Robert Winwood PhD
DSM Nutritional Products, Switzerland

Unexpected pervasive Vitamin D deficiency in people living in the Middle East
Programme

• Introduction
• Vitamin D status in the Middle East
• Some Unexpected Results
• Final Thoughts
Synonyms and Chemical Structure

Vitamin D (inactive form) is a fat soluble vitamin, taken up by diet (cholecalciferol, ergocalciferol) or produced in the skin (cholecalciferol) by the sun. The active form of vitamin D in the body is 1,25-dihydroxyvitamin D.

Synonyms: “Sunshine” vitamin, anti-rachitic factor, vitamin D, cholecalciferol, ergocalciferol

IUPAC name:
3-{2-[7a-Methyl-1-(6-methylheptan-2-yl)-2,3,3a,5,6,7-hexahydro-1H-inden-4-yliden]ethyliden}-4-methyliden-cyclohexan-1-ol
Vitamin D Pathway

**Major source** – sunlight
UVB
290-315 nm

Skin

Cholecalciferol (vitamin D₃)

7-Dehydrocholesterol

**Minor source** – dietary intake

Vitamin D₃ (fish) / food fortification

Liver

25-hydroxy D₃

Kidney

1,25 dihydroxy D₃ (active metabolite)

Human body has evolved to produce ~10'000 IU (250μg) of Vitamin D₃ every day (within ~ 15 – 30 min)

Nutritional Vitamin D sources are rare, mainly:
1. Fatty fish
2. Fortification

Chen TC, Arch Biochem Biophys. 2007

Ca Absorption & Bone Metabolism
Dietary Sources

Animal products (main source for D₃)

- Oily fish

Plant products (main source for D₂)

- Mushrooms

Others:

- Synthesized in the skin by the action of ultraviolet light

<table>
<thead>
<tr>
<th>Food</th>
<th>Vitamin D (µg/100g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salmon, sockeye, cooked, dry heat</td>
<td>13.1</td>
</tr>
<tr>
<td>Tuna, light, canned in oil, drained solids</td>
<td>6.7</td>
</tr>
<tr>
<td>Halibut, Atlantic and Pacific, cooked, dry heat</td>
<td>5.8</td>
</tr>
<tr>
<td>Sardine, Atlantic, canned in oil drained solids with bone</td>
<td>4.8</td>
</tr>
<tr>
<td>Herring, Atlantic, pickled</td>
<td>2.8</td>
</tr>
<tr>
<td>Butter</td>
<td>1.4</td>
</tr>
<tr>
<td>Mushrooms, white, cooked, boiled, drained, without salt</td>
<td>0.2</td>
</tr>
<tr>
<td>Milk, whole, 3.25% milk fat, without added vitamin A and vitamin D</td>
<td>0.1</td>
</tr>
</tbody>
</table>

USDA National Nutrient Database for Standard Reference
http://www.nal.usda.gov/fnic/foodcomp/search/
Vitamin D Status

- About half the world’s population has an inadequate vitamin D status
- Listed as a critical nutrient for all fourteen countries evaluated in the European Nutrition and Health Report
- Levels are even low in sunny climates such as Saudi Arabia, Africa and India and in countries with vitamin D fortification of foods such as the United States and Canada
- Obvious deficiency is less than 20 nmol per liter of serum 25-(OH)D levels
- Hidden deficiency is defined below 70 nmol per liter of serum 25-(OH)D levels

![Diagram of Vitamin D Status]

- Intake / day
  - 5 μg (200 IU)
  - 25 - 50 μg (1000 - 2000 IU)
  - 100 μg (4000 IU)

25(OH)D blood level [nmol/L]
- 20
- 50
- 80
- 150
- 250
- 400 - 1'250

- Obvious Deficiency
- Hidden Deficiency
- Beneficial Level
- Toxic Level

- treatment of clinically obvious deficiency
- chronic disease risk reduction
- adverse effects (hypercalecemia)
Vitamin D Deficiency
http://www.iofbonehealth.org/facts-and-statistics/vitamin-d-studies-map

Vitamin D status in adults (≥18 years)
Vitamin D deficiency in Europe: pandemic?\textsuperscript{1,2}

Kevin D Cashman\textsuperscript{3,4,6} Kirsten G Dowling\textsuperscript{3} Zuzana Škrabáková\textsuperscript{3} Marcela Gonzalez-Gross\textsuperscript{6,7} Jara Valmeña\textsuperscript{6}

**Conclusions:** Vitamin D deficiency is evident throughout the European population at prevalence rates that are concerning and that require action from a public health perspective. What direction these strategies take will depend on European policy but should aim to ensure vitamin D intakes that are protective against vitamin D deficiency in the majority of the European population. *Am J Clin Nutr* doi: 10.3945/ajcn.115.120873.
Health Benefits of Vitamin D

Bone Homeostasis

Diseases potentially associated with vitamin D deficiency

Holick, Am J Clin Nutr, 2002
25(OH)D status important for various health outcomes

Optimum plasma level is above 75 nmol/L

Adapted from Bischoff-Ferrari: Optimal Serum 25-Hydroxyvitamin D levels for multiple health outcomes
Vitamin D and mortality in general populations

Lowest mortality risk at 75 to 87.5 nmol/L

Air pollution increase the risk of vitamin D deficiency

- Vitamin D status is usually dependent on skin exposure to sun’s UVB radiation
- Air pollution decrease UVB light and thereby reduce skin vitamin D synthesis

Relationships among vitamin D status and sun exposure index in Belgian urban and rural postmenopausal women

Manicourt et al. 2008
Vitamin D status levels in the Middle East
FOOD & HEALTH

Vitamin D, a must for Saudi women

Rima Al-Mukhtar | Published – Wednesday 6 August 2014
A recent study of 10,735 adults from the Kingdom of Saudi Arabia that took place during the spring/summer of 2013 demonstrated that 63% of females and 41% of males were deficient in Vitamin D (i.e. plasma levels less than 28 ng/mL as defined by the Saudi Ministry of Health.)
Serum 25(OH)D status in Young Saudi Females (Abdelkarem et al., Saudi Med J 2016)

Study looked at 147 female Saudi students aged 18-25 years BUT 54.6% of OBESE students presented with insufficient status (< 50 nmol/L)
An observational study of 10,709 hospital patients in Saudi Arabia aged 19-60 years revealed:

For females:
- 51.2% Insufficient serum 25(OH)D ie < 25 nmol/L
- 44.1% Inadequate serum 25(OH)D ie 25-75 nmol/L

For males:
- 40.2% Insufficient serum 25(OH)D ie < 25 nmol/L
- 53.5% Inadequate serum 25(OH)D ie 25-75 nmol/L
Vitamin D status levels in the UAE

Typically Vitamin D insufficiency, deficiency and severe deficiency as defined as 50-75 nmol/L, 27.5-50 nmol/L and <27.5 nmol/L respectively

The results of a recent study * on young women aged 11 -18 years in the United Arab Emirates produced the following results for each category respectively were 1%, 19.8% and 78.8% respectively i.e. over three quarters of the girls had severe deficiency which is likely to lead to problems for them and their offspring in later life.

*Narchi H et al., Paediatrics and International Child Health 2015. 35(1): 36-43
Prevalence of Vitamin D Deficiency in the Middle East i.e. serum 25(OH)D <50 nmol/L

Hwalla M et al, Nutrients 2017, 9(3):229
The Issue in the Middle East:

- Prominent deficits in Vitamin D are noted among children, adolescents, women of child bearing age, pregnant women and the elderly.

- Food Fortification is sporadic and ineffective.

- Traditional clothing results in minimal skin exposure.

- The use of dietary supplements is low.

- Nutritional monitoring is limited.

(Hwalla N et al, Nutrients 2017)
Vitamin D replacement treatment RCT in Lebanese school children
El-Hajj et al.; J Clin Endocrin Metab 2006

- 179 girls aged 10-17 received interventions weekly oral doses of Vit D equivalent to either 200 or 2,000 IU/d for 1 year. Bone mineral density and bone mineral content (BMC) was made at baseline and at completion.
- Lean Mass increased in both treatment groups.
- Bone area and total hip BMC increased in the high dose group.
El-Hajj et al.; J Clin Endocrin Metab 2006

FIG. 2. Box plots showing the median and interquartile range of the percent change in lean mass (A), the percent change in hip trochanteric BMC (B), and the percent change in total hip BMC (C) by treatment group in premenarchal girls. *P* values displayed represent results from post hoc *t* testing on ANOVA. There was a significant effect of treatment on changes in lean mass and changes in trochanteric BMC at both doses. There was a trend for a significant effect of treatment on percent changes in total hip BMC in premenarchal girls.
Juvenile Vit D status is a concern in UAE

- A study of a total of 7883 juvenile patients admitted to the Burjeel Hospital of VPS Health care in Abu Dhabi, United Arab Emirates (UAE) from October 2012 to September 2014.
- Out of patients considered in this study, almost 58.1% of females and 43.3% of males in the age group of 1-18 years were found to have low serum 25(OH)D levels.
- Vitamin D deficiency was shown to be a clinical problem and 82.5% of the study cohort had inadequate serum 25(OH)D levels.
Vitamin D supplementation/correction is advised in all persons whose serum 25(OH)D falls below 50 nmol/l (20 ng/ml), and achieving a target of 75 nmol/l (30 ng/ml) is particularly suited for frail, osteoporotic, and older patients

BUT Despite overwhelming prevalence of vitamin D deficiency, universal screening is not recommended
Could fortified milk be an answer?

Alvi et al* examined 5 replicate samples of 5 brands of fortified low fat cows milk bought in Riyadh said to contain 400 IU/L (10 ng/mL) Vitamin D. 20% of the samples were more than 20% less or more than the label claim.

Table 1. Measured levels of Vitamin D in 125 samples from five producers of fortified low-fat cow milk.

<table>
<thead>
<tr>
<th>Producers</th>
<th>&lt;8 ng/mL</th>
<th>8-12 ng/mL</th>
<th>&gt;12 ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>NA</td>
<td>11.2</td>
<td>13.6</td>
</tr>
<tr>
<td>B</td>
<td>7.6</td>
<td>10.0</td>
<td>13.0</td>
</tr>
<tr>
<td>C</td>
<td>7.4</td>
<td>9.5</td>
<td>NA</td>
</tr>
<tr>
<td>D</td>
<td>7.7</td>
<td>9.4</td>
<td>NA</td>
</tr>
<tr>
<td>E</td>
<td>7.2</td>
<td>10.8</td>
<td>12.4</td>
</tr>
</tbody>
</table>

Intra-batch variation: 1.6-20.8%
Inter-batch variation: 8.2-20.8%
Intra-producer variation: 16.1%
Overall: Low fat milk is a reliable form of Vit D fortification

But of standard dairy products, only fresh milk helps - and only in children and women*

*Al Daghri N et al.; Int J Clin Exp Pathol 2015; 8(7); 8480-8486
Some unexpected results....
Curious CVD marker association with Vit D

Fig. 1 Association between serum log vitamin D and cholesterol concentrations in vitamin D deficient women. In the vitamin D deficient sub-group of women [25(OH)D <25 nmol/L; n = 350], the relation between serum levels of log 25(OH)D/vitamin D and total cholesterol was determined by Pearson correlation coefficient analysis. Results are presented as a scatter plot.

Al-Ajlan et al, 2015 BMC Pregnancy and Childbirth
Figure 2: Association between serum log vitamin D and triglyceride concentration in vitamin D deficient women. In the vitamin D deficient sub-group of women [25(OH)D <25 nmol/L; n = 350], the relation between serum levels of log 25(OH)D/vitamin D and total triglycerides was determined by Pearson correlation coefficient analysis. Results are presented as a scatter plot.

Al-Ajlan et al, 2015 BMC Pregnancy and Childbirth
Does covering up really reduce overall Vit D intake? (1)

Typical dress in Saudi Arabia

Effect of female dress style on Vitamin D status in Egypt
(derived from Fawzi MM et al, Life Sci J 2012; 9:763-767)

Healthy female students average 21 years

www.baldridge21.com photographer LoriPaul Roy
Does covering up really reduce overall Vit D intake? (2)

Botros RM et al 2015 studied 208 Egyptian women mean age 32 years (Endocrinol Nutr 62:314-321)

Source: www.bbc.co.uk
But low Vit D status is associated with increased risk of Cardiovascular Disease in KSA

Aljefree et al., Healthcare 2016, 4, 77.

In Saudi Arabia, CVD is the leading cause of admission to hospital and third most prominent cause of hospital based mortality.

The new study by Aljefree et al of 130 CHD patients from a hospital in Makkah Demonstrated that patients with a serum 25(OH)D <20 ng/mL were 6.5 times more likely to suffer from CHD than subjects with an adequate Vitamin D status (serum 25(OH)D ≥ 20 ng/mL ).

Similar results were seen in a previous study in Qatar where males with Vitamin D deficiency had a 3 times higher risk of MI than males with an adequate Vit D status

Final thoughts:-

Vitamin D deficiency/inadequacy is rife in the Middle East

- Nutritional monitoring is limited
- Food Fortification is sporadic and ineffective
- The use of supplements is low
- As the population is only likely to spend more time indoors in the future, it seems prudent for “at risk” groups, such as children and females over the age of 50 years to consume daily supplements.
Some people think scientists exclaim

*Eureka!*

When doing experiments.

But they’re way more likely to say...

*Bollocks!*

*oh...sh*t!*

*F**!*

*Ahse!*

*Stupid piece of crap machine!*

*I hate science!*

[Drawing of scientists reacting to experiments with swear words]
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References (1):

References (2)

- Fawzi MM, Swelam E & Said NS; “Plasma levels of 25-hydroxy vitamin D and dress style in a sample of Egyptian female university students”; Life Sci J 2012; 9:763-767
- Haq A, Svobodova J, Sofi NY et al.; “Vitamin D status Among the Juvenile Population: A Retrospective Study”; J Steroid Biochem 2017, Jan 17