Zeitschrift: Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften = Bulletin de l'Académie suisse des sciences médicales = Bollettino dell' Accademia svizzera delle scienze mediche

Herausgeber: Schweizerische Akademie der Medizinischen Wissenschaften

Band: 31 (1975)

Artikel: Subclinical and covert malnutrition

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DOI: https://doi.org/10.5169/seals-308008

Bull. schweiz. Akad. med. Wiss. *31*, 279–290 (1975)

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Subclinical and Covert Malnutrition

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Overt (obvious) malnutrition is clearly defined on the basis of specific clinical signs. In cases of mild deficiencies the significance of clinical signs becomes debatable; for example epithelial signs such as fissuring of the tongue, hypertrophic and hyperaemic papillae and cheilosis are debated as early signs of tissue depletion of B vitamins; Bitot's spots and hyperfollicular keratosis are debated signs of vitamin A deficiency.

Sub-clinical malnutrition is a somewhat vague condition where inadequate intake has led to abnormalities of biochemical systems and low body stores of the nutrient in question but no clinical signs are evident. It is a stage of nutritional status that precedes structural or functional change and must be regarded as an unstable situation since if the same conditions continue, i.e. inadequate dietary intake, then subclinical malnutrition must inevitably lead to clinical malnutrition.

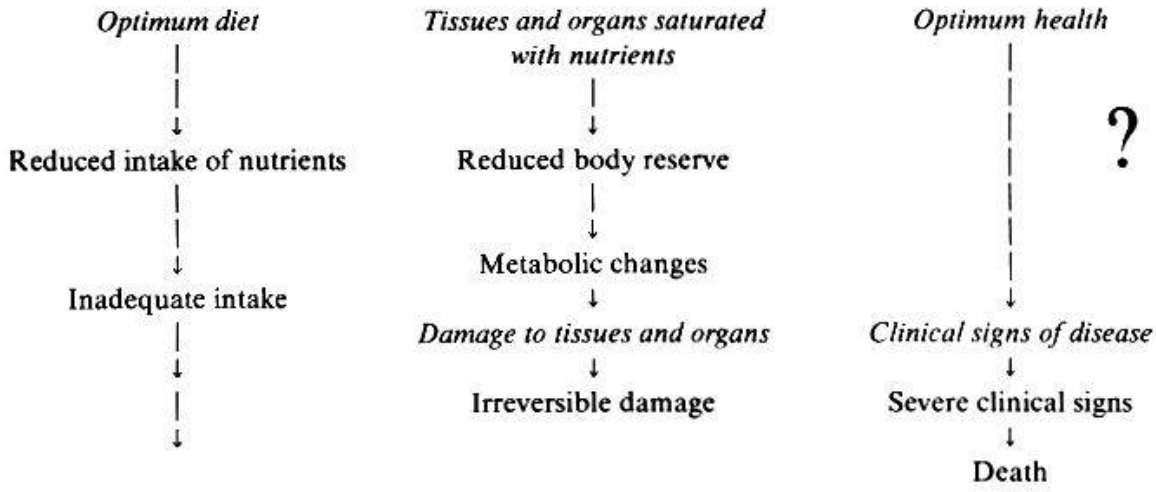
Covert (hidden) malnutrition describes a stable state; the subject has adapted to low body reserves of the nutrient in question, possibly by abnormal biochemistry of the tissues, so that even if the intake continues to be inadequate no change will take place.

An example, further discussed below, is where children with an inadequate intake of vitamin A do not show any signs of deficiency because their growth is inhibited by the poor diet. When extra food (but not extra vitamin A) is supplied, growth ensues and clinical signs of vitamin A deficiency follow.

Optimum diets

Fig. 1 illustrates the relation between diet, biochemical parameters and clinical condition. By definition the optimal diet fills the body stores with nutrients and results in optimal health. If the intake of a nutrient falls below optimal the earliest result is simply a fall in body stores. If the subject continues to consume an inadequate diet the body stores fall still further and when they approach depletion there is some departure from normal metabolic function (biochemical lesion). This may not incapacitate the subject in any way but is a

Fig. 1. Merging states of nutrition.



prelude to clinical abnormalities, so is termed sub-clinical malnutrition. It is not clear whether there is any impairment of health. A possibility that it may be detrimental is indicated by the observations of NALDER et al. (1972). These workers showed that when rats were fed a diet diluted by the addition of sucrose there was a fall in antibody production in response to infection. Similarly a deficiency of protein, vitamins or minerals can interfere with antibody production.

It is only when the nutrient level is reduced sufficiently to cause the first mild clinical symptoms that the condition of malnutrition becomes clear.

Although the area between 'optimal health' and overt malnutrition is necessarily vague, there are recognisable signs of sub-clinical malnutrition, for example in the instance of the vitamins. The raised blood levels of lactate and pyruvate that precede clinical wet beri-beri provide an example; Fig. 2 shows the several subclinical stages of rickets that may be found: radiological, biochemical rickets when the serum alkaline phosphatase is raised, and chemical rickets when serum 25-hydroxycholecalciferol is reduced.

Covert malnutrition

There are several examples of covert malnutrition where the subject shows no apparent signs and the condition remains stable until a stress is applied.

1) It has been established that 5–10 mg of ascorbic acid daily will prevent or cure scurvy but that 20 mg are required to promote the optimum rate of wound healing. A subject who is subsisting on 5–10 mg of the vitamin will therefore show no clinical signs and the condition will remain quite stable even if he continues on this inadequate diet. At this level of intake, however, he would generally be regarded as undernourished with respect to vitamin C – this state is covert malnutrition, it is not revealed until the stress of a wound is imposed.

Fig. 2. Subclinical rickets (PREECE et al., 1973)

	Normal	Chemical rickets	Bio-chemical rickets	Radio-logical rickets
Serum phosphate (mg/100 ml)	4	4	4	3
Serum alkaline phosphatase (KA units/100 ml)	15	15	40	100
Serum 25 HO CC (ng/ml)	12	4.7	2.2	0
Parathyroid hormone (ng/ml)	0.4	0.4	0.8	1.4

2) Children whose growth is limited by a poor diet and also short of vitamin A or vitamin D do not show signs of vitamin deficiency. The old aphorism was 'no growth, no rickets'.

SINHA and BANG (1973) reported seasonal variations in vitamin A deficiency as diagnosed by night blindness and/or Bitot's spots, and other workers have also reported seasonal variations in hospital admissions. SINHA and BANG studied 312 children of 0–4 years of age in W. Bengal over a period of years and revealed a small peak of high prevalence in November–December (5% of the subjects) with a larger peak April–June (16% of the subjects) and a sharp decline July–October (Fig. 3). The peaks are not apparently related to the availability of vitamin A-rich foods since these are in short supply throughout the year but appear to be related to growth. The peaks of deficiency follow the growth peaks and coincide with the rice harvest in November–December when almost everyone has enough to eat. When the children are short of both energy (and protein) and vitamin A, the deficiency of vitamin A is covert.

A similar observation was made in Central America in 1965 on 3,200 subjects. Intakes of vitamin A and serum levels were low but there was no xerophthalmia or keratomalacia.

3) WIDDOWSON (1973) referred to an experiment in which male rats survived on a diet low in vitamin E when the protein level was 1.5% or 20% but died when the diet provided 40–50% protein.

4) Requirements for protein are usually derived from the amount needed to maintain nitrogen balance. By this criterion 5% casein is adequate for the adult rat. BENDER et al. (1973) anaesthetised rats with pentobarbitone at various levels of dietary protein. At 10% and 20% casein the animals remained anaesthetised for 2¼ hours, but at 5% casein on the same dose of pentobarbitone 25% of the group died and the rest remained anaesthetised for 4 hours. The animals had shown no signs of deficiency at 5% protein but were unable to withstand the stress imposed.

5) PATHAK (1958) studied the diet of medical students and a group of 160 beggars in India. So far as could be ascertained the latter were consuming an

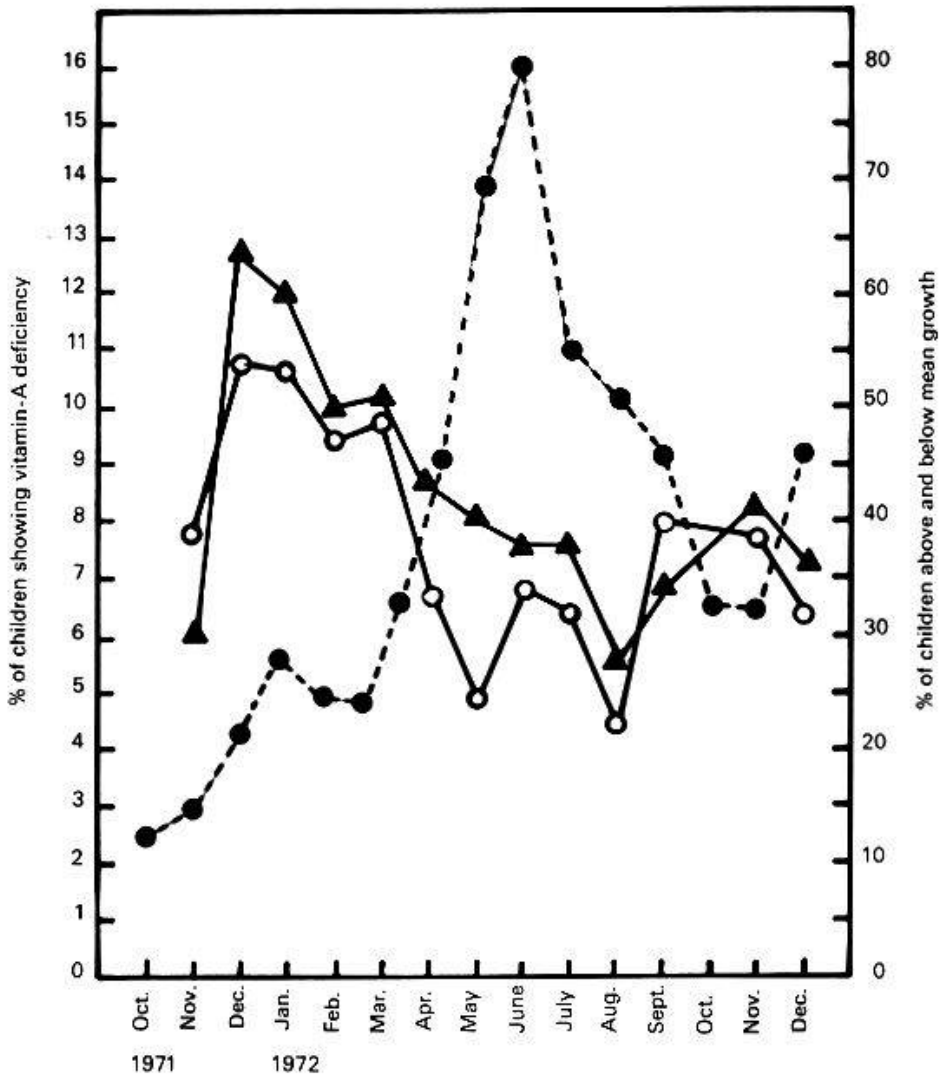


Fig. 3. Relation between vitamin A deficiency and growth of children (Ichag, 1971–73). ●-----● = vitamin A deficiency; ▲ = arm/head circumference above and below 0.280; ○ = weight above and below 50th percentile according to Singur percentile chart, which is the local growth chart for West Bengal children. (From SINHA and BANG, 1973.)

extremely poor diet grossly deficient in vitamins A, B_1, B_2, iron and energy and protein – both groups were of the same weight and height and considerably below those of the American standards. However, 94% of the beggars were free from any signs of avitaminosis (3 had deformed bones, 1 child had rickets and 1 had beri-beri, 3 had evidence suggestive of B vitamin deficiency and 2 had vitamin A deficiency).

Adaptation

There is a considerable body of evidence to show that both animals and man can adapt to reduced intake of nutrients so that they do not suffer any apparent ill-health on intakes well below those considered necessary. This is a

stable condition and may be included among the examples of covert malnutrition.

An example of energy adaptation, of which there are many in the literature, was a subject examined over a long period at Queen Elizabeth College (HOLDSWORTH, 1975). The subject was overweight at 195 lb and consuming 2,450 kcal per day. The daily intake was reduced to 1,000 kcal for 6 weeks and a loss of 18 lb resulted. The reduced weight was maintained for one year during which the subject consumed only 1,710 kcal per day. She was then given 800 kcal daily for 6 weeks and lost 8.75 lb. After this body weight was maintained at the new level with an intake of only 1,350 kcal – there was no further loss of weight at this level of intake so the subject had adapted to the low energy intake.

As long ago as 1919 BENEDICT reduced the daily energy intake of 25 young men from 3,200–3,600 kcal to 1,400 kcal for 3 weeks. After a loss of 12% of body weight they were able to maintain weight on only 1,950 kcal for a further 4 months. KEYS (TAYLOR and KEYS, 1950) made similar observations. When the energy intake of the subjects was reduced to half normal there was a fall of 25% in body weight and 19% in BMR – subjects were able to maintain their weight at 75% of starting weight on 45% of the original energy intake.

JACKSON (1937) maintained young rats at 50 g weight for 15 weeks. The protein was fed separately and after 3 weeks the amount of protein needed to maintain constant body weight decreased by 13%. At the same time the voluntary intake of energy decreased by 25%.

WATERLOW et al. (1966) described adaptation to low protein intakes by a decrease in protein turnover and a more economical use of amino acids, i.e. a greater proportion of the amino acid pool was used for protein synthesis and a correspondingly smaller amount excreted as urea. HOBERMAN (1951) showed that the half life of proteins was 16 days in animals fed high protein diets increasing to 21 days on low protein diets.

Adult rats were shown to be in nitrogen equilibrium on 5% dietary casein (KHAN, 1973). Their food intake was restricted to 70% of normal, thus not only reducing the intake of protein but leading to the oxidation of protein to satisfy the demand for energy. As expected the animals went into severe negative nitrogen balance, accompanied by an increase in hepatic glutamic-pyruvate transaminase and arginase indicating increased protein degradation. However, after periods varying in different groups of animals from 20–36 days nitrogen balance gradually returned to equilibrium and the activities of these enzymes returned to normal levels. The animals were now able to maintain body weight only a few grams below initial weight and also maintain nitrogen equilibrium on the reduced level of protein and energy. This was achieved by reducing resting oxygen consumption to 66% of normal.

All these examples of adaptation to reduced energy or nutrient intake can be regarded as covert malnutrition. With some of the vitamins the compensatory mechanism has been explained. For example, KATUNUMA et al. (1971)

showed that niacin deficiency resulted in a decrease of the enzyme systems that require niacin (NAD), namely lactic dehydrogenase (due to an increase in the enzyme that inactivates apolactic dehydrogenase) and apoglutamic dehydrogenase. Similarly rats with a pyridoxine deficiency decreased the pyridoxal-dependent enzyme ornithine transaminase in the small intestine. The authors suggest that the level of certain apoenzymes may be reduced in less essential tissues to make the vitamin-coenzyme available for more vital systems.

There is no evidence to indicate whether covert malnutrition as exemplified by such adaptations is harmful or even beneficial.

Nutritional enigmas

Further examples of covert malnutrition are found in subjects who have abnormally low intakes of energy and nutrients. All dietary surveys show a wide range of intakes, with some subjects, in apparent good health, consuming abnormally small amounts. For example, a collection of data (HARRIES et al., 1962) of energy intakes among 500 men showed a range from 1,000 to 5,000 kcal per day and among 800 women from 1,000 to 4,000 kcal. Those at the lower end of the range were consuming less than half the average intake. So far as energy intake is concerned, this presumably met their needs but, assuming that all subjects were consuming similar types of food, those at the lower end of the range obtained less than half the average intake of vitamins, minerals and protein. Unless the requirements of nutrients fall in parallel with the requirements for energy, these subjects are possibly suffering covert malnutrition.

Similarly elderly persons, whose energy expenditure and in most instances intake fall to two-thirds of what it was when they were younger, may also be suffering covert malnutrition.

There have been several reports of energy intakes so low as to barely satisfy basal requirements. These findings were an enigma until GARROW (1974) recently offered a feasible explanation. He demonstrated that some subjects reduce their metabolic rate considerably during sleep so that the total energy needs are less than calculated from BMR plus activity. Since such 'hibernators' have adapted to a low level of energy and presumably nutrient intakes, they are also in the class of covert malnutrition.

Very low apparent intakes of vitamin C in some subjects were shown by COOK et al. (1973). They measured the food intake of 780 schoolchildren and the widest range was shown for vitamin C (Fig. 4). This refers to schoolgirls aged 12–14 years; recommended intake for this group is 25 mg per day, mean intake was 54 with a standard deviation of 52 mg. This means that if the distribution had been normal one-sixth of the group received less than 2 mg per day; in fact the lowest intake was 5 mg per day. If the calculated figures for one week are indeed representative of the average intake of these children, since they were reported to be free from symptoms, they fall into the category of covert

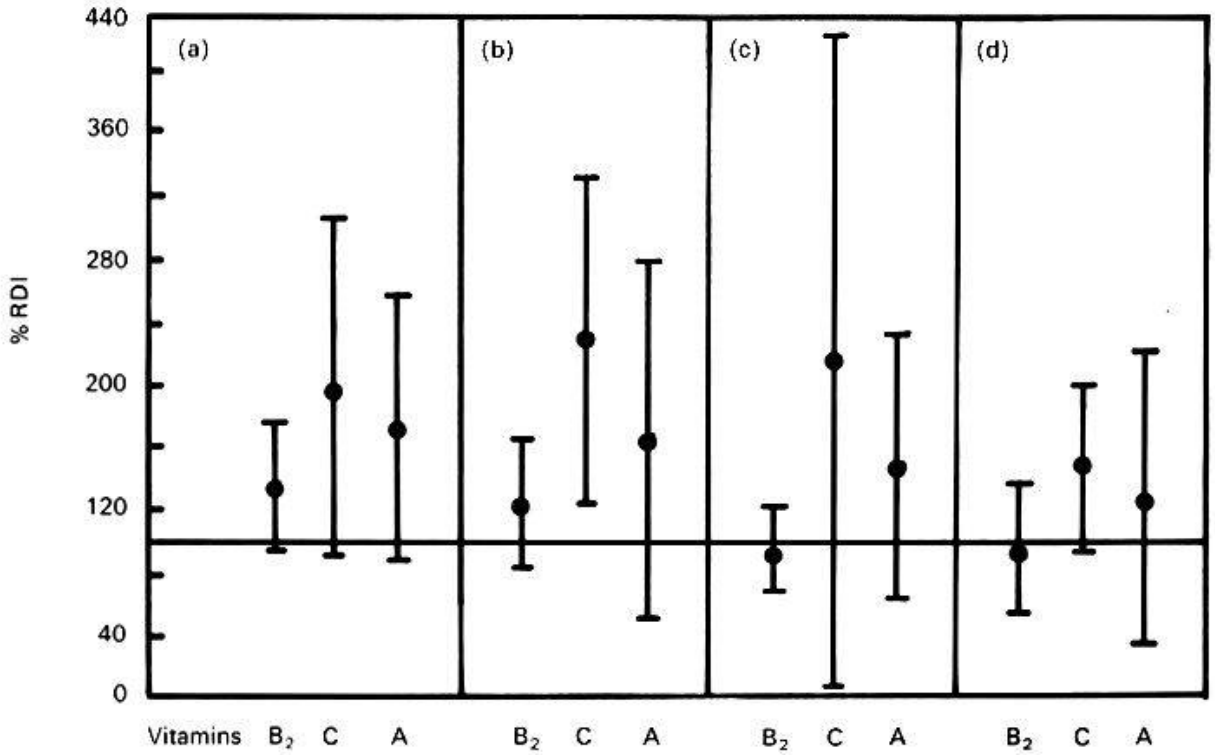


Fig. 4. Mean daily intakes of vitamins, expressed as a percentage of the recommended daily intake (RDI), for various groups of children: (a) boys, 9–11 years old (n = 198); (b) boys, 12–14 years old (124); (c) girls, 12–14 years old (110); (d) girls, 15–17 years old (81). Vertical bars indicate standard deviation. (Adapted from COOK, ALTMAN, MOORE, TOPP, HOLLAND and ELLIOTT, 1973.)

malnutrition. Fig. 5 shows a similar range from an earlier survey with, again, extremely low intakes at the lower end of the range.

A more dramatic example is provided by the work of HOPPNER et al. (1968) in Canada. One hundred samples of human liver were analysed at post mortem – 8 had no vitamin A, 32% of subjects over 10 years of age had levels between 0 and 40 μg/g wet liver; overall mean value was 100 μg (normal values are accepted as 100–300 μg).

It is known that vitamin A status is affected by a variety of diseases and that requirements are increased in certain diseases, so it is possible that these low levels were caused by the disease that led finally to death although no consistent correlation could be found between cause of death and liver vitamin A content. 13 subjects who died from accident had low values of 25 μg vitamin A per g liver. Furthermore RAICA et al. (1972) examined livers from 372 subjects from 5 areas of the United States and found 22% with levels 0–40 μg, and 26.6% with 41–100 μg; similar values were found in subjects dying accidentally.

Similar values have been reported from SMITH and MALTHUS (1962) and UNDERWOOD et al. (1970). Presumably all these subjects were suffering covert malnutrition.

The problem of categorising stages of nutritional status is exemplified by the recent reappraisal of iron deficiency anaemia. Haemoglobin levels below 13 g

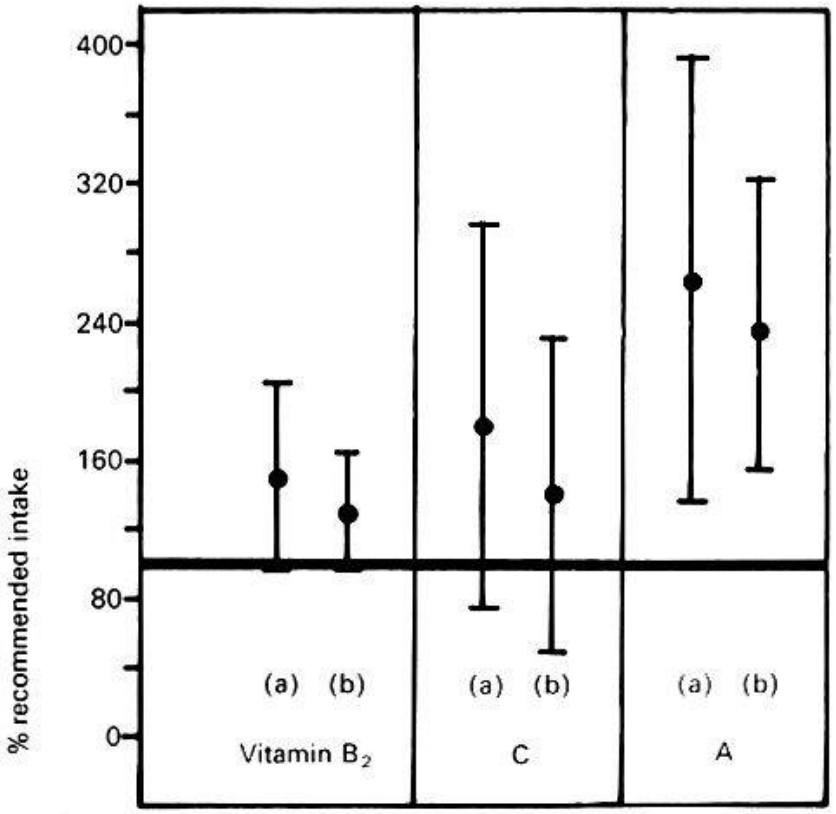


Fig. 5. Mean intake of vitamins in 4–5 year-old children as % RDI ± S.D. – (a) BRANSBY and FOTHERGILL, Brit. J. Nutr. 8, 195 (1954). (b) Ministry of Health 1968, Report No. 118.

per 100 ml in males and 12 g in females are defined as indicative of anaemia. ELWOOD (1973, 1974) found no impairment of function with low haemoglobin levels, and when these levels were restored by treatment, there was neither clinical nor subjective improvement. ELWOOD concluded that harmful effects are unlikely unless haemoglobin levels fall below 10 g per 100 ml. Others have suggested that at near maximal effort any decrease in haemoglobin levels causes impairment of work output. This would fit mild anaemia into the category of covert malnutrition – a stable state that shows no apparent harm until a stress is imposed.

The problem of assessing the optimal intake of nutrients is shown in Fig. 6. At low and obviously inadequate levels of intake of a nutrient (horizontal axis) clear signs of deficiency are seen (vertical axis). As intake increases, deficiency signs disappear until a stage is reached when there is no corresponding increase in benefit. This must be defined as optimal nutrition. Between the dose at which all signs disappear and the dose at which no further benefit accrues is the doubtful zone. This has long been recognised. However, the criterion of adequacy is open to question; Fig. 6 shows three possible criteria – disappearance of all clinical signs, saturation of coenzymes, and, at the highest level of intake, saturation of tissues. For example, with respect to thiamin, at least four criteria could be used; these are, with increasing dosage levels: growth; higher levels in

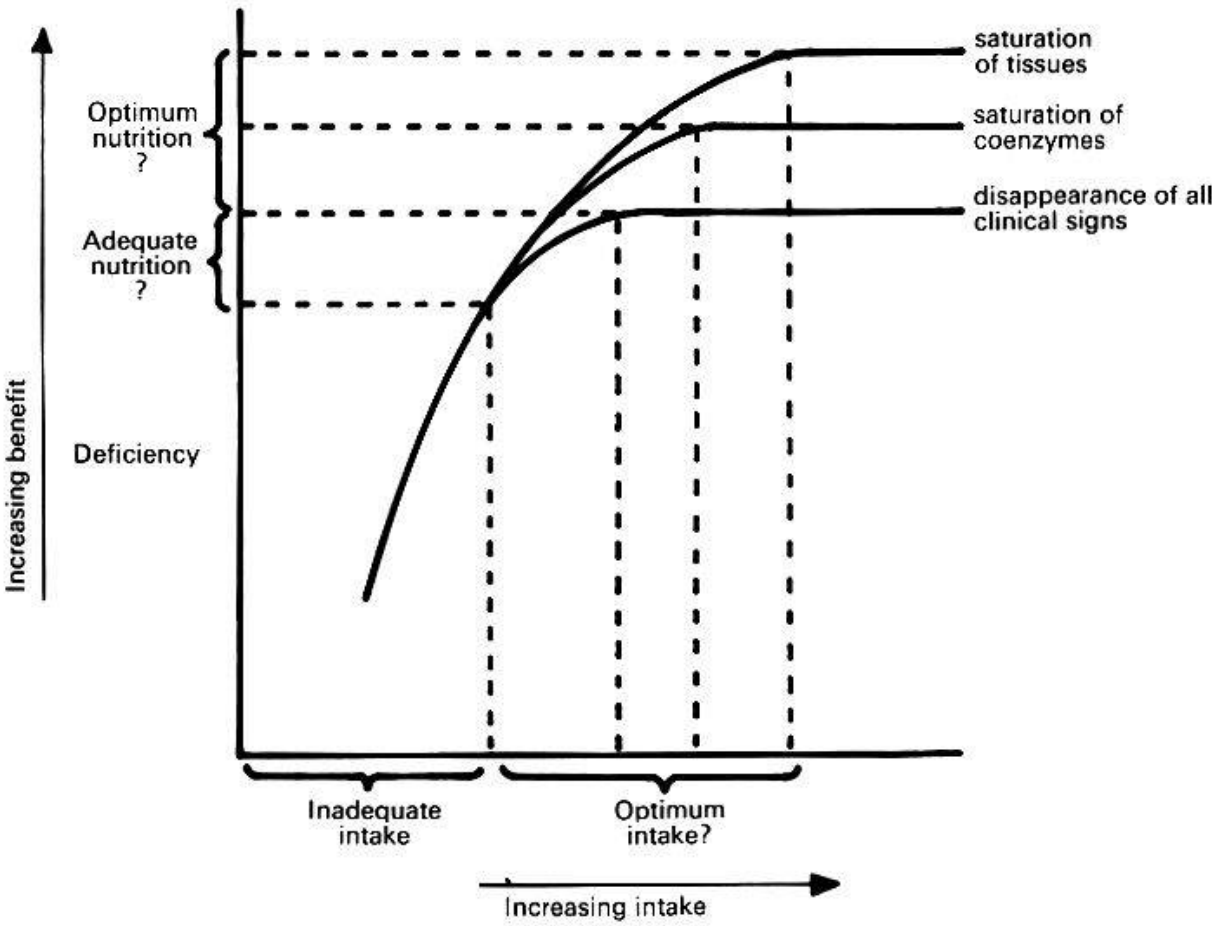


Fig. 6. Problem of minimum, adequate and optimum nutrient intake.

the red and white blood cells; greater total body thiamin, and finally, urine excretion increases. The converse of attempting to define the optimal intake, is attempting to define states of relative undernutrition.

Until there is a clearer basis for establishing criteria of nutritional adequacy, the term covert malnutrition may have a use.

Summary

Obvious or overt malnutrition is diagnosed from characteristic clinical signs. Subclinical malnutrition is revealed only by biochemical changes but is an unstable state which, if untreated, will develop to clinical malnutrition.

There appears to be a stable state where the subject has adapted to low levels of nutrient intake for which the name 'covert malnutrition' is suggested. Examples are: (1) vitamin C intake of 10 mg per day which is adequate to prevent scurvy and where no clinical signs appear until the stress of wounding is applied to the tissues; (2) inadequate intake of vitamin A without signs of deficiency because the poor diet limits growth – deficiency shows up when growth is

resumed: (3) protein intake which is adequate to maintain N balance but not adequate to withstand stress.

All dietary surveys reveal apparently healthy individuals whose intake of nutrients appears to be grossly inadequate – these may be 'suffering' covert malnutrition, although there is no evidence to indicate whether or not this stable condition is harmful.

Zusammenfassung

Die manifeste Fehlernährung kann auf Grund charakteristischer klinischer Symptome diagnostiziert werden. Bei der subklinischen Form muss man hingegen biochemische Störungen suchen; es handelt sich um einen labilen Zustand, der sich, wenn er vernachlässigt wird, in eine manifeste Fehlernährung entwickeln kann.

Es scheint andererseits einen beständigen Zustand zu geben, in dem sich das Individuum einer niedrigeren Nahrungszufuhr angepasst hat: es wird die Bezeichnung «versteckte Fehlernährung» vorgeschlagen. Einige Beispiele davon sind: 1. Geringere Vitamin-C-Zufuhr als 10 mg pro Tag genügen, um einem Skorbut vorzubeugen und um keine klinischen Symptome hervorzurufen, solange keine Gewebsverletzungen auftreten. 2. Mangelzustände an Vitamin A ohne klinische Symptome, da ein solcher Mangel das Wachstum hindert, sich aber nur dann zeigen würde, wenn dieses beendet ist. 3. Eine Proteinzufuhr, die genügend ist, um das Stickstoffgleichgewicht zu erhalten, aber ungenügend, um einen Widerstand gegenüber Stresszuständen zu sichern.

Alle Ernährungsstudien zeigen, dass es anscheinend gesunde Menschen gibt, deren Nahrungszunahme aber ungenügend ist: sie könnten an versteckter Fehlernährung «leiden», obwohl keine Sicherheit besteht, ob dieser beständige Zustand schädlich ist oder nicht.

Résumé

On peut diagnostiquer les syndromes de malnutrition manifeste sur la base de symptômes cliniques caractéristiques. Pour d'autres cependant, sans signes cliniques, il est nécessaire de recourir à la recherche d'anomalies biochimiques. Il s'agit là de situations instables, qui peuvent évoluer, si on les ignore, vers des dystrophies manifestes.

Il existe un état stable dans lequel le sujet s'est adapté à un bas degré de nutrition et on suggère la dénomination de «dystrophie alimentaire occulte», dont voici quelques exemples: 1. Doses de vitamine C inférieures à 10 mg par jour, en quantité suffisante pour prévenir le scorbut et sans symptômes cliniques en absence de blessures aux tissus. 2. Manque de vitamine A sans signes cliniques d'hypovitaminose, vu que l'apport insuffisant de cette substance freine la croissance et qu'il se révèlera seulement quand celle-ci sera terminée. 3. Un

apport de protéines suffisant pour maintenir l'équilibre de l'azote, mais insuffisant pour assurer une résistance vis-à-vis des états de stress.

Toutes les études alimentaires révèlent l'existence d'individus apparemment sains, dont l'alimentation est cependant franchement inadéquate. Ceux-ci peuvent «souffrir» de malnutrition occulte, bien qu'il n'y ait pas d'évidence indiquant si telle condition stable soit ou non nuisible.

Riassunto

Le distrofie alimentari manifeste si possono diagnosticare sulla base di segni clinici caratteristici. In quelle subcliniche invece è necessario ricercare anomalie biochimiche; si tratta in questi casi di situazioni instabili che, se trascurate, possono evolvere in distrofie manifeste. Ci sono d'altra parte degli stati stabili nei quali il soggetto si è adattato ad un livello alimentare inferiore e viene suggerito il termine di «distrofie alimentari occulte». Ne sono esempi: 1. Dosi di vitamina C inferiori a 10 milligrammi al giorno, quantità sufficiente a prevenire lo scorbuto e che non si accompagna di sintomi clinici in assenza di ferite ai tessuti; 2. Carenze di vitamina A, senza segni di deficienza, dato che un suo apporto insufficiente limita la crescita e che si rivelerà soltanto quando questa sarà finita; 3. Un apporto di proteine adeguato a mantenere l'equilibrio dell'azoto, ma insufficiente ad assicurare una resistenza in situazioni di stress. Tutti gli studi alimentari rivelano l'esistenza di individui apparentemente sani, la cui alimentazione è tuttavia inadeguata: costoro potrebbero «soffrire» di distrofie alimentari occulte, sebbene non ci sia evidenza alcuna che tali condizioni stabili siano o no dannose.

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