Cocaine

Christine Rizkalla, Young-Jin Sue and Henry M. Adam

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Technical Tip

Corneal Abrasions

Ann U. Stout, MD*

Author Disclosure

Dr Stout did not disclose any financial relationships relevant to this tip.

The father of a healthy 16-month-old boy brings him in to "check his eye." The evening before, which had been rather windy, he had taken the child for a walk in the stroller. During the walk, the boy began fussing and rubbing one eye. The father noticed that the eye was watery and red but could not see anything in the eye. He gave the boy some acetaminophen, and he slept well. Today, however, the eye is still teary and irritated, and the boy is fussy. You inspect the eye and find no foreign body.

Fluorescein staining viewed with a Wood lamp shows a 2-mm corneal abrasion and fine linear vertical streak defects. You suspect a hidden foreign body because the abrasion probably occurred yesterday and should have healed overnight. Upon eversion of the upper lid, you see a small black particle stuck to the tarsus that is removed easily with a cotton swab (Fig. 1). You prescribe analgesics as needed, topical antibiotic ointment, and reassurance. The next day, the father reports that his son's eye is back to normal.

Corneal abrasions (Fig. 2) occur often in children of all ages. The cornea is one of the most richly innervated tissues of the body, so discomfort may range from mild to severe, depending on the size of the defect. Symptoms include photophobia, tearing, and intermittent sharp pain due to ciliary body spasm. Physical findings include irritability, blurry vision, conjunctival injection, blepharospasm, irregular red reflex, dulled corneal light reflex, and fluorescein staining of the epithelial defect.

Examination is facilitated by the use of topical anesthetics (proparacaine or tetracaine), which provide temporary pain relief. Fluorescein helps define the size of the defect, although large defects may be seen without any dye. Fluorescein strips can be moistened and touched to the lower fornix to apply the stain or combination anesthetic/fluorescein drops can be used. The dye stains the exposed corneal stroma, but washes off of intact epithelium. The yellow dye is visible with regular white light, although blue or ultraviolet light (Wood lamp) may make it more visible and be better tolerated by a child who has photophobia.

The conjunctival cul de sac and upper tarsus should be examined to rule out retained foreign bodies, which may cause persistent abrasions, unless the cause of the abrasion is known to be external. The upper lid can be everted over a cotton-tip applicator or a fingertip to examine the tarsus. Abrasions that involve the entire cornea, such as after chemical exposure, may be overlooked because no normal epithelium remains for comparison.

Corneal abrasions heal rapidly, often within 24 hours, although larger defects may take longer. Antibiotic ointment may help lubricate the surface until healing occurs, but aminoglycosides should be avoided because they may delay epithelial regrowth. The chance of secondary infection is low, unless foreign matter is retained. Therefore, a course of topical antibiotics is not requisite. Tight patching with two eye pads may help with comfort by blocking light and preventing the irritation of repetitive blinking. The patch must be tight enough to prevent inadvertent lid opening under the patch, which could result in subsequent additional abrasions from the patch material. Patching is not believed to speed healing unless the defect encompasses more than 75% of the corneal surface area. Most younger children dislike the patch, so it can be applied in the office

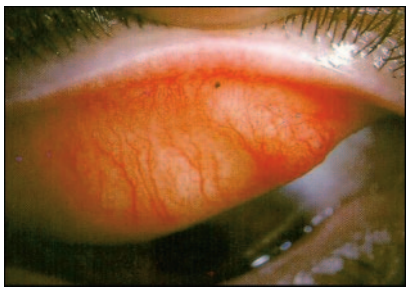

Figure 1. Foreign body in the eye.

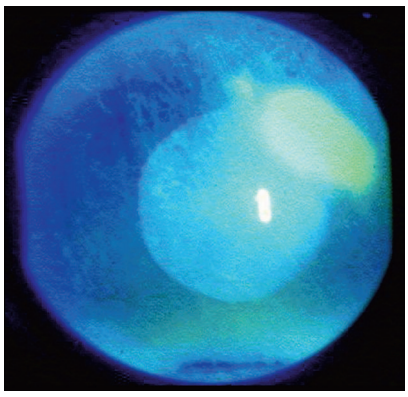

Figure 2. Corneal abrasion.

*Casey Eye Institute, Oregon Health & Science University, Portland, Ore.

and removed by the family if it is poorly tolerated. The family should not reapply it because it might be too tight or not tight enough.

Over-the-counter analgesics or codeine may be used for pain management if needed. The pain of an abrasion should not be underestimated, and treatment should be tailored to the child's comfort level. Pupillary dilation with a cycloplegic agent (tropicamide 1% or cyclopentolate 1%) may help to block ciliary spasm and relieve pain. Topical nonsteroidal drops (ketorolac) may provide additional relief, but may delay healing. Topical anesthetics NEVER should be dispensed because they not only retard healing but can lead to corneal melting and perforation.

Most small abrasions heal overnight. The patient can be seen the next day as needed or feasible. If symptoms and signs have resolved, it can be assumed that the abrasion has healed. A small group of patients are at risk of developing recurrent erosions from poor initial healing. During the night, the lid sticks to the new epithelial cells and pulls them loose upon awakening. These small abrasions are symptomatic upon awakening and often improve throughout the day. Nightly lubrication with ointment sometimes can break this cycle. Patients who have nonhealing abrasions should be referred promptly for additional evaluation because such abrasions can be due to secondary infections, occult foreign bodies, or lacerations.

In Brief

Ampicillin and Amoxicillin

Zainab A. Malik, MD
Nathan Litman, MD
Children's Hospital at Montefiore
Bronx, NY

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The Use of Antibiotics. Kucers A. In: Crowe KS, Grayson ML, Hoy J, eds. *The Use of Antibiotics: A Clinical Review of Antibacterial, Antifungal and Antiviral Drugs.* 5th ed. Oxford, United Kingdom: Butterworth-Heinemann Publishing; 1997:108–143, 192–208

Penicillins. Chambers HF. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and Practice of Infectious Diseases.* Vol 1. 6th ed. Philadelphia, Pa: Elsevier Churchill Livingstone; 2005: 281–293

Diagnosis and Management of Acute Otitis Media. Subcommittee on Management of Acute Otitis Media. American Academy of Pediatrics and American Academy of Family Physicians. *Pediatrics.* 2004;113: 1451–1465

Management of Sinusitis. Subcommittee on Management of Sinusitis and Committee on Quality Improvement. American Academy of Pediatrics. *Pediatrics.* 2001;108:798–808

Ampicillin and amoxicillin are aminopenicillins derived from the penicillin nucleus. Their basic structure consists of the beta-lactam ring and a side chain. The ring structure confers antimicrobial activity, and the side chain determines the antibacterial spectrum and pharmacologic properties. The antibacterial activity of aminopenicillins is similar to that of other penicillins via inhibition of bacterial cell wall synthesis. Penicillin-sensitive reactions in bacterial cell wall synthesis are catalyzed by a class of proteins called penicillin-binding proteins (PBPs), which are inhibited by beta-lactam antibiotics.

The antibacterial spectrum of aminopenicillins includes nonbeta-lactamase-producing gram-positive cocci, anaerobes, and gram-negative cocci, including *Neisseria* and *Enterobacteriacae* that do not produce beta-lactamase. These agents are not active against *Pseudomonas* sp and are hydrolyzed by beta-lactamases, making them ineffective against beta-lactamase-producing strains of bacteria.

Ampicillin is effective in treating upper and lower respiratory tract infections caused by *Streptococcus pneumoniae*, beta-hemolytic streptococci, and nonbeta-lactamase-producing strains of *Haemophilus influenzae*. It also is effective in the treatment of meningitis caused by group B streptococci, *Listeria monocytogenes*, *N meningitidis*, and all except highly resistant strains of *S pneumoniae*. Ampicillin previously was a first-line agent for treating urinary tract infections (UTIs) caused by *Escherichia coli* and gastroenteritis caused by *Salmonella enterica* or *Shigella* sp. However, due to the rising prevalence of beta-lactamase-producing strains of these organisms, ampicillin no longer is the agent of choice for UTIs unless susceptibility has been documented.

The in vitro activity of amoxicillin is similar to that of ampicillin. Ampicillin usually is given intravenously (IV) or

intramuscularly (IM), whereas amoxicillin is the preferred oral agent because it is less likely to cause diarrhea and can be administered less frequently than oral ampicillin. Amoxicillin is indicated in the treatment of otitis media, sinusitis, pneumonia, and susceptible UTIs. Among the oral penicillins and cephalosporins, amoxicillin can achieve therapeutic minimum inhibitory concentrations in body tissues for nonmeningeal infections caused by penicillin-resistant pneumococci, except highly resistant strains. Amoxicillin is not useful in the treatment of shigellosis because it is well absorbed in the small intestine. Oral ampicillin is indicated for this purpose; its poor intestinal absorption allows significant levels of the antibiotic to reach the site of infection in the large intestine.

Ampicillin can be given IV or IM in the form of its sodium salt. For neonates weighing more than 2,000 g and younger than 7 days old, a dose of 25 mg/kg every 8 hours is recommended for mild-to-moderate infections. With serious infections such as meningitis, the dose should be increased to 50 mg/kg every 8 hours. Neonates older than 7 days and weighing more than 2,000 g who have mild infections can receive a dose of 25 mg/kg every 6 hours; for meningitis, the dose should be increased to 200 mg/kg per day divided every 6 hours. For older infants and children, doses of 100 to 400 mg/kg per day, divided every 4 to 6 hours, are recommended. Because ampicillin is relatively nontoxic, dose adjustment is not imperative in mild-to-moderate renal failure, although it may be required for patients who have severe renal dysfunction.

Ampicillin is well distributed throughout the body. Although the peak interstitial tissue concentrations are lower than those achieved in serum, the drug persists in the interstitium for a longer period of time. It achieves therapeutic concentrations in septic joint effusions, ascitic fluid, and parapneumonic effusions. Very low concentrations of ampicillin can be detected in normal cerebrospinal fluid, but higher levels are achieved in patients who have bacterial meningitis due to ongoing meningeal inflammation.

The serum half-life of ampicillin declines with increasing postnatal age. In neonates 2 to 7 days old, the serum half-life is 4 hours; in 8- to 14-day-old neonates, it is 2.8 hours; and in 15- to 30-day-old neonates, it is 1.7 hours. In older children and adults, ampicillin has a serum half-life of 1 hour. After parenteral administration, 75% of the dose is excreted in the urine and 0.1% of the dose is excreted unchanged in bile. Because high concentrations of ampicillin are excreted in the urine, it was an agent of choice for UTIs prior to the emergence of microbial resistance.

The major adverse effects associated with ampicillin use are rashes, which tend to occur more commonly than with other penicillins (7.7% versus 2.75%). Ampicillin rashes may be urticarial or macular, resembling measles or rubella. The macular rashes usually appear 4 to 5 days after therapy has begun, without any other associated signs of allergy, and often subside with ongoing treatment. The nonurticarial rashes do not indicate true ampicillin hypersensitivity. Parenteral ampicillin therapy also can cause nausea and diarrhea, which are more common in younger children. Ampicillin and amoxicillin can both be responsible for *Clostridia difficile*-associated pseudomembranous colitis. Very large doses that achieve serum levels of 800 mcg/mL may cause central nervous system toxicity, resulting in convulsions.

Amoxicillin is available in the trihydrate preparation for oral use. The standard dose is 45 mg/kg per day in two divided doses or 80 to 90 mg/kg per day in two divided doses for indications that require high-dose amoxicillin. It is well absorbed after oral administration, and food does not alter its absorption. Almost 60% of an oral dose of amoxicillin is excreted unchanged in urine within the first 6 hours. It has a tissue distribution similar to that of ampicillin, and tissue levels are 40% of serum levels. Because amoxicillin achieves high levels in the gastric mucosa, it is a good antibiotic for treating *Helicobacter pylori* infections in combination with other agents. Oral amoxicillin is not indicated for treating central nervous system infections.

Amoxicillin is relatively nontoxic and may be given in the usual recommended dose to patients who have mild renal failure. The dose should be reduced for patients whose renal failure is moderate to severe. Amoxicillin is the drug of choice for treating acute bacterial sinusitis and acute otitis media. Factors that justify its use as a first-line agent include its narrow antimicrobial spectrum, pleasant taste, low cost, activity against susceptible and intermediately resistant pneumococci, and acceptable safety profile in children.

There is a high prevalence of beta-lactamase-producing strains of *H influenzae* and *Moraxella catarrhalis* in upper respiratory tract isolates in the United States, making them resistant to amoxicillin. Of the *S pneumoniae* isolates from the upper respiratory tract, an average of 30% are resistant to penicillin. Some 50% of these organisms are highly resistant, reflected in their lack of response to standard-dose amoxicillin therapy. Penicillin resistance among S *pneumoniae* results not from the production of an enzyme, but from an alteration in PBPs on the bacterial cell wall, which confers resistance to penicillins and cephalosporins.

Conventional doses of amoxicillin (45 mg/kg per day) are effective against all susceptible strains of *S pneumoniae* and most strains that are intermediate in resistance to penicillin. Highly resistant strains are not susceptible to conventional doses of amoxicillin. High-

dose amoxicillin (80 to 90 mg/kg per day) achieves high middle ear and sinus fluid levels, making it effective against all intermediately resistant strains and some, but not all, highly resistant strains. In practice, the response rate to high-dose amoxicillin among children who have acute otitis media is approximately 80%.

Risk factors for the presence of intermediate or highly resistant S *pneumoniae* necessitating the use of high-dose amoxicillin include child care attendance and having received antibiotics in the preceding 3 months, particularly among children younger than 2 years of age.

Amoxicillin and ampicillin are cross-allergenic with other penicillins and are contraindicated in penicillin-allergic patients. Amoxicillin generally is well tolerated, although it has a propensity to cause rashes and results in a morbilliform rash if given to a patient acutely infected with Epstein-Barr virus. The maculopapular eruptions produced by amoxicillin are similar to those seen with ampicillin. Amoxicillin also may cause nausea and diarrhea, although less commonly than ampicillin.

Comment: Despite newer and newer (and more expensive) antimicrobial agents, amoxicillin remains the drug of choice for both otitis media and sinusitis in most children. It's nice when oldies are still goodies.

Henry M. Adam, MD
Editor, In Brief

In Brief

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Christine Rizkalla, MD
Young-Jin Sue, MD
Children's Hospital at Montefiore
Bronx, NY

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History of Cocaine. Petersen RC. *NIDA Res Monogr*. 1977;13:17–34

Cocaine: History, Use, Abuse. Karch S. *J R Soc Med*. 1999;92:393–398

Cocaine Use: 2002–2003. *The NSDUH Report*. 2005. Available at: http://www.oas.samhsa.gov/2k5/cocaine/cocaine.htm

Intersecting Epidemics—Crack Cocaine Use and HIV Infection among Inner-city Young Adults. Edlin BR, Irwin KL, Faruque S, et al. Multicenter Crack Cocaine and HIV Infection Study Team. *N Engl J Med*. 1994;331:1422–1427

Cocaine and the Critical Care Challenge. Shanti C, Lucas C. *Crit Care Med*. 2003;31:1851–1859

TOX-ACLS: Toxicologic-oriented Advanced Cardiac Life Support. Albertson T, Dawson A, de Latorre F, et al. *Ann Emerg Med*. 2001;37(4 suppl):S78–S90

Cocaine, Amphetamines and Other Sympathomimetics. Rao R, Hoffman R. In: Marx JA, Hockberger RS, Walls RM, eds. *Rosen's Emergency Medicine: Concepts and Clinical Practice*. 5th ed. St. Louis, Mo: Mosby; 2002:2386–2392

Body Packing: The Internal Concealment of Drugs. Traub S, Hoffman R, Nelson L. *N Engl J Med*. 2003;349:2519–2526

According to one legend, before it was a plant, coca was a beautiful woman, executed for adultery. Evidence of humans consuming *Erythroxylon coca*, a South American shrub from which cocaine (benzoylmethylecgonine) is derived, dates to more than 1,000 years ago. Regarded as divine in the northern Andes of Peru and Bolivia, cocaine played a role in religious ceremonies and inspired colorful mythology regarding its origin. Chewing coca leaves was promoted for its healing powers, to ease hunger and thirst, and to improve the stamina required for daily labors and life at great altitudes. Spanish colonists of the region introduced the leaf to Europe, and the pure and far more potent chemical, cocaine, ultimately was extracted. The mid-1800s saw the production of coca-infused wines and tonics. Early surgeons discovered its utility for local anesthesia. Sigmund Freud praised the drug for its multiple medicinal uses. In 1886, Dr John Pemberton produced a new beverage named Coca Cola, combining coca and caffeine from the African kola nut plant, touting it as tonic for multiple ailments and nervous disorders, particularly for the elderly. Gradually, more products contained greater amounts, and consumption increased. Sir Arthur Conan Doyle described his celebrated fictional detective Sherlock Holmes using cocaine when occupied by boring cases. By the advent of the 20th century, increasing prevalence and nonmedicinal use of pure cocaine brought with it the awareness of its toxic and addictive potential. Beginning with the

Harrison Act of 1914, the United States government passed legislation to attempt to control its availability, but public demand remained.

Far from myth and legend, cocaine now is popularly known as bazooka, white lady, Charlie, snow, tornado, kryptonite, dust, bones, sugar, and blow, among other names. Estimates in both 2002 and 2003 were that more than 5.9 million people in the United States older than age 12 years (2.5% of the population) had used cocaine within the past 12 months, primarily within the 18- to 25-year-old group.

Cocaine is abused by several routes. Water-soluble cocaine hydrochloride is snorted as a powder or injected as an aqueous solution. Alkaloid preparations are smoked as "free-base" or as the precipitated crystal form known as crack. As a base, cocaine is highly purified, heat-stable, and lipid-soluble, thereby readily crossing the blood-brain barrier and yielding an intense and immediate "high." Both smoking and intravenous (IV) injection produce a high within seconds to minutes that lasts 15 to 30 minutes unless repeated hits are delivered. The effects of insufflated cocaine peak at 20 to 30 minutes (due to local vasoconstriction, which slows its absorption) and last approximately 1 hour. Cocaine may be adulterated to augment its mass (eg, with sugars or talc) or to enhance its effects (eg, with heroin—known as a "speedball"—phencyclidine, lidocaine, or strychnine). Use with alcohol produces the metabolite cocaethylene, which may augment its toxicity.

The physiologic effects of cocaine result from the release of norepinephrine from adrenergic nerve terminals and from inhibited reuptake of dopamine, epinephrine, serotonin and norepinephrine. Sympathetic overstimulation manifests as mydriasis, diaphoresis, tachycardia, hypertension, and hyperthermia. This may be followed by the complications of myocardial infarction, stroke, seizure, pulmonary hemorrhage, gastrointestinal ischemia, rhabdomyolysis, and renal failure. Use in pregnancy may lead to placental abruption or fetal demise. Behavioral manifestations of this sympathetic overstimulation include euphoria, confidence, agitation, aggression, and hallucinations ("coke bugs").

Cocaine blocks sodium transport across cell membranes, slowing nerve impulses, which accounts both for its anesthetic properties and for its potential to induce fatal ventricular arrhythmias and cardiac arrest. IV use carries the additional risks of local infection, sepsis, and endocarditis. Human immunodeficiency virus transmission is an additional risk of IV drug use, both from needle-sharing and because high-risk sexual encounters are associated with drug-seeking behavior.

Chronic use of cocaine is associated with cachexia, poor nutrition, and "crack dancing" (choreoathetotic movements from decreased dopamine stores). Upregulation of dopaminergic receptors exacerbates tolerance as well as the drug craving and dysphoria that follow each high. With greater intake needed to achieve the same effects, cocaine users increase their potential for morbidity and mortality.

Cocaine users may not be forthcoming about their drug taking. Urine screening is widely available, employing a highly specific immunoassay for the metabolite benzoylecgonine, which is excreted for 24 to 48 hours. However, depending on the chronicity of use, urine may remain positive for several days.

As with all medical emergencies, individuals who present with symptoms of toxicity should be evaluated for airway stability. The most rapidly fatal complications in cocaine use are related to hyperthermia, hypertension, and cardiac dysrhythmias. Benzodiazepines and aggressive external cooling are the foundation of management of such complications. Potentially life-threatening hyperthermia results from agitation, increased motor tone, and vasoconstriction, interrupting the body's cooling mechanisms. Once identified, hyperthermia must be addressed emergently with: benzodiazepines to decrease agitation; paralysis and airway stabilization if indicated; IV access for aggressive fluid management; and rapid cooling with ice.

The clinician also must monitor levels of creatine kinase, electrolytes, creatinine, coagulation parameters, and urine myoglobin because rhabdomyolysis may be an associated complication. A direct-acting alpha-adrenergic antagonist such as phentolamine and a vasodilator, usually nitroprusside, are used to treat critical hypertension. Beta blockers should be avoided because resultant unopposed alpha-adrenergic stimulation may exacerbate the hypertension. Computed tomography (CT) scanning of the brain and lumbar puncture should be strongly considered for patients who have persistent headache or altered mental status.

Evaluation of chest pain in association with cocaine use requires radiographs of the chest (for pneumothorax, widened mediastinum, and pneumonia), electrocardiography (ECG), measurement of cardiac enzymes and electrolytes, a complete blood count, and blood cultures. Acute coronary syndromes due to cocaine should be managed initially with nitrates and benzodiazepines, with use of alpha-adrenergic antagonists considered in refractory cases. Sodium bicarbonate is appropriate for treating the sodium channel blockade that results in ventricular dysrhythmias, manifested as a widened QRS interval on ECG. Class 1A and 1C antidysrhythmic agents generally are contraindicated in such situations because exacerbation of sodium channel blockade may ensue.

A unique set of problems arises with individuals who have ingested densely contained, well-sealed packets of the

drug for transport (body packers) or who have hastily swallowed poorly sealed aliquots to conceal them from law enforcement officers (body stuffers). Body packers may harbor up to 100 packages, each containing a lethal quantity of the drug. Body stuffers, while concealing a lesser amount of drug, may be at greater risk for toxicity from rupture of poorly secured packets. Plain radiographs may reveal air trapped between the wrappers (often condoms) used for packaging ("double-condom sign"), and contrast CT scans may demonstrate foreign bodies surrounded by gas. Bowel perforation is an additional concern. Because of the potential for lethal overdosing, a positive urine assay accompanied by symptoms of cocaine toxicity in such individuals should prompt rapid surgical decontamination, with treatment of associated toxicity as described previously. Stable individuals should be managed with whole bowel irrigation, using polyethylene glycol to facilitate gut emptying, and observation until passage of all packages.

With considerable numbers of adolescent users and accidental toddler exposures, cocaine continues to present a complex and sometimes fatal public health challenge that includes the pediatric population. Familiarity with the manifestations and management of cocaine intoxication is imperative for practitioners who work with children and adolescents.

Comment: So, at least initially, there really was a difference between Coke and Pepsi!

Henry M. Adam, MD
Editor, In Brief

Correction

For question #11 on page 345 in the September 2006 issue of *Pediatrics in Review*, the answer should be D rather than E.

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University of Rochester School of Medicine Rochester, NY 14642-8777
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