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STANDARDS FOR THE DIAGNOSIS OF VITAMIN DEFICIENCY IN MAN

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INTRODUCTION

The spectrum of vitamin deficiency states, as any other nutritional deficiency, extends between two theoretical limits: that of optimal nutrition, when the metabolic needs for the vitamin are amply satisfied, and that of extreme deficiency, when the lack results in such severe metabolic and organic alterations as to interfere with the life process. In between, however, there is a continuum of stages approaching either extreme to different degrees. This concept is suggestive of the difficulties involved in the definition of standards, since the implication is that they must be quantitative, and express in measurable terms the distance between the particular situation of an individual or a group of population from either or both of these two extremes.

It is evident, then, that the first task in the elaboration of standards is to define as clearly as possible the characteristics of the subjects that lie in these two extremes. The second would be to design means to express, quantitatively, deviations from them. To define these points, several criteria have been used that, at the risk of oversimplification, can be classified as follows: dietary, biochemical, clinical and functional. I have separated functional criteria from the rest despite the fact that good function is dependent

on the normality of the biochemical aspects of the organism; but the expression of these functions is dynamic and may be best referred to as "performance", whether this be biochemical, physiological, physical, mental or otherwise. Actually, functional tests should provide the ultimate criteria, but unfortunately, they are also the most difficult to evaluate.

In view of the latter difficulty, efforts have been made to develop indices, particularly dietary and biochemical. In general, these are, numerical expressions of measurable characteristics which ideally are, or may be, related to a state of functional alteration, but which are practical to apply to human subjects. They express arbitrary estimates of the position occupied by the subjects in the spectrum delimited by the two extremes mentioned in the previous paragraphs. Unfortunately, this relationship of the indices with function is as yet in many instances, poorly defined.

CLINICAL CRITERIA

Clinical criteria are of limited use as standards because of various reasons: a) they are often unspecific or, in other words, seldom pathognomonic of a particular deficiency; other factors in the physical and microbiological environment

may result in the same or similar alterations; b) the concomitant presence of several deficiency states obscures the appearance of clear-cut clinical signs, thus making their interpretation doubtful. Unfortunately, this is often the case with human populations; c) in general, their presence in the individual reflects the already extreme state of deficiency and therefore, they do not lend themselves to the evaluation of the gradient-type of situation characteristic of vitamin deficiency.

May I present, however, a positive point regarding clinical signs. There is one situation in which they may lend themselves to mathematical, or rather, to statistical treatment. When dealing with population groups, and provided that their nutritional origin can be demonstrated, prevalence figures could conceivably be set up as standards. The bases to define these limiting acceptable prevalences are still empirical, but they have value in comparative studies of population groups. An example of such an effort by Jolliffe is given in Table 1 (12). I will not comment on the soundness of the specific prevalences proposed. They are several years old and, perhaps, the time is due for a revision of these standards by a group of clinical nutritionists.

DIETARY AND BIOCHEMICAL CRITERIA

I deem it impossible to discuss these two approaches separately because in most instances the criteria to establish the dietary standards have been based on biochemical alteration.

Efforts have been directed towards the determination of some biochemical characteristics of subjects who are at the lower limit of the spectrum of deficiency and there is a great deal of information on this point for many vitamins. The determination of the other extreme, the extreme of sufficiency, is somewhat more vague, because here we either have a level of intake of a vitamin which will be sufficient to satisfy all metabolic needs and no more, and which will determine certain biochemical characteristics of the subjects, or on the other hand, we can have an excess of the vitamins which produce no harm but no further benefits either, and will, nevertheless, change some biochemical measurements. The danger here lies in not being able to discriminate between sufficient and excessive, and thereby run the risk of setting unduly high standards. I have partaken in the efforts of at least two scientific groups that have proposed standards to assess vitamin deficiency or adequacy, and I guarantee that, to the extent of our present knowledge, this danger has

been carefully considered.

The next question is how to establish standards to judge situations in between these two limits. In reviewing the literature, I have come to the conclusion that the prevailing criterion has been based on the following: a) values occurring in individuals who are in a definite deficiency state. These have been produced experimentally, both in animals and humans. Conditions of practically "complete depletion" have been obtained in which histological and physiological alterations are clearly evident; b) values occurring in individuals who present no evidence whatsoever of abnormality whether physical or physiological, and who, furthermore, possess a certain amount and concentration of the vitamin in question in their body or specific tissues which acts as a reasonable insurance against rapid depletion under conditions of deprivation; c) the intermediate values between the upper range of values under (a), and the lower range of values under (b) may be, and in general are, considered indicative of undesirable situations at "risk" to a smaller or larger extent. Subjects in these intermediate stages represent situations that can be changed from a doubtful status by increasing the supply of the nutrient to the body.

It would be impossible, in the allotted time, to review the approaches which have been used by groups of experts or individual investigators to set up dietary standards and corresponding biochemical indices for all the vitamins concerned. Depending on the extent of our knowledge, these proposed standards range from what could be considered "educated guesses" to relatively well-documented figures.

DERIVATION OF STANDARDS

I will discuss only three cases which can be taken as models of what has been done to elaborate standards perhaps under the best circumstances, that is, when a relatively adequate amount of knowledge has been available. There are less fortunate cases. But emphasis is made on one point: whatever information is available now with regard to standards cannot be improved by discussion or criticism, it has to be done through research.

Ascorbic Acid:

There is still much controversy regarding the amount of ascorbic acid to be recommended as an adequate intake for humans. I believe that this controversy is due more to differences of opinion than to contradictory data. If we take two standards, those of the National Research Council of

the United States (NRC) (17) and those of the Canadian Council on Nutrition (CCN) (5), we can readily realize that their traditionally divergent standards are both derived from the same data. While NRC recommends a daily intake of 60 mg for the adult man, the Canadian standard recommends exactly half (30 mg). Another U.S. group, the Interdepartmental Committee on Nutrition for National Defense (11), went somewhat further, proposing categories of levels of intake and corresponding expected plasma ascorbic acid concentrations which could be used as indices. These are shown in Table 2.

What are the data on which these standards are based? In Figure 1 are represented some of the pertinent associated phenomena in relation to levels of dietary intake. The data are mainly those from Lowry et al. (15) and Rally et al. (18). The intake which results in maximum plasma levels with minimum urinary loss is approximately 80-100 mg per day. Levels of 8-10 mg are sufficient to prevent scurvy. Information regarding intakes below that level is scarce and doubtful, but there is some evidence that 4 mg per day is not enough for adequate reversal of some clinical alterations (7). Studies with ^{14}C ascorbic acid, indicate furthermore, that the actual metabolic utilization by healthy men is around

22 mg per day (2,3,19).

In support of the recommendation of the NRC for the higher standard, two main arguments have been brought forward: a) that animals which can synthesize ascorbic acid, maintain a tissue concentration at saturation levels; and b) that the higher amount provides a margin of safety in cases of increased need, and also protects a proportion of individuals who, by the mere fact of individual variability, may have a higher requirement. In favor of the lower standards are the following arguments: a) that 30 mg is at least three times the intake needed to prevent scurvy; b) that it provides an amount somewhat above the ascorbic acid actually metabolized daily by a normal man; and c) that it has not been possible to demonstrate satisfactorily any further benefits from amounts in excess of this standard.

Thiamine:

Several criteria have been considered in the determination of standards for thiamine nutrition. Among the most informative we may list: a) the attainment of a point of minimum urinary excretion of the vitamin. It is based on the observation that as the thiamine intake is gradually lowered from a high level, the urinary excretion decreases proportionally to a point,

after which further lowering of the intake results in only minor changes in urinary output. This point is assumed to represent the minimal intake of thiamine which will maintain the tissues with a physiologically adequate thiamine concentration. Intakes higher than this critical point result in spilling and wasting of the vitamin; b) closely related to the above are the so-called dose-retention tests. They are conducted by the administration of a dose of thiamine either orally or parenterally and the determination of the percentage of the dose which is excreted in the urine during the subsequent four hours. The values obtained are also supposed to represent the extent of saturation of the tissues with thiamine; c) appearance of abnormalities in carbohydrate metabolism. These abnormalities are judged mainly by alterations in the concentrations of pyruvate and lactate in the blood and are particularly useful when the metabolic paths involved are subjected to a metabolic stress, such as a load of glucose plus physical exercise. Recently, transketolase activity in erythrocytes has been shown to depend on a minimum intake of thiamine, but so far, no direct application to the estimation of minimum requirement has been reported; d) appearance of early clinical signs such as impaired appetite,

lowered blood pressure, slight edema, diminution of deep reflex activity and dulling of vibration sense. The estimation of plasma and red blood cell thiamine has also been used, but they appear to be too insensitive.

Several independent groups of investigators have searched for the minimum daily intake required by humans using either one, or a combination of the above criteria in a comprehensive approach.

There is general agreement in expressing the requirements as mg daily per 1000 calories. The available evidence has been reviewed and carefully analyzed by several groups of experts. There is little question that intakes of 0.3 - 0.5 mg of thiamine per 1000 calories are about the highest range in values reported as minimum requirement. One exception is the work of Williams et al. (21) who concluded that even 0.45 mg per 1000 calories was slightly less than required. Their criterion, however, is open to question because it was based on an arbitrary set excretion level in the urine which has no definite basis, and on a slight elevation of the blood pyruvate after a glucose load, which may not necessarily be abnormal. Values of 0.20 - 0.25 mg can be considered as the lowest range of the values reported as minimum intakes.

Keys et al. (13) for example, conclude that "for the periods studied, no benefit of any kind was observed to be produced by an intake of more than 0.23 mg of thiamine per 1000 calories". These authors state, however, that no conclusions can be drawn for more prolonged periods of time. Their observation period lasted only from 10 to 12 weeks. Another very carefully conducted study in adult men in which levels in this low range were evaluated by comprehensive criteria was that of Horwitt and his group (9), who concluded that 0.40 mg of thiamine was below the minimal requirement for subjects who were consuming about 2000 calories per day (about 0.20 mg of thiamine per 1000 calories).

An interesting observation is that the extrapolation to man of the formulas developed by Cowgill in 1934 for mice, rats, pigeons, and dogs, indicate that the calculated thiamine requirement for a 60 kg woman and a 70 kg man would be 0.25 and 0.30 mg per 1000 calories respectively (16).

The stimulatory effect produced by the addition of thiamine pirophosphate (TPP) to the transketolase activity of red blood cell hemolyzate is increased under conditions of dietary thiamine restriction (4). Data are beginning to appear indicating that a TPP effect of more than 20% correlates with

"deficient" thiamine intake and excretion, and more than 25% may be regarded as an index of thiamine deficiency (6).

Reference to other works only serves to confirm what has already been stated. This discussion leaves a situation of relative agreement, but the decision regarding a minimum requirement figure still has to be made. A figure corresponding to the lowest range mentioned, of approximately 0.20 mg per 1000 calories, might be selected. This is the position adopted by the Canadian Council of Nutrition (5) which states that the results of the available studies indicate that "for the adult person 0.2 mg of thiamine per 1000 calories is at the lower limit of adequacy and that 0.3 mg per 1000 calories is near the level to produce tissue saturation, and is undoubtedly adequate". On these bases the Council adopts 0.3 mg per 1000 calories as the recommended amount.

It is interesting to note that in the latest edition of the Recommended Dietary Allowances, the National Research Council of the United States of America (NRC) (7) also bases the "dietary allowance" for thiamine on the evidence that the minimal requirement approximates 0.2 mg per 1000 calories. The NRC, however, recommends 0.5 mg/1000 cal on the assumption that this amount maintains whole blood thiamine levels and

permits relatively high urinary excretion.

The Joint FAO/WHO Expert Group on Requirements of Vitamin A, Thiamine, Riboflavin and Niacin (7) proposes 0.4 mg/1000 cal. They state that on the basis of available evidence, a value of approximately 0.33 mg/1000 cal represents the requirement and "with an allowance of 20% for individual variation, the recommended intake for thiamine is 0.40 mg per 1000 calories".

Data obtained from nutrition population studies seem to support this "critical" relationship between intake and urinary excretion. Figure 2 shows data collected by the Interdepartmental Committee on Nutrition for National Defense (U.S.A.) (11). These data are for adults only and were collected by different groups from 18 communities. In the Nutrition Survey of Central America and Panama, it was possible to derive similar relationships for a large number of subjects of different ages using the same biochemical and dietary techniques (1). The results are illustrated in Figures 3 and 4.

In fact, the "critical intake", i.e., the level at which the tissues become "saturated" (the excess thiamine being excreted in the urine) is usually found to be around 0.35 mg/1000 cal that is the mid-point between the Canadian and the FAO/WHO recommended figures. Measurements of the thiamine

metabolites excreted in the urine have indicated that the actual metabolic utilization of the vitamin is approximately 0.33 mg (per 1000 cal per day) and suggest this as the minimum daily requirement (22). A model curve illustrating this relationship is shown in Figure 5, which also presents the intakes recommended by the Canadian Council on Nutrition, the NRC and the FAO/WHO. The ICNND guide to interpretation of thiamine intake data is also included. Its scientific basis is quite evident. We must emphasize again that these figures are all based on the same set of data and that the difference between the views of the two groups is a question of balance between the degree of risk accepted as reasonable, and the feasibility of attaining in practice an intake to meet a relatively high recommendation.

Vitamin A:

In theory, the standards for the assessment of vitamin A deficiency should be based on the interrelationship of four types of data: dietary intake, concentration of vitamin A in liver, blood levels of the vitamin, and the appearance of clinical signs including abnormal dark adaptation which could be considered as a functional test.

In practice, the data available are difficult to interpret because of several factors: a) vitamin A accumulates

in liver tissue and can be used as a reserve to supply it to other tissues for variable periods of time, depending on the extent of these reserves; b) there is a need for more studies in humans to establish the quantitative relationship between vitamin A serum levels and vitamin A liver reserves, as well as to determine factors other than nutrition which affect this relationship; c) the scarcity of information on the biological activity of the carotenes as provitamin A compounds.

In this discussion I will follow the recommendation of the Joint FAO/WHO Expert Group that, because of the availability of crystalline vitamin A alcohol (retinol) as a reference standard, the practice of expressing vitamin A values in terms of International Units should be discontinued.

Intakes of compounds with vitamin A activity must, therefore, be expressed in "retinol equivalents". The retinol equivalency of the different carotenes will not be discussed here. The reader is referred to the literature (7).

The determination of blood plasma concentrations of retinol is still the only feasible biochemical tool to assess the state of vitamin A nutrition. I will try to describe the situations along the spectrum of vitamin deficiency states. At the upper extreme, the situation of sufficiency is obtained, with an intake which will be compatible with normal function,

particularly dim light vision and with complete absence of clinical signs. Furthermore, it is accepted that at this desirable level the liver should contain significant amounts of retinol. After reviewing thoroughly the available evidence, the FAO/WHO Expert Group (7) concluded that an intake of 750 mcg of retinol (2500 I.U.) ensures this situation in the human adult. This figure was proposed by them as the daily recommended intake. The Sheffield study (20) is the main source of data on which these conclusions are based. The intake of 750 mcg/day in two individuals maintained the plasma retinol levels at approximately 25-27 mcg/100 ml. Another "landmark" to be derived from these studies is the plasma level of 15 mcg/100 ml (50 I.U.). To quote: "A fall of the average plasma level to below 50 I.U. (15 mcg) per 100 ml in every case preceded the deterioration of dark adaptation by a few weeks, and no abnormal values for dark adaptation were noted in any subject as long as the plasma level of vitamin A remained above 50 I.U. per 100 ml". The next lower "landmark" set by the Sheffield study is 12 mcg (40 I.U./100 ml), since this was the average plasma level found at the time the deterioration of night vision was pronounced. Furthermore, none of the deprived individuals

whose dark adaptation remained normal had average plasma levels below 12 mcg/100 ml.

A few other observations in humans, in the literature reviewed, do little more than confirm the general magnitude of the figures given above. For example, the retinol levels of large groups of urban children or adults in Central America fall mostly between 20 and 50 mcg/100 ml (10).

As seen by the Group of Experts of the ICNND (11) these data would support the guide to interpretation of blood vitamin A data shown in Table 3.

In my opinion, this is a reasonable approximation of great practical value. As seen in Figure 6, data from Lewis et al. (14) indicate that intake and plasma levels relate quite linearly to each other up to plasma levels of 25-30 mcg/100 ml. Liver retinol behaves differently, since it does not begin to accumulate until the plasma values are around 18-20 mcg/100 ml. These data permit three conclusions: a) that a low plasma level results from a low intake and is undesirable because it means a low vitamin A availability to the tissues and the absence of reserves in the liver; b) that a higher intake of vitamin A, sufficient to elevate significantly the plasma levels, does not necessarily result in appreciable

liver reserves ("risk situation"). Under these conditions the supply of retinol to the tissues will be operating; but in terms of the economy of vitamin nutrition of the population, the situation is one of risk; c) that with an even higher intake (upper extreme of the spectrum), both high plasma and liver retinol levels are ensured.

From the Sheffield experiments (20) it can be deduced that intakes of around 390 mcg/day (1300 I.U.) of retinol, would place the subjects under situation (b). One could also suppose that intakes below that would eventually lead to depletion of hepatic reserves.

A reasonable guide to interpret "retinol equivalent" intakes (mcg/day) would be, for the FAO reference man, that *these 4* presented in Table 4.

COMMENTS

Other standard values have been constructed on bases similar to those illustrated here. The Appendix includes those which have been proposed by ICNND for some vitamins of public health significance, and those for blood serum and red blood cell folates, and for serum vitamin B₁₂ used by INCAP.

In conclusion, I would like to state that the standards are to be recognized for what they are. They are "yardsticks" against which to assess the relative position of subjects in

the spectrum of vitamin deficiencies. Furthermore, they define a goal, or the position in the spectrum which, within reason, represent the smallest probability of being deficient or at risk. They are most useful when taken as the basis for the statistical expression of the nutritional characteristics of a population.

It is not my intention to defend the specific figures proposed, but rather to emphasize the soundness of the principles involved in their development, as well as the general usefulness and limitations of the standards.

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FOOTNOTES

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TABLE 1

Nutrient	Clinical sign	Abnormal	
Calories:	Obesity	<i>Skin thickness:</i> Scapulae Lower Axillae	Over 30 mm.
			Over 25 mm.
Leanness	Height-weight tables <i>Skin thickness:</i> Scapulae Lower Axillae	Over 10 percent.	
		Under 8 mm. Under 8 mm.	
Protein.	Height-weight tables <i>Dependent edema</i>	Over 0 percent ¹ under age 50. In absence of beriberi starvation, and pregnancy.	
Vitamin A	<i>Follicular Keratosis of arms</i>	Over 5 percent ¹ in adults and pre-adolescents. Not reliable in starvation and in adolescents.	
Vitamin D.	Under six months <i>Cranio tabes</i>	Over 0 percent. ¹	
	Six mo. to two years <i>Bending of the ribs.</i> Over two years () and <i>X deformities of legs.</i>	Over 0 percent. ¹	
Thiamine.	Absent Achilles tendon reflexes.	Over 1 or 2 percent. ¹	
Niacin	<i>Tongue lesion more advanced than hypertrophy of papillae at tip.</i>	Over 5 percent. ¹	
Riboflavin	Reddened tongue . . .	Over 1 or 2 percent. ¹	
	Pellagrous dermatitis . . .	Over 0 percent. ¹	
	Angular stomatitis . . .	Over 5 percent ¹ in non-denture wearing population.	
Ascorbic acid	Conjunctival hyperemia (circum corneal infection).	Over 5 percent. ¹	
	Magenta tongue . . .	Over 0 percent. ¹	
	Red hyperemic gums . . .	Over 1 or 2 percent ¹ in children. Over 5 to 10 percent ¹ in adults.	
	Perifolliculosis	Over 0 percent. ¹	

¹ An educated guess of frequency that these signs might occur in a well-nourished population group.

From: "Methods for Evaluation of Nutritional Adequacy and Status".
Nat. Research Council, 1954.

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TABLE 2

GUIDES FOR THE INTERPRETATION OF ASCORBIC ACID INTAKES AND PLASMA LEVELS
(Young adult male)

	Deficient	Low	Acceptable	High
Dietary Intake (mg/day)	< 10	10 - 29	30 - 49	≥ 50
Plasma Concentration (mg/100 ml)	< 0.10	0.10 - 0.19	0.20 - 0.39	≥ 0.40

From: Manual for Nutrition Surveys, 2nd Ed., 1963. ICNND, Bethesda, Md.

TABLE 3

PLASMA VITAMIN A (mcg/100 ml)

Deficient	Low	Acceptable	High
< 10	10 - 19	20 - 49	\geq 50

From: Manual for Nutrition Surveys, 2nd Ed., 1963. ICNND,
Bethesda, Md.

TABLE 4

INTAKE OF RETINOL EQUIVALENTS
(mcg/day)

Deficient	Low	Acceptable or High
< 390	390 - 740	≥ 750

APPENDIX

INCAP¹ SUGGESTED GUIDES TO INTERPRETATION OF BLOOD FOLATES AND VITAMIN B₁₂
 (all ages)

Constituent	Deficient	Low	Acceptable or High
Serum folates (ng/1 ml)	< 3.0	3.0 - 4.9	≥ 5.0
Serum vitamin B ₁₂ (pg/1 ml)	< 100	100 - 149	≥ 150

¹ Prepared by Dr. Fernando Viteri and Dr. Jorge Alvarado, Division of Biomedical Research, INCAP.

SUGGESTED GUIDE TO INTERPRETATION OF VITAMIN INTAKE DATA
FOR REFERENCE MAN

	Deficient	Low	Acceptable	High
Ascorbic Acid: mg/day ¹	< 10	10 - 29	30 - 49	≥ 50
Thiamine: mg/100 cal ¹	< 0.20	0.20 - 0.29	0.30 - 0.40	≥ 0.50
Riboflavin: mg/day ¹	< 0.7	0.7 - 1.1	1.2 - 1.4	≥ 1.5
Niacin: mg/day ¹	< 5	5 - 9	10 - 14	≥ 15
Retinol equivalents: mcg/day ²	< 390	390 - 740	≥ 750	

¹ ICNND

² Suggested by author of present paper.

ICNND SUGGESTED GUIDE TO INTERPRETATION OF URINARY VITAMIN EXCRETION DATA

	Deficient	Low	Acceptable	High
ADULTS (MALES AND NONPREGNANT, NONLACTATING FEMALES)¹				
Thiamine:				
μg/6 hours-----	< 10	10 - 24	25 - 49	≥ 50
μg/gm creatinine-----	< 27	27 - 65	66 - 129	≥ 130
Riboflavin:				
μg/6 hours-----	< 10	10 - 29	30 - 99	≥ 100
μg/gm creatinine-----	< 27	27 - 79	80 - 269	≥ 270
N ¹ Methylnicotinamide:				
mg/6 hours-----	< 0.2	0.2 - 0.59	0.6 - 1.59	≥ 1.6
mg/gm creatinine-----	< 0.5	0.5 - 1.59	1.6 - 4.29	≥ 4.3
PROVISIONAL GUIDE FOR URINARY EXCRETIONS IN CHILDREN²				
Thiamine: μg/gm creatinine:				
Age (years):				
1-3-----	< 120	120 - 175	176 - 600	> 600
4-6-----	< 85	85 - 120	121 - 400	> 400
7-9-----	< 70	70 - 180	181 - 350	> 350
10-12-----	< 60	60 - 180	181 - 300	> 300
13-15-----	< 50	50 - 150	151 - 250	> 250
Riboflavin: μg/gm creatinine:				
Age (years):				
1-3-----	< 150	150 - 499	500 - 900	> 900
4-6-----	< 100	100 - 299	300 - 600	> 600
7-9-----	< 85	85 - 269	270 - 500	> 500
10-15-----	< 70	70 - 199	200 - 400	> 400

¹ The urinary values indicated above for adults are based on an expected creatinine excretion of 1.5 gm daily for a reference man weighing 65 kg, for creatinine coefficient of 23.

² The guides offered here for children are based on considerably less extensive data than are the guides for adults.

ICNND SUGGESTED GUIDE TO INTERPRETATION OF BLOOD VITAMIN DATA¹
(Young adult males)

Constituent	Deficient	Low	Acceptable	High
Plasma ascorbic acid: mg/100 ml	< 0.10	0.10 - 0.19	0.20 - 0.39	≥ 0.40
Plasma vitamin A: mcg/100 ml	< 10	10 - 19	20 - 49	≥ 50
Red Blood Cell Riboflavin: mcg/100 ml	< 10.0	10.0 - 14.9	15.0 - 19.9	≥ 20.0

¹ Serum levels of nutrients in children do not differ appreciably beyond infancy from those of adults. Similarly plasma levels of these blood constituents in women of child-bearing age are comparable to those of males. No guide is suggested by ICNND for RBC riboflavin during pregnancy. For ascorbic acid and vitamin A, the same values are given.

Legend to Figures

Figure 1: Relation of intake of ascorbic acid and blood plasma concentration.

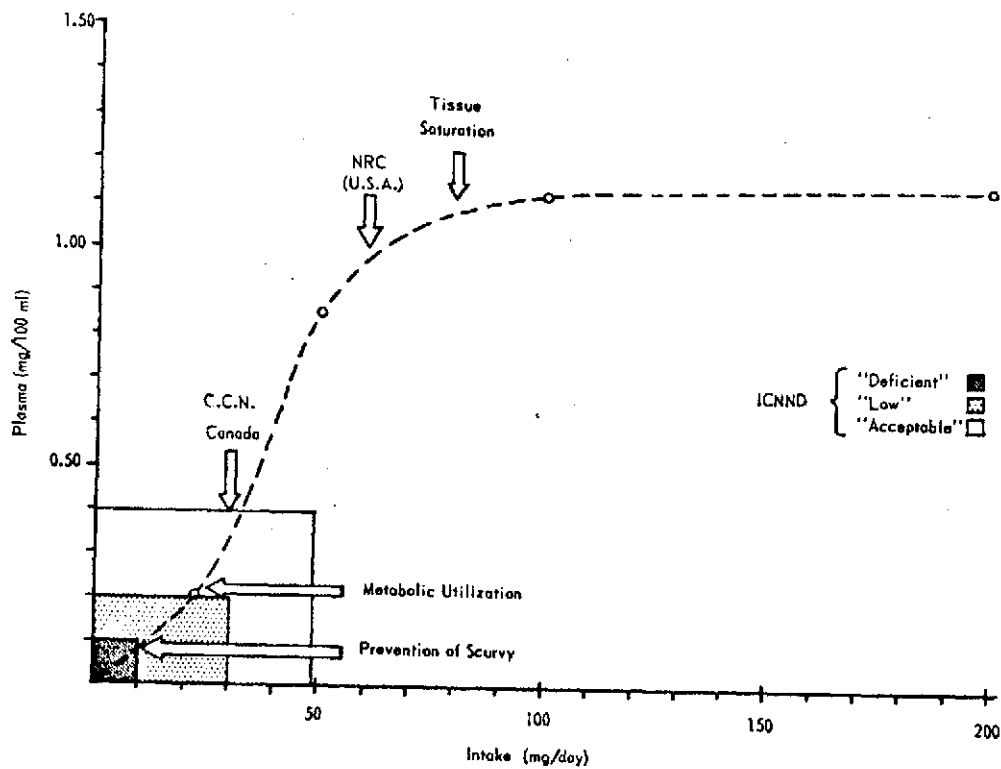
Figure 2: Relationship between thiamine intake and thiamine urinary excretion in adults of 18 countries.

Figure 3: Relationship between intake and urinary excretion of thiamine in Central America.

Figure 4: Relationship between intake and urinary excretion of thiamine in Central America.

Figure 5: Relationship of thiamine intake and urinary excretion.

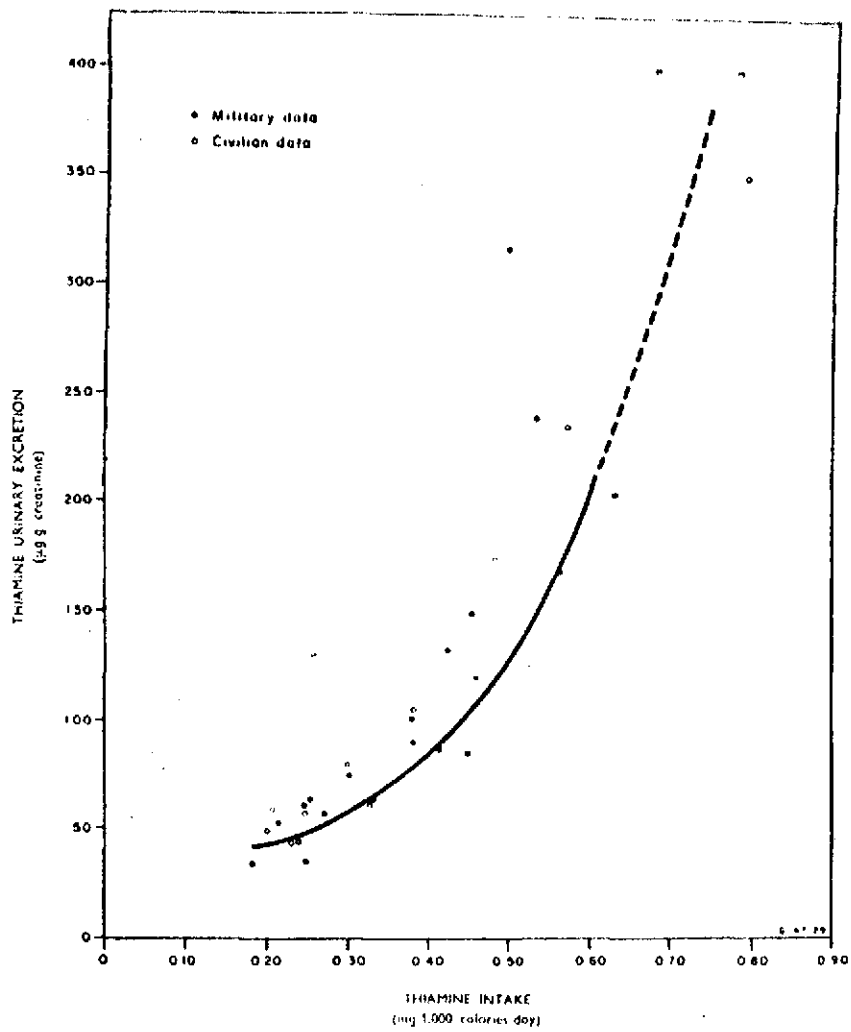
Figure 6: Relationship of vitamin A intake to blood plasma and liver concentration.



Based on data from Lowry *et al.* J. Biol. Chem., 166: 111, 1946, and Rally *et al.* Proc. Soc. Exp. Biol. Med., 40: 604, 1939.

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FIGURE 1

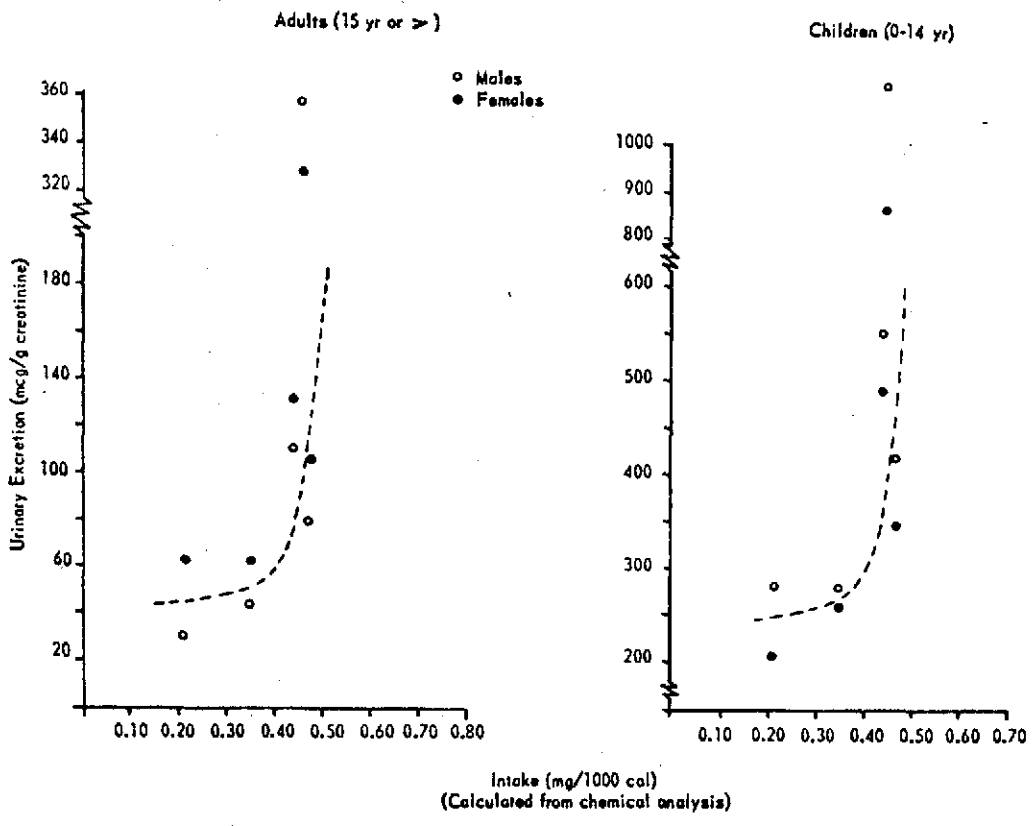


¹ Data from civilian and military groups surveyed by the Interdepartmental Committee on Nutrition for National Defense of the United States of America

From: FAO Nutrition Meetings Report Series No. 41.

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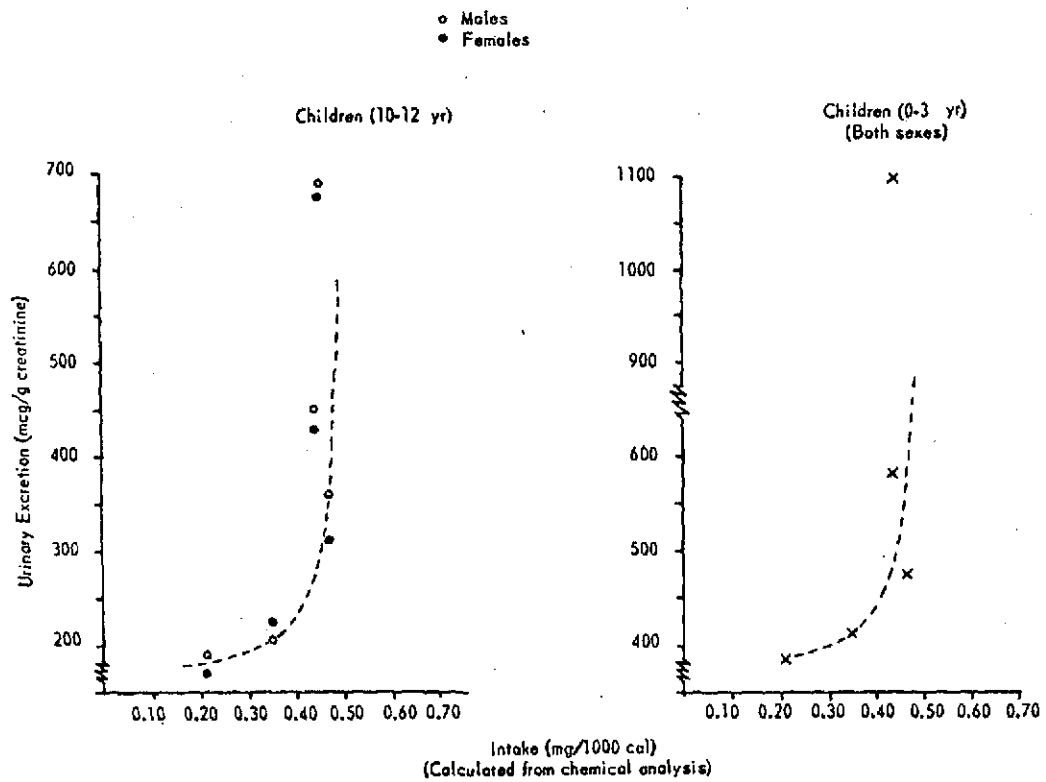
FIGURE 2



From: Arch. Latinoamer. Nutr., 18: 375, 1968.

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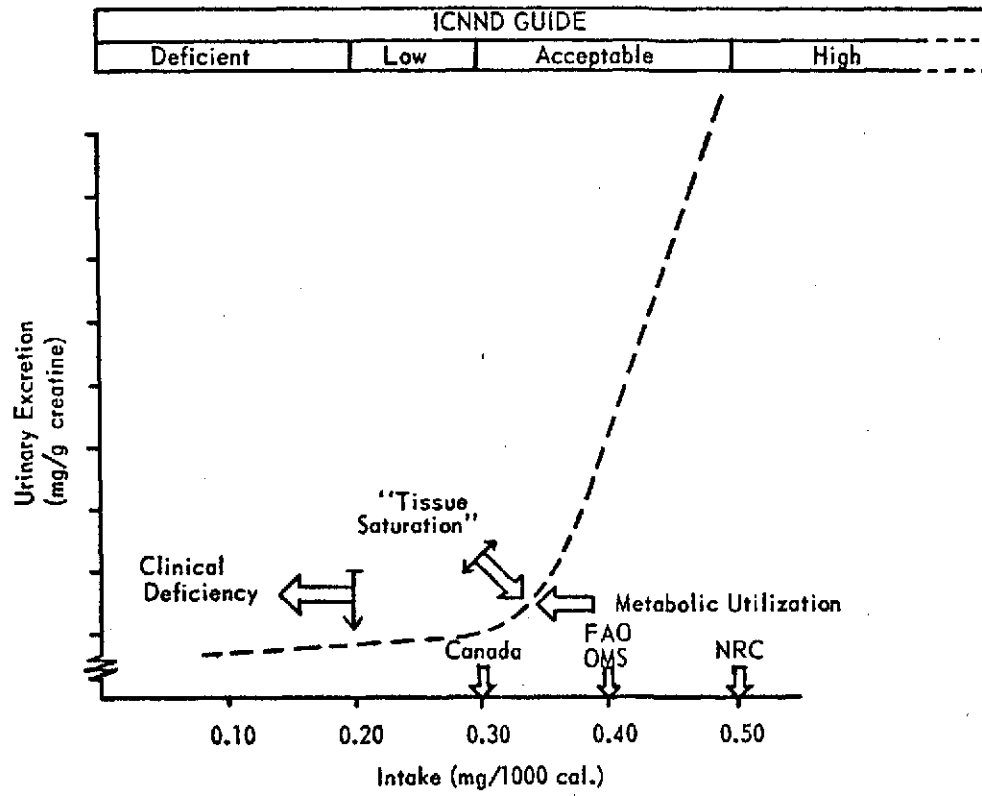
FIGURE 3



From: Arch. Latinoamer. Nutr., 18: 375, 1968.

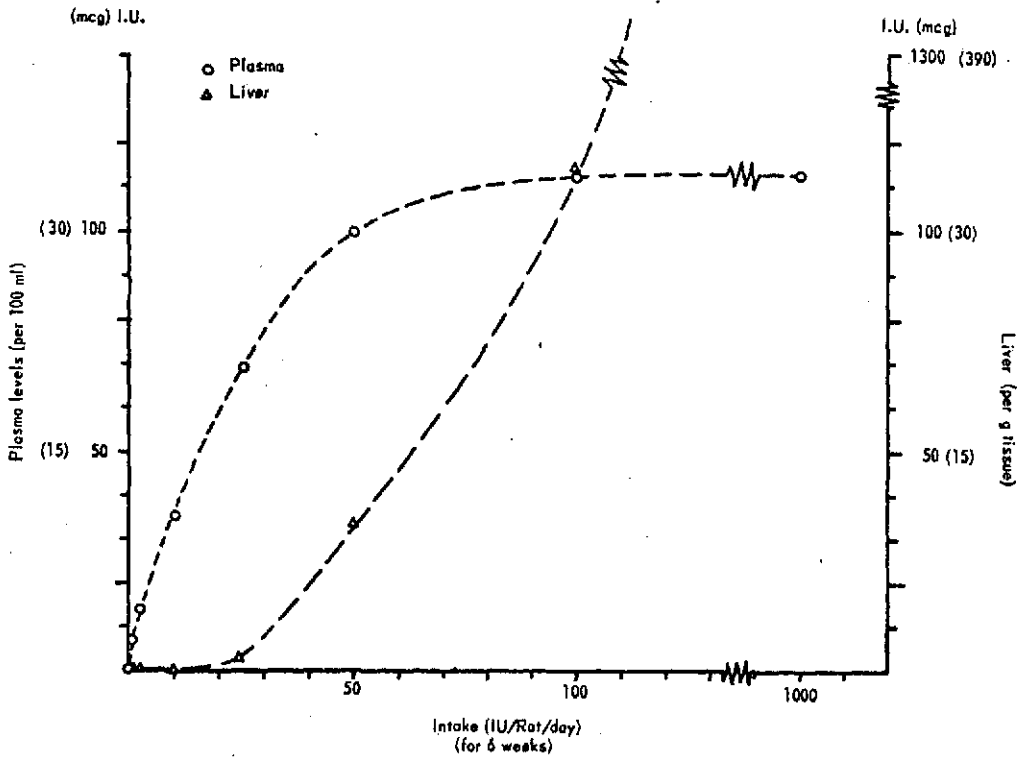
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FIGURE 4



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FIGURE 5



Based on data from Lewis et al., J. Nutrition, 23: 351, 1942.

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FIGURE 6