VITAMIN D IN THE PERINATAL PERIOD-
MYTHS AND REALITIES

Dr Sheila S Mathai, MD, DNB, DM
(Neonatology)
Professor & HOD (Pediatrics)
Armed Forces Medical College
Pune
"Real knowledge is to know the extent of one's ignorance."
Confucius
Peer reviewed articles on vitamin D in PubMed have increased from about 100 articles per year in 1975 to >3000 in 2015.

Time magazine has reported the newly realized importance of Vitamin D as one of the top 10 medical breakthroughs in 2007.

Sir Edward Mellanby discovered Vitamin D in the late 1890s.
Alpha calcidiol
(1 OH cholecalciferol): synthetic form
1. In sunny countries like ours we easily get our daily requirement of Vit D
2. Vit D is mainly important for bone health
3. Vit D deficiency is a nutritional problem seen in malnourished children with rickets
4. Normal neonates get enough Vit D from the maternal stores and breastmilk
5. Requirements of Vit D are the same for all ages
6. The hype about Vit D is just a passing fad…
Myth No1 : We easily get our daily requirement of Vit D from sunlight in countries like ours
SUNLIGHT VS ORAL INTAKE

- Just 10 minutes of >70% body exposure to mid-afternoon sunlight in a fair-skinned adult produces about 2000 units of vitamin D over the next 24 hours.

- This is equivalent to drinking 20 glasses of fortified milk (at 100 IU per glass) or taking 8 standard calcium tablets (250 IU per tablet) in one day.
Caveats of Sun-induced Vitamin D

- Depends on
  - Amt of skin exposed
  - Skin type (brown and dark skin absorbs less UV rays)
  - UVB Index (maximum between 1200-1500 hrs)
  - Geographical location

- Vitamin D from sunlight can actually vary from <100 IU/day to >2000 IU/day
Myth No 2: Vitamin D is only important for bone health

REALITY NO 2
VITAMIN D- MULTI-FACETED HORMONE

Calcium and Bone metabolism

Brain development

Diabetes

Cancers

Immunity & Inflammation

Cardiovascular disease

“Hormone” D
VITAMIN D AND CALCIUM METABOLISM

- Dietary Ca, P
- Intestinal tract
- Activity of parathyroid regulated by level of serum Ca
- Extracellular fluid Ca
- 1,25(OH)2D stimulates absorption of Ca and P from gut
- Parathormone regulates conversion of 25-OH-D to 1,25(OH)2D in the kidney
- Parathormone increases resorption of Ca and decreases resorption of P
- Calcitonin suppresses Ca release by suppression of osteoclast
- Parathormone releases Ca from bone
 Normally 30% of dietary intake of calcium is actually absorbed from the gut

This decreases to < 10% in Vit D deficient states
VITAMIN D AND BRAIN DEVELOPMENT

- Gestational vitamin D deficiency causes permanent changes in the developing rat brain.
- It disrupts the balance between cell proliferation and apoptosis.
- Results in epigenetic changes and has been implicated in autism.

T and B lymphocytes, macrophages and Langerhans cells express the Vitamin D receptors through TLRs.

- Regulates the production of the antimicrobial proteins cathelicidin and beta defensin.
- Induces the generation of CD25⁺/CD4⁺

LONG-TERM EFFECTS ON CHILDREN

- Maternal intake reduces the risk of recurrent wheeze and allergies in children at 3 y of age
- Intake of vitamin D in pregnancy reduces risk of type 1 diabetes: a birth-cohort study
Myth No 3: Vitamin D Deficiency is a nutritional problem
VITAMIN D FROM DIETARY SOURCES

- Fish oil
- Alfafa (seaweed)
- Mushrooms
- Spinach
- Small amts from egg yolk
VITAMIN D DEFICIENCY IS A LIFESTYLE DISEASE

Because we shun the sun....
VIT D DEFICIENCY WITH ‘NORMAL’ NUTRITION

- 40-50% of inner city children have been found to be deficient

- Maternal Vitamin D deficiency at or near term has ranged from 5-20% in light-skinned populations to 30-70% amongst dark-skinned people

- 98 infants aged 2.5 to 3.5 months, born at term with appropriate weight and their mothers were enrolled
- Vitamin D deficiency was found in 66.7 per cent of infants and 81.1 per cent of mothers; and insufficiency in an additional 19.8 per cent of infants and 11.6 per cent of mothers.
- Radiological rickets was present in 30.3 per cent of infants with 25OHD < 10 ng/ml.
Myth No 4: Normal neonates get enough Vit D from breastmilk and Vit D deficiency is not a big problem
The mother is the only source of Vitamin D
Cholecalciferol and 25-OH Vit D cross the placenta
Hydroxylation occurs in placenta and fetal kidney to 1-25 (OH)2D3
Half life of Vitamin D is 3-4 weeks and stores get depleted by 6-8 weeks
The Vitamin D content of breast milk is 20-40 IU/L
Requirement for a term baby is 200-400 IU/day in infancy which is equivalent to taking 4-8 L of breast milk/day!
CALCIUM AND VIT D METABOLISM

NORMAL
CALCIUM INTAKE

PREGNANCY
CALCIUM INTAKE

LACTATION
CALCIUM INTAKE

SERUM Ca^{2+}

URINE

33 gm of Ca

Only 10-20% of Ca is absorbed without Vitamin D

45 gm of Ca

Kovacs C S Am J Clin Nutr 2008;88:520S-528S
Fetal serum Ca is always higher than mother’s but Vit D level is always lower.....
2nd twin born to a primi after ART at 36+ weeks POG by Em LSCS (Ind IUD of first twin)

BW 1.9 Kg, Cried Immediately and started on feeds on D1

On D2 developed jerky movements of upper limbs with normal sensorium

During USG cranium had excessive crying followed by tetanic, opisthotonic spasms with laryngospasm requiring intubation

Baby’s SCa was 6.5mg with ionic Ca of 0.6mmol/L

Vit D was 10ng/ml; mother’s 12ng/ml, mother’s Ca was 6mg%!)
FACT...

Breast fed babies born to mothers with Vit D deficiency are very likely to develop both calcium and Vit D deficiency in early infancy unless supplemented from birth or exposed daily to sunlight.

- 60 infants with hypocalcaemic seizures and their mothers were compared with apparently healthy controls

- Hypovitaminosis D (25(OH)D levels <10 ng/mL) was observed in 85% of study mothers (6.54 ± 5.32 ng/mL) and 90% of study infants (4.92 ± 4.62 ng/mL)
Myth No 5: Requirements of Vit D are the same for all
What is considered normal is controversial.

1 ng/ml = 2.5 nmol/L

**WHAT ARE NORMAL LEVELS ...**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Range (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficiency</td>
<td>20</td>
</tr>
<tr>
<td>Insufficiency</td>
<td>30</td>
</tr>
<tr>
<td>Physiological</td>
<td>50</td>
</tr>
<tr>
<td>Upper limits</td>
<td>150</td>
</tr>
<tr>
<td>Undesired levels</td>
<td></td>
</tr>
</tbody>
</table>

Recommended Target Range for Newborns and children: 50 ng/mL

Adapted from: N England J Med 2007;357:266-81
Requirement of Vitamin D in Infancy

- Old recommendations: 200 IU/day (1 µg = 40 IU)
- 2008 recommendations of AAP: 400 IU of Vit D to be started in all breast fed babies from the first few days of life till on full complementary feeds to ensure a minimal serum level of 50 nmol/L

The ESPGAN recommendation of 800 to 1,600 IU/day vitamin D for preterm infants is promoted by at least three randomized, controlled trials.

- Sarah N. Taylor, Bruce W. Hollis and Carol L. Wagner. Vitamin D Needs of Preterm Infants. *NeoReviews* 2009;10;e590-e599
Daily vitamin D supplementation to babies born at 28-34 weeks at a dose of 800 IU compared with 400 IU significantly reduces the prevalence of vitamin D deficiency in preterm infants.

Primary outcome was VDD (serum 25-hydroxyvitamin D levels, 20 ng/mL) at 40 weeks’ PMA. Secondary outcomes were VDD, bone mineral content, and bone mineral density at 3 months’ corrected age (CA).
A randomized, controlled trial with mothers who were supplemented with 6000 IU (study) or 400 IU/day (controls).

The vitamin D levels in the breast milk of study group and in the exclusively breastfed infants themselves were found to be equivalent to the infants who received 300 IU per day with no toxic effects.

Vitamin D deficiency is rampant in our country both in pregnant mothers and young infants. It mostly remains subclinical and undetected but can manifest as frank hypocalcaemia in neonates. Deficiency can have long term implications not only on bone health but on immune responses, allergies, neurodevelopment and incidence of diabetes, cancers and cardiovascular disease in adulthood.
**TAKE HOME MESSAGES**

- All pregnant and lactating women in our country MUST be supplemented with ADEQUATE amounts of Vit D (800-1000 IU/day should be considered along with 1000 mg Ca/day)
- Supplementation of all term, breast-fed neonates with Vit D STARTING FROM THE FIRST FEW DAYS OF LIFE with 400 IU/day should be considered
- Preterms will need higher doses (800-1000 U/day) of Vit D depending on GA along with calcium and phosphate
Myth No 6: The hype about Vit D is just a passing fad...

REALITY NO 6
'If we cannot change our minds we cannot change anything'

George Bernard Shaw