The concept of healthy mother and healthy baby is an important aspect of reproductive health care programme. In a developing country like India, poverty, illiteracy and multiple pregnancies take their toll of mother’s health and that of the breast-fed infant. High prevalence of anemia and malnutrition among the reproductive age group women, particularly during pregnancy and lactation can have irrevocable effects on the infant’s health. This necessitates development of field centers to monitor the nutrition status and anemia in the population at large and to introduce user-friendly supplementation programmes to alleviate the nutrition related disorders. Also in a country like ours, infections and ill health necessitate long term drug therapy of the mother even during lactation and it is well established that most of the drugs present in the maternal circulation get transferred to breast milk. However, the effects of these maternal drugs on the nurslings have received scant attention. Studies have therefore been undertaken in the following areas: (i) transfer of drugs from maternal circulation to breast milk and its effect on the nursing infant; (ii) studies related to nutritional supplementation with iodine fortified salt in field conditions; and (iii) development of simple methods for monitoring hemoglobin status in adolescent girls and pregnant mothers.

4.1 Model to Predict Milk to Plasma Ratio of Maternal Therapeutic Drugs: Potential Effect on Infants’ Drug Metabolizing Enzymes (Funded by Indian Council of Medical Research Under The Functional Genomics and Molecular Medicine Program)

Principal Investigator: Anurupa Maitra


Duration: 2002-2005

In India, ill health of nursing mothers necessitating chronic medication is a common feature. Transfer of these drugs from maternal circulation to breast milk has now been well documented making the nursling an ‘un-intended recipient’ of these drugs. An in vitro model developed to determine this transfer potential from circulation to breast milk has been described earlier (Annual Report 2001-2002, p.73). However, the possibility of harmful effects of exposure to these drugs on the nurslings, when they are in their rapid growth and development phase, has not yet been studied. The present study is aimed at assessing the effect on the drug metabolizing capacity of these nurslings and studies have been initiated with anti-tuberculosis drugs in view of the wide prevalence of the disease, that necessitates long-term chronic therapy. The specific objectives of the study are to:
(i) determine transfer potential of the anti-tuberculosis drugs using the *in-vitro* model and correlate it with that observed *in-vivo*; (ii) investigate variations in the genomic profile with regard to drug metabolizing enzymes in children exposed to maternal anti-tuberculosis drugs during lactation; and (iii) determine significance of the gene variants detected with regard to drug metabolizing capacity.

The anti-tuberculosis drugs to be studied include rifampicin, isoniazid and ethambutol. The enzymes to be studied include cytochrome P450 3A4 (CYP3A4) and N-acetyltransferase 2 (NAT 2) which are the major enzymes involved in the metabolism of these drugs. Drug metabolizing capacity will be assessed based on probe drugs viz. paracetamol for CYP 3A4 and caffeine for NAT 2. HPLC-based analysis of all these drugs in serum and breast milk are being established. Fig. 61 shows the typical chromatogram obtained for the probe drug paracetamol.

![Fig. 61: HPCL pattern of paracetamol standard.](image)

Mutation analysis of the two genes, CYP3A4 and NAT 2, based on PCR-RFLP, PCR-SSCP and DNA sequencing is in progress. The study will provide novel information on the potential long-term effect of maternal anti-tuberculosis therapy on the breastfeeding infant.

### 4.2 Operational Evaluation of the Stability of Iodine in Double Fortified Salt: A Multicentric Study

**Principal Investigator:** M.G. Gupta

**Project Associate:** M.I. Khatkhatay

**Duration:** 2001-2002

An ICMR multicentric study to evaluate iodine loss in double fortified salt over a period one year has been completed. Iodine was estimated in 1600 salt samples stored at three different conditions namely laboratory, shop-like conditions and in the corridor. Analysis were carried out at 3, 6, 9 and 12 month intervals. Final decoding and analysis of the data will be done by ICMR.
4.3 Establishing a Centre for Estimating Haemoglobin Levels Using Whatman No. 1 Filter Paper Method *(Contractual Project funded by UNICEF)*

Principal Investigator: U.M. Donde

Duration: 2002-2003

The study aims to: (i) survey at the district level the nutritional status of children, adolescent girls and pregnant mothers as part of Reproductive and Child Health (RCH) programme of the Government of India; and (ii) make policy decisions regarding nutritional status, based on haemoglobin estimation, as part of RCH survey.

Anaemia, a debilitating disorder is a major public health problem for developing countries. Children, adolescent girls, pregnant women are the most vulnerable. Blood haemoglobin levels are indicators of anaemia as well as a key nutritional indicator. The commonest cause of anaemia is iron deficiency. Blood samples are collected by a needle (Lancet) prick on the finger, measured volume of blood is drawn into the capillary tube and dispensed onto Whatman no. 1 filter paper. In the laboratory, the area around soaked blood is cut and the contents eluted into the liquid reagent for the estimation of haemoglobin by colorimetry.

Ministry of Health and Family Welfare, New Delhi, has been coordinating this study. The reagents, equipments and other supplies required for the estimation of haemoglobin are being provided by UNICEF. Since June 2002, more than 60,000 samples have been analyzed. These samples were received from the states Maharashtra, Gujarat, Part of Madhya Pradesh, Bihar, Jharkhand, Daman, Dadra and Nagar Haveli. In addition, samples were also received from collaborating centers (NIN, Hyderabad; NIFPHW, New Delhi) as a part of the quality control programme. The laboratory reports were directly communicated to the respective NGO agencies from where the samples were received. The day-to-day analysis of the samples is in progress.