Phosphate Additives in Food

a health hazard in CKD

Eberhard Ritz
Heidelberg (Germany)
Phosphate additives in food – a health hazard

- Phosphate: what does zoology teach us?
- Phosphate – adverse effects in CKD and beyond kidney disease
- Phosphate in food items – do we know what we eat?
- Not all phosphate in food is created equal
- Information for educated patients - labelling of P content in food items?
Phosphate modulates life span of Drosophila in evolution “nutrient sensing pathways“ are highly conserved restriction of phosphate supply prolongs life span

Another lection from the animal kingdom
phosphate concentration and life span

Earth worm: short life span,
  high S-phosphate-concentration
Tortoise: long life span,
  low S-phosphate-concentration

coincidence
or are there reasonable explanations?

It had been known for decades: that high phosphate intake in racing horses has negative consequences for skeleton and muscles.

When racing horses (without kidney disease) had grazed in meadows fertilized with manure or phosphate, secondary hyperparathyreoidism and subperiostal resorption zones occurred. Painful tendons render the horse unfit for races during the entire racing season.

For a long time this was the only known P related health hazard.
Phosphate additives in food – a health hazard

- Phosphate - what does zoology teach us?
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Grain market (Kornmarkt)
Even in “normophosphatemic“ individuals the serum-phosphate-concentration is associated with:

- increased overall mortality
- more frequent and worse outcome of cardiovascular and
- more frequent and worse outcome of renal disease

Tonelli, Circulation (2005) 112:2627
Kestenbaum, JASN (2005) 16:520
Conall, Nephrol Dial Transplant (2011) 26:2885
Serum Phosphate Predictor of **ESRD**
*(endstage renal disease)*

**NHANES III**

$n=13\,372$ participants $>18$ years

mean age 44.3 years; 52% women

follow-up 9.1 years

**ESRD** = start of dialysis

Serum Pi *(mg/dl)*

<table>
<thead>
<tr>
<th>Serum Pi (mg/dl)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$&lt; 4$ mg/dl</td>
<td>1.0</td>
</tr>
<tr>
<td>$&gt;4$ mg/dl</td>
<td>2.41 (95% CI 1.29-4.5)</td>
</tr>
</tbody>
</table>

$p<0.007$

Higher S-Pi concentration in the normophosphatemic range increases risk of endstage renal disease
(3rd National Health and Nutrition Examination Survey; NHANESIII)

n=13 372; follow-up 9.1 years

S-phosphate (mg/dl) at start of observation

<table>
<thead>
<tr>
<th>&lt;4.0</th>
<th>&gt;4.0</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESRD</td>
<td>43 / 11‘308</td>
<td>22 / 2064</td>
</tr>
<tr>
<td>rel.Risiko ESRD</td>
<td>1.0</td>
<td><strong>2.41</strong></td>
</tr>
</tbody>
</table>

(adjusted for age, gender, race …)

Conall, Nephrol.Dial.Transplant.(2011) 26:2885
Adjusted hazard ratio (Confidence-Interval 95%): terminal renal failure correlated to baseline serum-phosphate

94,989 individuals without CKD, Kaiser Permanente program, 11 years follow-up mean age 50 years
In patients with CKD, high phosphate accelerates loss of renal function.

High serum-phosphate-concentration accelerates loss of renal function in CKD patients. The effect of ACE inhibitors to slow down progression is abrogated by high serum-phosphate-concentration.

Ramipril attenuating loss of renal function.
Metaanalysis of 17 Studies with different Cohorts
(n = 327,644)

Association between S-P and mortality chronic kidney disease

per 1 mg/dl higher S-P - 18 % higher mortality

rel. risk 1.18 (95 % CI 1.12 – 1.25)

Palmer, JAMA (2011) 305:1119
24h urine phosphorous excretion and all-cause mortality in CKD

880 patients
stable CKD
24h P excretion
7.4 years follow-up

**Urine Phosphorous Tertiles**

<table>
<thead>
<tr>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;508 mg/d</td>
<td>508-748 mg/d</td>
<td>&gt;748 mg/d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>unadjusted</th>
<th>adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>0.74</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>1.00</td>
<td>0.84</td>
<td>0.72</td>
<td></td>
</tr>
</tbody>
</table>

*Palomino, CJASN (2013) 8: e-pub March 28th*
High S-phosphate before renal transplantation - worse function after kidney transplantation

(\textit{longterm effects !!})

Medians within quartiles and interquartile-range (mg/dl)

\begin{align*}
4.2 & \ (3.7-4.5) \\
5.4 & \ (5.1-5.7) \\
6.4 & \ (6.1-6.8) \\
8.5 & \ (7.7-9.7)
\end{align*}

\begin{itemize}
  \item \textbf{1. \textit{delayed graft function}}
  \begin{itemize}
    \item \textit{adjusted odds ratio}
    \begin{itemize}
      \item \textbf{OR 1.68} (95\% CI 1.05-2.71)
    \end{itemize}
  \end{itemize}
  \item \textbf{2. \textit{graft-failure}}
    \begin{itemize}
      \item progressively higher in higher quartiles
        \begin{itemize}
          \item \textit{(p for trend = 0.015)}
        \end{itemize}
    \end{itemize}
\end{itemize}

Serum-Phosphate predicts mortality in kidney graft recipients
(prospective observational study; 379 patients; 6 years follow-up; corrected for eGFR)

Cumulative survival rate

< 0.92 mmol/L
0.92 – 1.12 mmol/L
> 1.12 mmol/L

Tage

Connolly, Transplantation (2009) 87:1040
Phosphate: a novel cardiovascular risk factor

Markus Ketteler, Myles Wolf, Kai Hahn, and Eberhard Ritz*

The above findings justify the recommendation to include fasting serum phosphate as a risk predictor in patients with kidney malfunction or cardiovascular disease. In addition, dietary advice to minimize food items containing added inorganic phosphates would constitute a measure for patients with chronic kidney or cardiovascular disease. Therefore, appropriate food labelling seems warranted. Elucidation of the pathogenetic pathways triggered by phosphate will be a fascinating issue in current and future cardiovascular research.
Association Serum-Phosphate and LVH (Echo)
3,300 participants without heart failure or CKD

Dhingra, Eur J Heart Fail (2010) 12:812
Serum Phosphate and left ventricular hypertrophy
(Echocardiography)

4,055 young adults with normal renal function

Odds ratio LV mass vs. S-phosphate

1.27 (95 %, CI 1.09 – 1.47)

Foley, JASN (2009) 20:397
Patients with chronic kidney disease serum-phosphate is associated with LV-Hypertrophy (cardiac magnetic resonance) even in early stages of the disease!

208 nondiabetic patients CKD 2-4
mean GFR 50 ± 15 ml/min/1.73m²
S-phosphate 1.11 ± 0.21 mmoll

Serum phosphate correlated with LVM (r=0.173;p=0.01)

# LVM increasing progressively with higher quartiles of serum phosphate concentration,

Chue, Heart (2012) 98:219
In patients with CKD, serum-phosphate is associated with LV-hypertrophy (cardiac magnetic resonance)

Chue, Heart (2012) 98:219
24h urine phosphorous excretion and CV events in CKD

Palomino, CJASN (2013) 8: e-pub March 28th
Serum-phosphate concentration in the normal range and cardiovascular events in the general population (Framingham offspring study)

3368 individuals, observation period 16.1 years, 524 CV events

Highest vs lowest quartile HR 1.55 (1.16-2.07) p=0.004

Serum-Phosphate and onset of heart failure

Prospective study
3,300 participants without heart failure or CKD
17.4 years follow-up

per 1 mg/dl Δ S-phosphate onset of heart failure OR 1.74
(95% CI 1.17 – 2.59)

Dhingra, Eur J Heart Fail (2010) 12:812
Serum-Pi Quartiles and Cardiovascular Events in Coronary Patients (without kidney disease !)

Overall mortality

myocardial infarction (letan+nonletal.)

caused by $P_i \text{ per se or by FGF23 triggered by } P_i$ ?
Phosphate and cardiovascular events in patients with stable coronary heart disease

*(LURIC study)*

<table>
<thead>
<tr>
<th>Quartiles</th>
<th>all patients</th>
<th>CV events</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3.72</td>
<td>358</td>
<td>52</td>
</tr>
<tr>
<td>3.72—&lt;4.03</td>
<td>202</td>
<td>23</td>
</tr>
<tr>
<td>4.03—&lt;4.65</td>
<td>317</td>
<td>49</td>
</tr>
<tr>
<td>≥4.65</td>
<td>141</td>
<td>27</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Continuous</th>
<th>all patients</th>
<th>mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per 0.81 mg/dl (SD)</td>
<td>1018</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>1.07 (0.93 to 1.24)</td>
<td>1.41 (0.90 to 2.21)</td>
</tr>
</tbody>
</table>

“Phosphate toxicity“

**Direct** effects:
vascular calcification
endothelial cell dysfunction

*Di Marco, Kidn.Internat. (2013) in press*

Effects mediated **via hormones**:
FGF23/klotho, PTH

*Toussaint, Nephrology (2012) 17:433*
5/6 nephrectomy → cardiac hypertrophy and insufficiency

heart pathology reduced by blockade of the FGF23 receptor;

FGF23 (in response to phosphate retention) is the culprit

FGF23

- Increases in early stages of chronic kidney disease

- Strongly associated with
  - death
  - CVD
  - LVH
  - vascular calcification

Toussaint, Nephrology (2012) 17:433
Even in normophosphatemic patients in early stages of chronic kidney disease, the serum concentration of FGF23 decreases when phosphate binders (Sevelamer or Calcium) are used. (This finding suggests that it is high FGF23 which keeps S-Pi within the normal range.)

Oliveira, CJASN (2010) 5:286
Phosphate additives in food – a health hazard

- Phosphate - what does zoology teach us?
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ÜBERSICHTSARBEIT

Gesundheitsrisiko durch Phosphatzusätze in Nahrungsmitteln

Eberhard Ritz, Kai Hahn, Markus Ketteler, Martin K. Kuhlmann, Johannes Mann


Phosphate Industry Responds to “Phosphate Additives in Food – a Health Risk” by Ritz et al
International Food Additives Council, Atlanta Georgia

It is well documented that phosphorous, a component of food phosphates, is an essential nutrient....

The review by Ritz et al ... focused on a small subset of the general population...

i.e. chronic renal disease..

Humans require dietary phosphate for proper functioning of the body;

in healthy individuals excess phosphorous is excreted

IFAC and PAPA ...agree with the large body of scientific and regulatory evidence that inorganic phosphates are safe and provide nutritional and functional benefits (!!!) in foods
Phosphorus-containing food additives: An insidious danger for people with chronic kidney disease

Ray J. Winger\textsuperscript{a,*}, Jaime Uribarri\textsuperscript{b} and Lyn Lloyd\textsuperscript{c}

or absence of biomarkers in blood or urine and the level of Glomerular Filtration Rate (GFR). The level of kidney function tends to decline progressively over time in many people and kidney failure is the adverse outcome. CKD is classified in 5 stages (Table 1).

Recent regulatory changes, which require the mandatory labelling of sodium and salt, have greatly increased consumers’ knowledge about sodium in food and health professionals’ ability to advise dietary sodium intake. However, people with CKD stage 5, defined as End-Stage Renal Disease (ESRD), need to control their intake of a number of nutrients, including sodium, potassium and phosphorus (P) to optimise their health. The use and bioavailability of P in our processed foods is increasing and these foods are particularly dangerous to people with ESRD. There is little transparency within the food industry to identify the quantitative usage of P, which effectively
In which food items are phosphate additives?

- meat products and seafood
- pasta (to decrease cooking time)
- instant pudding
- non-dairy creamers
- spreadable cheese (aged cheeses have none)
- fortified orange juice
- baked goods (high in additives: leavening agents and dough conditioners)
- soft ice cream
- chicken (for "plumping") and pork (for "moisture")

Calvo, Nephrology News and Issues 2012, July p6
## Typical phosphate content of some commercial food items

**("processed foods")**

Winger, Uribarri, Lloyd;  
*Trends in Food Science and Technology* (2012) 24:92-102

<table>
<thead>
<tr>
<th>Product</th>
<th>P content (mg/100g food item)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meat products</strong></td>
<td></td>
</tr>
<tr>
<td>corned beef</td>
<td>1298</td>
</tr>
<tr>
<td>bacon fried</td>
<td>450</td>
</tr>
<tr>
<td>sausages</td>
<td>160-214</td>
</tr>
<tr>
<td><strong>Pasta</strong></td>
<td></td>
</tr>
<tr>
<td>noodle, rice</td>
<td>6</td>
</tr>
<tr>
<td>noodle wheat</td>
<td>40-52</td>
</tr>
<tr>
<td>pasta, wholemeal, boiled</td>
<td>140</td>
</tr>
<tr>
<td><strong>Snack foods</strong></td>
<td></td>
</tr>
<tr>
<td>corn chips</td>
<td>291</td>
</tr>
<tr>
<td>popcorn</td>
<td>358</td>
</tr>
</tbody>
</table>
Typical phosphate content of some commercial food items ("processed foods")

Winger, Uribarri, Lloyd;
*Trends in Food Science and Technology* (2012) 24:92-102

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<thead>
<tr>
<th>Product</th>
<th>P content (mg/100g food item)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beverages</strong></td>
<td></td>
</tr>
<tr>
<td>coffee whitener</td>
<td>420</td>
</tr>
<tr>
<td><strong>Cereal Products</strong></td>
<td></td>
</tr>
<tr>
<td>biscuits</td>
<td>155-304</td>
</tr>
<tr>
<td>bread gluten-free</td>
<td>242</td>
</tr>
<tr>
<td>bread wholemeal</td>
<td>173</td>
</tr>
<tr>
<td><strong>Milk Products</strong></td>
<td></td>
</tr>
<tr>
<td>cheese, processed</td>
<td>552</td>
</tr>
<tr>
<td>Yoghurt (no added calcium)</td>
<td>96-195</td>
</tr>
</tbody>
</table>
What are the motivations of food industry to add phosphate to food items?

one additional incentive:
phosphate “binds“ water,
thus increasing weight

↪ incentive for food industry:
water in food items guarantees easy money
Limited efficacy of phosphate binders

1 Sevelamer 800 mg - 1 tablet binds 27 mg phosphate
1 Calcium acetate tablet - 1 tablet binds 30 mg phosphate
1 Phosphoenol 1000 mg - 1 tablet binds 90 mg phosphate
...

Calvo, Nephrology News and Issues 2012, July p6
How long has all this been known?

(we are reinventing the wheel !!!“)

Postprandial serum-P concentration in healthy volunteers: food items with/without phosphate additives

4 weeks diet containing 1g phosphate without phosphate additive
4 weeks the same diet with addition of sodium-phosphate resulting in total P intake of 2.1 g/day

"the contribution to serum phosphate from P in food additives is greater than the contribution of P in the diet"

Postprandial **Serum-P** in Healthy Volunteers

*food with/without added phosphate*

<table>
<thead>
<tr>
<th>Subject</th>
<th>Calcium(^1)</th>
<th>Phosphorus(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control (mg/100\ ml)</td>
<td>High-phosphorus (mg/100\ ml)</td>
</tr>
<tr>
<td>1</td>
<td>11.11</td>
<td>10.38</td>
</tr>
<tr>
<td>2</td>
<td>10.34</td>
<td>10.31</td>
</tr>
<tr>
<td>3</td>
<td>10.58</td>
<td>10.61</td>
</tr>
<tr>
<td>4</td>
<td>10.65</td>
<td>10.30</td>
</tr>
<tr>
<td>5</td>
<td>10.47</td>
<td>10.21</td>
</tr>
<tr>
<td>6</td>
<td>10.61</td>
<td>10.13</td>
</tr>
<tr>
<td>7</td>
<td>10.85</td>
<td>10.33</td>
</tr>
<tr>
<td>8</td>
<td>10.69</td>
<td>10.23</td>
</tr>
</tbody>
</table>

**Mean±SD**

<table>
<thead>
<tr>
<th>Calcium</th>
<th>Phosphorus</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.66±0.24</td>
<td>3.76±0.38</td>
</tr>
<tr>
<td>10.31±0.14</td>
<td>4.43±0.30</td>
</tr>
</tbody>
</table>

Without added phosphate

Bell, *J. Nutr.* (1977) 107:42

**increase: 0.67 mg/dl**

27%
Urinary phosphate excretion in healthy volunteers 
food with/without added phosphate

% increase higher than % increase of S-phosphate

<table>
<thead>
<tr>
<th>Subject</th>
<th>Control Week 1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Avg.</th>
<th>High-phosphorus 5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>Avg.</th>
<th>Significance*</th>
<th>Increase %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>460</td>
<td>358</td>
<td>474</td>
<td>220</td>
<td>378</td>
<td>1,598</td>
<td>1,113</td>
<td>1,030</td>
<td>1,136</td>
<td>1,219</td>
<td>$P &lt; 0.001$</td>
<td>222</td>
</tr>
<tr>
<td>2</td>
<td>308</td>
<td>625</td>
<td>434</td>
<td>244</td>
<td>403</td>
<td>611</td>
<td>999</td>
<td>1,099</td>
<td>1,603</td>
<td>1,078</td>
<td>$P &lt; 0.05$</td>
<td>168</td>
</tr>
<tr>
<td>3</td>
<td>382</td>
<td>680</td>
<td>625</td>
<td>340</td>
<td>507</td>
<td>749</td>
<td>1,920</td>
<td>1,785</td>
<td>2,091</td>
<td>1,636</td>
<td>$P &lt; 0.02$</td>
<td>222</td>
</tr>
<tr>
<td>4</td>
<td>392</td>
<td>474</td>
<td>673</td>
<td>569</td>
<td>527</td>
<td>897</td>
<td>417</td>
<td>684</td>
<td>646</td>
<td>661</td>
<td>NS</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>449</td>
<td>501</td>
<td>461</td>
<td>453</td>
<td>466</td>
<td>1,096</td>
<td>1,549</td>
<td>1,307</td>
<td>1,850</td>
<td>1,450</td>
<td>$P &lt; 0.001$</td>
<td>211</td>
</tr>
<tr>
<td>6</td>
<td>264</td>
<td>657</td>
<td>580</td>
<td>396</td>
<td>474</td>
<td>968</td>
<td>872</td>
<td>1,016</td>
<td>797</td>
<td>913</td>
<td>$P &lt; 0.01$</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>127</td>
<td>540</td>
<td>579</td>
<td>298</td>
<td>386</td>
<td>436</td>
<td>735</td>
<td>380</td>
<td>583</td>
<td>534</td>
<td>NS</td>
<td>38</td>
</tr>
<tr>
<td>8</td>
<td>512</td>
<td>218</td>
<td>229</td>
<td>148</td>
<td>277</td>
<td>525</td>
<td>731</td>
<td>451</td>
<td>664</td>
<td>593</td>
<td>$P &lt; 0.05$</td>
<td>114</td>
</tr>
</tbody>
</table>

Overall mean ± SD

427 ± 156

1,010 ± 477

$P < 0.001$

137%

resulting from added phosphate


serum-phosphate underestimates P-load
Phosphate additives in food – a health hazard

- Phosphate - what does zoology teach us?
- Phosphate – adverse effects in CKD and beyond kidney disease
- Phosphate in food items – do we know what we eat?
- Not all phosphate in food is created equal
- Information for educated patients - labelling of P content in food items?
Diurnal variation of plasma phosphorous concentration

9 patients, eGFR 32 ml/min; 7 days vegetarian diet, 7 days meat diet

Plasma Phosphorous (mg/dl)

Moe, CJASN (2011) 6:257
FE (*fractional excretion*) of P - diurnal variation

9 patients, eGFR 32 ml/min; 7 days *vegetarian* diet, 7 days *meat* diet

Fractional excretion of P (%)

*Moe, CJASN (2011) 6:257*
Diurnal variation of fractional P excretion

9 patients, eGFR32 ml/min; 7 days vegetarian diet ○, 7 days meat diet ●

2h fasting fractional P excretion (%)
Conclusion:

“not all phosphate is created equal“

there are major differences between covalently bound and free phosphate
Phosphate additives in food – a health hazard

- Phosphate-what does zoology teach us?
- Phosphate – adverse effects in CKD and beyond kidney disease
- Phosphate in food items – do we know what we eat?
- Not all phosphate in food is created equal
- Beyond patient education – we need appropriate labelling of P content in food items?
Synthesis of P requires extreme conditions which are not available in the solar system. All phosphorous on earth is derived from sources outside of the solar system, loss of P from available P stock (mainly Morocco, US, China) is not renewable, thus potentially constraining world food supplies.
Phosphate additives in food – a health hazard

- Phosphate - what does zoology teach us?

  *phosphate impacts on life span*

- Phosphate in food items – do we know what we eat?

  *no; phosphate additives are not disclosed*

- Not all phosphate in food is created equal

  *P additives are preferentially absorbed*

- Information for educated patients - labelling of P content in food items?

  *P additives in food must be labeled*

prof.e.ritz@t-online.de
Serum Phosphate: *predictor of chronic kidney disease and terminal renal failure*

**NHANES III**

- **n** = 13,372 individuals age >18 years
- Mean age 44.3 years; 52% women
- Observation 9.1 years
- ESRD = start of dialysis

**Serum Pi (mg/dl)**

<table>
<thead>
<tr>
<th>&lt; 4 mg/dl</th>
<th>&gt;4 mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>2.41</td>
</tr>
</tbody>
</table>

(95% CI 1.29-4.5)  

p < 0.007

Serum Phosphate Predictor of Future CKD
*(chronic kidney disease)*

**Framingham Heart Study**

*2269 participants without CKD at start of study, 25.1 years follow-up*

<table>
<thead>
<tr>
<th>Serum $P_i$ (mg/dl) at start and odds ratio of onset of CKD</th>
<th>&lt; 2.5</th>
<th>2.5-3.49</th>
<th>3.5-3.99</th>
<th>&gt;4</th>
<th>$p &lt;$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio CKD</td>
<td>11.8</td>
<td>11.3</td>
<td>12.4</td>
<td>18.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Systol. BP (<em>mmHg</em>)</td>
<td>125</td>
<td>120</td>
<td>116</td>
<td>121</td>
<td>0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>24.4</td>
<td>33.4</td>
<td>39.7</td>
<td>55.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>eGFR</td>
<td>108</td>
<td>105</td>
<td>107</td>
<td>134</td>
<td>0.0001</td>
</tr>
<tr>
<td>(ml/min/1.73m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Normal range*: 2.7-4.5 mg/dl [0.87-1.45 mmol/L]

In CKD stage 3 or 4 oral calcium carbonate (1500 mg/day)

# positive calcium balance
# but no effect on P balance

Hill, Kidn.Internat.(2013) 83:959
Selbst **S-Phosphat**-Konzentration des **Spenders** beeinflusst **Transplantationsergebnis** beim Empfänger (Lebendspender Nieren-Transplantation)

Höhere **Serumphosphat**-Konzentration des **Spenders** korreliert zu:
- # höherem **Serumkreatinin** des Empfängers
  
  slope 0.087 (CI:0.004-0.169); \( p=0.041 \) vergesellschaftet mit

- # niedrigerer **eGFR** des Empfängers
  
  slope -4.32; (CI -8.17 - -0.48); \( p=0.028 \)

# unabhängige Korrelation zu:

**akute Transplantatrejektion** *(Biopsie gesichert)* und **verzögerte Funktionsaufnahme** nach Transplantation

*Chang, CJASN (2011) 6:1179*
Lebenserwartung

Maverick study
(Kaiser Permanente)

36,679 Patienten chronic kidney disease (CKD 3-5)
Serum – P korreliert zu:
- Gesamtmortalität
- (Hospitalisierung wegen CV Ereignisse)
- (akuter Herzinsuffizienz)

<table>
<thead>
<tr>
<th>Serum-P</th>
<th>Gesamtmortalität</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5-4.9</td>
<td>rel.Risiko 1.29 (1.15-1.45)</td>
</tr>
<tr>
<td>5.0-5.4</td>
<td>1.71 (1.46-2.0)</td>
</tr>
<tr>
<td>&gt; 5.5</td>
<td>2.72 (2.23-3.33)</td>
</tr>
</tbody>
</table>

Gesamtmortalität progredient höher bei höherer Serum-Phosphat-Konzentration
S-Phosphate – independent predictor of: overall mortality/ CV mortality/ atherosclerosis

# even in patients without CKD
# even for S-Pi values within the “normal” range

# CARE study (Pravastatin after MI)
  eGFR>60ml/min/1.73m²
  per 1 mg/dl higher S-Pi → HR overall mortality 1.22 and MI 1.22
  Tonelli, Circulation (2005) 112:2627

# VA study (Veterans with CKD, observational study)
  per 1 mg/dl higher S-Pi → HR overall mortality 1.2

# Framingham offspring study (eGFR>60ml/min/1.73m², 16 years)
  per 1 mg/dl higher S-Pi → HR 1.31 for incident CVD event

# ARIC study (13,340 patients without CKD or cardiac disease)
  carotis intima media thickness: higher in progressively higher S-Pi quintiles
  (even at GFR >90 ml/Min/1.73m²)
Ausgangswert von S-P (aber nicht von S-Ca) korrelierte 15 Jahre später zu neu aufgetretenem Koronarkalk (EB scan) (3015 gesunde junge Männer in der CARDIA Studie)

Multivariante Assoziation: Koronararterien-Verkalkung und S-Phosphat (und S-Kalzium) Quartilen