VITAMIN D DEFICIENCY IN THE NEONATAL PERIOD

Leena Mamilly, MD
Objectives

1. Recognize vitamin D deficiency-related hypocalcemia in the neonate as a result of maternal vitamin D deficiency
2. Manage vitamin D deficiency in the neonatal period
3. Recommend maternal vitamin D screening and supplementation during pregnancy for prevention of neonatal vitamin D deficiency
Clinical Case

- 6 day old full term male neonate presented to the emergency department for seizure-like activity. The infant had an episode of hand twitching on day 5 of life. Generalized seizure activity was noted on the sixth day leading to the ED visit.
- The infant had a Hispanic mother and Caucasian father. His mother reported an uneventful pregnancy. She reported taking prenatal vitamins for a short period of time in the beginning of pregnancy. No other medications. She does not have any health issues. Denied excessive calcium supplementation.
- On physical examination, the infant had normal vital signs and a normal baseline examination.
- Admitted to the PICU after full septic workup was performed.
- He was found to have a severely decreased calcium level (Total Ca 6.3 mg/dL).
# Laboratory Evaluation of the Infant and Mother

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>6.3 mg/dL</td>
</tr>
<tr>
<td>Ionized Ca</td>
<td>3.1 mg/dL</td>
</tr>
<tr>
<td>Phosphate</td>
<td>9.9 mg/dL</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.7 mEq/L</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>216 unit/L</td>
</tr>
<tr>
<td>PTH</td>
<td>24 pg/mL</td>
</tr>
<tr>
<td>25-OH Vitamin D</td>
<td>&lt;8 ng/mL</td>
</tr>
<tr>
<td>1,25-OH Vitamin D</td>
<td>52.4 pg/mL</td>
</tr>
<tr>
<td>Urine Calcium</td>
<td>3 mg/dL</td>
</tr>
<tr>
<td>Urine Creatinine</td>
<td>8.0 mg/dL</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>9.1 mg/dL</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>106 unit/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.1 g/dL</td>
</tr>
<tr>
<td>PTH</td>
<td>38 pg/mL</td>
</tr>
<tr>
<td>25-OH Vitamin D</td>
<td>9 ng/mL</td>
</tr>
<tr>
<td>1,25-OH Vitamin D</td>
<td>22.6 pg/mL</td>
</tr>
</tbody>
</table>

Neonatal Hypocalcemia

Calcium levels
• < 8.8 mg/dL in term infants
• < 7 mg/dL in preterm infants

Classified as:
• Early-onset: First 3-4 days of life. Usually secondary to an exaggeration of the normal decline in serum calcium after birth
• Late Onset: 5 to 10 days after birth. More frequent in term neonates. Not correlated with birth trauma or asphyxia
Bone Metabolism in the Fetal Period

- Pregnant mother’s serum ionized calcium and PTH are stable
- PTHrP produced by the placenta and other fetal structures (high maternal levels)
- Increased maternal calcitriol to double the norms, increased intestinal calcium absorption
- Active transport of Ca across the placenta. 1:1.4 maternal to fetal calcium gradient
- PTHrP as the main regulator of fetal ionized calcium
- In the first two trimesters, calcium deposition contributes to linear growth
- Third trimester rapid bone mineralization
- Fetal circulating calcium levels increase with advancing gestational age
- At term the fetus is hypercalcemic relative to maternal levels
Bone Metabolism in the First Few Days of Life

- Birth leads to sudden interruption of calcium supply
- Falling ionized calcium with insufficient PTH response
- Relative resistance of the immature kidney to PTH
- Renal retention of phosphorus contributing to hypocalcaemia
- Elevated intake of phosphate (Cowmilk-derived formulas)
- Exaggerated calcitonin secretion in preterm infants
- Physiological nadir within the first 2 days of life
- The newborn’s vitamin D status is directly related to maternal vitamin D status
- Serum levels of both 25-hydroxyvitamin D and calcitriol are lower than maternal levels
Presenting Signs and Symptoms of Neonatal Hypocalcemia

- Nonspecific, often clinically silent
- Neuromuscular irritability: myoclonic jerks, ‘twitching’, exaggerated startle responses or seizures
- Apnea
- Cyanosis
- Tachypnea
- Tachycardia
- Vomiting
- Laryngospasm
- Prolonged QT interval
- Heart failure
Causes of Neonatal Hypocalcemia: Early Onset

- Maternal diabetes
- Preeclampsia
- Maternal hypercalcemia
- Asphyxia
- Sepsis
- Prematurity
- Low birth weight
- Hypomagnesemia
- Respiratory distress syndrome
- Blood transfusion
- Alkalosis
Causes of neonatal hypocalcemia: Late Onset

- Increased phosphate load
- Vitamin D deficiency (nutritional, genetic)
- Nutritional calcium deficiency
- Hypomagnesemia
- Renal insufficiency
- Hypoalbuminemia
- Transfusion
- Diuretics
- Organic acidemias
- Transient PTH resistance

Primary Hypoparathyroidism

- DiGeorge syndrome
- Familial hypoparathyroidism
- CaSR-activating mutation
- Pseudohypoparathyroidism
- Kenny-Caffey syndrome
- Pearson mitochondropathy
- Kearns-Sayer mitochondropathy
- PTH gene defects
- Partial deletion of GCMB
Workup of a Neonate with Hypocalcemia

Infant Evaluation
- Serum total and ionized calcium
- Serum phosphorus
- Serum magnesium
- Spot urine for calcium-to-creatinine ratio
- Total protein and albumin
- Intact PTH
- Electrolytes
- BUN and creatinine
- Vitamin D metabolites

Maternal Evaluation
If maternal cause is suspected
- Serum calcium and ionized Calcium
- Phosphorus
- Magnesium
- PTH
- 25 (OH)D
- 1,25 (OH)D
- Spot urine for calcium-to-creatinine ratio
Vitamin D Deficiency in the Mother-Infant Dyad
Synthesis and Metabolism of Vitamin D in the Regulation of Calcium, Phosphorus, and Bone Metabolism

Vitamin D Deficiency: Definition

Endocrine Society Guidelines

• Screening for vitamin D deficiency only in persons at risk
• Defines vitamin D deficiency as total serum 25-(OH)D levels <50 nmol/L (<20 ng/mL)
• Defines vitamin D insufficiency as 25 (OH)D level of 52.5 to 72.5 nmol/L (21 to 29 ng/mL)

<table>
<thead>
<tr>
<th>nmol/L**</th>
<th>ng/mL*</th>
<th>Health status</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>&lt;12</td>
<td>Associated with vitamin D deficiency, leading to rickets in infants and children and osteomalacia in adults</td>
</tr>
<tr>
<td>30 to &lt;50</td>
<td>12 to &lt;20</td>
<td>Generally considered inadequate for bone and overall health in healthy individuals</td>
</tr>
<tr>
<td>≥50</td>
<td>≥20</td>
<td>Generally considered adequate for bone and overall health in healthy individuals</td>
</tr>
<tr>
<td>&gt;125</td>
<td>&gt;50</td>
<td>Emerging evidence links potential adverse effects to such high levels, particularly &gt;150 nmol/L (&gt;60 ng/mL)</td>
</tr>
</tbody>
</table>
Epidemiology

http://dx.doi.org/10.1016/j.jsbmb.2013.11.003
Factors Associated with Maternal Vitamin D Deficiency

- Maternal diet
- Latitude
- Seasonal variations
- Adiposity
- Ethnicity/skin pigmentation
- Use of sun screen
- Use of sun protective clothing
- Use of prenatal vitamins
High Prevalence of Vitamin D Insufficiency in Black and White Pregnant Women Residing in the Northern United States and Their Neonates

Lisa M. Bodnar, Hyagriv N. Simhan, Robert W. Powers, Michael P. Frank, Emily Cooperstein, and James M. Roberts

2Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA 15261; 3Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Pittsburgh School of Medicine, Pittsburgh, PA 15213; and Magee-Women’s Research Institute, Pittsburgh, PA 15213


• 200 black women and 200 white women, all nulliparous
• Maternal blood samples in early gestation and late gestation. Cord blood samples.
• The majority of black women were vitamin D deficient or insufficient. No deficiency noted in white women, insufficiency was common
• Multivitamin users had higher 25 (OH)D levels
• Although levels were higher in the summer and lower in the winter and spring for both groups, black women had a smaller mean difference in vitamin D levels compared to white women from winter to summer.
<table>
<thead>
<tr>
<th></th>
<th>White women, ( n = 200 )</th>
<th>Black women, ( n = 200 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-21 wk gestation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum 25(OH)D, ( \text{nmol/L} )</td>
<td>73.1 (69.4, 76.9)</td>
<td>40.2 (37.9, 42.7)*</td>
</tr>
<tr>
<td>Vitamin D status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficient: 25(OH)D &lt;37.5 nmol/L</td>
<td>2.0</td>
<td>44.9**</td>
</tr>
<tr>
<td>Insufficient: 25(OH)D 37.5-80 nmol/L</td>
<td>60.3</td>
<td>51.0</td>
</tr>
<tr>
<td>Sufficient: 25(OH)D &gt;80 nmol/L</td>
<td>37.3</td>
<td>4.1</td>
</tr>
<tr>
<td>37-42 wk gestation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum 25(OH)D, ( \text{nmol/L} )</td>
<td>80.4 (76.0, 85.1)</td>
<td>49.4 (46.1, 52.9)*</td>
</tr>
<tr>
<td>Vitamin D status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficient: 25(OH)D &lt;37.5 nmol/L</td>
<td>5.0</td>
<td>29.2**</td>
</tr>
<tr>
<td>Insufficient: 25(OH)D 37.5-80 nmol/L</td>
<td>41.2</td>
<td>54.1</td>
</tr>
<tr>
<td>Sufficient: 25(OH)D &gt;80 nmol/L</td>
<td>53.8</td>
<td>16.7</td>
</tr>
<tr>
<td>Cord blood</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum 25(OH)D, ( \text{nmol/L} )</td>
<td>67.4 (63.8, 71.3)</td>
<td>39.0 (36.3, 41.8)*</td>
</tr>
<tr>
<td>Vitamin D status, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deficient: 25(OH)D &lt;37.5 nmol/L</td>
<td>9.7</td>
<td>45.6**</td>
</tr>
<tr>
<td>Insufficient: 25(OH)D 37.5-80 nmol/L</td>
<td>56.4</td>
<td>48.8</td>
</tr>
<tr>
<td>Sufficient: 25(OH)D &gt;80 nmol/L</td>
<td>33.9</td>
<td>7.6</td>
</tr>
</tbody>
</table>

1 Values are geometric means (95% CI) or %. *Different from white women, \( P < 0.001 \) (student’s \( t \) test); **different from white women, \( P < 0.001 \) (chi-square test).

2 Log-transformed to ensure normality.
Widespread Vitamin D Deficiency in Urban Massachusetts Newborns and Their Mothers
Anne Merewood, Supriya D. Mehta, Xena Grossman, Tai C. Chen, Jeffrey S. Mathieu, Michael F. Holick and Howard Bauchner
*Pediatrics* 2010;125:640; originally published online March 22, 2010:
DOI: 10.1542/peds.2009-2158

- 375 newborns and 433 mothers
- Blood samples within 72 hours of delivery
- 58% of the infants and 35.8% of the mothers were Vit D deficient: 25 (OH)D <20 ng/mL
- Severe deficiency (<15 ng/mL) in 38% of the infants and 23.1% of the mothers
- Risk factors for infant Vit D deficiency: maternal deficiency, winter birth, black race and a maternal BMI of ≥ 35
- Maternal prenatal-vitamin use was protective against both infant mother deficiency
- 30% of the women who took prenatal vitamins were still vitamin D deficient at the time of birth.
Pregnancy Outcomes In Relation to Vitamin D Deficiency
### Vitamin D supplementation for women during pregnancy (Review)

#### Anticipated absolute effects (95% CI)

**Risk with no treatment/placebo (no vitamins or minerals)**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Risk</th>
<th>Study Population</th>
<th>Anticipated absolute effects (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia (ALL)</td>
<td>RR 0.22 (0.23 to 0.30)</td>
<td>219 (2 RCTs)</td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes (ALL)</td>
<td>RR 0.43 (0.25 to 0.74)</td>
<td>219 (2 RCTs)</td>
<td></td>
</tr>
</tbody>
</table>

#### Relative effect (95% CI) (studies) (GRADE)

- Quality of evidence: LOW
- Quality of evidence: VERY LOW

#### Comments

Risk with treatment with vitamin D alone

Risk with treatment with vitamin D plus placebo

Moderate

Pre-eclampsia (ALL) 150 per 1000

Study population

Gestational diabetes (ALL)

Study population

12 per 1000

24 per 1000

10 per 1000

(11 to 94)

(11 to 82)

12 per 1000

24 per 1000

10 per 1000

(11 to 94)

(11 to 82)
| Maternal vitamin D concentration at term (25-hydroxyvitamin D) (nmol/L) (ALL) | The mean maternal vitamin D concentration at term (25-hydroxyvitamin D) (nmol/L) (ALL) in the intervention group was 47.24 higher (35.17 to 59.31 higher) | 888 (7 RCTs) | LOW 1, 4 |
| Adverse effects | Study population | RR 0.17 (0.01 to 4.06) (1 RCT) | 135 | LOW 2 |
| Preterm birth (less than 37 weeks' gestation) (ALL) | Study population | RR 0.36 (0.14 to 0.93) (3 RCTs) | 477 | MODERATE 1 |
| Low birthweight (less than 2500 g) (ALL) | Study population | RR 0.40 (0.24 to 0.67) (3 RCTs) | 493 | MODERATE 1 |
| Moderate | 22 per 1000 | 4 per 1000 (0 to 90) | |
| 99 per 1000 | 35 per 1000 (14 to 92) | |
| 46 per 1000 | 17 per 1000 (6 to 43) | |
| 199 per 1000 | 80 per 1000 (58 to 133) | |
Neonatal Outcomes in Relation to Maternal Vitamin D Deficiency
78 infants < 31 days of age hospitalized (mean = 8 days) for moderate to severe hypocalcemia (< 1.0 mmol/L or 4 mg/dL)

- 76 presented with seizure-like activity
- 67 exclusively formula-fed
- 25 (OH) D levels were checked in 42 infants
  - All 42 infants ≤ 62 nmol/L (25 ng/mL)
  - 35 infants < 50 nmol/L (20 ng/mL)
  - 10 infants < 30 nmol/L (12 ng/mL)

- 71.8% males
- 62% Hispanic
Biochemical Characteristics

- Hyperphosphatemia
- Hypomagnesemia
- Low or inappropriately normal PTH levels

Treatment

- IV calcium used in 69 infants
- Oral calcium carbonate
- Oral calcitriol n=60, median dose 0.25 mcg daily
- Low phosphorus formula
- Magnesium replacement n=42
- Median duration of treatment 1.8 months (1.0-2.5)
Incidence of Hypocalcemic Seizures Due to Vitamin D Deficiency in Children in the United Kingdom and Ireland

Emre Basatemur and Alastair Sutcliffe

- Physician-reported cases of seizure activity and both hypocalcemia (<2.0 mmol/L) and Vit D deficiency (25(OH)D < 50 nmol/L)
- N = 91
- 24 infants < 1 month of age (27%)

<table>
<thead>
<tr>
<th>Test</th>
<th>Age &lt; 1 month</th>
<th>Age &gt; 1 month</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-OH-D (nmol/l) (n=81)</td>
<td>Median (95% CI)</td>
<td>Median (95% CI)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>25-OH-D (nmol/l) (n=89)</td>
<td>20.1 (13.9 - 25.9)</td>
<td>10.3 (10 - 11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alkaline phosphatase (iu/l) (n=89)</td>
<td>351 (256 - 406)</td>
<td>816 (719 - 922)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parathyroid hormone (pmol/l) (n=72)</td>
<td>5.9 (2.8 - 8.6)</td>
<td>28.3 (22.4 - 33.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Corrected calcium (mmol/l) (n=91)</td>
<td>1.54 (1.44 - 1.63)</td>
<td>1.38 (1.33 - 1.43)</td>
<td>0.002</td>
</tr>
<tr>
<td>Phosphate (mmol/l) (n=86)</td>
<td>2.97 (2.71 - 3.24)</td>
<td>1.82 (1.69 - 1.96)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Lower vitamin D levels are associated with increased risk of early-onset neonatal sepsis in term infants

M Cetinkaya¹, F Cekmez², G Buyukkale¹, T Erenler-Ercan¹, F Demir¹, T Tunc², FN Aydin³ and G Aydemir²


- 50 term infants with clinical and laboratory findings of early onset sepsis (The first 3 postnatal days). 50 controls.
- Neonatal and maternal serum 25(OH)D levels
- Both maternal and neonatal 25(OH)D levels were lower in the study group compared to control
- 84% of infants in the sepsis group had a mean 25(OH)D level of < 11 ng/mL ($P<0.05$)
- 10% maternal regular vitamin D supplementation in the sepsis group vs 645 in the control group
- Mean maternal vitamin D levels 22.2 ± 6.8 ng/mL in the sepsis group compared to 36.2 ± 1.8 ng/mL in the control group ($P <0.001$)
- Positive correlation between maternal and neonatal levels
Long Term Outcomes Related to Maternal Vitamin D Status

Effect on future risk of asthma, wheezing and upper respiratory infections

• Multiple publications with contradicting results. Camargo et al found reduction in the risk of recurrent wheezing in the offspring of mothers with higher vitamin D levels during pregnancy.

• Chawes et al. 2016: RCT: supplementation with vitamin D3: 2400 IU (n=315) or placebo (n=308). Children followed for 3 years. Vit D supplementation decreased the incidence of “troublesome respiratory symptoms”, although no statistically significant reduction in the risk of asthma was found.

The risk of type 1 diabetes

• J Dong et al 2013: Meta-analysis of 13 studies (vitamin D intake during pregnancy or early in life). “vitamin D intake during early life may be associated with a reduced risk of type 1 diabetes. However, there was not enough evidence for an association between maternal intake of vitamin D and risk of type 1 diabetes in the offspring”

Areas of active research

• Lasting effects of fetal and early infancy vitamin D deficiency on later adult disease such as anatomical changes of the brain, schizophrenia, multiple sclerosis, certain cancers, cardiovascular disease, and various other autoimmune diseases such as diabetes and lupus
Treatment of neonatal hypocalcemia and Vitamin D Deficiency

• Oral calcium supplementation
• Intravenous calcium repletion (recurrent seizures, prolonged QT interval)
• Oral calcitriol might be needed to normalize calcium levels quickly
• Vitamin D replacement 2000 IU daily
• Low phosphorus formula (such as Similac PM 60/40) along with oral calcium supplementation
• Magnesium replacement for 1-2 weeks when indicated
• Most patients require treatment for 1-2 months
Our Patient’s Clinical Course

- Initially started on IV calcium gluconate 100 mg/Kg/day, along with PO calcitriol 0.25 mcg twice a day
- He was also started on Vitamin D3: 2000 units by mouth daily
- Due to recurrent seizures, calcium gluconate was increased to 200 mg/Kg/day and calcitriol to 0.5 mcg twice daily.
- He developed hypomagnesemia on day 2 of admission, requiring replacement with magnesium sulfate 50 mg/Kg/dose
- Infant was started on oral calcium replacement with calcium carbonate on day 3 of admission (Ca 7.5 mg/dL)
- Other studies, including blood culture, EEG, CT scan of the brain and cardiac echo were negative
- Testing for DiGeorge syndrome was not deemed necessary
- Length of hospital stay: 5 days
- All medications were discontinued (as lab improvement allowed) at 7 weeks of age except for vitamin D3 replacement
Current Guidelines: Where We Stand on Maternal Vitamin D Deficiency
Recent evidence suggests that vitamin D deficiency is common during pregnancy especially among high risk groups. Newborn vitamin D level are largely dependent on maternal vitamin D status. An optimal serum level during pregnancy has not been determined (20 versus 32 ng/dL). Most experts agree that 1000-2000 IU of vitamin D per day is safe. At this time there is insufficient evidence to support a recommendation for screening all pregnant women for vitamin D deficiency. There is insufficient evidence to recommend vitamin D supplementation for the prevention of preterm birth or preeclampsia.
Evaluation, Treatment, and Prevention of Vitamin D Deficiency: An Endocrine Society Clinical Practice Guideline
Guidelines For Screening and Supplementation

- “We recommend using the serum circulating 25(OH)D level, measured by a reliable assay, to evaluate vitamin D status in patients who are at risk for vitamin D deficiency”. Pregnant and lactating women considered within the individuals at risk
- Daily doses of 600 IU do not prevent vitamin D deficiency in pregnant women
- Recommended prenatal vitamin containing 400 IU with a supplement of at least 1000 IU
- Lactating women should take at least a multivitamin containing 400 IU vitamin D along with at least 1000 IU supplement daily
- 4000 to 6000 IU/d to transfer enough vitamin D into her milk if they choose not to give the infant a vitamin D supplement
- Both the AAP and Endocrine Society recommend supplementation for infants with 400 IU daily of vitamin D
<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>AI (IU, μg)</th>
<th>EAR (IU, μg)</th>
<th>RDA (IU, μg)</th>
<th>UL (IU, μg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 to 6 mo</td>
<td>400 (10, pg)</td>
<td>—</td>
<td>—</td>
<td>1,000 (25, pg)</td>
</tr>
<tr>
<td>6 to 12 mo</td>
<td>400 (10, pg)</td>
<td>—</td>
<td>—</td>
<td>1,500 (38, pg)</td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–3 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>2,500 (65, pg)</td>
</tr>
<tr>
<td>4–8 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>3,000 (75, pg)</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>14–18 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>19–30 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>31–50 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>51–70 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>&gt; 70 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>800 (20, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9–13 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>14–18 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>19–30 y</td>
<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
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<td>31–50 y</td>
<td>—</td>
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<td>600 (15, pg)</td>
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</tr>
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<td>—</td>
<td>400 (10, pg)</td>
<td>600 (15, pg)</td>
<td>4,000 (100, pg)</td>
</tr>
<tr>
<td>&gt; 70 y</td>
<td>—</td>
<td>400 (10, pg)</td>
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NOTE: AI = Adequate Intake; EAR = Estimated Average Requirement; IU = International Units; RDA = Recommended Dietary Allowance; UL = Tolerable Upper Intake Level.
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