Vitamin D and Breast Cancer Prevention

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UK Breast Cancer Statistics

- Breast Cancer
  - 48,000 cases 2008
  - $75,000 cost/case (US/NIH:2008)
  - Total Cost/year: $3,600,000,000

20% Potential Prevention (up to 75%)
9600-38,400 people wouldn’t get it
Cost savings/year (20%): $720,000,000

www.grassrootshealth.net
Aging of UK Population

- 15% over 65 in 2010
- 40% expected over 65 in 2030

Where’s the budget?
Technology and Cancer

- Benefits of all this spending are marginal.

- Cutler shows that since 1960
  - Life expectancy has increased 6.97 years
  - Increase from cardiovascular disease changes—almost all HTN 4.88 years
  - Increase from cancer change 0.19 years

Ezekiel J. Emanuel, M.D., Ph.D. NIH
Technology and Cancer

- Increase over 40 years of average life expectancy because of cancer treatment is:

10 weeks of life

Ezekiel J. Emanuel, M.D., Ph.D. NIH
Meta-analysis of breast cancer risk

Dose–response gradient of risk of breast cancer according to serum 25-hydroxyvitamin D concentration, pooled analysis.
80% Breast Cancer Incidence Reduction

Source: Garland et al. (2007) based on data in Lowe et al. (2006)
Breast Cancer Dose Response Risk Reduction


VITAMIN D & CANCER*

* Lappe et al. AJCN 2007

77% reduction
## CANCERS BY TREATMENT (YRS 2–4)

<table>
<thead>
<tr>
<th>Site</th>
<th>Placebo (n=266)</th>
<th>Ca+D (n = 403)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>7 (2.6%)</td>
<td>4 (1.0%)</td>
</tr>
<tr>
<td>Colon</td>
<td>2 (0.7%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Lung</td>
<td>3 (1.1%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Marrow/Lymphoma</td>
<td>4 (1.5%)</td>
<td>2 (0.5%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td><strong>Total</strong>*</td>
<td>18 (6.8%)</td>
<td>8 (2.0%)*</td>
</tr>
</tbody>
</table>

* P < 0.05
Distant Disease-Free Survival
Breast Cancer

Proportion distant disease free

Years since diagnosis

Serum level $\geq 75$ nmol/L
Serum level $< 50$ nmol/L
Higher D: 50% less likely to spread

Overall Survival VITAMIN D DEFICIENCY IN BREAST CANCER
Goodwin PJ, Ennis ME, Pritchard KI, Koo J, Hood N
Mount Sinai Hospital, University of Toronto, Canada

www.grassrootshealth.net
Mice Without Vitamin D Receptors Have High Risk for Cancer Development

Normal No VDR

Early Stage Cancer

Tumor Incidence

<table>
<thead>
<tr>
<th></th>
<th>WT</th>
<th>VDR HET</th>
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</thead>
<tbody>
<tr>
<td>Incidence (%)</td>
<td>42%</td>
<td>70.9%</td>
</tr>
</tbody>
</table>

Slide courtesy of J. Welsh, PhD
DINOMIT - Theory of Breast Cancer
Cedric F. Garland, Dr. P.H.

- Disjunction – Loss of Tight Junctions
- Initiation – Genetic variation
- Natural selection – Competition for growth
- Overgrowth – Palpable mass and invasion
- Metastasis – Remote colonization
- Involution – Growth inhibition
- Transition – Coexistence with normal tissue
In vitamin D deficiency, the first lesion is harm to the intercellular junction.

This unleashes natural selection. Natural selection is the engine of growth of the cancer.
Normally adherent cells
Decoupling: Loss of tight junctions
Decoupling advances
Decoupling becomes complete
Mild Dysplasia due to loss of tight junctions
DNA variation due to infidelity of reproduction or carcinogens
DINOMIT- Initiation

Continued variation in DNA and epigenetics
DINOMIT - Initiation

Continued variation in DNA and epigenetics
Natural selection >> rapidly reproducing clones
DINOMIT - Natural Selection

Natural selection $\Rightarrow$ rapidly reproducing clones
DINOMIT - Overgrowth

New clone rapidly mitotic
DINOMIT- Overgrowth

Infidelity of DNA and epigenetics
DINOMIT- Overgrowth

Infidelity of DNA and epigenetics
DINOMIT- Overgrowth

Overgrowth creates crowding
DINOMIT - Overgrowth

Overgrowth creates crowding
DINOMIT- Overgrowth

Beginning penetration of basement membrane
DINOMIT- Overgrowth

Ongoing penetration of basement membrane
DINOMIT - Overgrowth

Fuller penetration of basement membrane
DINOMIT - Overgrowth

Penetration of basement membrane continues
DINOMIT - Overgrowth

Penetration of basement membrane continues
Penetration of basement membrane continues
Malignant cells enter lymphatic circulation
Malignant cells enter lymphatic circulation
Malignant cells enter lymphatic circulation
Malignant cells enter lymph nodes
DINOMIT - Metastasis

Malignant cells enter lymph nodes
DINOMIT - Metastasis

Malignant cells enter lymph nodes
Malignant cell population grows
Expansion of malignant clone in lymph node
DINOMIT- Metastasis

Expansion of malignant clone in lymph node
Expansion of malignant clone in lymph node
Malignant cells transported from lymph node
Malignant cells transported from lymph node
DINOMIT- Metastasis

Malignant cells transported from lymph node
Malignant cells transported from lymph node
What do we do to PREVENT it?

Get serum level to 100-150 nmol/L

1200-1500 mg/day of calcium
(from all sources)
Beyond Clinical Trials to a Population Level Intervention Project
D*action Project

A population level public health intervention

1. Solve the deficiency epidemic- - now!
2. Create Evidence- Based Public Health Policy Recommendations
   • Large scale intervention
   • Education
   • Testing
   • Voluntary/ individual intake adjustment
   • Documentation
Project Study Results to Date
D*action Project: Serum Level vs Intake

Vitamin D Intake IU/day (N=3667)
Rise in serum 25(OH)D per 1,000 IU D3 per day
<table>
<thead>
<tr>
<th>Current Serum Level (nmol/L)</th>
<th>50</th>
<th>75</th>
<th>100</th>
<th>125</th>
<th>150</th>
<th>175</th>
<th>200</th>
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<td>25</td>
<td>1000</td>
<td>2200</td>
<td>3600</td>
<td>5300</td>
<td>7400</td>
<td>10100</td>
<td>13800</td>
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<tr>
<td>38</td>
<td>500</td>
<td>1700</td>
<td>3200</td>
<td>4900</td>
<td>7000</td>
<td>9700</td>
<td>13400</td>
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<tr>
<td><strong>50</strong></td>
<td>1200</td>
<td>2600</td>
<td><strong>4300</strong></td>
<td>6400</td>
<td>9100</td>
<td>12800</td>
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</tr>
<tr>
<td>63</td>
<td>600</td>
<td>2000</td>
<td>3700</td>
<td>5800</td>
<td>8600</td>
<td>12300</td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>1400</td>
<td>3100</td>
<td>5200</td>
<td>7900</td>
<td>11600</td>
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<tr>
<td>88</td>
<td>800</td>
<td>2500</td>
<td>4600</td>
<td>7300</td>
<td>11000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>--</td>
<td>1700</td>
<td>3800</td>
<td>6500</td>
<td>10200</td>
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<tr>
<td>113</td>
<td>--</td>
<td>900</td>
<td>3000</td>
<td>5700</td>
<td>9400</td>
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<tr>
<td>125</td>
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<td>--</td>
<td>2100</td>
<td>4800</td>
<td>8500</td>
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<tr>
<td>150</td>
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<td>--</td>
<td>2700</td>
<td>6400</td>
<td></td>
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</tr>
<tr>
<td>175</td>
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<td>--</td>
<td>--</td>
<td>3700</td>
<td></td>
<td></td>
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Example: To go from 50 nmol/L to 125 nmol/L would require an average additional intake of 4300 IU/day
D*action Study Data plotted on previously published data

diamond-shaped are the means of controlled dosing studies (n=48)
square symbols, individual values from reported cases (n=21) of vitamin D intoxication

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Next Steps

- Further analyze health outcome data
- Expand endorsements of the Call to Action—get serum levels to 100-150 nmol/L

**Key medical group in Canada has fully endorsed with their membership**
Next Steps, continued

- Enroll additional groups
  - Disease specific, e.g., MS, breast cancer, falls
  - Other large population groups
    - Communities
    - Research groups
    - Government groups/regions
  - Expand sponsorship
Reality must take precedence ... for nature cannot be fooled.

Richard Feynman
Thank you!

Get your Vitamin D blood serum level to 100-150 nmol/L (40-60 ng/ml)
Special Thanks

- Cedric F. Garland, Dr. P.H.
- Robert P. Heaney, MD
- Leo L. Baggerly, Ph.D.
- JoEllen Welsh, Ph.D.
- ALL 8000 sponsors!