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THE CHALLENGE OF INTERACTION OF NUTRITION AND INFECTION

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In this paper the authors dilate on the application of research findings to the health problems of communities. The most frequent kinds of malnutrition and their interaction with infections as well as the groups at risk have to be identified.

The developing countries have a very high prevalence of malnutrition as well as incidence of infection. Usually low income groups are most at risk. Physiological and cultural factors combine to make children under 3 years the vulnerable group. Their rapid growth creates high nutritional demands which are often not met. Moreover, children between 6 months and 3 years are most susceptible to infection as they no longer enjoy passive immunity and have yet to acquire active immunity. Traditional infant feeding practices often result in very inadequate weaning diets. Consequently protein calorie malnutrition is very common among children. Extreme syndromes like kwashiorkor or marasmus are most often the outcome of synergism between protein calorie malnutrition and infection. Sometimes infectious diseases of childhood seem to initiate major interaction with malnutrition.

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THE CHALLENGE OF INTERACTION OF NUTRITION AND INFECTION*

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In this paper we will not attempt to be comprehensive but will only indicate areas where more research is needed in order to tackle this problem in human populations. The spadework done by several generations of biochemists and bacteriologists in the laboratory leaves little doubt that nutritional deficiencies generally reduce the capacity of the host to resist the consequences of infection and that almost all infections can result in nutritional diseases in borderline deficient persons (Ascoli *et al.*, 1967).

The major challenges in the study of interaction of nutrition and infection lie in the area of research methodology and the implementation of findings.

Classical unifactorial research has only limited relevance to the problem of interaction of nutrition and infection in natural populations. Schneider (1946, 1950, 1951, 1956) demonstrated the danger of over-simplification in unifactorial research designs. He chose 3 strains of mice: Two pure inbred strains and one random bred strain. One inbred strain was known to have high resistance to salmonella infection. The other inbred strain was susceptible to this infection. The random bred strain, however, had a heterogenous resistance. He also selected 3 strains of salmonella: one highly virulent, one avirulent and one of heterogenous virulence. The nine genetic combinations of these strains of mice and salmonella were exposed to an adequate as well as an inadequate diet. Only the experimental group with random-bred mice and heterogenous salmonella culture showed natural diet as an important factor in their survival. Since the heredity of natural populations tends to be heterogenous the experience of random bred mice infected with a salmonella strain of mixed virulence is most relevant to the needs of human populations confronted with infections. Gordon (1958, 1965) formulated another aspect of the methodological challenge by stressing on the " multifactorial causality " of disease, where he wrote: " Too often the clinician and the public health worker are encouraged to identify the agent of disease and then, in attempts at prevention or control to concentrate on measures directed against this agent. Such a limited attack may fail miserably, however, in preventing a relapse once the patient returns to his home environment. For prevention of disease in the general community, measures based on a narrow etiological approach are also frequently ineffective. Preoccupation of public health authorities with the causative agents of disease is likely to result in control measures that are uneconomical and unsuccessful because they do not attack the most vulnerable links in the multiple chains of causation ". Thus if we want to study

* For a detailed review of the literature on the subject of interaction of nutrition and infection refer to WHO Monograph No. 57 by N. S. Scrimshaw, C. E. Taylor, and J. E. Gordon.

the interaction of nutrition and infection it should not be a sum total of unilateral influence but as complicated web of reverberating interactions in which heredity, previous disease history and age of the host play a vital role. Therefore research methodology for the study of these interactions needs real innovative thinking and we hope to spend considerable effort to solve some aspects of this challenge in the next years.

In this paper we will dilate on the second challenge viz., the application of research findings to the health problems of communities. The most frequent kinds of malnutrition and their interaction with infections as well as the groups at risk have to be identified.

The developing countries have a very high prevalence of malnutrition as well as incidence of infection (Behar *et al.*, 1958; Wolstenholme and O'Connor, 1967). Usually low income groups are most at risk. Physiological and cultural factors combine to make children under 3 years the vulnerable group (Behar *et el.*, 1960; Gordon *et al.*, 1967). Their rapid growth creates high nutritional demands which are often not met. Moreover, children between 6 months and 3 years are most susceptible to infection as they no longer enjoy passive immunity and have yet to acquire active immunity. Traditional infant feeding practices often result in very inadequate weaning diets. Consequently protein calorie malnutrition is very common among children (Behar *et al.*, 1960; Gordon and LeRiche, 1950). Extreme syndromes like kwashiorkor or marasmus are most often the outcome of synergism between protein calorie malnutrition and infection (Morley *et al.*, 1968; Platt, 1958a; Suzman, 1955; Scrimshaw, 1959; 1965; Scrimshaw *et al.*, 1960). Sometimes infectious diseases of childhood seem to initiate major interaction with malnutrition.

It has been shown beyond dispute that measles (Gordon *et al.*, 1965b; Morley, 1962, 1967; Morley and MacMillan, 1961; Morley *et al.*, 1963; Scrimshaw *et al.*, 1966) and chickenpox (Salomon *et al.*, 1966, 1968) claim high fatality among malnourished children due to a disastrous protein catabolism (Beisel, 1966; Belfrage, 1963; Scrimshaw, 1963).

Although immunization can provide effective protection against infectious diseases of childhood, it has also been demonstrated that they provoke a negative nitrogen balance (Gandra and Scrimshaw 1961; Scrimshaw, Taylor and Gordon, 1968) and therefore present a potential danger to malnourished children.

Similarly diseases without lasting immunity such as furonculosis, diarrhoea (Gordon, *et al.*, 1964a, b, c; 1965a; 1968; Gordon, Behar and Scrimshaw, 1964a, b; Gordon, Chitkara and Wyon, 1963; Scrimshaw *et al.*, 1957) and malaria (Oomen, 1957) act in strong synergism with malnutrition. In the case of diseases that do not leave lasting immunity and for which no simple preventive measures are available repeated attacks are likely to occur, resulting in a tremendous adverse impact on the nutritional status of the children.

Sometimes the vicious circle seems initiated by nutritional deficiencies. Infections occurring among humans (adults as well as children) with low intakes of vitamin A and carotene (Oomen, 1957, 1959), vitamin B or C (Dodin 1955; Platt, 1958a, b; Smith and Woodruff, 1951; Stern, 1923, Suzman, 1955) intensify the deficiencies and cause further complications.

Iron deficiency anemia is very common in developing countries. Limited supply of iron is only a cause of secondary importance for this syndrome, (Scrimshaw, Taylor, and Gordon, 1959). Intestinal parasites mostly influence iron metabolism through blood loss. Especially notorious in this respect are Nector Americanus and Ancyclostoma duodenale (Giles, 1964; Tasker, 1961). Chronic bacterial or viral infections can provoke anemia due to diminished iron binding capacity and reduced erythrocyte life span (Bush *et al.*, 1956; Cartwright *et al.*, 1946; Cartwright and Wintrobe, 1952; Giles and Brown, 1962; Haris, 1963; Princiotto *et al.*, 1964). Acute infections sometimes induce hemolytic anemia (Jandl, Jacob and Daland, 1961).

Little is known about the interaction of protein calorie malnutrition and infection. Fitzpatrick (1948) was able to demonstrate through pair-feeding experiments that rats on low casein diets (5%) also deficient in thiamine were more sensitive to typhus infection. The general undernutrition resulting from anorexia caused by thiamine deficiency seemed to be responsible for their greater sensitivity for typhus.

Most of the children in developing countries suffer from some degree of protein calorie malnutrition. Studies in Guatemala (Gordon *et al.*, 1965a; Gordon, Behar and Scrimshaw, 1964a, b; Gordon, *et al.*, 1964c; Gordon, *et al.*, 1962; Scrimshaw *et al.*, 1962, 1966) have established a direct correlation between degree of malnutrition (Gomez classification) and incidence and fatality of weanling diarrhoea. (Gordon, Singh and Wyon, 1961; Gordon, Wyon and Ascoli, 1967). Similar observations have been made in Punjab.

A review of relevant literature by Scrimshaw, Taylor and Gordon (1968) has led them to conclude that " Infections so consistently worsen nutrition status that they must be taken into account in all clinical problems and public health programs that involve persons whose diet is inadequate or whose nutritional status is suboptimal ". The converse of this would be that malnutrition so consistently worsens resistance against infections that we must take into account the nutrition of the individual or that of the population whenever we deal with infectious diseases.

The first step in the process of identifying efficient methods of preventing health problems resulting from the interaction of nutrition and infection is " the identification of the weakest links in the chains of causation " (Gordon, 1958, 1965). Equally important is the need to identify simple methods of containing such interaction once it has started.

Not many systematic investigations have been done on the relative merits of nutritional supplementation and medical care and their synergistic action in the control of illness. In an extensive study on weanling diarrhoea carried out in Guatemala during 1959-64, provision of a food supplement promoted physical growth and reduced the incidence of disease although not to a striking extent. Medical care alone resulted in lower mortality but had no effect on either morbidity or growth rate. This study pointed to the need for combining nutritional and medical care.

In Narangwal we were interested in pursuing this hypothesis. Investigations were initiated in 1966 to study the relative merits of nutritional care, medical care, both combined, or neither, in reducing morbidity and mortality.

Children under three years in nine villages were included in the study. Baseline data were obtained in all these villages with regard to major ecological features, pregnancy, history of women in the 15-49 yrs age group, socioeconomic status etc.

Since the beginning of the experiment a tightly carried out schedule of morbidity survey, anthropometric survey and vital registration is being followed. The baseline anthropometry showed that exactly half of the study children were malnourished. Five percent of all children under three years suffered from third degree malnutrition (Gomez classification); about 10% had second degree malnutrition, and about 35% had first degree malnutrition. More than eight out of 10 children below three years had less than 10 g% hemoglobin. Intestinal parasitose generally associated with the condition was not identified only as a minor problem in this age group. The morbidity survey also revealed a high prevalence of gastro-intestinal, respiratory and skin complaints. Vital registration showed high mortality of children: about 250/1000 children died before 3 years of age. This included 100/1000 neonatal deaths.

The number of children included in this study in the various groups are shown below:

	First Experimental Year		*Second Experimental Year*	
	No. of villages	*No. of children*	*No. of villages*	*No. of children*
Control of infection and Nutr. Care	2	199	3	324
Control of infection only	1	125	2	169
Nutrition care only	1	110	4	284
Control	5	343	2	150

In the areas with nutrition care a dietary survey is combined with advice and supplementation where needed. The dietary survey is being carried out of all children under 3 years of age. Mothers are educated on the need to introduce semisolids right from the fourth month onwards and solid foods from the tenth. Mothers are advised to prolong breast feeding upto 18 months. Some features of the supplementation programme are indicated below:—

(i) Oral iron and folic acid supplements are provided to premature, low birth weight babies and to children born to anemic mothers from second month onwards and to all detected anemia cases among children.

(ii) Food supplements are given twice a day to all children with second or third degree malnutrition (Gomez classification) and to children with first degree malnutrition, who do not gain weight at the desired rate.

(iii) Day care centres are set up for Ramadaisia (scheduled caste) children during harvesting season.

The Programme for the control of infections includes preventive and curative services.

(i) The preventive program includes immunization (measles, diphtheria, pertussis, tetanus both antenatal and pediatrics, tuberculosis) and health education on methods of prevention of disease.

(ii) The curative service stresses early detection of illness and treatment through a resident lady visitor, smooth referral of selected cases to the project pediatrician, to the health centre and/or the hospital.

While the experiment is continuing the statistical team regularly measures actual service input by each worker. Likewise results obtained in terms of growth and information about current morbidity and mortality are periodically tabulated. This helps us to regularly review our standing orders. Field observations made by professional staff and the statistical feed-back also determine the subjects for discussion in our weekly in-service training for field staff.

A preliminary analysis of the first year of our work shows a decline in the morbidity (measured as number of illness days) in our combined medical care and nutrition care villages (Table 1). In order to confirm that this is no chance effect, one village, which in the first year of the study was subjected to medical care only is now being given combined medical care and nutrition treatment in its second experimental year. The results during the second experimental year show a decline in morbidity in this new medical care and nutrition village, thus seeming to support the conclusion of the Guatemala study. This confirmation legitimizes the hope that one of the major scourage of humanity can be tackled. Health workers, however, will still be left with the difficult task of adapting these findings on a massive scale to tackle the major health problems of children in developing countries.

Planning health services which would use these principles should also take into account that most people in rural areas are unable to get adequate medical care because even when such care is theoretically free, they are unable to afford the cost of transport to the nearest hospital in terms of time and money, attendants, special diets, medicines etc. In one of our studies about 260 episodes of illness per 1000 population in a year are treated by private practitioners and the average cost of treatment is Rs. 2/- per episode or 52 paise per capita per year.[1] In contrast, the government spends Rs. 2.85 per capita per year.[2] This clearly shows that the medical services are by no means operating economically.

In the words of Maurice King " medical care must be made available to the people as close to their homes as possible in the smallest, cheapest, most humbly staffed and most simply equipped unit...." and that there is an urgent need in these countries to obtain maximum return in human welfare from the limited money and skills available. He also

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1 Functional Analysis Study of the Rural Health Research Projects, Narangwal Ludhiana, Punjab.

2 Health Statistics of India, 1963. Central Bureau of Health Intelligence, Ministry of Health and Family Planning, New Delhi, India. 1967, p. 243.

points out the need for training auxiliary workers in adequate numbers and imparting them appropriate skills for treating common diseases and in setting up decentralized services with minimum investment in building[1]."

TABLE 1

Morbidity Data on children in Narangwal project

Month	*No. of illness days per 100 children month observations*			
	Control	*Medical care + Nutrition*	*Medical care*	*Nutrition*
September, 1968	**1806**	**2253**	**1966**	**2125**
October	1748 (97)	1967 (87)	2160 (110)	2030 (95)
November	1415 (78)	1894 (84)	1995 (101)	—
December	1341 (74)	1957 (86)	1833 (93)	—
January, 1969	1456 (80)	1675 (74)	2136 (108)	1982 (93)
February	1564 (86)	1623 (72)	2373 (72)	2020 (95)
March	1389 (77)	1444 (64)	2206 (117)	1560 (73)
April	1278 (71)	1322 (54)	2263 (115)	1426 (67)
May	1389 (77)	1399 (62)	2285 (116)	1595 (75)
June	1596 (88)	1474 (65)	2254 (114)	1435 (67)
July	1964 (109)	1745 (77)	2371 (120)	1610 (76)
August	1873 (104)	1881 (83)	2004 (102)	2070 (97)
September	1657 (92)	1740 (77)	2030 (103)	1915 (90)
October	1665 (92)	1423 (63)	2489 (126)	1970 (93)
November	1600 (89)	1420 (63)	2452 (124)	2333 (110)
Average from January 1969 onwards	1585 (87)	1559 (69)	2259 (115)	1810 (89)

The values in parentheses are percentages of the baseline values in September, 1968.

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1 Medical Care in Developing Countries, London, Oxford, 1966, Axioms 3 and 5, 1 : 7.

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