CAUTION: Beware of the Impact of Intravenous Vitamin C on Renal Function
Intravenous Vitamin C- Safety

- Relative safety well documented in the medical literature
- Predominantly minor side effects (thirst, nausea).\(^6,7,8,9,10,11,12,18,20,21\)
- CAM study 2008
- However, 2 reported deaths in patients with acute renal failure \(^{19,26}\)
- The proposed mechanism of death: acute oxalate nephropathy.
- Contraindications: glucose-6-phosphate dehydrogenase deficiency\(^{13}\), hemochromatosis \(^{14}\)
- Precautions: Hx of renal oxalate stones, renal impairment or renal failure \(^{15,16,17,18,19,20,21}\)
Our Experience

- Safe administration of i.v. vitamin C for > 30 years.
- Treatment 1-2 infusions/week
- No serious adverse events
  - Definition: Serious adverse event - events where the patient either died, required hospitalisation or prolonged existing hospitalisation, required intervention to prevent permanent disability/incapacity, resulted in a congenital abnormality, or where the event was life-threatening. [www.medsafe.govt.nz](http://www.medsafe.govt.nz)
RNZCGP CQI Activity

- Looked at renal function in ~ 200 consecutive patients
- Renal function measured at start, 4 weeks, then 12 weekly
- 9/200 patients -> 15-20% decline in s.creatinine
- GP review
- Identification of causative/ confounding factors
Potential Causative and Confounding Factors

- Dehydration
- Autoimmune disorder
- Uncontrolled BP
- Uncontrolled DM
- Urinary tract outflow obstruction e.g. BPH, intra-abdominal tumour, Ca prostate, mets
- Renal stone, reflux nephropathy or other renal abn
- Medications e.g. NSAIDs, diuretics, anti-viral agents, aminoglycosides, cephalosporins et cetera
- Infection/ sepsis
- Dietary confounders: eggs, bacon, steak, oral vitamin C
- Proximity of the blood test to the ascorbic acid infusion.
### Vitamin C and Renal Function

<table>
<thead>
<tr>
<th>#</th>
<th>Age</th>
<th>Date (Start)</th>
<th>Creatinine</th>
<th>eGF R</th>
<th>Date (End)</th>
<th>Post-Creatinine</th>
<th>Post-eGF R</th>
<th>% Change</th>
<th>Possible contributing factor</th>
<th>Date (Outcome)</th>
<th>Creatinine (Outcome)</th>
<th>eGF R (Outcome)</th>
<th>% Change</th>
<th>Outcome</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>07/10/10</td>
<td>68</td>
<td>90</td>
<td>02/03/11</td>
<td>98</td>
<td>75</td>
<td>44%</td>
<td>Oral vit C and scrambled eggs on toast</td>
<td>11/03/11</td>
<td>82</td>
<td>90</td>
<td>21%</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>12/11/10</td>
<td>59</td>
<td>89</td>
<td>08/04/11</td>
<td>73</td>
<td>70</td>
<td>24%</td>
<td>chronic left ear otitis externa</td>
<td>29/04/11</td>
<td>70</td>
<td>73</td>
<td>19%</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>29/04/10</td>
<td>65</td>
<td>80</td>
<td>11/03/11</td>
<td>78</td>
<td>65</td>
<td>20%</td>
<td>Oral vit C</td>
<td>22/03/11</td>
<td>71</td>
<td>72</td>
<td>9%</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>03/02/10</td>
<td>76</td>
<td>88</td>
<td>08/03/11</td>
<td>104</td>
<td>61</td>
<td>37%</td>
<td>Steak and oral vitamin C</td>
<td>22/03/11</td>
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<td>74</td>
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<td>N</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>19/01/11</td>
<td>75</td>
<td>73</td>
<td>09/03/11</td>
<td>91</td>
<td>58</td>
<td>21%</td>
<td>Took alpha lipoic acid and oral vitamin C</td>
<td>16/03/11</td>
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<td>63</td>
<td>13%</td>
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</tr>
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<td>6</td>
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<td>18%</td>
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<td>03/06/11</td>
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<td>76</td>
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<td>N</td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>05/11/11</td>
<td>70</td>
<td>71</td>
<td>18/03/11</td>
<td>77</td>
<td>63</td>
<td>10%</td>
<td>Ibuprofen and iv vitamin C on same day</td>
<td>26/04/11</td>
<td>72</td>
<td>68</td>
<td>3%</td>
<td>N</td>
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<tr>
<td>8</td>
<td>61</td>
<td>26/01/11</td>
<td>70</td>
<td>74</td>
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<td>Oral vit C</td>
<td>12/04/11</td>
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<td>76</td>
<td>-3%</td>
<td>N</td>
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<tr>
<td>9</td>
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<td>01/12/10</td>
<td>60</td>
<td>86</td>
<td>22/02/11</td>
<td>99</td>
<td>48</td>
<td>65%</td>
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<td>05/05/11</td>
<td>55</td>
<td>80</td>
<td>-8%</td>
<td>normalised</td>
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### Renal function returns to pre-treatment levels

<table>
<thead>
<tr>
<th>Age</th>
<th>Date</th>
<th>Creatinine</th>
<th>eGFR</th>
<th>Date</th>
<th>Post-Creatinine</th>
<th>Post-eGFR</th>
<th>% Change</th>
<th>Possible contributing factor</th>
<th>Date</th>
<th>Rpt Cr</th>
<th>Rpt eGFR</th>
<th>% change</th>
<th>Outcome</th>
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</thead>
<tbody>
<tr>
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<td>07/10/10</td>
<td>68</td>
<td>90</td>
<td>02/03/11</td>
<td>98</td>
<td>75</td>
<td>44%</td>
<td>Oral vit C and scrambled eggs on toast</td>
<td>11/03/11</td>
<td>82</td>
<td>90</td>
<td>0%</td>
<td>N</td>
</tr>
<tr>
<td>64</td>
<td>12/11/10</td>
<td>59</td>
<td>89</td>
<td>08/04/11</td>
<td>73</td>
<td>70</td>
<td>24%</td>
<td>chronic left ear otitis externa</td>
<td>29/04/11</td>
<td>70</td>
<td>73</td>
<td>-18%</td>
<td>N</td>
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<tr>
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<td>65</td>
<td>80</td>
<td>11/03/11</td>
<td>78</td>
<td>65</td>
<td>20%</td>
<td>Oral vit C</td>
<td>22/03/11</td>
<td>71</td>
<td>72</td>
<td>-10%</td>
<td>N</td>
</tr>
<tr>
<td>73</td>
<td>03/02/10</td>
<td>76</td>
<td>88</td>
<td>08/03/11</td>
<td>104</td>
<td>61</td>
<td>37%</td>
<td>Steak and oral vitamin C</td>
<td>22/03/11</td>
<td>88</td>
<td>74</td>
<td>-16%</td>
<td>N</td>
</tr>
<tr>
<td>45</td>
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<td>75</td>
<td>73</td>
<td>09/03/11</td>
<td>91</td>
<td>58</td>
<td>21%</td>
<td>Took alpha lipoic acid and oral vitamin C</td>
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<td>76</td>
<td>17/03/11</td>
<td>80</td>
<td>63</td>
<td>18%</td>
<td>Oral vitamin C</td>
<td>03/06/11</td>
<td>68</td>
<td>76</td>
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<td>N</td>
</tr>
<tr>
<td>75</td>
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<td>70</td>
<td>71</td>
<td>18/03/11</td>
<td>77</td>
<td>63</td>
<td>10%</td>
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<td>30/03/11</td>
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<td>56</td>
<td>27%</td>
<td>Oral vit C</td>
<td>12/04/11</td>
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<td>76</td>
<td>3%</td>
<td>N</td>
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<tr>
<td>69</td>
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<td>60</td>
<td>86</td>
<td>22/02/11</td>
<td>99</td>
<td>48</td>
<td>65%</td>
<td>Played golf in the heat and got dehydrated, taking voltaren plus low dose aspirin</td>
<td>05/05/11</td>
<td>55</td>
<td>80</td>
<td>-7%</td>
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</table>
Renal function remains stable

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Date</th>
<th>Creatinine after re-challenge iv vit C</th>
<th>eGFR after re-challenge iv vit C</th>
<th>% change as compared with baseline</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>38</td>
<td>19/07/11</td>
<td>71</td>
<td>90</td>
<td>0%</td>
<td>stable</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>64</td>
<td>21/06/11</td>
<td>70</td>
<td>73</td>
<td>-18%</td>
<td>stable</td>
<td>chronic left ear infection persists</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>15/07/11</td>
<td>61</td>
<td>86</td>
<td>-6%</td>
<td>stable</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>73</td>
<td>28/06/11</td>
<td>91</td>
<td>71</td>
<td>-19%</td>
<td>stable</td>
<td>obstruction due to unknown metastatic nodal disease in right ileocolic vessels</td>
</tr>
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<td>5</td>
<td>45</td>
<td>16/06/11</td>
<td>71</td>
<td>77</td>
<td>-5%</td>
<td>stable</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>63</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>75</td>
<td>26/05/11</td>
<td>74</td>
<td>66</td>
<td>0%</td>
<td>stable</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>61</td>
<td>26/04/11</td>
<td>74</td>
<td>69</td>
<td>0%</td>
<td>stable</td>
<td></td>
</tr>
</tbody>
</table>
Vitamin C and serum Creatinine

- Cephalosporin antibiotics, NSAIDs, aminoglycosides, anti-viral agents, diuretics, lithium all may cause elevations in serum creatinine.

- Vitamin C causes a false rise in s. creatinine by ~26% by reduction of the chemical analyte picrate to picramate.\(^{27,28,29,30}\)

- Laboratory measurement of s. creatinine may vary by 20-30%.

- Other interesting things:
  - Protein, eggs, bacon and steak, glucose may also interfere in the assay causing falsely high values.\(^{29,30}\)
Vitamin C and Renal Stones

- Controversial
- Oxalate stone formers more at risk?
- Vitamin C appears to cause a modest increase in urinary oxalate excretion........
Vitamin C and Renal Stones

- Urinary oxalate excretion affected by diet e.g. leafy greens, spinach, nuts, chocolate, cranberry, high animal protein, low calcium, low fluid intake
- And by age, gender, ethnicity, BMI, gut health and transport, enzyme deficiencies et cetera
- Ascorbic acid converts to oxalate during storage, handling, processing, and analysis 11,12, 15-20, 22-25
- When the urine sample is stored, handled and processed correctly <0.5% of the administered dose of vitamin C is recovered as oxalic acid 12
- Oxalate stones take months/ years to develop......
- Does vitamin C cause oxalate stones?
A prospective study of the intake of vitamins C and B6, and the risk of kidney stones in men.
Curhan, G.C., Willett, W.C., Rimm, E.B. & Stampfer, M.J.

**Abstract**: PURPOSE: The association between the intake of vitamins C and B6, and kidney stone formation was examined. MATERIALS AND METHODS: We conducted a prospective study of the relationship between the intake of vitamins C and B6 and the risk of symptomatic kidney stones in a cohort of 45,251 men 40 to 75 years old with no history of kidney calculi. Vitamin intake from foods and supplements was assessed using a semiquantitative food frequency questionnaire completed in 1986. RESULTS: During 6 years of followup 751 incident cases of kidney stones were documented. Neither vitamin C nor vitamin B6 intake was significantly associated with the risk of stone formation. For vitamin C the age-adjusted relative risk for men consuming 1,500 mg. daily or more compared to less than 250 mg. daily was 0.78 (95% confidence interval 0.54 to 1.11). For vitamin B6 the age-adjusted relative risk for men consuming 40 mg. daily or more compared to less than 3 mg. daily was 0.91 (95% confidence interval 0.64 to 1.31). After adjusting for other potential stone risk factors the relative risks did not change significantly. CONCLUSIONS: These data do not support an association between a high daily intake of vitamin C or vitamin B6 and the risk of stone formation, even when consumed in large doses.

Intake of vitamins B6 and C and the risk of kidney stones in women.
Curhan, G.C., Willett, W.C., Speizer, F.E. & Stampfer, M.J.

[Abstract] [URL]
A prospective study of the intake of vitamins C and B6, and the risk of kidney stones in men.
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[Abstract]

Intake of vitamins B6 and C and the risk of kidney stones in women.
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[Abstract] [URL]

Abstract: Urinary oxalate is an important determinant of calcium oxalate kidney stone formation. High doses of vitamin B6 may decrease oxalate production, whereas vitamin C can be metabolized to oxalate. This study was conducted to examine the association between the intakes of vitamins B6 and C and risk of kidney stone formation in women. The relation between the intake of vitamins B6 and C and the risk of symptomatic kidney stones were prospectively studied in a cohort of 85,557 women with no history of kidney stones. Semiquantitative food-frequency questionnaires were used to assess vitamin consumption from both foods and supplements. A total of 1078 incident cases of kidney stones was documented during the 14-yr follow-up period. A high intake of vitamin B6 was inversely associated with risk of stone formation. After adjusting for other dietary factors, the relative risk of incident stone formation for women in the highest category of B6 intake (> 40 mg/d) compared with the lowest category (< 3 mg/d) was 0.66 (95% confidence interval, 0.44 to 0.98). In contrast, vitamin C intake was not associated with risk. The multivariate relative risk for women in the highest category of vitamin C intake (> or =1500 mg/d) compared with the lowest category (< 250 mg/d) was 1.06 (95% confidence interval, 0.69 to 1.64). Large doses of vitamin B6 may reduce the risk of kidney stone formation in women. Routine restriction of vitamin C to prevent stone formation appears unwarranted.
26 August 2011

Dr Penny Warring
Level 3, 110 Remuera Rd
Remuera
AUCKLAND 1050

Dear Penny

Ethics ref: NTX11/EXP/189 (please quote in all correspondence)
Study title: Monitoring renal function and kidney stones after intravenous vitamin C
Principal investigator: Dr Penny Warring
Co-investigators: Dr Nicky Baillie, Dr Anne O’Reilly

Thank you for your application received 23 August 2011. This study was given ethical approval by the Deputy Chairperson of the Northern X Regional Ethics Committee on 24 August 2011.
Be Aware

- Laboratory measurement of s. creatinine may vary by 20-30%.
- Multiple factors including drugs, medical conditions, level of hydration, high dietary protein and supplement intake affect s. creatinine.
- Advise patients to wait 48 hours after consuming steak, eggs, bacon, oral or intravenous vitamin C; and to be well hydrated, prior to renal function testing.
- Consider repeating the test before jumping to conclusions.
- Monitor, evaluate, reflect, and repeat measures.
PDF Library References

QuickSearch: oxalate  clear Number of matching entries: 156/4174.

Ascorbic acid as suspected cause of oxalate nephrotoxicosis in a goat.
Adair, H.S. & Adams, W.H.
[Abstract]

Apparent absorption of copper and zinc from composite vegetarian diets in young Indian men.
Agte, V., Chiplonkar, S., Joshi, N. & Paknikar, K.
[Abstract]

Determination of serum oxalate using peroxyoxalate chemiluminescence of free oxalic acid.
Albrecht, S., Hornak, H., Freudt, T., Böhm, W.D., Wells, K. & Reinschke, A.
[Abstract] [URL]

Secondary oxalosis: a cause of delayed recovery of renal function in the setting of acute renal failure.
Alkunad, A.M. & Chau, L.
[Abstract] [URL]
Thank you
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- Consider repeating the test before jumping to conclusions.
- Monitor, evaluate, reflect, and repeat measures.
References


References continued


References continued


27. Qing H Meng; William C Irwin; Jennifer Fesser; K Lorne Massey Interference of ascorbic acid with chemical analytes Annals of Clinical Biochemistry; Nov 2005; 42, ProQuest Health and Medical Complete pg. 475

