood Cell Count of the enrolled women.....	78
Table 8:	Liver function and serum creatinine level of the enrolled women.....	79
Table 9	Type of delivery among the studied women.....	80
Table 10:	Neonatal characteristics.....	81
Table11:	Concentrations of total mercury in maternal blood and umbilical cord blood.....	82
Table 12:	Distribution of maternal mercury level according to Rfd.....	83
Table 13:	Distribution of cord mercury level according to Rfd.....	84
Table14:	Mean maternal blood mercury levels by demographic characteristics of studied women.....	85
Table15:	Mean cord blood mercury levels by demographic characteristics of studied women.....	86
Table16:	Distributions of maternal and cord blood mercury concentrations among different fish consumption rate.....	87

Table17:	Distribution of maternal blood mercury concentrations by neonatal characteristics.....	88
Table18:	Distribution of cord blood mercury concentrations by neonatal characteristics.....	89
Table19:	Correlations between mercury concentration and fish consumption frequency.....	90
Table 20:	Correlations between mercury concentration and parity.....	91
Table 21:	Correlations between mercury concentration and fetal weight.....	92
Table 22:	Correlations between mercury concentration and laboratory findings	93

LIST OF FIGURES

Figure I: Natural processes leading to mercury emission	7
Figure II: Acrodynia: Exanthema due to mercury intoxication from a mercury thermometer broken in the children's room 4 months previously	39
Figure 1: Distribution of maternal mercury level according to Rfd	83
Figure 2: Distribution of cord mercury level according to Rfd.....	84
Figure 3: Mean maternal and cord blood mercury levels by amount of fish consumption.....	87

LIST OF ABBREVIATIONS

ATSDR	Agency for Toxic Substances and Disease Registry
CFL	Compact fluorescent light bulbs
DHA	Docosahexaenoic acid
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
Hg	Mercury
MeHg	Methyl mercury
NRC	National Research Council
OSHA	Occupational Safety and Health Administration
Rfd	Reference dose
UNEP	United Nations Environmental Program

INTRODUCTION

Mercury (Hg) and its compounds are recognized as potentially hazardous material and are rated in the top category of environmental pollutants (**Lipfert et al., 1995**).

Mercury occurs naturally and distributes throughout the environment by both natural process and human activities. Inorganic Hg released into the environment from natural or anthropogenic sources is transformed to organic Hg (mainly methylated form), which is then accumulated in higher trophic animals through food chain (**Boudou and Ribeyre, 1997; Morel et al., 1998**).

Methyl mercury (MeHg), biomagnifies in the aquatic food web, hence, large predatory species have the highest concentrations (**UNEP, 2002**). Methyl mercury is received by humans through long-lived fish and seafood caught in the seas contaminated by mercury (**Myers et al., 2003**).

People are exposed to MeHg mainly through their diet, especially through the consumption of freshwater and marine fish, and consumption of other animals that consume fish (such as marine mammals). The highest levels are found in fish that are apical predators of older age such as king mackerel, pike, shark, swordfish, walleye, barracuda, large tuna, scabbard, marlin and fish-consuming mammals such as seals and toothed whales (**UNEP, 2002; Miklavcic et al., 2011**).

Trimming, skinning off and cooking the mercury-contaminated fish does not reduce the mercury content of the fillet portion. However, people who

consume moderate amounts of a variety of fish are not at risk **(UNEP, 2002)**.

In addition, humans are exposed to methylmercury through food (especially fish) and elemental mercury vapor from amalgam dental fillings **(Jiang et al., 2010)**.

Fish MeHg is easily absorbed by gastrointestinal tract and rapidly enters the blood stream. It is distributed throughout the body within 3–4 days. It is estimated that 5% of dietary MeHg is found in the blood and 10% in the brain, with a half-life ranging between 45 and 70 days **(Castoldi et al., 2003)**.

Ingested MeHg readily crosses the placenta and blood–brain barriers **(Ramirez et al., 2000)**.

Exposure to mercury is especially important for pregnant women. Since, there is no barrier preventing transmission of mercury from mother to fetus. Therefore, the prenatal period is believed to be the most susceptible stage of life, and there is an increasing concern about the neurotoxic effect of prenatal Hg exposure on the fetus **(Goldman and Shannon, 2001)**.

Exposure to high doses of methyl mercury during pregnancy, such as occurred in Minamata, Japan and in Iraq during the 1970s can cause fetal death, serious birth defects, mental retardation, long-term disabilities, and blindness **(NRC, 2000)**. Prenatal exposure to lower doses has been linked to subtle learning delays and alterations of the autonomic nervous system **(Clarkson, 2002; USEPA, 2001; Sorenson et al., 1999)**.

The toxic limit of mercury for human fetus specified by The US EPA

(Environmental Protection Agency) is 0.1 µg/ kg/day (**Counter and Buchanon, 2004; Goldman and Shannon, 2001**).

This reference toxic limit of mercury is stated for maternal daily intake because that is how the fetus is exposed. The toxic limit level for fetus could be lower than the mother's values. The fetus was considered to be the most sensitive group (**Steuerwald et al., 2000; Schetter, 2001; Weil et al., 2005**).

AIM OF THE WORK

To evaluate the levels of methyl mercury in the serum of pregnant mothers and cord blood for 3rd trimester pregnant females who exposed to:

- a) Amount of fish > 350 gm/week
- b) Amalgam (mercury vapor > 0, 28 µg/day)

Research question

Survey levels of methyl mercury in maternal and cord blood for 3rd trimester pregnant females who exposed to:

- a) Amount of fish > 350 gm/week
- b) Amalgam (mercury vapor > 0, 28 µg/day)

Medical applications

If the hypothesis of the study become true, it is advisable to develop mass screening program for pregnant mothers, and design campaign to inform pregnant mothers about hazards of eating such foods and thus prevent exposure to these substances.

LITERATURE REVIEW

HISTORY OF MERCURY

During the past three decades, concerns about environmental mercury contamination have emerged because of its wide distribution and persistence in the environment, as well as its tendency to accumulate in food chains, with possible adverse effects at the top of food webs, especially for humans (**Briggs, 2003**).

Mercury is an inorganic, naturally occurring element with ubiquitous distribution throughout the environment (**Oken and Bellingerb, 2008; Gundacker et al., 2010a; Ramon et al., 2011**). It is a global contaminant of increasing concern, ranked as top three-priority pollutant out of 275 substances on the Agency for Toxic Substances and Disease Registry's Substance Priority List (**ATSDR, 2011**).

Mercury was considered the basis of metals, close to gold and it was named after the planet Mercurius, which was the planet nearest to the sun (gold). Others say that because of its mobility it is named after Mercurius, the messenger of the gods in Roman mythology (**Scerri, 2007**). It is symbolized as Hg; an abbreviation derived from the ancient Greek word *Hydrargyrum* which means liquid quicksilver (**Clarkson and Magos, 2006**).

Mercury and the other noble metals were the first elements to be discovered and utilized by humans, as they exist in nature either in Free State or as easily decomposable compounds (**Carpi, 2001**). The Chinese, Greek and Roman people have recognized its presence and applications since ancient times. In the 4th century B.C., Aristotle discussed the use of 'fluid silver' for religious ceremonies. The ancient Egyptians used it to form amalgams, Greeks used it in ointments and

the Romans used vermillion (the red-colored sulphur salt of Hg) as a cosmetic and decorative (**Forrai, 2007**).

Despite the fact that, the predominant use of Hg in pre-industrial times was for the extraction and purification of gold and silver because of its ability to combine with other metals and form amalgams, gold mining remains a major use of the metal today (**Carpi, 2001**).

The unique chemical and physical properties of Hg are used widely in industry. Currently, Hg is used industrially in the chloralkali production of batteries, incorporation in thermometers, barometers, other scientific apparatus', streetlights, fluorescent lamps, advertising signs. Medicinally, it is used in dental amalgam fillings and vaccine preserver (**Virtanen et al., 2007; Chen et al., 2009**).

SOURCES AND FORMS OF ENVIRONMENTAL MERCURY

Mercury is released in environment in substantial quantities through natural events as well as from a wide range of anthropogenic activities (**Burger et al., 2004; Holmes et al., 2009**).

It occurs naturally at trace levels in the environment by tillage of the earth's crust (Figure I). It is a natural component of rocks and minerals and it is emitted to the environment through weathering of rock in mountains, the degassing of the earth's crust through volcanic eruptions and seismic activity, evaporation from the oceans (**Nriagu and Becker, 2003; Gray and Hines, 2006; Gustin et al., 2008; Bose-O'Reilly et al., 2010**), photo-reduction of divalent mercury in natural waters and biological formation from methylation of elemental Hg (**UNEP, 2002**).

Increasing amounts are also released through human activity; since industrialization the amount of Hg found in the environment has increased by a

factor of three (**Jones, 2004**). Anthropogenic mercury emissions account for about two-thirds of the total global output (**ATSDR, 2001; Swain et al., 2007**).

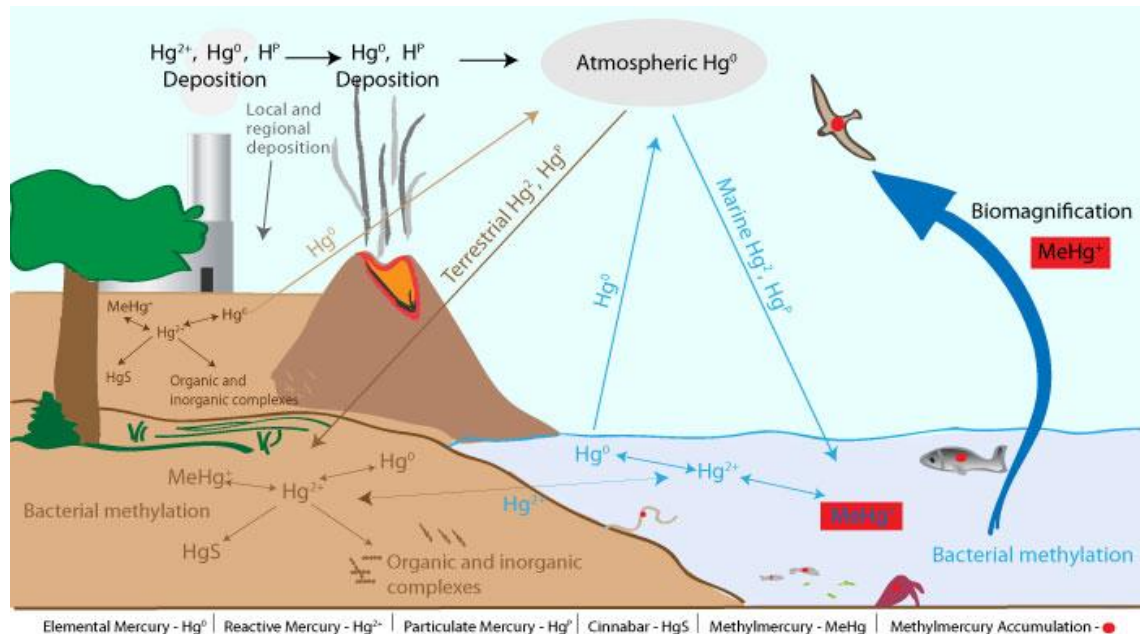


Figure I: Natural processes leading to mercury emission

United Nations Environmental Program (UNEP) classified anthropogenic sources into three categories: (1) mobilization of Hg impurities from coal-fired power plants, fossil burning, or cement production; (2) releases of Hg from intentional activities, as mercury mining, artisanal gold and silver mining, chloralkali production, manufacturing of mercury-containing medicinal products and other products (batteries, switches) and the use of fluorescent lamps and amalgam fillings; (3) combinations of intentional releases and mobilization of mercury impurities as waste incineration, landfills from mining tailings or vaporizing of amalgam fillings in crematoria (UNEP, 2002).

Mercury exists in the environment as one of three forms, namely, metallic mercury, also known as elemental mercury, inorganic mercury and organic mercury. For organic and inorganic compounds, Hg may have a valence state of either +1,