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## Nutrition And Drug Metabolism A review of recent Indian studies

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The metabolic interactions between dietary constituents and drugs are varied and complex. Drugs can adversely affect nutritional status, while nutrients in foods can affect the metabolism of drugs and their therapeutic efficacy and toxicity. In a country like ours, where undernutrition is widespread and where the wide prevalence of several infectious diseases calls for the intensive use of a range of potent drugs, a proper understanding of drug-nutrient interactions and their implications is extremely important. Unfortunately this subject has not received the attention it deserves from either physicians or nutrition scientists. In this communication, work carried out in India in recent years (largely at the National Institute of Nutrition, Hyderabad) in this area is briefly discussed.

Before a drug exhibits its activity, it has to get absorbed, bind to plasma proteins and get transported, to be delivered to various organs and target tissues in adequate concentrations. It is only when these processes are complete that a drug can exert its therapeutic (or toxic) response. The fate of the drug in terms of absorption, binding, distribution, metabolism and excretion can be influenced by the patient's diet and nutritional status.

### Absorption

Considerable attention has been directed to effects of food on absorption of drugs.<sup>24,36</sup> When a drug is administered orally, it undergoes processes such as disintegration, dissolution,

absorption and passage through liver. Foods can affect one or many of these stages. The quantity and quality of foods have been shown to enhance bio-availability of a number of drugs such as anti-hypertensives (beta-blockers, hydralazine), antibiotics (erythromycin stearate, nitrofurantoin) and anti-convulsants (phenytoin, carbamazepine). For example, high fat diet enhances the absorption of griseofulvin and a high protein diet increases propranolol bioavailability. It has recently been demonstrated that rice and wheat diets improve the bio-availability of the anti-malarial drug chloroquine.<sup>38</sup>

Foods can also reduce the absorption of many other antimicrobial agents such as isoniazid, rifampicin, penicillin and ampicillin. Several mechanisms are implicated in such food-drug interactions in the gastro-intestinal tract. Binding of drugs to substances in the food, alterations in pH, gastric emptying time, intestinal transit time, mucosal absorption and splanchnic hepatic blood flow account for food-induced variations in absorption of drugs. These variations will directly influence the onset, intensity as well as duration of action of drugs.

Most drugs, in practice, are administered by the oral route and therefore altered absorption would be of clinical significance for drugs such as antibiotics, anti-convulsants, anti-hypertensives and anti-malarials. As a general rule, solutions and suspensions are less susceptible to food drug interactions. On the other hand, enteric coated drug preparations are more prone to food interactions. The effect on drug absorp-

tion is inversely proportional to the time gap between food intake and drug dosing, being maximal when the drug is taken immediately after meals. Studies on chloroquine and rifampicin clearly indicate that chloroquine, a gastro-intestinal irritant, has to be administered along with food for better therapeutic efficacy while rifampicin has to be administered on an empty stomach.<sup>1,27</sup> Caution needs to be exercised when administering bactericidal drugs which are given once a day depending on the effects of food on their bio-availability.

Our studies have shown that malnutrition decreases and delays absorption of antibiotics and nutrients used as medicaments which may result in therapeutic failures.<sup>30</sup>

### Protein Binding And Volume Of Distribution

An important pharmacokinetic parameter which determines the plasma concentration of a drug is its apparent volume of distribution. This, in turn, is dependent on plasma protein binding.

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The binding of a drug to plasma proteins is a significant determinant of the intensity and duration of the drug's pharmacological actions and its eventual elimination. Drug protein binding may be expected to vary in varying grades of malnutrition and can change in relation to endogenous nutrient-related substances such as fatty acids, bilirubin, tryptophan, uric acid, etc. which bind to albumin. Significant reduction in binding of several drugs had been documented in malnutrition in both adults and children in several Indian and other studies.<sup>6,13,17</sup>

Clearance of drugs such as phenylbutazone, rifampicin and doxycycline in undernourished subjects has been shown to correlate with protein binding.<sup>22,23,32</sup> In malnutrition, protein binding of the drug propranolol was observed to be higher due to greater amounts of  $\alpha_1$  acid glycoproteins.<sup>10</sup> Our observations on tetracycline in the malnourished indicate that the tissue uptake and binding of this drug is significantly reduced in malnutrition, with a decrease in volume of distribution.<sup>31</sup> Data on tissue binding of drugs in human malnutrition are, however, generally scanty.

In addition to plasma proteins, in the malnourished humans, there is a reduction in body fat which could also alter the distribution of highly lipid soluble drugs. The consequent elevation of free (unbound) drug concentration with a decrease in the distribution are likely to result in higher toxicity.<sup>17</sup>

### Detoxification Of Drugs

Detoxification of drugs involves Phase I (oxidation, reduction, hydroxylation) and Phase II (conjugation) processes, mediated by mixed function oxidases. The conjugating enzymes are located in the liver, kidney, lungs, gastro-intestinal tract, placenta, skin and blood cells. The microsomal drug metabolising enzymes, located in the endoplasmic reticulum, directly determine the rate of metabolism and plasma therapeutic efficacy and toxicity of drugs. These enzymes are also concerned in the detoxification of a wide range of chemicals such as pesticides, mycotoxins, environmental pollutants (carcinogens), cosmetics and dyes. These major enzyme systems with wide substrate specificity, therefore, determine not only the pharmacological, but also toxicological properties of drugs and chemicals.

Most nutrients participate directly or indirectly in the functioning of the above

enzymes involved in the detoxification process of the drugs. Literature in experimental nutrition provides ample evidence that nutritional constraints alter drug metabolism.<sup>3,8,9,12</sup> However, experimental data cannot always be extrapolated to human situations for reasons such as species variations and poor predictability of pharmacological effects in experimental nutritional deficiencies. Further, enzyme activity in vitro and clearance of drugs in vivo need not be identical.

In general, experimentally induced nutritional deficiencies, except deficiencies of thiamine and iron, decrease the activity of enzymes involved in drug detoxification. Severe protein and fat (lipoprotein) restriction invariably decrease the enzyme activity. On the other hand, chronic semi-starvation appears to increase the enzyme activity and metabolism of certain drugs.

### Studies On Detoxification Of Drugs In Humans

Studies on drug detoxifications can be considered under the above two phases of metabolism, namely, oxidative metabolism (Phase I) and conjugation of drugs (Phase II).

**Oxidative Metabolism (Phase I):** Mixed function oxidases involved in Phase I of detoxification were evaluated in malnourished adult subjects by use of prototype and specific drugs such as antipyrine, doxycycline, phenylbutazone and rifampicin. These studies showed that the clearance of these drugs in general was delayed in severe malnutrition as encountered in cases of famine oedema.<sup>14,20</sup> These results indicate the need for altered dosage schedules particularly in severe malnutrition. Delayed clearance of drugs has been observed in severe states of malnutrition in children viz. kwashiorkor and marasmus.<sup>7,23</sup>

**Conjugations (Phase II):** Studies in malnourished children using chloramphenicol, paracetamol, sulfadiazine, isoniazid indicate that conjugation reactions are decreased.<sup>23</sup> Peak plasma concentrations are delayed, areas under plasma time concentration curves are higher and steady state levels are increased due to decreased conjugations. Therefore, in malnourished children, drugs such as chloramphenicol could evoke more severe toxic reac-

tions. It is necessary to reduce the dosage in order to have plasma steady state concentrations below the toxic range. However, conjugations of contraceptive steroids are not impaired in undernourished women.<sup>26,29</sup>

Our recent observations on in vitro enzymes such as benzo(a)pyrene hydroxylase,  $\gamma$  glutamyl transpeptidase, paranitrophenol and glutathione conjugations bring out the reciprocal effects on oxidation and conjugation systems with an increase in oxidation and decrease in conjugation of some substrates which can result in higher toxic effects.<sup>33,34</sup>

### Metabolic Experiments

Several metabolic experiments have been carried out to assess the effects of macronutrients on drug clearance. Our studies on varying protein and energy intake demonstrate that inadequate energy intake (60 percent of recommended dietary allowances [RDA] with 10 percent protein energy) diminishes drug clearance, whereas with energy intakes of 60-70 percent of RDA with 15 percent protein energy, drug kinetics are not altered significantly.<sup>19</sup>

On the other hand, carbohydrate energy with relative deficiency of protein intake (five percent protein energy) diminishes drug clearance even if the total energy intake is adequate (3000 kcal). Asian vegetarians are reported to have lower clearance of drugs<sup>25</sup>, whereas Caucasian vegetarians do not differ in drug clearance from non-vegetarians.<sup>5</sup> Data on the protein concentration of the two sets of vegetarian dietaries are necessary to know if the difference is truly ethnic or is related to differences in protein concentration of their dietaries. Studies on protein supplements suggest that isocaloric substitution of proteins for carbohydrate at constant energy intake (40 percent of protein energy) enhances the clearance of drugs such as theophylline and antipyrine.<sup>2</sup> When energy intake is a limiting factor and proteins are used for energy needs as happens in severe protein energy malnutrition, drug clearances will be impaired. Therefore drug doses need to be decreased in severe states of malnutrition. Nutritional status could also influence the clearance of drugs by the kidney.

Renal excretion of drugs has been investigated both in malnourished children and adults.<sup>31</sup> The results suggest

that elimination of drugs such as penicillin, cephoxitin, gentamicin, tetracycline and tobramycin are reduced in severe states of malnutrition<sup>7</sup> whereas in lesser grades of malnutrition, the drugs are eliminated faster due to decrease in protein binding. These results are similar to those with respect to the hepatic detoxification of drugs. Therefore, in conditions of faster elimination in order to maintain maximum and minimum inhibitory concentrations especially for antibiotics, dosage intervals have to be reduced. Plasma concentrations of nephrotoxic drugs such as gentamicin and other aminoglycosides require to be monitored in severe malnutrition.

### Toxicity Of Drugs And Chemicals In Malnutrition

Nutritional stress seems to be an important determinant of drug toxicity in experimental animals. Hypoalbuminemia has been shown to be associated with greater vulnerability to toxic reaction of drugs<sup>4</sup>. Several recent studies in kwashiorkor indicate that symptoms such as oedema, fatty liver and skin lesions can be indirectly attributed to free radical generations arising from impaired detoxifying capacities as the body reserves of antioxidants such as vitamins A and E, beta-carotene and zinc which are protective, are low in malnourished states.

Our recent studies on hepatotoxicity of antitubercular drugs in adults<sup>21</sup> and observations in children<sup>35</sup> confirm that toxic reactions to these drugs are higher in malnutrition, and stress the need for careful evaluation of drug dosage in undernourished subjects, from the point of view of therapeutic efficacy and toxicity. Toxicities in malnutrition seems to be determined by a balance of many events such as the chemical nature of the parent compound and its metabolite, alterations in pharmacokinetic parameters and the receptors.<sup>16</sup> Therefore various permutations and combinations of adverse effects and efficacy are possible in malnutrition including increased susceptibility to chemical carcinogens.<sup>11,18</sup> Drug induced nutritional disorders may further complicate and compound the picture.<sup>8,37</sup>

The studies briefly discussed here provide two important messages:

- Where drugs are being used for the treatment of ailments in undernourished population, the dosage schedules generally prescribed by the manufacturers

may need to be reviewed and modified. Currently, this aspect of drug therapy in our country is being totally neglected. As several factors determine the dosage schedules, it is necessary to have a fresh look into doses employed and therapeutic response in undernutrition.

- Undernourished populations are more susceptible to toxic effects of chemicals and potential carcinogens. The problem of environmental pollution therefore must claim even greater concern in the context of widespread prevalence of undernutrition. It is possible that several important factors of clinical importance remain unrecognised and therefore warrant further research.

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## ANNOUNCEMENT

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- Women and Nutrition in India — General Considerations — C. Gopalan
- Demographic Consequences of Low Status of Women in Indian Society — K. Srinivasan and Tara Kanitkar
- Nutrient Requirements and RDA of Girls and Women in India — B.S. Narasinga Rao
- Pattern of Growth and Development of Indian Girls and Body Size of Adult Indian Women — S.G. Srikantia
- Nutrition in Pregnancy — Prema Ramachandran
- Lactation-Nutrition-Fertility Interaction — Prema Ramachandran
- Nutritional Deficiency Diseases — S.G. Srikantia
- Women and the Health System — Saramma T. Mathai
- Socio-economic and Socio-cultural Influence on Women's Nutritional Status and Roles — Meera Chatterjee.

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## Reviews and Comments

# A Strategy For Basic Minimal Health Care Using UIP as the spearhead

Shanti Ghosh

The classic report of the Health Survey and Development (Bhore) Committee (1946) had provided an excellent blueprint for comprehensive basic health care for our country — long before the Alma Ata Declaration. Unfortunately, though four decades have elapsed since that Report was published, the outreach and quality of basic health care to our rural masses continues to be poor and inadequate — this in spite of the fact that during this period there has been an enormous expansion of our health infrastructure.

## The Present Picture

That our present health infrastructure is by no means unimpressive will be evident from the following data: As on March 31, 1988, there were more than 100,000 sub-centres (SCs), 15,000 Primary Health Centres (PHCs) and nearly 800 Community Health Centres (CHCs) in the country. An SC, to be "manned" by two Health Workers (one male and one female) is expected to serve a population of 5,000 (3,000 in tribal areas and difficult terrain) and a PHC (with six sub-centres in its jurisdiction) for 30,000 population. These infrastructural targets are being progressively achieved, though there is considerable shortfall in the number of health workers, particularly male health workers. As per the goals set in the Seventh Five Year Plan (which is nearing its end), a Village Health Guide (VHG) and a trained Dai (TBA) are being provided for 1,000 population. There is, however, as yet no evidence that with these inputs, outreach of the health facilities to the rural population is satisfactory.

The outlay for health and family welfare during the Seventh Plan was Rs. 67,000 million (3.7 percent of the total Plan outlay) which is 114 percent of the amount budgeted in the Sixth Plan. The allocation for MCH was Rs.10,000 million which is five times that budgeted in the Sixth Plan. Out of this amount, (a disproportionately high) Rs. 2,500 million has been earmarked for the Universal Immunisation Programme (UIP) alone! — an unfortunate distortion possibly arising from a mistaken sense of

priorities and perceptions.

While present overall investments on health are still below national needs, they are by no means unimpressive. What is obvious is that we are not getting adequate returns for the investments already made. The material, financial and manpower resources already available, and on the ground, are not being optimally deployed and managed. A few facts will serve to highlight this conclusion.

Taking cognisance of the high maternal mortality and high delivery-related mortality among infants, the Seventh Plan target was to provide ante-natal care to 60-75 percent of women and 100 percent coverage to them with two doses of tetanus toxoid (TT). Adequate ante-natal care along with health/nutrition education was expected to reduce the incidence of low birth weight babies. It is to be sadly admitted that the actual performance today falls far short of these targets. The achievement with respect to immunisation with TT has, however, been relatively better for reasons which we will consider presently.

## Utilisation of Health Services

According to a recent report by Kanitkar and Sinha (1989)<sup>4</sup>, only 20 percent of women in Maharashtra had received ante-natal care; the corresponding figures for Bihar and Rajasthan were less than five percent! Home visiting even in PHC or SC villages varied from 32.8 percent in Gujarat to 5.2 percent in Bihar, and in non-PHC and non-SC villages from 24 percent in Gujarat to 1.4 percent in Rajasthan. The percentages of women residing in the "centre villages" and actually availing of ante-natal services from the Health Centre were 27 percent in Maharashtra, 20 percent in Orissa, 13 percent in Gujarat, 11 percent in Rajasthan and five percent in Bihar; the percentages for the "non-centre villages" were 19, 16, 10, four and five respectively.

The reasons for poor utilisation of health services as gleaned from available reports pertain both to the community and to the health services. As for the

community, it would appear that the majority of women do not see any "necessity" for ante-natal care. Pregnancy is considered by them to be a normal physiological process hardly needing any medical advice unless something goes wrong. This is a reflection of the failure of present programmes of health education and community involvement. Other reasons for nonutilisation were: distance of Health Centre from the homes; possible loss of daily wage involved in the long trek to, and waiting at, the Health Centre; apprehension and fear of the "Governmental apparatus"; lack of confidence in the service; "no one to look after the young children at home".

While the community had the above reasons for nonutilisation of health services, the health services themselves, which also contributed significantly to the present situation, had their own "reasons" – some of them quite valid. They were not able to reach out to the community because of lack of mobility due to non-availability of transport, difficult terrain, scattered hamlets, insufficient priority being given to the programme in the health hierarchy, obsession with the tubectomy and Family Planning targets and (more recently) immunisation targets, lack of equipment and drugs, lack of skills, both managerial and clinical, lack of supervision, lack of clarity as to what to do and how to do it, lack of an organised information and referral system which would make home visits purposeful and worthwhile, and often lack of motivation. A recent evaluation by ICMR (1989)<sup>3</sup> showed poor registration of pregnant women in many health centres. Only 11 percent PHCs had registered more than 80 percent pregnant women in their jurisdiction, and in about half the number of PHCs, the figure was less than 40 percent. Ten percent of PHCs did not have any record of pregnant women! The situation regarding TT and iron and folic acid supplementation was also unsatisfactory.

Very few deliveries were being conducted by the health personnel, the majority being conducted by trained or untrained dais and by relatives and neighbours. Post-natal care and care of the baby also went by default because the health worker did not even know where a birth had taken place. The record of deaths was also incomplete.

As mentioned earlier, a quarter of the budget for MCH now has been earmarked for the UIP. A vast infrastructure

has been created with enormous inputs and equipment, vaccines, training, supervision, logistics and management. An earlier publication in this Bulletin<sup>2</sup> had indicated that even with this vast investment, immunisation coverage in many States has been inadequate. According to an evaluation carried out by the National Institute of Health and Family Welfare, immunisation coverage in several States has been no more than 40 percent following the institution of this vertical programme.

### UIP As A Spearhead

The essence of the strategy that is being suggested here is that we should take full advantage of the present "immunisation drive" and the procedures being employed in the UIP to achieve the immunisation coverage targets, in order to achieve a broad-based integrated programme of basic health care. The UIP offers an opportunity which we should not let slip.

Immunisation under the UIP is now being carried out at all the Health Services outlets, at the Anganwadi centres of the ICDS System and also at fixed points in villages (outposts) where none of these centres exist. An important element of the UIP strategy is adherence to a "fixed day schedule" – a schedule which people are beginning to remember and understand. According to this procedure, prior information is provided to the community by the health worker or VHG a day before the immunisation team is due, to act as a reminder, so that mothers and their children could be collected in a group for immunisation. It is through these means and special efforts that the UIP attempts to achieve a better population coverage and outreach than what our health services have so far been able to achieve for their operations.

There are legitimate misgivings regarding the present UIP strategy in which immunisation has been given the highest priority as the prime component of maternal and child health care in preference to other components, which cause many more deaths and result in much higher morbidity.

However, since a political decision to push the UIP almost as a vertical isolated programme has been taken and is being pursued, it is important that health workers and health scientists interested in the promotion of integrated primary health care evolve a strategy by which

this programme can be "captured" and used in a manner which will help to achieve the objective of broad-based health care. In short, we must evolve a strategy whereby other essential components of ante-natal and child health care, which are now being crowded out and neglected because of the single-pointed pursuit of UIP as a vertical programme, are enabled to "ride" on the UIP programme. In this strategy, the opportunities created by the UIP for the collection of mothers and children for immunisation purposes could be used for the delivery of other components of the health service package. Thus, the UIP will become the entry point for a broad-based programme of integrated maternal and child health care.

This approach is fully justified. On the one hand, it will not detract from the ongoing UIP and on the other hand, it will serve, with minimal additional inputs, to broaden the outreach and quality of health care to our rural people. Surely, while pregnant women and children need to be immunised against preventable diseases, this alone will give poor dividends as women and young children will continue to die of other causes which are not amenable to immunisation and these latter far outweigh those prevented by immunisation.

### The Proposed Strategy

In the UIP, every pregnant woman is supposed to get two doses of tetanus toxoid, the first one after around four to five months of pregnancy, and the second a month or two later. We must use the opportunity provided by the motivated gathering of pregnant women for immunisation, for providing them, at the same time, other ante-natal services besides immunisation. This can be done without disrupting the UIP and with minimal additional inputs in terms of time and resources. When pregnant women gather for immunisation, it should be possible to carry out an ante-natal examination, provide necessary advice regarding health care and diet and give them iron and folic acid tablets. The ante-natal check could include: identification of the "high risk mother" (from the history of past pregnancy outcome, i.e. a very low birth weight baby, one or more abortions, still-birth, instrumental delivery, caesarean section and a neonatal death) requiring special care; clinical examination for signs of anaemia, toxæmia, and any clinical abnormality.

Since 60-70 percent of women are anaemic and even the non-anaemic women are advised to take iron for prophylaxis, there does not seem any point in doing actual haemoglobin estimations.

It would be prudent to give the woman, at the time of the first contact as part of the UIP, one month's supply of iron and folic acid tablets (60 tablets at the rate of two tablets per day) containing 60 mg elemental iron and 500 mg folic acid per tablet, with necessary instructions. It would improve compliance if the tablets were nicer looking than at present (say, a nicer red colour) and dispensed in a plastic container or pouch or possibly a strip. Special care must be taken that these tablets do not, on any account, resemble the oral contraceptive pills.

Wherever possible, at least the weight of the mother should be recorded. If recording of height is possible, this could also be done. For this purpose, a cut-off point of 145 cm can be marked on the wall in the centre or in a suitable building in the village itself. Studies from NIN, Hyderabad (1985)<sup>5</sup> have shown a high association of low birth weight with maternal weight below 40 kg at 20 weeks pregnancy, haemoglobin below 8 g/dl, previous bad obstetric history and current obstetric problems. Extremes of age and parity above four pose special problems. All these cases will need special care and attention.

The above procedure can be repeated at the time when the women assemble for the second TT injection of the UIP. In this way it will be possible for the pregnant woman to get 100-120 tablets of iron during her pregnancy. There should be facility for checking of blood pressure to detect toxæmia. Urine examination is cumbersome and difficult to carry out in the field and may be dispensed with. A judgement as to whether delivery can safely take place at home or not must be made considering the past history and examination. During this second visit, a sterile cord care kit can be given to the pregnant woman for use at the time of delivery. It is mandatory, of course, that TBAs should be trained in the use of the cord care kit. There should be a mechanism for reporting births or for referral in problem cases.

**Care of the baby:** At the first contact with the mother after the birth of the baby, at the time when she brings the baby for the first dose of the UIP

immunisation schedule, apart from post-natal care and advice regarding breast-feeding, etc., information on the manner in which the cord care kit was used during her delivery should be enquired into and checked. This information would help to assess whether TBAs are applying the knowledge imparted to them during training and what improvements are needed with respect to their training.

It must be accepted that, for some years to come, most deliveries in rural areas will continue to be conducted by TBAs. It is, therefore, essential that good rapport and communication are established between the health workers and TBAs.

In the UIP, the first contact with the baby is at six to eight weeks (unless the delivery has taken place in an institution, where BCG might have been given). During this contact the baby can be given DPT, OPV and BCG, and its growth and nutrition can be assessed (preferably by weighing) and necessary advice given regarding breast-feeding. An observant health worker can also observe the movement of limbs, vision, hearing, etc., and assess development, and exclude physical handicap. The mother can be questioned about lochia or any other complaint. More time would have to be spent on primipara regarding advice on breast-feeding. The second and third UIP contacts can be used for strengthening advice regarding feeding. Around four to five months (third DPT), advice regarding introduction of appropriate semi-solid foods to the baby can be given. This will also be the opportune time to advise the couple about spacing and the use of contraceptives. The mother should be given iron tablets during these contacts. Every health centre should have a weighing scale; however, at the outreach site, it would be difficult to weigh the baby, for, after all there is a limit to the things that a worker can carry to the field. In this situation, one would have to rely on the assessment of the health worker rather than on weighing scales.

The timing of DPT and OPV at three, four, five months had the merit of facilitating contact at a crucial period when growth faltering is likely to occur and advice regarding continuation of breast-feeding and introduction of semi-solids has to be given. With the changed schedule (six, 10, 14 weeks), there is a large gap during the crucial period between 14 weeks and nine months when measles vaccine is due. In any

case, experience in the field has shown that a majority of mothers would like to wait for about three months for the first DPT and OPV, when the baby has "gained some weight" and there are no taboos about taking the baby out of the house. Besides, four to six months after delivery is the most suitable time to advise on family planning. So, one would have to balance the pros and cons of timing carefully.

It should be possible to develop a simple mother/child card in which all the relevant information can be entered.

The first-line drugs should be available at the health centre and carried to the outreach sites. Management of minor ailments on the spot would increase the credibility of the health personnel. The male health worker can help with this.

Many studies have shown that the VHG or TBA can facilitate the work of the health worker considerably. These workers belong to the village and can easily identify households with pregnant women and children under three years. These households can be contacted a day prior to the visit of the UIP team and advised to 'come to the immunisation site. Of course this arrangement can only work if these workers are motivated and treated as members of the health team and not as dispensable second-rate adjuncts.

In an earlier issue of this Bulletin Gopalan<sup>1,2</sup> had urged that "the infrastructure built for this operation (UIP) ... could be widely used for the implementation of broad-based primary health care operations". This paper sets out in brief outline a strategy aimed at achieving this objective.

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