

## Screening for Vitamin C in the Urine: Is it Clinically Significant? 298

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Humans cannot make vitamin C (ascorbic acid or ascorbate) and must obtain it through the diet or as supplements.<sup>1</sup> If taken orally several important things must occur to get an adequate supply of vitamin C to the tissues. The substance containing vitamin C must be digested, absorbed, metabolized and excreted. If given intravenously, the digestion and absorption process is, of course, bypassed.

Since vitamin C is a water-soluble vitamin, any excess in the blood should appear in the urine, providing there is normal renal function. Vitamin C disappears from the urine early in blood or tissue depletion. Plasma levels fall next and tissue levels (such as in leukocytes and platelets) are the last to fall.<sup>2</sup> In healthy human tissues the maximum vitamin C pool varies. Data from the literature gives three different ranges, from 1500 to 5,000 mg (20, 22, 32 mg per kg of body weight).<sup>3,4,5</sup>

The half-life of vitamin C in tissues varies depending on the literature data, from 16 to 20 days. Assuming a tissue level of 5000 mg, a lack of vitamin C in the diet for 16 days would reduce the tissue store to about 2500 mg; in 32 days it would be about 1250 mg; in 44 days it would be 625 mg and in 64 days it would be about 313 mg and clinical signs of scurvy should start to develop.<sup>5,6</sup>

Again, depending on the reference, the renal threshold of plasma vitamin C is 0.8, 1.4, or 1.7 mg/dL and further intake results in a rapid urine clearance.<sup>7,8,9</sup> Vitamin C levels in the body of 1500 mgs or less will result in no urinary

excretion of vitamin C.<sup>9</sup> However, certain medications such as aspirin, aminopyrine, barbiturates, hydantoins and paraldehyde as well as cold or heat stress are known to increase the excretion of vitamin C in the urine.<sup>10,11</sup>

When vitamin C stores are depleted, very little vitamin C appears in the urine after a test dose.<sup>9</sup> The U.S. RDA for vitamin C is 75 mg for females and 90 mg for males with an additional 35 mg if one smokes cigarettes.<sup>12</sup> It is important to remember that the RDA nutrient guide was designed to prevent deficiency diseases with a little nutrients to spare. It does not guarantee optimal or good health.

Many animals produce vitamin C at levels much higher than that recommended for humans. When an animal is under stress or has an illness, the amount of vitamin C produced increases tremendously. For example, a 70 kg goat (the average weight used in calculations for adult males) will produce vitamin C at 33 mg/kg/day or 2.31 g/day. Under stress or disease, the goat can produce 190 mg/kg/day or 13.3 g of vitamin C a day! The RDA for human males equals to about 1.3 mg/kg/day or about 91 mg a day (1.3 times 70 kg).<sup>1</sup>

Vitamin C can be excreted in the urine unchanged as ascorbic acid, as dehydroascorbic acid, 2,3-diketogluconic acid and oxalic acid. Since oxalate is a part of common kidney stones (calcium oxylate), some have suggested that high doses of vitamin C will cause kidney stones. The Center has a thirty year history of treating patients with vitamin C, sometimes in very large I.V. doses and large oral doses. There have been no serious health effects of vitamin C in these patients.

1. The Center for the Improvement of Human Functioning International, Inc., 3100 N. Hillside Ave., Wichita, KS 67219

Of course, patients who are prone to developing kidney stones should take vitamin C under a physician's supervision. If prone to kidney stones, they would probably develop the stones without vitamin C. If vitamin C was the sole cause of kidney stones, it would seem that herbivores, many who can make grams of vitamin C a day and usually have an alkaline urine (two parameters for formation of common kidney stones), would have an epidemic of kidney stones.

Vitamin C has many vital functions in the body. Therefore, it is important to have a way of measuring it. For over twenty-five years, Dr. Hugh D. Riordan included a plasma and urine vitamin C as part of the initial testing for all new patients. Measurement of plasma vitamin C is a very complicated procedure that takes several hours to perform. The Bio-Center Laboratory performs this test by HPLC. A sublingual, lingual or intradermal test using a dye has been tried, but with conflicting results. A capillary fragility test using a blood pressure cuff is useful in severe vitamin C deficiency.

Urine vitamin C can also be performed by HPLC, but it is much easier to do a screening test on the urine by a dipstick. Dr. Riordan first used the C-Stix® (Ames Division, Miles Laboratories, Elkhart, IN). This product is no longer available. The strip was dipped in fresh urine, excess urine removed and after 10 seconds, the reagent side was compared to a color chart on the bottle. The color chart was 0, 5, 10, 20, and 40 mg/dL. A vitamin C reagent area is included on many multiple strips as a check for vitamin C in the urine as an interfering substance for several of the other tests (blood, glucose, bilirubin and nitrite), depending on the manufacturer of the strip

Over the last two years, Dr. Riordan and one of the authors (JAJ), searched the various manufacturers of urine strips for a product similar to the C-Stix.® Dr. Riordan

wanted a strip that could be used by patients at home as well as in the laboratory to monitor urine vitamin C levels. It was decided that the color chart should have an extended range of 50 and 100 mg/dL.

A company, Teco Diagnostics (Anaheim, CA), agreed to make a strip to our specifications with a color chart that included a 50 and 100 mg/dL color areas. After evaluating the strip against other strips with a vitamin C area and various standards and numerous patients, we accepted the product and named the strip VitaChek-C®

As stated before, Dr. Riordan used the vitamin C reagent area as a screening test for nutritional amounts of vitamin C rather than a test for interfering substances. The theory being, if tissues were saturated, the water-soluble vitamin C would be excreted in large amounts in the urine. People on a regular diet with no illness or severe stress, should excrete about 20 to 30 mg/dL a day in their urine.<sup>13</sup> Dr. Riordan preferred to have the urine vitamin C 40 mg/dL or above.

After examining patient data (Table 1, p.261), it is obvious that the renal threshold of 1.4 mg/dL for vitamin C was not all that predictable.

The data showed 3,871 (59%) of patients had a plasma vitamin C of 0.1 to 1.3 mg/dL (normal is 0.6 to 2.0 mg/dL). This is below the "renal threshold" of 1.4 mg/dL. Of these, 881 (23%) had 30 to 40+ mg/dL of vitamin C in their urine. It is also interesting to note that 812 patients had plasma vitamin C levels of 0.1 to 0.5 mg/dL, or biochemical scurvy! There were 2,666 patients with plasma C levels above the "renal threshold." Of these 1,285 (48%) had urine vitamin C of "0" to 20 mg/dL.

We also compared the urine C results to the urine specific gravity in 276 patients. Specific gravity (SG) had no effect on the urine C results. Many dilute urines (SG 1.001- 1.010) had high levels of vitamin C while many concentrated urines (1.020- 1.035) had low levels of vitamin C.

Table 1.

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MONITORING their own urine for many years the common way to monitor CLINITE dipstick Division adults a blood glucose "meter" Other tests to measure course a supervisory We strip to is a common patients C. A common mg/dL or something

References

1. Levine biochem 1986; 3
2. Bralley in mol

Table 1. Comparison of plasma vitamin C with urine vitamin C in 6,537 patients.

Range of Plasma C mg/dL, (number of patients)*	Number (%)	
	0 - 20 mg/dL Urine C	30 - 40+ mg/dL Urine C
4.3 to 5.0 (n=36)	2 (6%)	34 (94%)
3.6 to 4.2 (n=55)	7 (13%)	48 (87%)
3.1 to 3.5 (n=80)	16 (20%)	64 (80%)
2.6 to 3.0 (n=187)	41 (22%)	146 (78%)
2.0 to 2.5 (n=627)	280 (46%)	347 (54%)
1.4 to 1.9 (n=1681)	939 (59%)	692 (41%)
0.6 to 1.3 (n=3059)	2303 (75%)	756 (25%)
0.1 to 0.5 (n=812)	687 (84%)	125 (16%)

\*= plasma vitamin C measured by HPLC (normal value is 0.6 to 2.0 mg/dL), urine by VitaChek-C<sup>®</sup>

Monitoring of diseases by testing their own urine has been used by patients for many years. Before the invention of the computer chip and microprocessors, many health professionals and patients monitored diabetes with urine and the CLINITEST<sup>®</sup> tablet, then later with a urine dipstick for glucose and ketones (Ames Division, Miles Laboratories, Inc). Now adults and children measure their own blood glucose with a glucose strip and "meter" to help control their diabetes. Other tests are also available for patients to measure blood cholesterol, etc. Of course any such test should be under the supervision of your physician.

We continue to use the VitaChek-C<sup>®</sup> strip to screen urine for vitamin C. It is a convenient way for physicians and patients to monitor the urine vitamin C. A consistent urine vitamin C of 20 mg/dL or lower may be trying to tell you something.

#### References

1. Levine M: New concepts in the biology and biochemistry of ascorbic acid. *N Engl J Med*, 1986; 314: 892-901.
2. Bralley A, Lord, RS: Laboratory evaluations in molecular medicine: nutrients, toxicants,

and cell regulators. *IAMM*, Norcross, Ga. 2001; 26-27.

3. Ginter E: In: *Understanding Vitamin and Minerals*, Rodale Press, Emmaus, Pa., 1984: 58-59.
4. Jacob RA: Vitamin C. In: *Modern Nutrition in Health and Disease*. Ninth Edition. Edited by Maurice Shiels, James Olsen, Moshe Shike, A. Catherine Ross. Baltimore: William and Wilkens, 1999: 467-482.
5. McEvoy GR: *Drug Information: The American Hospital Formulary Service*, American Society of Health System Pharmacists, Inc., 1993, MD.
6. Sauberlich HE: Bioavailability of vitamins. *Proc Food Nutr Sci*, 1985: 1-33.
7. Sauberlich HE: In: *Present Knowledge in Nutrition* (Edited by Brown ML). Nutrition Foundation, Washington, DC, 1990.
8. Hellman L, Burns JJ: Metabolism of L-ascorbic Acid-1-C14 in man. *J Biol Chem*, 1958, 230:923.
9. Groff JL, Gropper SS, Hunt SM: The water soluble vitamins. In: *Advanced Nutrition and Human Metabolism*. Minneapolis: West Publishing Company, 1995: 222-237.
10. Jacob RA: Assessment of human vitamin C status. *J Nutr*, 120(suppl 11): 1480, 1990.
11. Washko PW, et al: Ascorbic acid and dehydroascorbic acid analysis in biological samples. *Analyt Biochem*, 204:1, 1992.
12. Frei B, Traber M: The new US dietary reference for vitamin C and E. *Redox Rep*, 2001, 6: 5-9.
13. Product Insert, Urine Reagent Strip-11, *Teco Diagnostics* 1268 N. Lakeview Ave, Anaheim, CA. 92807.