MEGAVITAMIN THERAPY: THE REALITY
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To understand the reality of megavitamin therapy, it is first necessary to know what a vitamin is and how it functions in the body. A vitamin is "a general term for a number of unrelated organic substances that occur in many foods in small amounts and that are necessary for the normal metabolic functioning of the body." 1 Generally speaking, vitamins function metabolically as coenzymes. 2 In this capacity, vitamins join with apoenzymes (proteins produced by cells) to form holoenzymes. It is the holoenzyme which is capable of catalyzing chemical reactions in the body. With these basics in mind, it is possible to understand how much vitamin is needed.

The requirement for a vitamin which functions as a coenzyme is determined by the amount of apoenzyme a cell can produce. There is a limit to this amount, and a limit to the amount of reaction product the cell desires to be formed as a result of the chemical reaction catalyzed by the holoenzyme. Therefore, the amount of vitamin needed by a cell at any one time is limited. If vitamins are supplied in amounts exceeding the quantity capable of serving as coenzymes, vitamin function will not be served by these substances.

Recommended daily allowances (RDA) of vitamins have been formulated with this need in mind. 3 These amounts of vitamins are easily available if one consumes a diet of unrefined foods, many eaten raw. Megavitamin proponents, however, believe that some people need amounts of vitamins far in excess of what could be supplied in food. It has been stated that "in the human population there may be several alleles of the gene controlling the manufacture of each apoenzyme; in consequence the concentration of coenzyme needed to produce the amount of active enzyme required for optimum health may well be somewhat different for different individuals. In particular, many individuals may require a considerably higher concentration of one or more coenzymes than other people do for optimum health ... ." 4 This is true, but the conclusion that many people would thus need to take supplements is unsupported by any scientific evidence, except in the case of extremely rare genetic defects such as methylmalonic aciduria in which the need for vitamin B 12 may be 1000 times the RDA; 4 and, perhaps, in the case of severe malabsorption syndrome, also rare.

The fact that there are significant inter-individual differences in needs is reflected in the RDA. In fact, the RDA compensates so well for the fact that some people need more of a certain vitamin that it has been occasionally criticized as being too generous, for instance in the RDA for vitamin E. 5 It is therefore, important to reemphasize that no scientific evidence has ever been presented to prove that the vast majority of the population (99.99%) cannot function optimally on the amount of vitamins present in an unrefined food diet. This does not mean that deficiencies cannot develop on a refined food diet — in fact, the contrary is true. But the remedy would be to change the diet, not just add supplements.

There are those, however, who would claim that just in case scientific evidence is presented in the future, perhaps large quantities of vitamins should be consumed daily. But, this may be a dangerous practice for some people. Consider the following possible sources of harm from megavitamin therapy.

Megadoses of niacin have been used to treat hypercholesterolemia (3500 mg/day) 6 and mental illness (300-1500 mg/day). 7 These doses are approximately 20-200 times greater than the RDA. 3 Serious side effects include hepatic toxicity in up to 45% of subjects, 6,8,9 gastrointestinal distress in 20 to 40%, 10 hyperglycemia in 50 to 66% of nondiabetics, 10 hyperuricemia in 62 to 78%, 10,11 and miscellaneous side effects. 10 The effect causing hyperuricemia has been investigated and found to reflect "multipotential pharmacologic actions of 'megadoses' of a simple vitamin." 10 A review of the side effects of niacin concludes that "to be on the safe side one must urge caution in the prolonged use of this drug, as with any that has profound effects on several metabolic systems, the mechanisms of which remain to be elucidated." 9 Also, it should be noted that niacinamide, which may come into wide use since it does not cause the skin flush seen with nicotinic acid, is 2 to 3 times more toxic than the acid. 9

Megadoses of vitamin C are also not free of danger. If an individual with erythrocyte glucose-6-phosphate dehydrogenase deficiency (G-6-PD) consumes too much 'C', the consequences may be a hemolytic crisis. 11,12,13 Perhaps the first death from megavitamins has been recorded in a black male with G-6-PD deficiency. 11 This condition is present in about 15% of black males, and a smaller percent of black females and people of Eastern Mediterranean ancestry. 7

Both proponents 15 and opponents 16 of megadose 'C' therapy recognize that a result is diarrhea in many cases. Irritation of gastrointestinal tract mucosa by ascorbic acid clearly results in an attempt by the body to quickly eliminate this substance. In susceptible individuals, large doses of 'C' can increase urinary oxalate excretion to the point where renal calcification may occur. 17,18,19 Also, uricosuria is induced, possibly causing formation of uric acid stones. 20 Dr. Linus Pauling has, however, noted that if sodium ascorbate were used instead of ascorbic acid, then urine acidification and thus stone precipitation would not occur. 21 But ingestion of large amounts of sodium may cause problems on its own as is well known.

Another side effect is rebound scurvy. If a prolonged large intake of 'C' is reduced to the level found in a normal diet, scurvy may be precipitated due to systemic conditioning. 22,23 Apparently, increased metabolism or excretion of 'C' is induced by continual large doses. 22 While it may be true that this is not a hazard to most people as noted by Dr. Pauling, 21 studies show that it is a hazard to some people. 22,23 Furthermore, the rebound effect may last con-

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siderably longer than a "week or two" as stated by Dr. Pauling.11,22,23

Megadoses of 'C' interfere with normal mineral metabolism. Iron absorption is greatly enhanced 24,25 and this may cause iron overload (hemochromatosis)26, a serious disease. By interacting with absorption or metabolism of copper, 'C' was found to enhance copper deficiency in chicks, a "manifestation of ascorbic acid toxicity per se."27 Far reaching effects on skeletal mineral metabolism 27,28,29 have led some to postulate a possible risk of bone disorders in those who chronically use large doses of 'C'.30 'C' megadoses may destroy vitamin B1231,32 but this has been disputed.33,34 A clinical study, however, supports the possibility of significant destruction.35 Dr. Pauling, without mentioning this clinical study, has stated that there is no danger of this side effect.21 Careful examination of both sides of this argument reveals that the issue is not as yet settled and that, therefore, this side effect must still be regarded as potential.

Megadoses of 'C' may interfere with vitamin A metabolism with a detrimental effect.36 Interaction with anticoagulant drugs has also been observed.37 Also, false positive tests for glucosuria38; and false negative tests for stool occult blood39 may result from ingestion of large doses of 'C'. Dr. Pauling notes that modification of the tests may circumvent this problem 21 but, until such modified tests become widely used, a problem will remain.

Large doses of 'C' may interfere with the reproductive system and cause infertility 40,41 or even fetal death.42 The studies which have reported these findings have not been mentioned by Dr. Pauling when he concluded that "it seems unlikely that ascorbic acid causes abortions to any great extent"; no mention is made of the possibility of infertility.21

A final possible side effect of 'C' megadoses is diabetes.43 although there is not a great chance of this unless very large amounts are used for a long time. The possibility should not, however, be completely disregarded.

Vitamin E is also often used in megadose amounts.44 A review of its side effects, however, concludes that "the long term effects of human hypervitaminosis E cannot be accurately predicted, but there is sufficient published evidence of potential hazards to make the current situation disquieting."45 Negative side effects include deposition of cholesterol in the aorta 47,48; elevation of serum triglycerides 49; and cholesterol 50; reduced vitamin A status 51; coagulopathy, possibly causing hemorrhage in patients with vitamin K deficiency 52,53; enhanced growth of lung tumors 54; gastrointestinal disturbances 55,56; interference with iron metabolism, as reflected by delayed therapeutic response to exogenous iron in iron-deficient patients 57; skin rash 58; interference with thyroid gland function 59,60; creatinuria 61,62; and severe fatigue.46,59,60 The finding of creatinuria with fatigue suggests "induction of some degree of damage to skeletal muscles."59 Indeed it should be considered that "excess vitamin E, like the other fat-soluble vitamins, must be considered as potentially toxic."59

Dichloroacetate (DCA) or panganic acid, so-called "vitamin B15", has never been shown to take part in and be necessary for normal metabolic functioning; therefore, this substance is a drug, not a vitamin. Its side effects include: cyanosis and respiratory failure 61; mild sedation and increased uric acid levels in diabetics 62; possible oxalic acid stone formation and renal dysfunction 63; and mutations possible causing neoplasms.64 Although found in food, this substance seems to be one of the many "toxins occurring naturally in foods"65 and not a vitamin. Even the main proponents of DCA usage admit that "the efficiency and safety of chronic dichloroacetate administration are unknown."62

Studies with megadoses of vitamin B6 have revealed "major changes" in many metabolic functions thus suggesting that "further pharmacological studies on the metabolic effects and the potential toxicity of massive doses of vitamin B6... should be performed before they can be recommended for routine use with impunity."66 Effects on rats included a 20% increase in mean body weight and a 40% increase in mean liver weight, possible due to increased rate of fat deposition.67

The toxicity of megadoses of vitamin A are well known. If 20 to 30 times the RDA (100,000-150,000 IU) is taken for a prolonged period of time, the complications may include fatigue, malaise, lethargy, abdominal discomfort, bone and/or joint pain, severe headaches, insomnia and restlessness, night sweats, loss of body hair, brittle nails, constipa-

...tion, irregular menses, emotional lability, exophthalmos, peripheral edema, mouth fissures, and dry, scaly, rough skin.67

Toxic doses of vitamin D are in the range of 1000 to 3000 IU per kilogram body weight (RDA is 400 IU). Such amounts may cause nausea, diarrhea, weight loss, nocturia, renal damage, and soft tissue calcification.68

CONCLUSION

This article has reviewed the literature regarding the rationale and side effects of megadose vitamin therapy. Theoretical biochemical considerations have shown that megadoses cannot act as vitamins, since the body can only use a limited amount of these substances in a vitamin role. Vitamins supplied in excess of the body's needs, therefore, must be regarded as drugs. The literature on megadose vitamin therapy clearly shows pharmacological effects of these substances, replete with side effects. It should be no surprise that there are side effects if amounts of vitamins far in excess of what could be consumed in food are taken in supplement form. Any natural substance, including water, if used in too large an amount, can raise metabolic havoc.

It would seem that a general principle in nutrition might be that any fragmented food is potentially harmful since the body is only able to metabolize normally a food in the whole state. The term "fragmented food" could describe not only white flour and white sugar, but also large amounts of vitamins given apart from the food in which they would normally be found.

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