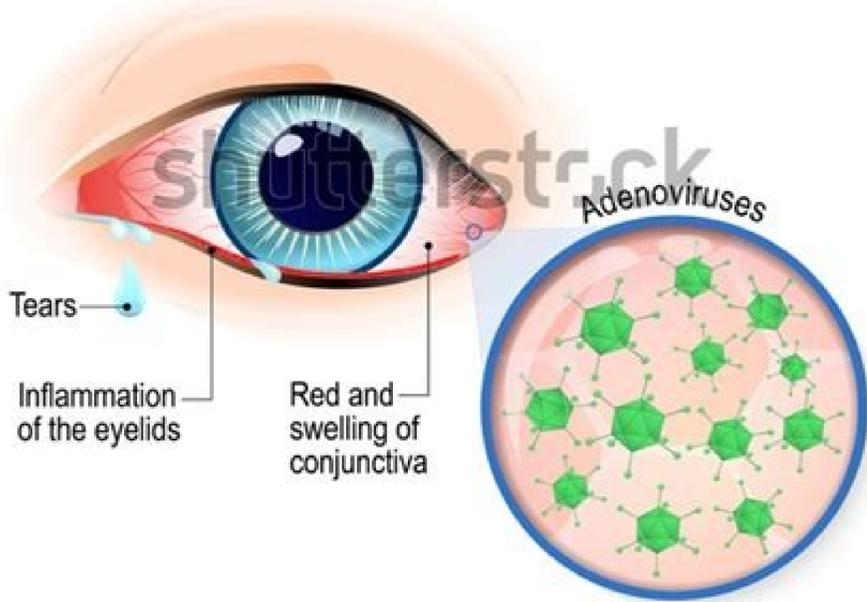


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# Viral conjunctivitis



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## Concepto

- La conjuntivitis neonatal es una inflamación conjuntival que aparece durante el primer mes de vida, también llamada oftalmia del recién nacido. Es una de las causas más comunes de infección neonatal; favorecida por la infección del tracto genital materno, o traumatismos obstétricos en el momento del parto



Rev. Inst. Med. trop. S. Paulo  
51(4):227-229, July-August, 2009  
doi: 10.1590/S0036-46652009000400010

## BRIEF COMMUNICATION

### MOLECULAR EPIDEMIOLOGY OF ADENOVIRUS CONJUNCTIVITIS IN RIO DE JANEIRO, BRAZIL, BETWEEN 2004 AND 2007

Adriana G. MARANHÃO(1), Caroline C. SOARES(1,2), Maria Carolina M. ALBUQUERQUE(1) & Norma SANTOS(1)

## SUMMARY

Viral conjunctivitis is a common, highly contagious disease often caused by adenovirus. We investigate the frequency of adenoviral conjunctivitis in the population of Rio de Janeiro, Brazil, between March 2004 and May 2007 and identified the predominant serotype circulating among this population. Seventy-five ocular swabs were collected from 66 patients with clinical presentation of conjunctivitis. The specimens were analyzed for detection of adenovirus (AdV) by polymerase chain reaction (PCR). The PCR products were further analyzed for virus typing by sequence analysis and/or heteroduplex mobility assay (HMA). Forty-five samples (60%) were positive for AdV of which 21 samples were typed as AdV19 (46.7%), 7 AdV8 (15.5%), 3 AdV31 (6.7%), and one each AdV1, AdV2, AdV3, AdV4 and AdV6. For nine samples the serotype was not determined. AdV19 was the predominant serotype circulating in Rio de Janeiro during the studied period.

**KEYWORDS:** Adenovirus; Conjunctivitis; Ocular infection.

Adenoviruses (AdV) are one of the major causes of conjunctivitis representing 15 to 70% of all conjunctivitis cases worldwide<sup>(1,2,3,4)</sup>. These viruses belong to the *Adenoviridae* family, *Mastadenovirus* genus, which is divided into six species (A - F) and 51 serotypes. The serotypes AdV8, 19 and 37 are often associated to epidemic keratoconjunctivitis (EKC) although other serotypes such as 2, 3, 4, 5, 7, 10, 11, 21, 22, 29 and 34 have also been associated to this illness<sup>(1,3,5,6,7)</sup>. Pharyngeal-conjunctival fever, a disease commonly affecting children, is most commonly caused by serotypes 3 and 7 whereas serotypes 1 to 11, 15, 16, 17, 19, 20 and 22 are agents of non-specific follicular conjunctivitis<sup>(8)</sup>. The purpose of this study was to investigate the frequency of adenoviral conjunctivitis in the population of Rio de Janeiro, Brazil, and to identify the predominant serotype circulating among this population.

Between March 2004 and May 2007, 75 ocular swabs were collected from 66 patients with a clinical presentation of conjunctivitis in the city of Rio de Janeiro, Brazil. The protocol was approved by the Committee of Ethics in Research of the involved institution and all patients had given informed consent, in accordance with Resolution 196/96, of the Brazilian Ministry of Health. The swabs were placed in virus transport media and kept at 4 °C until the moment of DNA extraction. Adenovirus DNA was extracted by using the Wizard® Purification Kit (Promega, Madison, USA) according to the manufacturer's instructions. The extracted DNA

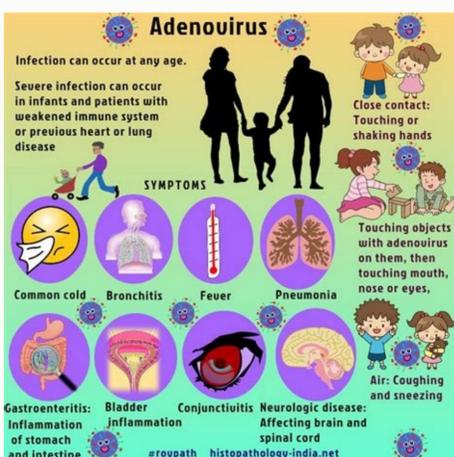
was amplified by polymerase chain reaction (PCR) using specific primers for a conserved region of the hexon gene that yield a 303bp fragment<sup>(9)</sup>. The amplified fragments were subjected to heteroduplex mobility assay (HMA) as described by previously<sup>(9)</sup> and/or sequencing analysis for serotype identification. For the HMA the samples were hybridized against control viruses belonging to serotypes AdV3, AdV4, AdV7, AdV8, AdV11, and AdV19. For sequencing, the amplified DNAs of positive samples were purified using the Wizard SV gel and PCR Clean-Up system kit (Promega), and the sequences determined using the PCR primers and the BigDye® Terminator Cycle Sequencing Kit and the ABI PRISM® 3100 automated DNA sequencer (Applied Biosystems, Foster City, CA, USA). DNA sequences were assembled and analyzed with the programs SeqMan, EditSeq, and MegAlign in the Lasergene software package (DNASTAR, Madison, WI, USA).

Forty-five samples (60%) were positive for AdV of which 21 samples were typed as AdV19 (46.7%), seven AdV8 (15.5%), three AdV31 (6.7%), and one each AdV1, AdV2, AdV3, AdV4 and AdV6 (Fig. 1). For nine samples the serotype was not determined because of the poor quality of the DNA. Five other samples were positive for Coxsackievirus A24 (data not shown). The seasonal distribution of the positive samples demonstrates that the AdV19 was the predominant strain between March and May of 2004. The other AdV serotypes were detected throughout the studied period (Fig. 2).

(1) Departamento de Virologia, Instituto de Microbiologia, Universidade Federal do Rio de Janeiro, 21941-900 Rio de Janeiro, RJ, Brazil.

(2) FICOR/12, Rio de Janeiro, 21045-900 Rio de Janeiro, RJ, Brazil.

Correspondence to: Norma Santos, Departamento de Virologia, Instituto de Microbiologia, Universidade Federal do Rio de Janeiro, Cidade Universitária, CCS-BL I, Blo de Fundão, 21941-900 Rio de Janeiro, RJ, Brazil. Phone: +55 21 2562-6740, Fax: +55 21 2560-8344. E-mail: nsantos@micro.ufrj.br





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Adenoviral conjunctivitis (Ad-CS) has never been so popular a topic as it is right now. With over 26 million viewers tuning in to watch the Olympics, Americans have watched Bob Costas’s unilateral conjunctivitis worsen, then become bilateral. His ocular condition prompted many commentators to remark, “Can’t someone help him?” Members of the RAPID (Reducing Adenoviral Patient-Infected Days ) research group, along with many other ophthalmetrists, sat helplessly staring at our television screens, wishing we could send him a bottle of Betadine! So why didn’t he get that treatment? Why aren’t more patients correctly diagnosed with Ad-CS and treated with Betadine?EpidemiologyAdenoviral conjunctivitis (Ad-CS), also known as “pink eye,” is one of the most common eye infections worldwide. Ad-CS is highly symptomatic, causing discomfort, tearing, lid swelling, photophobia, and decreased vision. Some 15%-35% of the patients develop subepithelial corneal infiltrates that can progress to permanent visual impairment. Because of the epidemic potential of some adenoviral serotypes, Ad-CS is a reportable condition in Germany and Japan.1,2Outbreaks of viral conjunctivitis spare no nationality, age, gender, or social class.3-6 Patients with acute conjunctivitis typically present to a primary-care provider and are estimated to comprise as much as 2% of a general practitioner’s practice.7 Medical management of Ad-CS is estimated to cost \$670 million annually with patients losing 5 or more days of work or school per infection.8Ad-CS is more contagious than other forms of conjunctivitis (or even other viral conditions including herpes simplex virus or human immunodeficiency virus) partly due to the virus’s ability to remain infectious in the desiccated state for weeks at room temperature.9Adenoviruses have no outer lipid bilayer and are highly resistant to disinfection.10 The virus is transmitted directly through droplets or smears of infected bodily fluids, primarily tears or respiratory secretions, and by fomites on towels, doorknobs, soap, counters, instruments, eye drops, and eyeglasses. The hands of nearly 50% of patients with Ad-CS presenting for care were culture positive.11 The period of contagion lasts about 3 weeks.1 Incubation period for Ad-CS is about 10 days (range 7-16 days) prior to the onset of symptoms. Symptoms typically persist for 7 to 28 days.Studies report that most eyes test negative with culture by 13 days after the onset of symptoms.12,13 The duration and severity of symptoms and complications differ among the more than 20 adenovirus serotypes associated with conjunctivitis; however, serotypes 8, 19, 37, and 53 are known to have the greatest epidemic potential.14Next: Diagnostic difficultyDiagnostic difficulty Research for effective treatment of Ad-CS has been seriously hampered by the lack of clear diagnostic indicators to differentiate Ad-CS from other causes of conjunctivitis. The proportion of infectious conjunctivitis due to viral infections has been reported anywhere from 20%-70% and that 65%-90% is thought to be due to adenoviruses. The etiology of acute conjunctivitis is often made based on clinical signs and symptoms, but the diagnostic accuracy is less than stellar, ranging from 40%-72%.The diagnostic conundrum of Ad-CS may be resolved by the availability of the first point-of-care test, the Rapid Pathogen Screening AdenoPlus Detector, distributed by Nicox. AdenoPlus, which has FDA approval, CLIA waiver, and a CPT code, yields a bivariate “yes/no” for the presence of adenovirus antigen to a lower limit of 40-50 virions. Its sensitivity was 85% (29 of 34) and specificity was 98% (89 of 91) compared to qPCR in a sample of 128 consecutive patients with acute conjunctivitis.15However, its accuracy has been brought into question by a study of 9 patients tested with both AdenoPlus and qPCR. AdenoPlus gave negative readings in 6 of 9 eyes with high qPCR adenovirus titers and positive readings in 3 patients with zero PCR titers.16Treatment Currently there are no drugs that are FDA approved for use in the management of Ad-CS. The use of topical ganciclovir (Zirgan, Bausch + Lomb) is currently being investigated, but the adenoviral structural characteristics may prove too hardy for this anti-viral agent.The ideal treatment for Ad-CS would be safe, effective, low cost, and widely accessible. Ophthalmic Betadine 5% (povidone iodine, Alcon) meets these criteria. Melton and Thomas reported that since they began using the single, in-office protocol of 5% Betadine “…we have not had a patient to go on to develop the legendary subepithelial infiltrates.”17 There is preliminary evidence from in vivo animal and human studies.18-20 but a definitive clinical trial that determines Betadine’s efficacy against Ad-CS has yet to be conducted. Anecdotally, practitioners using Betadine on a regular basis are proponents of its efficacy. Betadine’s safety profile has been demonstrated with decades of use as a topical antiseptic in neonates, children, and adults. The cost per 30 mL single-use bottle of 5% ophthalmic Betadine is approximately one quarter the cost of a 5gm tube of ganciclovir.The urgency for a randomized clinical trial with 5% ophthalmic Betadine increases as more eyecare providers adopt off-label use of Betadine for the treatment of Ad-CS. Evidence from a well-designed randomized trial, whether the result is no effect or positive, would have high public health impact. A positive trial outcome of a single, in-office treatment of Betadine could revolutionize management of Ad-CS.Almost all clinical studies of Betadine demonstrated quicker resolution of disease as compared to controls receiving standard care. In a series of 36 patients, Abel stated that 83% reported decreased lid swelling and decreased crusting 1 day after treatment with 10% Betadine or 2 days of 5% Betadine used 3 times daily. The vast majority of patients, 94%, reported “marked improvement” of symptoms within 24 to 48 hours of treatment.7In a prospective study of 61 patients using 2% Betadine 4 times a day for 7 days, 46% recovered completely within a week, and 77% reported “absence of general ocular discomfort” within 7 days.6 A Web-based, uncontrolled, unmasked trial of Betadine is now underway. All of these studies are uncontrolled, unmasked, or both.Next: Anecdotal useAnecdotal use Despite the lack of well-designed clinical studies, the utilization of Betadine in the management of Ad-CS is widespread among clinicians.In 2013, optometrists and ophthalmologists at seven clinical meetings were queried using either audience response systems (clickers) or paper surveys regarding their use of Betadine. Of the 649 responses, 29.3% of practitioners utilized Betadine at least some of the time in their management regimen of Ad-CS (see Figure 1).Of those using Betadine, approximately 23% reported using it for at least 76% of their patients presenting with Ad-CS (see Figure 2).This indicates that this juice have found Betadine to be a viable treatment option incorporate it most or all of the time. Additional questions were asked of attendees at a course presented by Drs. Melton and Thomas at the American Academy of Optometry. Attendees were asked about the utilization of AdenoPlus to aid in the diagnosis of acute conjunctivitis. Only 10% of the 340 attendees reported utilizing this point-of-care test (see Figure 3).Those using Betadine in the management of Ad-CS were more likely to incorporate AdenoPlus (15.4% vs. 6.3% of those not using Betadine) as illustrated in figure 4.There was some difference in the frequency of use of AdenoPlus based on how often Betadine was utilized. In those who used Betadine in at least 76% of their Ad-CS cases, the AdenoPlus was employed 33.3%, which was the highest utilization among all groups (see figure 5).Until research provides the definitive answer if Betadine is effective or not, it seems a reasonable treatment regimen to try when these patients present within the first few days of infection onset. It is rapid, inexpensive, and has the potential to significantly lessen the duration of a patient’s infection. The decision to use Betadine can be guided by the results of AdenoPlus, which should improve the clinician’s accuracy at diagnosing Ad-CS.ODTReferences:1. Meyer-Rusenberg B, Loderstadt U, Richard G, Kaulfers PM, et al. Epidemic keratoconjunctivitis: the current situation and recommendations for prevention and treatment. Dtsch Arztebl Int. 2011 Jul;108(27):475-80.2. Aoki K, Tagawa Y. A twenty-one year surveillance of adenoviral conjunctivitis in Sapporo, Japan. Int Ophthalmol Clin. 2002 Winter;42(1):49-54.3. 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Adenovirus can spread through droplets when someone with an infection coughs or sneezes. Fecal material (poop) can spread the infection via contaminated water, dirty diapers, and poor hand washing. Outbreaks of adenovirus at summer camps are linked to contaminated water in swimming pools and lakes. A child might also pick up the virus by touching someone who has ... 2019-08-28 · consider adenoviruses as possible causes of upper respiratory infection, lower respiratory infection such as pneumonia, and conjunctivitis (individual cases or outbreaks) report unusual clusters (e.g., respiratory, conjunctivitis) potentially caused by adenoviruses to the state or local health department Adenovirus serotype 14 (Ad14) is a serovar of adenovirus which, unlike other adenovirus serovars, is known to cause potentially fatal adenovirus infections.According to the United States Centers for Disease Control and Prevention (CDC), as of September 2007, outbreaks have been identified in four states in the U.S., with ten identified deaths since May 2006. 2020-03-15 · Adenovirus conjunctivitis: The most common type Coronavirus is front and center right now, but you may not have heard of the most common cause of viral pink eye: adenoviruses. The symptoms of adenovirus infection can resemble a cold or the flu and may include: Fever. Gastrointestinal symptoms such as diarrhea and nausea 2017-02-24 · Adenovirus conjunctivitis infection usually settles by itself within 2-4 weeks. You can help make it more comfortable with cold compresses and lubricants, such as chilled artificial tears (available from pharmacies). Occasionally a pharmacist or doctor may suggest antibiotic drops to prevent additional bacterial infection. Preventing transmission of viral conjunctivitis is ... 2020-01-13 · adenovirus — by far the most common; herpes virus — uncommon but more dangerous; People can get viral pink eye from an infection that spreads from the nose to the eyes. It can also be ... 2020-08-11 · adenovirus types 8, 19, 37, 53, and 54, which can cause highly contagious conjunctivitis adenovirus types 40 and 41, which causes gastroenteritis, especially among children Symptoms If the person does not require referral to ophthalmology, manage infective conjunctivitis in primary care according to likely cause. Acute (non-herpetic) viral conjunctivitis. Reassure the person that most cases of acute, infectious conjunctivitis are self-limiting and do not require antimicrobial treatment — viral (non-herpetic) conjunctivitis usually resolves within one to two ... Allergic conjunctivitis C onjunctivitis caused by allergies can be seasonal, occurring at certain times of the year (when due to pollen or grasses), or continuous or ongoing (when caused by allergens such as dust mite or pets). Allergic conjunctivitis is not infectious or contagious. Read more about allergic conjunctivitis. Viral conjunctivitis MedTerms medical dictionary is the medical terminology for MedicineNet.com. Our doctors define difficult medical language in easy-to-understand explanations of over 19,000 medical terms. Viral conjunctivitis is much more common than bacterial conjunctivitis. It can be difficult to differentiate from bacterial conjunctivitis and they can coexist as viral conjunctivitis with bacterial superinfection. The RPS Adenodetector can be used to identify some strains of adenovirus responsible for infection. pink eye (conjunctivitis) acute gastroenteritis (inflammation of the stomach or intestines causing diarrhea, vomiting, nausea and stomach pain) Less common symptoms of adenovirus infection include. bladder inflammation or infection; neurologic disease (conditions that affect the brain and spinal cord) Adenoviruses can cause mild to severe illness, though serious illness is less ... 2017-10-27 · Viral pink eye is caused by viruses like adenovirus and herpes virus. It usually clears up without treatment in 7 to 14 days. It usually clears up without treatment in 7 to 14 days. 2022-07-28 · FPnotebook.com is a rapid access, point-of-care medical reference for primary care and emergency clinicians. Started in 1995, this collection now contains 7117 interlinked topic pages divided into a tree of 31 specialty books and 741 chapters. An adenovirus infection can occur in a child of any age. Children ages 6 months to 2 years who are in child care are more likely to become ill with these viruses. Adenovirus infections of the digestive tract are more common in children under the age of 5. Most children have had at least one adenovirus infection by age 10. The types of specimens you should collect for human adenovirus detection depend on the patient’s clinical presentation and the type of infection. Before collecting any specimens, discuss with a laboratory and a clinician familiar with adenovirus. To improve human adenovirus detection, you should collect specimens within a week of symptom onset. 2021-04-14 · Adenovirus infections can often cause common cold or flu-like symptoms, fever and sore throat, according to the CDC. They can also cause pink eye, or conjunctivitis; inflammation in the airways of ... Viral conjunctivitis is a highly contagious acute conjunctival infection usually caused by an adenovirus. Symptoms include irritation, photophobia, and watery discharge. Diagnosis is clinical; sometimes viral cultures or immunodiagnostic testing is indicated. Infection is self-limited, but severe cases sometimes require topical corticosteroids. Adenovirus types 8, 19, 37, 53, and 54, which can cause epidemic keratoconjunctivitis Enteric adenovirus types 40 and 41, which cause gastroenteritis, usually in children Some adenoviruses (e.g., 4 and 7) that spread in bodies of water such as small lakes or swimming pools without adequate chlorine and can cause outbreaks of conjunctivitis 2022-04-21 · Adenovirus type 41 commonly causes pediatric acute gastroenteritis, which typically presents as diarrhea, vomiting, and fever; it can often be accompanied by respiratory symptoms [4]. While there have been case reports of hepatitis in immunocompromised children with adenovirus type 41 infection, adenovirus type 41 is not known to be a cause of hepatitis ... Modified virus (adenovirus) This is the vaccine active ingredient. Adenoviruses are a group of common viruses that can cause a variety of illnesses (e.g. Bronchitis, conjunctivitis). Most people will have been exposed to some kind of adenovirus during their lifetime. The AstraZeneca vaccine has been made from a modified adenovirus which causes the ... 2019-08-28 · The illnesses can range from the common cold to pneumonia, croup, and bronchitis. Depending on the type, adenoviruses can cause other illnesses such as gastroenteritis, conjunctivitis, cystitis, and, less commonly, neurological disease People with weakened immune systems are at high risk for developing severe illness caused by adenovirus ... An immunosassy is a test that relies on biochemistry to measure the presence and/or concentration of an analyte. The analyte can be large proteins, antibodies that a person has produced as a result of an infection or small molecules. 2018-12-04 · Conjunctivitis or pink eye: Inflammation of stomach or intestines; Less commonly, urinary tract or bladder infections; What’s most challenging about identifying and treating adenoviruses? Dr. Grein: Respiratory symptoms are most common, and they really can look and feel a lot like a cold or the flu—especially if it’s flu season. But adenovirus is with us year ... Most often, an adenovirus infection develops in the respiratory tract. When this happens, symptoms of infection are usually similar to the ... Children can also develop symptoms of pinkeye, which is also called conjunctivitis. Some strains of adenovirus will cause infections in the stomach and gastrointestinal tract. This can lead to diarrhea, abdominal cramps, and other ... Epidemics of febrile disease with conjunctivitis are associated with waterborne transmission of some adenovirus types. ARD is most often associated with adenovirus types 4 and 7 in the United States. Enteric adenoviruses 40 and 41 cause gastroenteritis, usually in children. For some adenovirus serotypes, the clinical spectrum of disease ...

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