INTRODUCTION
The infamous thalidomide incident of the 1960's proved that the human population was not immune to chemically induced developmental abnormalities. This tragedy claimed over 10,000 victims - infants born with severe and shocking physical deformities - before the cause was identified and thalidomide removed from the market (Farrar and Blumer, 1991).

Warnings of such a disaster were present nearly thirty years prior to the tragedy but they went unheeded. Experimental studies had shown that dietary variation of vitamin A during pregnancy could produce birth defects (Hale and Warkany, 1930). The first observation that fetal cells were susceptible to the carcinogenic action of chemicals was probably that of Law (1940) who injected 1,2,5,6-dibenzanthracene directly into the amniotic fluid of mouse fetuses. Most of the mice developed lung tumors within seven months of birth. In 1947, Larsen first reported transplacental tumor induction in experimental animals. He observed a high incidence of lung adenomas in the offspring of mice treated with urethane during the last three days of gestation. Surprisingly, these observations were neglected for a good 20-30 years before their importance was recognized and work in the direction of identifying chemicals capable of passing the placental barrier began.

The classic papers of Druckrey et al. (1966, 1967) showed that a large number of N-nitroso compounds were teratogenic as well as carcinogenic in the F1 progeny. They seriously warned against the consequences of prenatal exposure to chemical carcinogens. Since then, the transplacental effect of a large number of chemicals have been demonstrated using different animal model systems (for reviews see Tomatis, 1979, 1988). Pediatricians soon established a connection between rubella infection in early pregnancy and the birth of severely deformed infants. It was also in the 1960's that the first evidence for an increased human cancer risk following prenatal exposure was put forward when childhood leukemia was associated with in utero radiation exposure (Stewart et al., 1956). In 1971 reports by Herbst et al. (1971) and Greenwald et al. (1971) established a relationship between prenatal diethylstilbestrol (DES) exposure and subsequent occurrence of clear-cell adenocarcinoma of the vagina and cervix in young women. Upto date, DES is the only established human transplacental carcinogen known (Herbst et al., 1978; Kleihues, 1982).
With the years, other exposure routes were identified. Prezygotic exposure of the germ cells of one or both parents to a carcinogen/mutagen may result in the incorporation of a mutation in the germ line and increase the risk of cancer in subsequent generations. The male germ cells appear to be at a greater risk of mutation than mature oocytes (see Tomatis et al., 1990). Several epidemiological studies, although limited and contradictory, relate cancer in children with parental occupational exposures, parental cigarette smoking and household exposures to electric and magnetic fields (Preston-Martin, 1989). Experimental evidence of the possible role of prezygotic events in increasing cancer risk is accumulating. In amongst the first studies in this field, Tomatis and Goodall (1969) demonstrated that the progeny of male mice treated with 7,12-dimethylbenz(a)anthracene (DMBA) prior to mating did not show increased tumor incidence while the progeny of treated females did. Exposure of either parent to X-rays or urethane increased the incidence of tumors in the subsequent untreated generations of mice (Nomura, 1975; 1982; 1989). Napalkov et al. (1987) demonstrated an increase in the incidence of 12-O-tetradecanoyl phorbol-13-acetate (TPA)-induced skin papillomas in the progeny of parents exposed to DMBA prenatally. The progeny of male rats exposed to ethylnitrosourea (ENU) before mating also showed significantly higher thyroid tumor incidence rates (Tomatis et al., 1990).

The postnatal period has also been recognized as a critical developmental period. The increased vulnerability of infants to xenobiotics compared to adults may be due to the numerous characteristic risk factors associated with the stage. As for example a larger infant body surface area w.r.t. weight, a higher infant metabolic rate and oxygen consumption, different body composition, special dietary needs, the immaturity of the organs and organ systems, low levels of drug metabolizing and DNA repair enzymes and the absence of the blood-brain barrier, to name a few (WHO, 1986). In addition the rapid cell proliferation may be conducive to the formation of DNA-carcinogen adducts, making these stages privileged sites for neoplastic transformations.

An infant may directly come into contact with xenobiotics through air, water or clothes. Another important postnatal exposure route identified is the milk. Breast
milk is the ideal food for the infant, but it has been shown to be a reservoir for lipophilic chemicals and the means for translactational delivery of the same.

As early as the last century it was known that the breast milk from a mother occupationally exposed to toxic chemicals might contain sufficient amounts of chemical that could adversely affect the nursing infant (Reed, 1908). But again many years passed before the first environmental chemical was detected in human milk - the organochlorine insecticide DDT (Laug et al., 1951). Later with the development of sophisticated gas-chromatography techniques, other chemicals like DDE, DDD, dieldrin, hexachlorocyclohexanes, heptachlor epoxide, HCB, aroclor, PCBs, PBBs, TCDD (Jensen, 1988), nitrosamines (Lakritz, 1984), carcinogens (see Jensen, 1988), heavy metals (Jensen, 1983), therapeutic drugs (Welch, 1981) and viruses (see Ichimaru et al., 1991) were also detected in human milk. Human milk in general contains 10-50 times more of these environmental contaminants than cow's milk or milk substitutes (Jensen, 1988). Most of the contaminants of human milk are inherently toxic (especially the organohalogens and the heavy metals). Their adverse effects tend to be directed against the neonatal liver, skin, immune and nervous systems.

Neonatal exposure via the translactational route may be an addition to a previous in utero exposure. Toxic effects need not be manifested at birth or during infancy, but can remain hidden and appear in later years as behavioural or biochemical abnormalities and also as cancers.

Obviously, the concern over toxic exposures of human infants is growing. Hard facts about the hazards of perinatal xenobiotic exposure is not available and continued surveillance is necessary.

Investigators have tried to prevent or reduce the formation of perinatally-induced tumors by using different chemopreventive strategies. Rao (1982; 1989) demonstrated the reduction of DMBA-induced transplacental and translactational tumors in mice and their subsequent generations by the dietary additives BHA and disulfiram (Rao et al., 1989). Other laboratories have used
various synthetic and naturally occurring chemopreventives to inhibit perinatal carcinogenesis (see Alexandrov et al., 1990).

The aim of this work was to study the influence of the translactational passage of certain dietary chemopreventive agents as well as of some environmental substances. The milk used as a delivery route for chemoprotective principles may counteract perinatal carcinogenesis by preventing promotion of a prenatally initiated carcinogenic event or postnatal initiation. The concept of using milk as a delivery route originated in the 15th century B.C. when it was used as a route for administration of medicines to the suckling infant.

In our studies, the modulation of activities of xenobiotic metabolizing enzymes in the neonatal liver have been used as biochemical parameters for the detection of the presence of active principle(s) in the translactational system.

The modulation of neonatal enzymes could greatly affect the toxicity/carcinogenicity of many xenobiotics encountered via maternal exposures, and may prevent the development of childhood cancers.