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## Pediatric conjunctivitis

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### Summary

Pediatric conjunctivitis is a common condition in childhood. It has often benign etiology and a self-limited course. Conjunctivitis may occur due to infectious and non infectious causes. Infectious causes include bacterial and viral conjunctivitis; noninfectious causes include allergic and chemical conjunctivitis. The diagnosis should be done according to clinical symptoms and findings. Also the treatment should be applied according to causes. In this review; the etiology, diagnosis, course and treatment of pediatric conjunctivitis will be described. (*Turk Arch Ped* 2012; 47: 237-243)

**Key words:** Allergic conjunctivitis, bacterial conjunctivitis, child, viral conjunctivitis

### Introduction

Conjunctivitis is one of the complaints which is frequently encountered in the pediatric emergency. It is characterized by redness in the conjunctiva related to hyperemia and congestion in blood vessels and discharge with varying severity and content (1). It may have mild symptoms and a mild clinical course or present as a severe problem which may lead to death. In children, conjunctivitis usually has a benign etiology and frequently leads to a self-limiting picture. In this review, the etiology, clinical picture, diagnosis, prognosis and treatment of pediatric conjunctivitis will be described. Neonatal conjunctivitis will be described under a separate title because of its clinical characteristics and differences.

### Etiology and clinical picture

Infections (bacterial and viral), allergic hypersensitivity or chemicals may lead to conjunctivitis. The etiology varies depending on the age.

The signs and symptoms of conjunctivitis are usually similar. Independent of the cause the conjunctival tissue is edematous and hyperemic locally or diffusely. In addition, watery, mucoid or purulent discharge accompanies the picture. The redness of the conjunctiva does not extend to the limbus and is usually intensified in the combination region of the palpebra and bulbar conjunctiva (2). When the limbus is involved, inflammation of the cornea (keratitis) or the uveal tissue (uveitis) should be

considered (2). Ocular pain and photophobia are not observed except for adenoviral conjunctivitis. In addition, decrease in vision is not observed in conjunctivitis and should be evaluated by an ophthalmologist in terms of uveitis, glaucoma, keratitis or corneal erosion (3). Itching and sense of a foreign body are usually related with allergic causes (2,4). Clean or mucoid discharge may be caused by allergic and viral conjunctivitis (3) and yellow-green purulent discharge which has to be cleaned frequently may be caused by bacterial agents (2,4,5). In a study, it was reported that four clinical factors (age  $\geq$  6 years, presence of complaints in April-November, absence of watery discharge or absence of adhesion in the eyes due to purulent discharge in the morning) might be defined as low-risk for bacterial conjunctivitis in children (6).

Preauricular adenopathy may suggest viral etiologies (4). In children of advanced ages with adenoviral conjunctivitis, pharyngitis may also be observed (2). Allergic conjunctivitis is usually observed together with rhinitis, asthma and eczema in advanced childhood and early adulthood and conjunctival edema may accompany.

In conjunctivitis, light reflex (pupilla reaction) is not affected and if a change is observed uveitis, retinal damage and optic neuropathy should be considered.

### Neonatal conjunctivitis (Ophthalmia neonatorum)

This conjunctivitis observed in the first month is the most common infection in the neonatal period (7). The most common

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causes in order of frequency include chemical, bacterial, chlamydial and viral causes (8). Although similar symptoms are observed with all these etiologies, the time of onset of symptoms frequently give a diagnostic clue (9). Conjunctivitis observed in the first 24 hours of life is frequently an irritant reaction against prophylactic eye drops (7). This is most commonly observed against silver nitrate and occurs with a lower rate in prophylaxis with erythromycin or tetracycline. The clinical course of chemical conjunctivitis includes conjunctival hyperemia which is observed in the first 24 hours of life and improves in the first 48 hours, bilateral palpebral edema and watery discharge. No bacteria are observed on gram staining of conjunctival scrape smear and no treatment is needed, since it is self-limiting (7).

Many different bacteriae leading to neonatal conjunctivitis have been reported. The most important microorganism is *Neisseria gonorrhoea*. Because of institutional prophylactic neonatal eye treatment the frequency of gonococcal conjunctivitis is decreasing rapidly in the Western countries (7,8). The typical clinical picture includes palpebral edema, bulbar hyperemia and conjunctival hyperemia accompanying sudden, painful, abundant purulent discharge in the first 2-5 days of life (7,8). If the diagnosis is not made, the organism shows rapid progression, leads to corneal ulceration and perforation of the eyeball and blindness may occur (7). When gonococcal infection is suspected, gram staining and culture should be performed from conjunctival scraping (7,8). In addition, chlamydial culture should also be performed (7,10). The diagnosis is based on observation of intracellular gram (-) diplococci (11). The treatment consists of hospitalization, adequate eye irrigation with saline for a few times a day and a single dose of intravenous or intramuscular ceftriaxone (25-50 mg/kg) in patients limited to conjunctivitis (10,12). Topical antibiotic use alone is inadequate and unnecessary (10,12). Treatment of the mother and her partner in terms of gonorrhea should also be done (7). In addition, the patients should be evaluated in terms of systemic infections including arthritis, meningitis and sepsis (10).

*S. aureus*, *s. pneumoniae*, *s. viridans*, *h. influenzae*, *escherichia coli*, *pseudomonas spp.*, *klebsiella spp.*, *enterobakter spp.*, *proteus spp.* and viruses may also lead to neonatal conjunctivitis after the 72nd hour postnatally (7,8,13,14). Most infections caused by these organisms except for *pseudomonas* can be treated by topical antibiotics alone. *Pseudomonas* conjunctivitis may be observed as edema and erythema in the palpebras, purulent discharge, pannus formation, corneal perforation or endophthalmia and may lead to sepsis, shock and mortality (7,15). The diagnosis is made by observation of gram (-) rods in the exudate and growth in the culture (7). Since systemic and local antibiotics enter the anterior chamber poorly, systemic and local aminoglycosides are given together for treatment (15,16). Sometimes, subconjunctival antibiotic injections may be needed (16,17). All infants should be "isolated" and ophthalmologic consultation should be requested (16,17).

The most common organism leading to neonatal conjunctivitis is *c. trachomatis* (7,8,10). It occurs in the first 5-14 days of life (10). Various clinical pictures including mild-moderate conjunctival erythema, little, mucoid or abundant, purulent discharge, ocular edema, conjunctival edema or pseudomembrane formation may be observed (7,8,18). Approximately 50% of the newborns delivered vaginally from mothers with active chlamydial infection were found to have a risk for acquired infection (7,8,18). 25-50% of these infants have conjunctivitis (18). Chlamydial infections have also been found in infants born by cesarean section (8,18). Unfortunately, silver nitrate, erythromycin and tetracycline can not prevent chlamydial conjunctivitis in newborns (8,18,19). In infants younger than 30 days, *Chlamydia* should be considered in the etiology of conjunctivitis (7,18). The diagnosis is made by culture, direct fluorescent antibody, enzyme immunoassay, polymerase chain reaction or ligase chain reaction and demonstration of intracytoplasmic inclusion bodies by Giemsa stain (10,18). The treatment of chlamydial neonatal conjunctivitis consists of 50 mg/kg/day oral erythromycin in four doses for 10-14 days (10,18). Use of local antibiotics is ineffective and unnecessary. Treatment of the mother and her partner should be done (10,18). Untreated chlamydial conjunctivitis may result in conjunctival and corneal scar of varying degrees (7).

Herpes simplex virus-2 may lead to neonatal conjunctivitis passing through the birth canal, though rarely (20). It should be suspected in presence of history of infection in the mother, vesicular blepharitis and ocular dendritic ulcer. Conjunctivitis is observed in the first two months and different eye tissues may be involved. The diagnosis is made by immunofluorescence, smear and culture. While local treatment is enough, systemic antiviral agents may be administered in disseminated cases; steroids should be avoided (21). A complete septic evaluation should be performed in HSV infection (21).

### Protective treatment in neonatal conjunctivitis

For many years Crede prophylaxis (1% silver nitrate) were used for gonococcal infection, but this was ineffective for chlamydia and other bacteria. 0.5% erythromycin and 1% tetracycline eye pomades were used for prophylaxis. In recent years, 2.5%-5% povidon-iodine drop was shown to be the most effective wide-spectrum antimicrobial agent on neonatal conjunctiva and had a lower toxicity compared to silver nitrate (22). In addition, fucidic acid was reported to be promising in treatment (23). In a study performed in Turkey in which the current status in prophylactic treatment of neonatal conjunctivitis was analysed in 24 universities and 24 public hospitals, the most commonly used two drugs were reported to be gentamycin and tobramycin, whereas povidon-iodine was reported not to be used (24). For deliveries by cesarean section prophylactic treatment is not necessary (22).

## Bacterial conjunctivitis

### Microbiology (pathogenic agents)

The pathogenic bacteria vary according to age. In newborns, bacterial agents are observed more commonly compared to children of advanced ages. The most commonly isolated microorganisms in infants with conjunctivitis have been reported to include *Chlamydia trachomatis*, *s.taphylococcus aureus*, *staphylococcus epidermidis*, *streptococcus viridans*, *haemophilus türleri* and *streptococcus pneumoniae* (13,14). Conjunctivitis caused by neisseria gonorrhoea is not observed frequently because of institutional prophylactic treatment (8,13,14).

Bacterial agents are more common in children of advanced ages with nonepidemic conjunctivitis (5,25,26). At these ages, the most commonly isolated pathogenic agents include *h. influenzae*, *s. pneumoniae* and *moraxella catarrhalis*. In addition, *s.aureus* may be grown as a result of contamination in eyes with normal flora or blepharitis (5,25). No tests are needed in normal subjects for diagnosis. In cases resistant to treatment, investigations for differentiation of the agent may be needed in newborns and in patients with immune deficiency.

### Acute bacterial conjunctivitis

Except for the neonatal period, bacteria are responsible of acute conjunctivitis with a two fold higher rate compared to viruses (5,25,26). The most commonly isolated organisms include *H. influenzae*, *S. pneumoniae* and *Branhamella catarrhalis* (*Moraxella catarrhalis*) (1,5,25,26). Since staphylococcus species are isolated with an equal rate in asymptomatic children and children with conjunctivitis, the role of staphylococci in the pathogenesis of conjunctivitis is controversial (5,25,26). The signs and symptoms in children include itching, burning, mucopurulent or purulent discharge, palpebral edema or conjunctival erythema (Picture 1) (5,26). The clinical course consists of sudden unilateral onset and invasion to the other eye in 48 hours. Although there is no diagnostic sign to differentiate bacterial and viral conjunctivitis, some clues may be useful for making the diagnosis: presence of complaints in the preschool childhood, presence of



**Picture 1.** A child with bacterial conjunctivitis accompanied by heavy mucopurulent discharge, palpebral edema and conjunctival erythema in both eyes

accompanying otitis media, development of papilla in the conjunctiva or papillary response and bilateral involvement suggest bacterial agents (5,26). On the other hand, the etiology can not be predicted based on the the clinical examination, since the signs and symptoms of bacterial and viral conjunctivitis can overlap (27). To support the diagnosis gram staining of conjunctival exuda may be performed (27,28).

Another pathogenic agent which deserves to be mentioned is *n. gonorrhoea*, though it is not frequently observed. It may also be observed in children of advanced ages, though rarely. Sudden onset, abundant purulent discharge, palpebral edema and fever are observed in the patients (5,19). Treatment consists of a single dose of ceftriaxone (50 mg/kg, maximum dose 1 g) and frequent washing of the eye with saline until purulent discharge disappears (12). Since the organism is transmitted by sexual contact, all children with gonococcal conjunctivitis should be investigated in terms of sexual abuse.

Although acute bacterial conjunctivitis is treated with topical antibiotics, it is a self-limiting disease. Treatment is requested, because it provides eradication of the bacteria and more rapid clinical improvement, decreases the rate of reinfection, prevents the invasion of infection, provides relief of the symptoms, shortens the disease time and decreases the risk of development of complications which threaten vision (28,30-34). Ophthalmic antibiotics which are administered for a shorter period and with simpler doses increase the efficiency of treatment (35). The treatment usually consists of a 7-10-day course of broad-spectrum topical antibiotics (32). Topical antibiotics may be drops or ointments. Ointments may lead to blurred vision especially in school-aged children (36).

Although there are many topical antibiotics, the spectrum of the antibiotic, potential side effects, expense and the child's age should be considered in selection of the drug. Bacitracin-polymixin B and trimethoprim-polymixin have little side effects and a broad spectrum (5,37). Although aminoglycosides act on gram negative bacteria, they have a weak action on streptococci. They have been reported to cause epithelial toxicity and corneal ulcer especially in long-term use (5,37). Although chloramphenicol has also a broad spectrum, it has been shown to cause aplastic anemia, when used topically for the eye (5,38). Although erythromycin acts on gram positive bacteria and chlamidia, it has a weak action on *h.aemophilus species*, *b. catarrhalis*, *s.taphylococcus species* and gram-negative organisms (5,37). Although fluoroquinolones have a broad spectrum and high efficiency, they have few side effects except for local irritation and resistance of gram-positive and gram-negative bacteria against this antibiotic with a high rate (5,37,39). In a study performed in Turkey, the most efficient antibiotics against the bacteria isolated from 47 patients with acute bacterial conjunctivitis included vancomycin, netilmicin, chloramphenicol and tobramycin with sensitivity rates of 100%, 96%, 93% and 91%, respectively (40). On the other hand, topical eye drop form of vancomycin is not available commercially. Conclusively, the best options for initial empiric treatment may be netilmicin or tobramycin.

On the other hand, it has been reported that 1,25% povidon-iodine ophthalmic solution may be a treatment option in treatment of bacterial and chlamydial conjunctivitis, when topical antibiotics are not available or can not be purchased because of economic reasons (41).

Corticosteroids may sometimes be used in combination with ophthalmic antibiotic drops. Use of these agents should be avoided, since they prevent eradication of the bacteria, worsens herpetic keratitis which are erroneously diagnosed as conjunctivitis and increase intraocular pressure (37).

A frequently asked question asked to clinicians is if "isolation" is needed (for example, when will the child be able to go back to school?). In a study in which *h. influenzae* chains which caused an epidemic of conjunctivitis were compared, it was reported that *h. influenzae* chains showed variance from one child to another child in the same center and therefore contagiousness was low (42). Therefore, "isolation" of these children is not necessary (43).

### Conjunctivitis-otitis syndrome

It has been reported that ¼ of the patients with conjunctivitis have otitis media, though they have no ear pain (44,45). Therefore, all children with bacterial conjunctivitis should be investigated in terms of otitis media. *H. influenzae*, *s. pneumoniae* and other bacteria have been reported to grow in conjunctiva and middle ear fluid obtained from children with conjunctivitis and otitis media (44,46). Since beta-lactamase is found with a high rate in *h. influenzae*, treatment with beta-lactamase resistant antibiotics is recommended (46).

### Viral conjunctivitis adenoviral conjunctivitis

The causative agent in most viral conjunctivitis cases is adenovirus. It is responsible of 20% of conjunctivitis cases especially in autumn and winter months (47). Adenoviral infections are very contagious and have many forms. These include follicular conjunctivitis, pharyngoconjunctival fever, epidemic keratoconjunctivitis and acute hemorrhagic conjunctivitis



**Picture 2.** A child with unilateral right viral conjunctivitis accompanied by mild erythema and mild palpebral edema

(2,5,48). It may lead to mild erythema or intense palpebral edema and watery discharge (Picture 2). Although the symptoms involve both eyes, it starts earlier in one eye and rapidly transfers to the other eye. The signs and symptoms may be different in the two eyes (49). The history usually includes contact with a person with red eye and upper respiratory infection (50). The clinical picture may last for a few weeks. If corneal involvement is present, recovery may take months. Preauricular lymphadenopathy is frequently present (49). The diagnosis of adenoviral conjunctivitis is generally based on the clinical picture (9).

All of its forms are very contagious. The transmission of the disease usually occurs by contact with infected employees and contaminated objects (2,5,48). Therefore, the main approach in treatment is prevention of contamination. Attention should be paid to personal hygiene (51). Healthcare workers related to ophthalmology should wear gloves and apply good hand-washing techniques. The devices used in the examination of patients should be cleaned after use (2,5,48). The family should be informed that the towels and bed linens of the patient should be separated from the other family members (2). The child should be kept at home for approximately one week after the onset of the symptoms (1,3,48). Treatment is supportive independent of the type of adenoviral conjunctivitis and consists of cold compress, artificial tears and topical vasoconstrictors (3,50,52). No significant difference could be found in studies which compared antiviral agents and combination of artificial tears and antiinflammatory agents (52,53). Topical corticosteroids should be avoided, since they cause side effects including super-infection, glaucoma and cataract, worsen undiagnosed herpetic keratoconjunctivitis, increase adenoviral growth and lengthen the time of adenoviral virus shedding (52,54). Topical antibiotic treatment is not necessary, since secondary bacterial infection is rare (3). On the other hand, it was reported that use of broad-spectrum antibiotics including trimethoprim, polymixin B may be efficient, since it shortened the course of the disease (55). If the disease does not recover in 7-10 days or if vesicles are present, an ophthalmologist should be consulted for a possible diagnosis of herpes simplex (36).

### Follicular conjunctivitis

The most common type of adenoviral conjunctivitis causes follicular reaction (48,50). Follicles are formed by aggregation of the lymphocytes and appear as small, pale, veinless areas surrounded by the plexus formed by blood vessels (3,48). The other findings include preauricular lymphadenopathy, hyperemia, watery discharge, palpebral edema, rhinitis, pharyngitis and other symptoms of upper respiratory infection (48,50). The patient complaints of itching and a sense of foreign body (50).

### Pharyngoconjunctival fever

The most common causative agents are adenovirus type 3,4 and 7 (2,5,48,50). Epidemics occur by insufficiently chlorinated swimming pools and contaminated pools (5,48). The characterized findings include pharyngitis, fever,

conjunctival edema, hyperemia and bilateral preauricular lymphadenopathy (2,48,50). Sometimes, small petechial hemorrhages may be observed in the conjunctiva (48). Improvement of the symptoms takes a period ranging between 4 days and 2 weeks (5,48,50).

### Epidemic keratoconjunctivitis

The most common causative agents in epidemic keratoconjunctivitis include adenovirus type 8, 19 and 37 (2,5,48,50). It is the most severe form of conjunctivitis caused by adenoviruses. Children of advanced ages and adults are affected (5). Objects contaminated with the virus can be contagious for two months (2). Although the patient has findings of upper respiratory infection, ophthalmic symptoms including severe irritation, photophobia, conjunctival edema, punctal epithelial defect, follicular (early) or papillary (late) response and small petechial hemorrhages are predominant (5,48,50). Corneal involvement is the predominant finding on examination (56). In the advanced stage, cloudy, grey-white subepithelial infiltrates may form and these infiltrates do not resolve in a few months (48,50). Severe cases may be misdiagnosed as preseptal or periorbital cellulitis (5,48,50).

### Acute hemorrhagic conjunctivitis

The most common causative agents are picornaviruses which include the enterovirus and coxsackievirus groups. Adenovirus type 11 may also cause acute hemorrhagic conjunctivitis (48,50,57). It is highly contagious and usually occurs as epidemics (50). The patients have hyperemic and chemotic conjunctiva which develops suddenly, subconjunctival hemorrhage, palpebral swelling, excessive tearing, photophobia and pain (50,57). The symptoms develop in 24-48 hours and last for 3-5 days. Afterwards, they gradually improve in 10 days (50,57).

### Herpes virus conjunctivitis

Herpes virus conjunctivitis may be primary infection or recurrence. It involves one side only in 80% of the cases. The most common agent leading to ophthalmic infections is HSV-1. In newborns, the most common agent is HSV-2 (2). Primary infection occurs most commonly at the ages of 1-5 years (5). Conjunctivitis occurs in the first 5 days-2 weeks of life. Relapsing infections usually occur in adults. While the primary infection heals spontaneously, relapses may result in corneal opacification and vision loss. The characteristic findings include follicular inflammatory response, serous discharge and preauricular lymphadenopathy (2,5). Most cases of herpetic conjunctivitis (80%) are unilateral. Other accompanying findings may include labial vesicles, upper respiratory tract infection, gingivostomatitis and keratitis and these findings are useful in the diagnosis (2,5,50). It is difficult to differentiate primary HSV infection from adenoviral and chlamydial infection:

the diagnosis is usually made clinically. In suspicious cases, viral culture and antibody tests may be performed (3,50,58).

For treatment of conjunctivitis caused by herpes simplex virus an ophthalmologist should be absolutely consulted (50,59). Topical trifluridine, iododeoxyuridine or vidarabine are used for treatment (2,50,59). Oral acyclovir may be used in severe cases or to inhibit relapsing lesions (2,59). In newborns, both topical and intravenous acyclovir should be administered. Steroids should be avoided, since they may aggravate the infection.

### Allergic conjunctivitis

Allergic conjunctivitis is a chronic disease characterized by frequent relapses. It may be considered in children presenting with excessive tears, red and itching eyes (32). In conjunctivitis without itching, care should be taken in the diagnosis of allergy. A history of other atopic diseases including eczema, asthma or most commonly rhinitis is frequently present (3,4,60). It most frequently occurs in the late childhood and early adulthood (4). It may be divided as acute form and chronic form. The acute group includes seasonal (pollens, grass, greensward, soil) and long-term (perennial) (dust, mite, cockroach) allergic conjunctivitis. The chronic group includes vernal keratoconjunctivitis, atopic keratoconjunctivitis and giant papillary conjunctivitis.

The symptoms are bilateral. They may be persistent or seasonal. The most common symptom is itching. Excessive tears, mucoid discharge, mild erythema, palpebral edema and conjunctival edema may be observed (Picture 3) (3,4). The acute form usually occurs during the months between April and July, but may also spread the whole year. Vernal conjunctivitis is a different disease. It may lead to permanent sequela. When the weather gets warm, the complaints increase. The cornea may be involved, intense and raised papillar formations are present.



**Picture 3.** A child with allergic conjunctivitis accompanied by increased tears and mild conjunctival erythema in both eyes

Treatment consists of avoiding allergen agents (staying away from grass, use of hat and eyeglasses, washing the face and hands in the evening, changing clothes after arriving home, ventilating and solarizing clothes), cold compress to relieve itching, vasoconstrictors, antihistaminics, decongestants, H1-receptor antagonists, mast cell stabilizers and non-steroid antiinflammatory drugs (3,61). Antihistaminics and decongestant agents should be used for a short period, since they may cause "rebound" when used in combination for a long period (4,61). Mast cell stabilizers (lodoxamide, nedocromil and pemirolast) are efficient in treatment of seasonal allergic rhinitis, but improvement of the symptoms takes a few days to a few weeks (61,62). H1-receptor antagonists (emadastin and levocabastin) are efficient and their efficiency start more rapidly (61,63). In addition, ketotifen and olopatadine are mast cell stabilizers and H1-receptor antagonists. They are efficient drugs (61,64). The use of olopatadine 0.1% opthalmic solution as 1-2 drops every 6-8 hours in allergic conjunctivitis was approved in children aged 3 years and older (36). Lodoxamide tromethamine and cromolyne sodium should be preferred in severe cases (65).

### Rare causes of conjunctivitis

#### Membraneous conjunctivitis

A membrane is formed on the conjunctiva and when it is attempted to be removed hemorrhage occurs in the conjunctiva. It is frequently observed in diphtherial, streptococcal and ligneous conjunctivitis. It is treated according to the causative agent.

#### Pseudomembraneous conjunctivitis

There is no real membrane, it is related with intense exudation and no hemorrhage occurs when removed. It is caused by high-virulent viruses and bacteria.

#### Ligneous conjunctivitis

It is a form of membraneous conjunctivitis which is observed rarely. It occurs more frequently in young children. The palpebras are thickened and bleed when peeled. It may cause deformity in the eye. Plasminogen deficiency and hydrocephaly are observed frequently (22). Treatment should absolutely be planned by an ophthalmologist.

Other causes of red eye including subconjunctival bleeding, lacrimal duct obstruction, blepharitis, keratitis, corneal foreign body, uveitis and acute glaucoma crisis should also be considered (49).

Conclusively, treatment can be administered in simple cases of conjunctivitis in children, if the differentiation can be made and preventive measures may be recommended, but steroids should not be used. If there is no response to treatment in 2 days, the patient should be referred to an ophthalmologist without delay. Delays which may be harmful for the patient should be avoided.

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