

When can doxycycline be used in young children?

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Tetracyclines are a class of naturally occurring compounds originally derived from *Streptomyces aureofaciens*. Tetracyclines have been used since the 1950s as broad-spectrum antimicrobial agents in adults and as growth promoters in animal feed.

Advances in the design of tetracyclines led to the development and licensure of doxycycline in 1967 (a second-generation tetracycline). Doxycycline has several differences when compared to older tetracyclines, including a greater spectrum of activity and improved solubility.

Clinical use of tetracyclines in children younger than 8 years of age has been limited because of the known binding of first-generation tetracyclines to teeth and bones in young children, which can lead to permanent staining of the teeth and enamel hypoplasia. Tetracycline use during pregnancy has been limited because of similar concerns regarding the fetus.

Doxycycline binds to calcium less readily than other tetracyclines and has not been shown to cause tooth staining. Although data are limited, evidence does not support dental staining as a consequence of doxycycline use in young children.



Courtesy of Billings RJ, et al. *Pediatrics*. 2004;113:1123

A blinded trial performed by the Centers for Disease Control and Prevention (CDC) and the Indian Health Service in 2013 evaluated dental staining following doxycycline use in children under 8 years of age in a community with high rates of Rocky Mountain spotted fever (Todd SR, et al. *J Pediatr*. 2015;166:1246-1251). No differences in teeth staining were found between children who received doxycycline and those who did not.

Other reviews and comparative trials have not found a risk of dental staining from doxycycline use in children younger than 8 years of age. The CDC recommends “doxycycline as the treatment of choice for

children of all ages with suspected tickborne rickettsial disease” noting that “Previous concerns about tooth staining in children aged <8 years stem from older tetracycline-class drugs that bind more readily to calcium than newer members of the drug class, such as doxycycline” (*MMWR Recomm Rep.* 2016;65(No. RR-2):1-44). The 2018 AAP *Red Book* states that “doxycycline can be used for short durations (ie, 21 days or less) without regard to patient age....”

Tetracyclines are considered first-line therapy for a number of infections, including those caused by *Rickettsia* (most notably Rocky Mountain spotted fever), *Ehrlichia* and *Anaplasma* spp., as well as for tularemia, brucellosis, cholera, *Chlamydia* genital infections, post-exposure prophylaxis following anthrax exposure and malaria prophylaxis. Doxycycline also is used for prophylaxis and treatment of Lyme disease caused by *Borrelia burgdorferi*.

Which of the following statements are correct?

- a) A sun lamp or tanning bed can be used while taking doxycycline as long as sunglasses are worn.
- b) Oral tetracyclines can be taken without regard to food ingestion.
- c) Oral doxycycline has been associated with increased intracranial pressure (pseudotumor cerebri), which generally resolves when medication is discontinued.
- d) Ribosomes are the site of protein synthesis in living cells.

Answer: c and d are correct

The antimicrobial activity of the tetracycline class is due to inhibition of protein synthesis. Tetracyclines inhibit protein synthesis by binding to the 16S ribosomal RNA subunit. Tetracyclines interfere with the binding of transfer-RNA to messenger-RNA. This is the site where protein synthesis occurs as amino acids are added to the growing polypeptide chain. Normally, bacterial protein synthesis proceeds at an amazing rate of 10 to 20 amino acids added per second.

Photosensitivity is a well-documented adverse reaction to tetracyclines among people who have extensive exposure to sun (or ultraviolet light) such as may occur in those taking doxycycline for malaria prophylaxis. Within 24 hours of sun exposure, a sunburn-like eruption may develop in skin exposed to the sun in association with pain and pruritis in patients taking doxycycline.

The first-generation oral tetracyclines should not be taken with dairy products or antacids due to the formation of insoluble chelation complexes. Complexes may form during simultaneous ingestion of products containing calcium, magnesium, aluminum, iron or zinc. When ingested with foods containing these metals, antibiotic absorption from the gastrointestinal tract is decreased. However, doxycycline absorption is not markedly influenced by simultaneous ingestion of food or milk.

Questions concerning doxycycline use in young children may arise in relation to treatment of infection by *Borrelia burgdorferi* sensu lato. Several antimicrobial agents offer efficacy in the treatment of Lyme disease in children: amoxicillin, cefuroxime axetil, ceftriaxone and doxycycline. Azithromycin has activity against the spirochete that causes Lyme disease and is likely to provide equivalent treatment to recommended antimicrobial agents, although azithromycin generally is considered to be a second-line drug.

Selection of an oral antimicrobial agent for treatment of Lyme disease will depend on a number of considerations, including history of drug allergy, possibility of meningitis or cranial involvement (doxycycline

has better cerebrospinal fluid penetration), possibility of co-infection with anaplasmosis or ehrlichiosis (doxycycline preferred) and extent of anticipated sun exposure.

Prophylaxis against Lyme disease following a bite from *Ixodes scapularis* tick in an endemic area is recommended if certain conditions are met, specifically if an engorged tick has been attached for more than 36 hours and prophylaxis can be started within 72 hours of tick removal. If these conditions are satisfied, a single dose of doxycycline may be recommended independent of age.

Aminopenicillins have not been evaluated for post-exposure prophylaxis and are not recommended partly because of a short half-life relative to doxycycline.

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