Safety of Vitamin C: Urban Legends

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Often the benefits of vitamin C observed in randomized double-blind placebo-controlled trials are disregarded, although at the same time authors may exaggerate the potential harm caused by vitamin C even when it is purely anecdotal (see for example Olson & Hodges 1987; Herbert 1993).

In a casual survey of 20 physician colleagues, Goodwin and Tangum (1998) found that all of them were aware that high-dose vitamin C ingestion can cause kidney stones. Goodwin and Tangum were, however, interested in where this common 'knowledge' comes from and they combed the medical literature without finding any articles in refereed journals reporting instances of high-dose vitamin C causing kidney stones. Review articles cited book chapters that in turn cited abstracts, letters, and other review articles. Goodwin and Tangum concluded that nowhere in the trail of citations was there any fundamental information on whether or how frequently high-dose vitamin C supplementation might lead to kidney stones. The authors simply stated that vitamin C may cause kidney stones, and as proof they cited other authors who had said the same thing. Thus, this description reveals a typical urban legend; a story that is retold, yet no-one confirms that the story is true.

The anecdote of vitamin C and kidney stones is mentioned in a major textbook of pharmacology: "…risks of megadose treatment ... include formation of kidney stones" (Marcus & Coulston 2001). The statement that vitamin C may cause kidney stones has been reiterated, e.g., in the Nordic Nutritional Recommendations without any references (NNR 2004 p 310).

When reviewing the health effects of vitamin C, Olson and Hodges (1987) and Herbert (1993) claimed that "Large intakes of vitamin C may reduce insulin production." This statement was based on a paper published in 1946. Levey and Suter (1946) reported that vitamin C potentiates the diabetogenic action of alloxan in rats, whose blood-sugar level was determined 3 days after injecting alloxan, or alloxan with vitamin C. Hyperglycemia was observed in 50% of the rats treated with alloxan and vitamin C, in contrast to 17% of the rats treated with alloxan alone. Nevertheless, the authors concluded from their own previous work that "ascorbic acid alone does not produce hyperglycemia" (Levey & Suter 1946). Thus, this old experiment with alloxan- treated rats was the basis for Olson and Hodges (1987) and Herbert (1993) to state that large doses of vitamin C alone may reduce insulin production in human subjects.

Olson and Hodges (1987) and Herbert (1993) stated that "Large intakes of vitamin C may interrupt pregnancies." This suggestion was based on a brief Russian paper published in 1964. Twenty women whose menstruation was delayed by 10-15 days were given 6 g/day of vitamin C, and 16 of them started to menstruate within 3 days (Samborskaya & Ferdman 1966). Pauling (1976a) wrote a letter to the authors inquiring whether any actual direct test of pregnancy was carried out, but he received only a copy of the publication by way of reply. Thus, there was no evidence that the women were pregnant to begin with. Possibly the women just had irregular menstruation, yet this report was valid enough for Olson and Hodges (1987) and Herbert (1993) to conclude that vitamin C may cause miscarriages.

Olson and Hodges (1987) and Herbert (1993) also argued that "Large intakes of vitamin C may lower plasma vitamin B12 levels." This claim was originally made by Herbert himself (Herbert & Jacob 1974), however, it was shown afterwards that the apparent breakdown of vitamin B12 was due to methodological shortcomings (Newmark et al. 1979; Marcus 1981), and the vitamin B12 level was not decreased in patients administered as much as 4 g/day of vitamin C for 11 months or more (Afroz et al. 1975), or in children administered gram-doses of vitamin C for years (Ekvall et al. 1981). However, these papers were not cited by Olson and Hodges (1987) or Herbert (1993).

In extreme cases, suggestions about vitamin C toxicity have been based on double-speculation. Herbert (1993) stated that (1) vitamin C might cause elevated iron levels, and (2) elevated iron levels might cause increased risk of coronary heart disease. However, (1) in order to quantify the effect of vitamin C supplementation on iron status, Cook et al. (1984) administered 2 g/day of vitamin C to 9 subjects for 2 years without finding indications of

iron accumulation, and (2) several studies with different types of settings were unable to corroborate the hypothesis that raised iron levels increase the risk of coronary heart disease (Bendich & Langseth 1995; Hemilä & Paunio 1997). In contrast to ordinary people, patients suffering from actual iron overload may derive harm from vitamin C; however, its harmful effect on these particular patients and the rationale of treating such patients with the combination of vitamin C and desferrioxamine has been known for a long time (Nienhuis 1981).

Rivers (1987) reviewed 74 publications dealing with the possible toxicity of vitamin C and concluded that "Large quantities of ascorbic acid will not result in calcium-oxalate stones, increased uric acid excretion, impaired vitamin B12 status, iron overload, systemic conditioning, or increased mutagenic activity in healthy individuals." In another review, Marks (1989) concluded that "A large number of adverse reactions have been alleged to occur with the use of large doses of ascorbic acid, but almost without exception further study has demonstrated that the allegations are without foundation ... an overview of all the information shows that the safe daily level is at least 100 times the RDA." The RDA level for vitamin C was 60 mg/day at that time. Hathcock (1997) stated that "Many hypothetical adverse effects of high intakes of vitamin C have been cited for decades. Most, with the exception of mild and transient gastrointestinal effects, seem to have little or no known factual basis." Several other reviews have also concluded that vitamin C is safe in doses around 1 g/day (Hanck 1982; Bendich & Langseth 1995; Diplock 1995; Hathcock et al. 2005). The recent US nutritional recommendations suggest that the safe range of vitamin C intake goes to 2 g/day for adults, but the basis for this upper limit of ‘safe doses’ is the appearance of loose bowels (FNB 2000 pp 155-65), which, however, is quite a trivial adverse effect and disappears quite quickly with a change to lower intake levels.

There are a few reports of severe harm caused by highdose vitamin C administration. Nevertheless, the death of a 68-year old African American man was not attributed to intravenous injection of 80 grams of vitamin C on 2 consecutive days per se, but to his coincident glucose-6-phosphate deficiency (Campbell et al. 1975). Such isolated instances have no public health relevance. In a recent pharmacokinetic study participants were administered up to 100 grams of vitamin C within a few hours indicating the safety of such a large dose per se in healthy people (Padayatty et al. 2004). There is much evidence indicating that vitamin C metabolism changes during infections and this may affect the relationship between doses and adverse effects (Hemilä 2006 pp 6-7; seeMetabolism). It has been reported that people with serious infections can ingest over 50 g/day of vitamin C without gastric problems (Luberoff 1978; Cathcart 1981).

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