

Introductory Remarks: Session on Developmental Factors Affecting Pollutant Toxicity

by Sergio Fabro*

The last century of human history has been characterized by an unprecedented geometrical growth of knowledge of the physical, chemical and biological sciences. This knowledge, combined with the technology of the continuing industrial revolution, has given us a remarkably increased ability to control infections, infestations, and to some degree malnutrition and famines.

This has resulted in a significantly longer life expectancy and, since human fertility has not significantly changed, overcrowding on this earth is expected in the near future. For these reasons, we have increasingly sharpened our focus on improving the quality of life while attempting to decrease fertility and accordingly the birth rate.

However, the same technological advances which allow us to enjoy a longer life now represent potential toxicological threats to human life and progeny. For example, the advances in knowledge of synthetic chemistry have made it possible to produce chemicals of novel structure not previously existing in nature. We are therefore being exposed to increasing numbers of chemicals which are man-made and whose toxicity, in most cases, is poorly understood. Some of these new chemicals are drugs with therapeutic value, others are industrial products or by-products, but all are associated to some extent with the risk of toxicity.

Furthermore, it appears that susceptibility to environmental toxicity differs with stage of human development, and that we are particularly sensitive to pollutant toxicity during our intrauterine life. We have become increasingly concerned about this problem, since apparently innocuous drugs to adults, such as thalidomide and DES, have resulted

in tragic human experiments in transplacental toxicology when given to pregnant women.

The realization of the dynamic complexity of the man-made environmental changes, combined with the medical recognition of the significant human reproductive wastage, made pollutant toxicity during pregnancy one of the most pressing environmental problems. Thus, human reproductive wastage is not only significant, but in most cases its etiology is poorly understood. For every 3 million live births per year in the USA there are approximately 600,000 abortions, and some 24,000 fetuses die *in utero*. Of those who are born alive, about 10% are premature, and some 12-14% have a low birth weight, with another 90,000 possessing some type of congenital malformation. In this country, about 30,000 babies per year die during the neonatal period, and some additional 26,000 do not survive into the beginning of their second year.

Although these figures are well established, nevertheless the etiology and pathogenesis of most of these effects is far from being understood. In particular, it is not clear how important a role environmental toxicity has played. Congenital heart disease is a predominant type of congenital abnormality occurring at about 4-5 per thousand live births, and it is a leading cause of neonatal and infant mortality. Despite the frequency with which this defect occurs, our understanding of its cause(s) and mechanism(s) is very scanty. For only 5% of the cases can we infer a genetic, metabolic or an exogenous environmental factor. The etiology of the remaining 95% is unknown, except that it appears to some extent to be familial. In absolute numbers, this means that every year about 15,000 new babies are born with some significant heart abnormality and for 14,250 of them we cannot find an apparent cause.

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Similarly, a large proportion of the cases of abortion, stillbirth, prematurity and intrauterine growth retarded babies has an unknown etiology.

Indeed, one is left to wonder what part the environment plays in determining at least a proportion of these defective offspring. However, intrauterine death or low birth weight are only the most obvious effects of abnormal human reproduction. We must add to them the offspring who seem perfectly normal at birth, but who later in life are afflicted with mental retardation or are suffering from transplacentally-induced disease including cancer, hypertension and infertility. At the present time, most of the evidence for this type of subtle toxicity

is derived from experiments in animals. Dr. Rice later will talk to us on transplacental carcinogenicity, and Dr. Tuthill will tell us the relationship between sodium exposure and the development of hypertension. The extent of this type of problem in the human is unclear, and represents an area of active concern, and a challenge to future investigations.

It is my opinion that a close monitoring of offspring of pregnant workers, combined with basic animal experimentation, will lead to a better understanding of the risk factors in environmental toxicity to human reproduction and development.