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جامعة أسيوط


## In This Issue…





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**This Bulletin is a free quarterly periodical issued by the Drug Information Center (DIC) located at Faculty of Pharmacy, Assiut University**

# Vitamin D deficiency

Vitamin D deficiency is a global public health issue. About 1 billion people worldwide have vitamin D deficiency, while 50% of the population has vitamin D insufficiency. In this issue we are going to discuss the essential points regarding vitamin D deficiency.

## 1- Introduction

Vitamin D is a fat-soluble vitamin that plays an important role in calcium homeostasis and bone metabolism. Dermal synthesis and dietary intake are the major sources of ergocalciferol (D2) and cholecalciferol (D3), both of which are converted to 25-hydroxy-vitamin D2 (25-OH-D2) and 25-hydroxy-vitamin D3 (25-OH-D3) respectively in the liver by hepatic enzyme 25–hydroxylase. Both 25-OH-D2 and 25-OH-D3 are then converted to the most active form of vitamin D (1,25 dihydroxyvitamin D) by the enzyme 1-alpha-hydroxylase in the kidneys. This active 1,25 dihydroxyvitamin D increases intestinal absorption of calcium and bone resorption and decreases renal excretion of calcium and phosphate.

Vitamin D deficiency can lead to osteomalacia and rickets in children and osteomalacia in adults**.**

## 2- Causes of vitamin D deficiency

1. Decreased dietary intake and/or absorption:

Certain malabsorption syndromes such as celiac disease, short bowel syndrome, gastric bypass, inflammatory bowel disease, chronic pancreatic insufficiency, and cystic fibrosis may lead to vitamin D deficiency. Lower vitamin D intake orally is more prevalent in the elderly population.

2. Decreased sun exposure:

About 50% to 90% of vitamin D is synthesized through the skin via sunlight while the rest comes from the diet. Twenty minutes of sunshine daily with over 40% of skin exposed is required to prevent vitamin D deficiency. Dark-skinned people have less cutaneous vitamin D synthesis. Decreased exposure to the sun as seen in individuals who are institutionalized, or have prolonged hospitalizations can also lead to vitamin D deficiency. Effective sun exposure is decreased in individuals who use sunscreens consistently.

3. Decreased endogenous synthesis:

Individuals with chronic liver disease such as cirrhosis can have defective 25-hydroxylation leading to deficiency of active vitamin D. Defect in 1-alpha 25-hydroxylation can be seen in hyperparathyroidism, renal failure and 1-alpha hydroxylase deficiency.

4. Increased hepatic catabolism:

Medications such as phenobarbital, carbamazepine, dexamethasone, nifedipine, spironolactone, clotrimazole, and rifampin induce hepatic p450 enzymes which activate degradation of vitamin D.

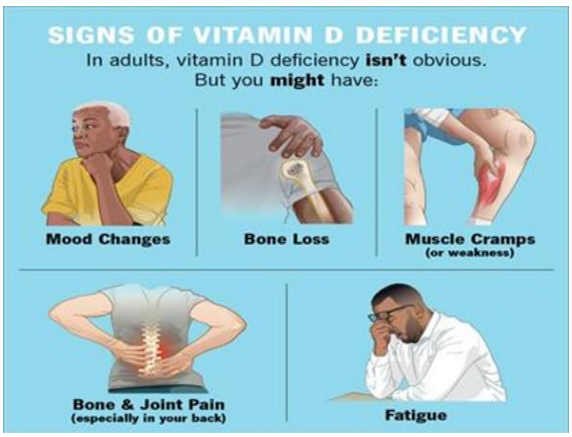
5. End organ resistance:

End organ resistance to vitamin D can be seen in hereditary vitamin D resistant rickets.

## 3- Testing of vitamin D

It is not recommended to screen asymptomatic individuals for vitamin D deficiency. High-risk individuals shall be evaluated. Vitamin D sufficiency or deficiency is evaluated by the measurement of serum 25-hydroxyvitamin D.

There are substantial differences in mineral metabolism amongst different races. African Americans, for example, have higher bone density and low fracture risk compared to other races. The International Society for Clinical Densitometry and International Osteoporosis Foundation



recommend minimum serum levels of 25-hydroxyvitamin D of 30 ng/mL to minimize the risk of fall and fractures in older individuals. There is insufficient data about the maximum safe up level of serum 25-hydroxyvitamin D, however, at high levels such as above 100 ng/mL, there is a potential risk of toxicity due to the secondary hypercalcemia.

## 4. Treatment and management of vitamin D deficiency:

Several preparations of vitamin D are available. **Vitamin D3 (cholecalciferol)**, when compared with **vitamin D2 (ergocalciferol),** has been shown to be more efficacious in achieving optimal 25-hydroxyvitamin D levels, thus favoring vitamin D3 as a treatment of choice.

The amount of vitamin D required to treat the deficiency depends largely on the degree of the deficiency and underlying risk factors.

- Initial supplementation for 8 weeks with Vitamin D3 either 6,000 IU daily or 50,000 IU weekly can be considered. Once the serum 25-hydroxyvitamin D level exceeds 30 ng/mL, a daily maintenance dose of 1,000 to 2,000 IU is recommended.
- A higher-dose initial supplementation with vitamin D3 at 10,000 IU daily may be needed in high-risk adults who are vitamin D deficient (African Americans, Hispanics, obese, taking certain medications, malabsorption syndrome). Once serum 25-hydroxyvitamin D level exceeds 30ng/mL, 3000 to 6000 IU/day maintenance dose is recommended.
- Children who are vitamin D deficient require 2000 IU/day of vitamin D3 or 50,000 IU of vitamin D3 once weekly for 6 weeks. Once the serum 25(OH)D level exceeds 30 ng/mL, 1000 IU/day maintenance treatment is recommended. According to the American Academy of Pediatrics, infants who are breastfed and children who consume less than 1 L of vitamin D-fortified milk need 400 IU of vitamin D supplementation.
- Calcitriol can be considered where the deficiency persists despite treatment with vitamin D2 and/or D3. The serum calcium level shall be closely monitored in these individuals due to an increased risk of hypercalcemia secondary to calcitriol.
  Calcidiol can be considered in patients with fat malabsorption or severe liver disease. (Vitamin D deficiency.

**Sources** :

*- Sizar O, Khare S, Goyal A, et al. Vitamin D Deficiency. [Updated 2022 Jul 18]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532266/*

*-Amrein, K., Scherkl, M., Hoffmann, M. et al. Vitamin D deficiency 2.0: an update on the current status worldwide. Eur J Clin Nutr **74**, 1498–1513 (2020). https://doi.org/10.1038/s41430-020-0558-y*

*-https://www.healthline.com/nutrition/vitamin-d-side-effects*

# Common Q & A

### 1. What are the natural sources of vitamin D?

There are a few foods that naturally have some vitamin D, including:

Fatty fish such as salmon, tuna and mackerel and sardines.

Beef (cow) liver.

Cod liver oil.

Mushrooms.

Egg yolks.

Cod liver oil.

You can also get vitamin D from fortified foods. Be sure to check the nutrition labels to find out if a food has vitamin D. Foods that often have added vitamin D include:

- Cow's milk and soy, almond and oat milk.
- Breakfast cereals.
- Orange juice.

## 2. Why taking vitamin D is important in pregnancy?

It has been demonstrated that vitamin D supplementation is able to reduce adverse pregnancy outcomes when a higher level is achieved, with an increasing efficacy when the target level is raised from 20 to 40 ng/mL or 50 ng/mL.Three major adverse pregnancy outcomes appear to improve with vitamin D supplementation: a 60% reduction in preeclampsia, a 50% reduction in gestational diabetes, and a 40% reduction in preterm delivery. Vitamin D deficiency during pregnancy also seems able to induce specific genomic pathways relevant to autoimmune disease in childhood and later in life .The placenta can convert 25(OH)D to the active form $1,25(OH)_2D$, similarly to the kidneys; therefore, more basic research should shed light in the future on the specific vitamin D metabolism during pregnancy. The FDA has recently approved the statement "Pregnant women who have higher serum vitamin D levels have a decreased risk of preterm birth." Taking into account the recent literature, vitamin D deficiency is associated with worse outcomes during pregnancy, and at least 400–600 IU of daily vitamin D supplementation is reasonable for women with a vitamin D level <40 ng/mL, with higher required doses in more severe deficiency.

## 3. Which populations are more susceptible to vitamin D deficiency?

- Breastfed infants.
- Older adults.
- Pregnant women.
- obese patients.
- People who have had gastric bypass surgery.
- People with osteoporosis, kidney disease, or liver disease.
- People with dark skin.
- People with Crohn's disease or celiac disease.

## 4. Can too much vitamin D become toxic?

Vitamin D supplements are considered very safe, and toxicity is uncommon. In order for vitamin D to reach toxic or dangerous levels in the body, it needs to exceed 100 ng/mL. Hypervitaminosis D is defined as blood vitamin D levels over 100 ng/mL, while vitamin D intoxication is defined as serum levels over 150 ng/mL.

**Symptoms and side effects related to vitamin D toxicity:**

1. Elevated blood level.
2. Elevated blood calcium level with Symptoms of hypercalcemia.
3. Gastrointestinal symptoms.
4. Altered mental status.
5. Kidney complications.

**However, vitamin D toxicity is more common in people with certain medical conditions. These include**:

- Granulomatous disorders.
- Congenital disorders.
- Some lymphomas.

**Sources**

*-https://www.healthline.com/nutrition/vitamin-d-side-effects.*

*- https://my.clevelandclinic.org/health/diseases/15050-vitamin-d-vitamin-d-deficiency*.

# Duchenne muscular dystrophy

It is a debilitating genetic condition that causes a gradual loss of muscle function that affects everyday movements and activities. Muscular dystrophy is a condition that causes progressive wasting of the muscles. Duchenne muscular dystrophy is a particular type of muscular dystrophy caused by a mutation in the DMD gene. It affects more boys than girls.The DMD gene helps produce a protein called dystrophin, which is important for muscle strength, support and repair. People with Duchenne muscular dystrophy don't produce the normal form of dystrophin, which means their muscles are more easily damaged and don't work properly. The genetic mutation of the DMD gene is either inherited from parents or caused by a genetic change in the child.

## Types of muscular dystrophy

There are many types of muscular dystrophy, with Duchenne muscular dystrophy being the most common in children. Becker muscular dystrophy is very similar to Duchenne muscular dystrophy. It has the same underlying cause but is usually less severe, presenting with slightly different symptoms. Other types as;

- Emery-Dreifuss muscular dystrophy.
- Facioscapulohumeral muscular dystrophy.
- Limb-girdle muscular dystrophy.
- Myotonia congenital.
- Myotonic dystrophy.

## Signs of Duchenne muscular dystrophy

The first thing parents usually notice is that their child isn't reaching their motor (muscle movement) milestones. They might also notice that their child falls over often, is clumsy and walks on their toes.Later, the child with Duchenne muscular dystrophy might develop:

- Muscle weakness that affects their posture, walking and running.
- Reduced joint movement due to shortening of their muscles.
- Problems with their heart muscle, affecting heart function.
- Difficulty breathing as their muscle weakness worsens.

## How is Duchenne muscular dystrophy diagnosed?

If the doctor suspects a problem like Duchenne muscular dystrophy, your child might have blood tests and genetic tests.

Blood tests look for elevated levels of the enzyme creatine kinase. This test can give a guide, but not a certain diagnosis. A genetic test for the DMD gene is the best way to diagnose DMD.

If genetic tests are unclear, as they sometimes are, your child might need a muscle biopsy to check for dystrophin in the muscle.

Duchenne muscular dystrophy is usually diagnosed between 3 and 7 years of age.

## Treatment

There's no cure for DMD, but there are medicines and other therapies that can ease child's symptoms, protect their muscles, and keep their heart and lungs healthy.

**Eteplirsen (Exondys 51)** has been approved to treat individuals with a specific mutation of the gene that leads to DMD. It is an injection medication. Its most common side effects are balance problems and vomiting. Although the drug increases dystrophin production, which would predict improvement in muscle function, this has not yet been shown.
The oral corticosteroid **deflazacort (Emflaza)** was approved in 2017 to treat DMD, becoming the first FDA approval of any corticosteroid to treat the condition. Deflazacort has been found to help patients retain muscle strength as well as helping them maintain their ability to walk. Common side effects include puffiness, increased appetite and weight gain.
**Steroids such as prednisone** slow muscle damage. Children who take this medicine are able to walk for 2 to 5 years longer than they would without it. The drugs also can help your child's heart and lungs work better.
For the small number of DMD patients with the gene mutation exon 45 skipping, the injectable **casimersen (Amondys 45)** has been approved. It is the first targeted treatment for this type of mutation and has been shown to help increase the production of dystophin.

Because DMD can cause heart problems, it's important for your child to see a cardiologist, for checkups once every 2 years until age 10, and once a year after that. Girls and women who carry the gene have a higher risk of heart problems, too. They should see a cardiologist in their late teens or early adult years to check for any problems.
• A cell therapy developed by the executive director of the Smidt Heart Institute stabilizes weakened muscles–including the heart muscle–in Duchenne muscular dystrophy patients, a new study published in the international peer-reviewed journal The Lancet shows,
***Repeated intravenous cardiosphere-derived cell therapy in late-stage Duchenne muscular dystrophy (HOPE-2): a multicenter, randomized, double-blind, placebo-controlled, phase 2 trial.*** Published in:
**www.thelancet.com Vol 399 March 12, 2022.**
If the HOPE-2 study's success is duplicated in the upcoming multicenter, randomized, placebo-controlled HOPE-3 clinical trial, the intravenous cell therapy could become the first Food and Drug Administration-approved treatment for Duchenne patients with advanced disease."This therapy is unique in that it addresses two vital needs in patients with Duchenne: physical movement and a healthy heart.

## Living with Duchenne muscular dystrophy

There is no cure for Duchenne muscular dystrophy, so treatment aims to manage symptoms and improve quality of life.
A neurologist usually oversees treatment, working with a range of different health professionals including physiotherapists, podiatrists, speech pathologists and psychologists.
Common treatments include stretching and exercising muscles, and wearing splints and orthotics for support. Counselling can also help with any issues that arise.
Steroids can be used to try and slow the progression of Duchenne muscular dystrophy.

**Source :** *Health Direct , Australian Government Department of Health and aged care.*

# Real Enquiries

**At the " Drug Information Center" we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center**:

**Enquiry received from** : A.A.- Assiut

**Enquiry**: Is Zanoglide suitable for a patient with heart disease?

**Summary of the answer:**

Pioglitazone , like other thiazolidinediones , can cause dose - related fluid retention when used alone or in combination with other antidiabetic medications and is most common when Pioglitazone and Glimepiride Tablets are used in combination with insulin . Fluid retention may lead to or exacerbate congestive heart failure . Patients should be observed for signs and symptoms of congestive heart failure .

According to a study , the administration of sulfonylureas ( glimepiride ) has been reported to be associated with increased cardiovascular mortality as compared to treatment with diet alone or diet plus insulin . Although only one drug in the sulfonylurea class ( tolbutamide ) was included in this study , it is prudent from a safety standpoint to consider that this warning may also apply to other oral hypoglycemic drugs in this class , in view of their close similarities in mode of action and chemical structure .

So , in summary , an alternative oral hypoglycemic should be considered .

**Sources:**

*1. Drugs.com , Pioglitazone and Glimepiride Tablets [ Online ] . Drugs.com [ Last updated : Feb 1 , 2018 ] . Available at : https://www.drugs.com/pro/pioglitazone - and - glimepiride - tablets.html [ Accessed : June 17 , 2018 ].*

*2. emc . Actos Tablets . [ Online ] . Electronic Medicines Compendium [ Last updated : May 26 , 2018 ] . Available at : https://www.medicines.org.uk/emc/product/1287/smpc [ Accessed : June 17 , 2018 ] .*

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# Test Your Knowledge

1. A deficiency of which of the following vitamins can cause night blindness
   a) D
   b) K
   c) A
   d) E
2. An organ of the body that is often damaged permanently by rheumatic fever is the
   a) Lung.
   b) Heart.
   c) Kidney.
   d) Liver.

3. A drug used as a preventative when traveling to areas in which malaria is endemic is
    a) Human immune globulin.
    b) Malarial vaccine.
    c) Quinine.
    d) Chloroquine phosphate.
4. A danger of prolonged use of pilocarpine salts as a miotic is
    a) Lens opacity.
    b) Glaucoma.
    c) Tearing.
    d) Detached retina.

***Answers:***

**1. (c)** **2. (b)** **3. (d)** **4. (a)**


## NEW FDA approved drugs

| Trade name | Active ingredient | Approval date | Use |
|---|---|---|---|
| Ztalmy | ganaxolone | 18/3/2022 | To treat seizures in cyclin-dependent kinase-like 5 deficiency disorder |
| Pyrukynd | mitapivat | 17/2/2022 | To treat hemolytic anemia in pyruvate kinase deficiency |
| Cibinqo | abrocitinib | 14/1/2022 | To treat refractory, moderate-to-severe atopic dermatitis |

**Source:** *https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drug-approvals-2022*