Skin manifestations of illicit drug use Manifestações cutâneas decorrentes do uso de drogas ilícitas

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Abstract: Illicit drug use and abuse is a major problem all over the world. The United Nations estimates that 5% of world population (aged 15-64 years) use illicit drugs at least once a year (annual prevalence) and half of them use drugs regularly, that is, at least once a month. Many adverse events of illicit drugs arise on the skin and therefore dermatologists should be aware of these changes.

Keywords: Street drugs; Street drugs/history; Street drugs/adverse effects; Skin; Review

Resumo: O uso e abuso de drogas ilícitas é um problema significativo e de abrangência mundial. A Organização das Nações Unidas estima que 5% da população mundial entre os 15 e 64 anos fazem uso de drogas pelo menos uma vez por ano (prevalência anual), sendo que metade destes usam regularmente, isto é, pelo menos uma vez por mês. Muitos dos eventos adversos das drogas ilícitas surgem na pele, o que torna fundamental que o dermatologista esteja familiarizado com essas alterações.

Palavras-chave: Drogas ilícitas; Drogas ilícitas/bistória; Drogas ilícitas/efeitos adversos; Pele; Revisão

HISTORY

More than five thousand years ago in Mesopotamia, the region where present-day Iraq is situated, the calming, somniferous and anesthetic properties of opium (from the Latin, *opium*, through the Greek, opion, meaning 'sap, juice') were already known by Sumerians. Obtained from unripe seeds of *Papaver somniferum* (poppy or opium poppy / mawseed / plant of joy), *opium* is the most ancient drug known. The Persians and Egyptians used it to prevent intense crying in children and to instill courage in soldiers. Figures of poppy seeds can be found in Greek coins dated at least one thousand years before the effects of opium were mentioned in Hellenic literature. It was the custom in ancient Greece to add opium to the hemlock infusion administered for suicide or

euthanasia in order to minimize the suffering of those condemned. Opium was probably the nephente drug Homer referred to as "the most powerful destroyer of grief."^{1,2}

During the seventh century, Turks and Arabs discovered not only the powerful effects of inhaling opium smoke but also its commercial potential. A growing commerce commenced with sales primarily to India and China. The eighteenth century witnessed the drug's arrival in Europe, via England, and during the following century, morphine and heroin, the two most consumed derivatives of opium, were isolated.

Morphine was isolated in 1804 by the German chemist Friedrich Wilhelm Adam Sertüner who

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named it in homage to Morpheus, the Greek god of dreams. Initially, its use was restricted, but as of 1853, with the advent of the hypodermic syringe, it soon experienced a wide range expansion. Due to its potent anesthetic effect, its use during the American Civil War resulted in a large number of addict soldiers.³

Heroin was synthesized in 1874 by the English chemist C.R. Alder Wright, by the acetylation of morphine. Felix Hoffman, lead chemist of the Bayer pharmaceutical industry in Germany, introduced heroin as a medication on August 21, 1897, less than two weeks after having produced aspirin (Figure 1). The name possibly derives from the German *beroisch* (heroic), a sensation described by the first volunteers in experimental studies. The manufacturer marketed the product from 1898 to 1910 as a cough sedative for children and a treatment for morphine addiction, until it was discovered that heroin is converted into morphine in the liver.^{4,5}

The use of cocaine also dates far back in time, as is suggested by the presence of coca leaves (from the Aymara language, meaning "the tree") in tombs of Peruvian Indians dated from 600 AD. The chewing of coca leaves by Andean highland natives is probably more of a cultural habit than an addiction itself. The feeling of well-being and relief of fatigue probably facilitated adaptation to high altitudes, a fact readily perceived by the Spanish settlers who soon taxed the production of coca leaves. For some time, these resources were the main source of support for the Catholic Church in that region.⁷

Initially isolated in 1855, cocaine (Figure 2) was the first local anesthetic known, and was introduced into medical practice by the Austrian ophthalmologist Carl Koller. One of the first reports on its effects was penned by no one else than Sigmund Freud.* Based on his observations that the effects of cocaine were so opposite to those of morphine, Freud erroneously concluded that the former would be a logical treatment for morphine-dependent individuals.

One of the most popular drinks in Italy during the nineteenth century was Vin Mariani, formulated in 1863 by the chemist Angelo Mariani with 6 mg of cocaine per ounce (29.6 ml) and advertised as tonic and restorative (Figure 3). The list of famous customers who endorsed its therapeutic effects included Thomas Edison, Julio Verne, Alexandre Dumas, and pope Leo XIII, who awarded Mariani the Gold Medal of the Vatican. At the end of



FIGURE 1. Source: National Library of Medicine



FIGURE 2. Source: Wikipedia

that century, the US manufacturer Parke-Davis sold cocaine in the form of powder, cigarettes, and even in a formulation for intravenous use that was accompanied by a needle. Among other indications, it proclaimed that the product would "supply the place of food, made the coward brave, and the silent eloquent." Trying to compete with Vin Mariani, John Styth Pemberton launched French Wine Cola in the US. Since the commercial success was far below expected, Pemberton dropped the wine from the formula and added a mixture of caffeine and cocaine. Coca-Cola, the best seller soft drink in the world, was so created. In 1906, to comply with legislation, its manufacturer began to use decocainized coca leaves. 8

^{*} Freud S. 1884;2:289-314 apud Gegler LL, Mark H. 1986;315:1495-500.



Figure 3. Source: Wikipedia

The 2006 report of the United Nations Office on Crimes and Drugs estimates that around 200 million people, the equivalent to 5% of the world population (age 15-64), use illicit drugs at least once a year (annual prevalence). Half of them do it on a regular basis (at least once a month). The number of addicts or problematic users is calculated as 25 million, the equivalent to 0.6% of the world population age 15-64. The world scenario as to the drug market (production and use) shows geographical variations. Overall, the tendency is towards stability or even a decline. One notable exception is marijuana, the dominant illicit drug in all regions of the world and with a growing rate of use.

COCAINE

Cocaine, or benzoylmethylecgonine, is an alkaloid (a chemical compound containing nitrogen, carbon, oxygen, and hydrogen) obtained from *Erythroxylum coca* leaves, a native plant in Andean countries such as Peru, Colombia, and Bolivia. Out of over 200 species *Erythroxylum*, only *E. coca, E. coca var. ipadu, E. novogranatense*, and *E. truxillense* produce reasonable amounts of cocaine, with a content that varies between 0.5 and 2%.¹⁰

The production process initially involves pressing the leaves along with an organic solvent. The resulting paste, which is 80% cocaine, is then treated with hydrochloric acid in order to remove impurities. This produces a white crystalline powder (cocaine hydrochloride) known by a wide variety of names such as brillo, powder, bird, Bogotá Bullions, snow, squib, white devil, yada, zing, etc. Since it is water-

soluble, it can be eaten/chewed, inhaled by the nose ("snorted"), or injected. On the other hand, since it is vulnerable to pyrolysis, smoking cocaine in cigarettes produces little or no euphorigenic effect.

During the 1980's, another form of cocaine was introduced on the market and obtained by dissolving cocaine hydrochloride in water and adding an alkali, usually baking soda, to the solution. Once heated, this solution crystallizes forming cocaine 'rocks' known as crack, which vaporize at low temperatures and are more appropriate for smoking. The name 'crack' is onomatopoeic and refers to the sound produced by the boiling of the hydric components of the rocks when heated. Since it is not soluble in water, this cocaine base is not appropriate for ingestion, inhalation or injection. Crack produces a high concentration of cocaine at relatively low prices, making it extremely popular among low-income users. It is readily absorbed in lung alveoli, and therefore produces a euphorigenic sensation almost immediately.

Cocaine is a potent stimulator of the central nervous system, producing an initial feeling of euphoria, well-being, outwardness, and increased libido. Higher doses may lead to tremors, convulsions, and ultimately, depression of vital spinal cord centers. Its best known mechanism of action is the blockage of presynaptic reuptake of neurotransmitters such as dopamine, noradrenalin, acetylcholine, and serotonin. This blockage potentiates and prolongs the peripheral and central actions of these catecholamines, particularly at the pleasure center of the brain (limbic system).11 The anesthetic effects on peripheral nerves occur by the inhibition of cell membrane repolarization, with a consequent blockage of nerve impulse generation and conduction. Cardiovascular effects are secondary to the increased plasma levels of catecholamines, leading to hypertension, tachycardia, and arrhythmias. There is a 24-fold increase in the risk of acute myocardial infarct one hour after cocaine use in individuals with low risk factors for this cardiac event. This risk is not related to the amount ingested, administration route, or frequency of use.12 Cocaine also displays a potent vasoconstritive effect. Administration routes of cocaine include nasal inhalation or snorting (the most popular), chewing leaves (a common habit among natives of Andean highlands), or injection, the latter being responsible for the most drastic dermatological alterations and addressed elsewhere in this text.

Aspirated through the nose over a prolonged period, its vasoconstrictor effects result in necrosis and perforation of the nasal septum. Cocaine has also been associated with cases of acute porphyria, ¹³ intra-

nasal warts,¹⁴ scleroderma,¹⁵ palpable purpura,¹⁶ Henoch-Schöenlein purpura,¹⁷ and Schurg- Strauss vasculitis.¹⁸ Generalized excoriations secondary to the parasite delusion and tingling sensations induced by cocaine are common.

Hofbauer et al. described recurrent lesions (two episodes) similar to those of Stevens-Johnson syndrome associated with cocaine use. Since on these two occasions the patient acquired the drug from a dealer who was not his/her usual supplier, and since the dermatosis did not recur with continuing cocaine use, the authors consider the possibility that the skin lesions were set off by fillers that are commonly incorporated to cocaine. ¹⁹ Bullous erythema multiform has also been reported in cocaine users with no other imputable factor. ²⁰

Crack smokers frequently present with punctiform, hyperkeratotic, blackened lesions located on palms and ventral surfaces of fingers, which are more evident on the dominant hand ("crack hands"). These lesions are attributed to burns from the pipe used to contain the drug and tend to be repeated, since the cerebral intoxication makes the user less aware of thermal traumas.²¹ The high temperatures reached by the vapors emanated during crack smoking also lead to eyebrow thinning (Figure 4). Acute cases of segmental epidermal necrosis are also reported, associated with reticular livedo and acrocyanosis, and possibly instigated by prolonged vasospasms.²²

HEROIN

Heroin (diacetylmorphine) is a derivative of morphine obtained by acetylation, which provides high liposolubility, rapid penetration through the hemato-encephalic barrier and intense euphoria. Once in the body, heroin is de-acetylated and converted into morphine. In the United Kingdom, it is available as a prescription drug for pain relief in terminal patients, myocardial infarct, and acute pulmonary edema. The classic form, white and crystalline, corresponds to diacetylmorphine hydrochloride. In the 1980's, brown heroin (black tar heroin) appeared on the market, a brownish paste with a gummy consistency produced primarily in Iran and Mexico that needs to be diluted for use.

In the United States alone, the number of people who have already experimented heroin is estimated at 3.5 million, and more than 1 million of these have become addicts. Between 1995 and 2002, it is estimated that more than 100 thousand individuals initiated addiction per year, with a great prevalence among youth 12 to 25 years of age.²³

Heroin can be consumed by inhalations of the vapors that are released when the drug is heated in pieces of aluminum paper or mixed with conventional cigarette tobacco and smoked. These two administration routes are not, however, very efficient. The preferred route is injection.

In the early 1980's, a novel epidemic of pigmented tongue lesions, clinically and histologically consistent with fixed drug eruption, was described in Holland. All patients shared the habit of smoking heroin²⁴ (Figure 5).

INJECTIING USE OF ILLICIT DRUGS

The intravenous route is used by cocaine and heroin addicts because it produces quicker and more intense effects. Preferred sites are the veins of the antecubital fossa of the non-dominant arm, not only because they are readily accessed, but also because it



FIGURE 4: Lateral eyebrow thinning in crack user



FIGURE 5: Hyperpigmentation of the tongue in heroin user

is possible to hide skin markings by using a long-sleeved shirt/blouse.²⁵

As the veins become less accessible, generally due to sclerotic phenomena, or in users fearful of the potent effects obtained by the intravenous route, cocaine and heroin can also be injected into the subcutaneous tissue, a technique known as skin-popping, or in the muscles (muscle popping). The injecting use of these drugs leads to the most drastic acute and chronic manifestations. Some are caused by the drug itself, but most are set off by adulterants or fillers. Both cocaine and heroin are mixed with substances that are incompatible with injection use, such as talcum, quinine, starch, sugar, and flour, among others, with the intention of increasing profit margins for drug dealers.

Acute Manifestations

The most common acute manifestations include skin and soft tissue infections, the main cause of hospital admissions among injecting drug users. The mechanism for the establishment of infections probably involves tissue trauma, effects of the drug and its fillers, tissue ischemia, and inoculation of bacteria. With repeat injections at the same site, the skin and adjacent tissues become more susceptible to infection.²⁶ The most common organism recovered is S. aureus, alone or associated with anaerobic bacteria, and the latter are predominantly of oral origin.27 Clinical manifestations and severity vary from superficial and meaningless abscesses to potentially fatal cases of necrotizing fasciitis,28 and include extensive cellulitis and even pyomyositis, a rare pyogenic and abscess-forming infection of skeletal muscles.29

TThe greatest risk factor for the formation of skin and soft tissue abscesses is the use of the subcutaneous route (skin-popping), with the introduction of irritant substances, even bacteria, directly into the tissues. Although it leads to other systemic risks, the intravenous route precludes the local concentration of irritants and microorganisms. Other risk factors are the use of non-sterile needles and the use of cocaine + heroin mixture (speedball).³⁰

Systemic candidiasis is the most common mycotic infection among heroin users and may manifest as endocarditis, endophthalmitis, and osteitis. Folliculitis by *Candida*, practically exclusive of this group of patients, is morphologically similar to bacterial folliculitis but with a few characteristics that allow its distinction. The most striking feature is that lesions are tender. They primarily affect areas of the scalp, beard, trunk, and pubic region. Bacterial cultures are negative, and lesions do not respond to antibiotics. Folliculitis by *Candida* is interpreted as

a secondary setting of systemic candidiasis, which is usually transitory. It is considered a probable form of contamination from the presence of the fungus in the drug itself, in lemons whose juice is used to dilute brown heroin, or even on the needles, since it is customary among addicts to moisten them with saliva before injections.³¹⁻³³

Transcutaneous botulism is a flaccid, descending, and potentially fatal paralysis, set off by the neurotoxin produced by *Clostridium botulinum* that germinates in the lesions. Since 1988, California has experienced a dramatic increase in number of cases of transcutaneous botulism, and the great majority is in individuals who inject brown heroin.³⁴ Similarly, more than half of the tetanus cases notified in California between 1988 and 2000 were related to the use of injecting drugs.³⁵

Between April 1 and June 20 of 2000, 62 cases of serious illness, with at least 30 deaths, were reported in injecting drug users in the United Kingdom and the Republic of Ireland. All patients were hospitalized, or found dead, with soft tissue infections (abscesses, cellulitis, fasciitis, or myositis) at the site of the injection, a serious systemic toxic condition, or as a necropsy finding of diffuse toxic or infectious process. The disease was associated with subcutaneous or intramuscular, but not intravenous, use of heroin. In eight cases, species of Clostridium (C. novyi e C. perfringens) were isolated, alone or in association with other microorganisms. Some characteristics suggest that this outbreak resulted from the contamination of a large batch of heroin: similar clinical features and injecting methods, temporal and geographical distribution, and a high proportion that knew, and injected with, each other.36 The outbreak was considered extinct in August of the same year, totaling 104 cases and 35 deaths. Similar cases were later described in Canada³⁷ and in California.³⁸

Excoriations are common, although it cannot be determined if they are consequences of the pruritis induced by the narcotics or by psychological disturbances. Opiates may produce degranulation of mast cells by non-immune mechanisms and therefore, urticaria is a relatively common complaint among heroin users. It is estimated that about 20% of patients who receive opiates postoperatively develop urticaria.³⁹

Chronic Manifestations

Chronic skin manifestations are also common and some of them pathognomonic of the injecting use of illicit drugs. Scars resulting from the prolonged habit of self-injecting into the subcutaneous tissue (skin-popping) are very distinct. They are relati-

vely small (0.5 to 3 cm de diameter), oval or rounded, generally multiple, slightly atrophic, and sometimes hyperpigmented, with a punch-out appearance. They are distributed on the extensor surface of arms and dorsal surface of the hands, preferred sites for this route of administration, as well as abdomen and thighs. In most instances they represent a scarring process of small abscesses, although they may be present even in the absence of abscesses (Figure 6).

Repeated and prolonged trauma to the veins leads to linear, sclerotic, and many times hyperpigmented scars. These lesions were first described in 1929 and called 'needle tracks' since their linear aspect resembled railroad tracks.** Intensity of the lesions and the rate at which they are established depends on what is injected and the contaminants and fillers present. Quinine, for example, is the contaminant with the highest sclerosing potential. Hyperpigmentation result from the inflammatory process and its degree depends on the individuals' skin color. Another possible explanation for this phenomenon would be the inadvertent introduction of soot that accumulates on the needles when they are sterilized over a flame.⁸

Necrosis of the extremities is still another dramatic consequence of the injected use of illicit drugs. Although it may occur with any drug, it is more common in cocaine users who deliberately or involuntarily employ an arterial route. The prolonged and repeated vasospasm induced by cocaine, a potent vasoconstriction agent, and the occlusive phenomena generated by the injection of contaminants that function as emboli, seem to be the main factors in the etiopathogenesis of the necrosis^{40,41} (Figure 7). Experimentally, the subcutaneous injection of cocaine hydrochloride produces necrotizing panniculitis and vascular necrosis in rats.⁴²

The contaminants, especially talc, are capable of forming granulomas at the injection sites or along the venous path. In patients who use injections of amphetamines, the talc itself, present in the tablets, may be responsible for forming cutaneous granulomas⁴³ (Figure 8).

MARIJUANA AND HASHISH

Cannabinoids are psychoactive chemical components present in plants of the *Cannabis genus*. The most potent, which has hallucinogenic properties, is Δ -9-tetrahydrocannabinol, commonly known as THC. Of the three existing species (*C. sativa, C. indica*, and *C. ruderalis*), only the first two produce high quanti-



FIGURE 6: Scars resulting from subcutaneous injection of cocaine (skin popping)

ties of the psychoactive components. *C. indica* is usually found in the Middle East and India, where it is used in the production of hashish.

Cannabis is an easily managed plant, potentially cultivated in any region of the world, even in indoors. I basically yields three forms of drugs: a) marijuana, obtained by grinding leaves, stems, and flowers, low concentrations of THC, and usually consumed by smoking; b) hashish, a resin extracted from the plant trichomes and compacted into blocks, with concentrations of THC, and usually consumed by smoking; and c) the oil (honey oil), with high concentrations of THC, extracted with the use of solvents



FIGURE 7: Extensive necrosis secondary to cocaine injection (courtesy Dr. Milton Viana, Belo Horizonte)

^{**}Biggam A. 1929;23:147-53. apud Karch SB. 1996. p.349-50.



FIGURE 8: Granuloma (foreign body) along the venous path due to cocaine injection

such as acetone or methanol, and added to conventional cigarettes or to marijuana cigarettes, or inhaled after heating.

Although the origin is controversial, the word assassin may have derived from the Arab word *bas-bsbashin*, a name used to designate a sect of blood-thirsty Islamic militants who were avid hashish users. Marijuana is, by far, the number 1 drug consumed worldwide. A great part of its popularity among young people may be attributed to its reputation of an innocent or weak drug, edowed with therapeutic properties. As with conventional cigarette smokers, classically, marijuana users bear a greater risk of premature skin aging, with accentuated lividness and prominent wrinkles.

The derivatives of Cannabis, however, share



FIGURE 9: Poppers (courtesy of Dr. Ronald Brancaccio, New York University)

many of the carcinogens found in tobacco and thus would be capable of acting as risk factors for malignant neoplasms of the lungs, upper respiratory tract, colon, and bladder, among others. A recent comprehensive review suggested that variables such as frequency, mode of use, and duration of exposition be analyzed in further studies for better reliability of results. 44 Such strictness is justified when some countries are considering marijuana availability as a therapeutic agent.

The components of *Cannabis* also possess atherogenic potential, as is shown by the growing number of case reports of artheritis in drug users.⁴⁵

ECSTASY

In 1914, the German pharmaceutical industry Merck received the patent for the drug 3,4-methylene-dioxymethamphetamine (MDMA), originally an intermediate chemical product that would be used in synthesis of a hemostatic drug. Legally commercialized in the US until 1985 and used as an adjuvant in psychotherapy, MDMA, popularly known as ecstasy or XTC, soon started to be consumed in nightclubs because of its euphorigenic and disinhibition effects. Since the drug has been banned in many countries, most of MDMA available is synthesized in clandestine laboratories and a great number of contaminants such as ephedrine, pseudoephedrine, caffeine, aspirin, and paracetamol, are added. Classically hepatotoxic, ecstasy may also be responsible for serious cases of depression, panic syndrome, and psychoses. The first report of skin lesion in users included a comedone-free acneiform dermatosis on the face with rapid onset. One possible pathogenic explanation for the skin lesions would be a disorder in sexual steroid metabolism secondary to hepatotoxicity of the drug, with a consequent stimulation of sebaceous glands.46

POPPERS

Alkyl nitrites comprise a large group of organic compounds. The most well known, amyl nitrite, has been used for years as a treatment for angina, while others are sold as room deodorizers or for recreational use.

Nitrites, commonly known as poppers, (Figure 9) produce muscle relaxation, including those of the vaginal and anal sphincters. The vasodilation that follows muscle relaxation, the rationale for its use in angina, is also considered as a factor for prolonging erection and orgasm. These characteristics have made the drug extremely popular in sexual experiences, especially among homosexuals.

Since they are highly volatile, nitrites may be inhaled directly from the containers in which they



FIGURE 10: Perioral contact dermatitis to poppers (courtesy of Dr. Ronald Brancaccio, New York University)

are sold. Immediate effects include tachycardia, facial flushing, and mild headache. Nitrites may cause contact dermatitis. Since the initial report by Fisher et al.,⁴⁷ in 1981, other studies have shown the possibility of immediate sensitization (contact urticaria) and delayed sensitization with these compounds⁴⁸ (Figure 10).

REFERENCES

- Brito Filho D. Toxicologia humana e geral. 2 ed. Rio de Janeiro: Atheneu; 1988.
- 2. Kritico P, Papadaki S. The history of the poppy and of opium and their expansion in antiquity in the Eastern Mediterranean area. Bull Narc. 1967;19:5-10.
- 3. Wikipedia [homepage on the internet]. Morphine [cited 2006 Jul 3]. Available from: http://en.wikipedia.org/wiki/morphine.
- 4. Wikipedia [homepage on the internet]. Heroin [cited 2006 Jul 3]. Available from: http://en.wikipedia.org/wiki/heroin.
- de Ridder M. Heroin: new facts about an old myth. J Psychoactive Drugs. 1994;26:65-8.
- Gegler LL, Mark H. Medical complications of cocaine abuse. N Eng J Med. 1986;315:1495-500.
- Wikipedia [homepage on the internet]. Cocaine [cited 2006 Jul 3]. Available from: http://en.wikipedia.org/ wiki/cocaine.
- 8. Karch SB. The pathology of drug abuse. 2nd ed. Boca Raton: CRC; 1996. p. 349-50.
- United Nations Office on Crimes and Drugs [homepage on the internet]. World Drug Report 2006 [cited 2006 Jul 3]. Available from: http://unodc.org.
- 10. Larini L, Carvalho D. Estimulantes centrais. In: Larini L, editor. Toxicologia. São Paulo: Manole; 1993. p.251-63.
- 11. Vasica G, Tennant CC. Cocaine use and cardiovascular complications. Med J Aust. 2002;177:260-2.
- 12. Ayman M. Drug-induced myocardial infarction secondary to coronary artery spasm in teenagers and young adults. J Postgrad Med. 2006;52:51-6.

- 13. Dick AD, Prentice MG. Cocaine and acute porphyria. Lancet. 1987;2:1150.
- 14. Schuster DS. Snorters' warts. Arch Dermatol. 1987;123:571.
- 15. Kerr HD. Cocaine and scleroderma. South Med J. 1989;82:1275-6.
- Enriquez R, Palacios FO, Gonzalez CM, Amoros FA, Cabezuelo JB, Hernandez F. Skin vasculitis, hypokalemia and acute renal failure in rhabdomyolysis associated with cocaine. Nephron. 1991;59:336-7.
- 17. Chevalier X, Rostoker G, Larget Piet B, Gherardi R. Schöenlein-Henoch purpura with necrotizing vasculitis after cocaine snorting. Clin Nephrol. 1995;43:348-9.
- 18. Orriols R, Munoz X, Ferrer J, Huget P, Morell F. Cocaine-induced Churg-Strauss vasculites. Eur Respir J. 1996;9:175-7.
- 19. Hofbauer GFL, Burg G, Nestlé FO. Cocaine-related Stevens-Johnson syndrome. Dermatology. 2000; 201:258-60.
- Tomecki KJ, Wikas SM. Cocaine-related bullous disease.
 J Am Acad Dermatol. 1985;12:585-6.
- 21. Feeney CM, Briggs S. Crack hands: a dermatologic effect of smoking crack cocaine. Cutis. 1992;50:193-4.
- 22. Zamora-Quezada JC, Dinerman H, Stadecker MJ, Kelly JJ. Muscle and skin infarction after free-basing cocaine (crack). Ann Intern Med. 1988;108:564-5.
- 23. Kreek MJ, Bart G, Lilly C, Laforge KS, Nielsen DA. Pharmacogenetics and human molecular genetics of opiate and cocaine addictions and their treatments. Pharmacol Rev. 2005;57:1-26.
- 24. Westerhof W, Wolters ECH, Brookbakker JTW, Boelen

- RE, Schipper MEI. Pigmented lesions of the tongue in heroin addicts fixed drug eruption. Br J Dermatol. 1983;109:605-10.
- 25. Vollum DI. Skin lesions in drug addicts. Br Med J. 1970;2:647-50.
- 26. Ebright JR, Pieper B. Skin and soft tissue infections in injection drug users. Infect Dis Clin North Am. 2002;16:697-712.
- 27. Summanen PH, Talan DA, Strong C, McTeague M, Bennion R, Thompson Jr JE, et al. Bacteriology of skin and soft-tissue infections: comparison of infections in intravenous drug users and individuals with no history of intravenous drug use. Clin Infect Dis. 1995;20 (Suppl 2):S279-82.
- 28. Chen JL, Fullerton KE, Flynn NM. Necrotizing fasciitis associated with injection drug use. Clin Infect Dis. 2001;33:6-15.
- 29. Hsueh PR, Hsine TR, Hsieh WC. Pyomyositis in intravenous drug abusers: report of a unique case and review of the literature. Clin Infect Dis. 1996;22:858-60.
- 30. Murphy EL, DeVita D, Liu H, Vittinghoff E, Leung P, Ciccarone D, et al. Risk factors for skin and soft tissue abscesses among injection drug users: a case-control study. J Infect Dis. 2001;33:35-40.
- 31. Leclerc G, Weber M, Contet-Audonneau N, Beurey J. Candida folliculitis in heroin addicts. Int J Dermatol. 1986;25:100-2.
- 32. Leclech C, Cimon B, Chennebault JM, Verret JL. Pustulose candidosique des heroïnomanes. Ann Dermatol Venereol. 1997;124:157-8.
- 33. Recio C, Pique E, Lluch J, Vidal JM. Foliculitis por Candida en usuários de drogas por via parenteral. Enferm Infecc Microbiol Clin. 2003;21:84-5.
- 34. Passaro DJ, Werner SB, McGee J, Mac Kenzie WR, Vugia DJ. Wound botulism associated with black tar heroin among injection drug users. J Am Med Assoc. 1998;279:859-63.
- 35. Vugia DJ, Werner SB, Woodfill CJ. Wound botulism, tetanus, and necrotizing fasciitis among injection drug users in Califórnia: the clostridial connection. In: Scheld WM, Murray BE, Hughes JM, eds. Emerging infections 6. Washington, DC: ASM Press; 2004. p.111-20.
- 36. McGuigan CC, Penrice GM, Gruer L, Ahmed S, Goldberg D, Black M, et al. Lethal outbreak of infection with Clostridium novyi type A and other spore-forming organisms in Scottish injecting drug users. J Med Microbiol. 2002;51:971-7.
- 37. Williamson N, Archibald C, Van Vliet JS. Unexplained deaths among injection drug users: a case of probable

- Clostridium myonecrosis. Can Med Assoc J. 2001; 165:609-11.
- 38. Kimura AC, Higa JI, Levin RM, Simpson G, Vargas Y, Vugia DJ. Outbreak of necrotizing fasciitis due to Clostridium sordellii among black-tar heroin users. Clin Infect Dis. 2004;38:87-93.
- 39. Withington D, Patrick J, Reynolds F. Histamine release by morphine and diamorphine in man. Anaesthesia. 1993;48:26-9.
- 40. Heng MCY, Haberfeld G. Thrombotic phenomena associated with intravenous cocaine. J Am Acad Dermatol. 1987;16:462-8.
- 41. Del Giudice P, Vandenbos F, Boissy C, Cua E, Marion B, Bernard E, et al. Cutaneous complications of direct intra-arterial injection in drug addicts. Acta Derm Venereol. 2005; 85:451-2.
- 42. Scott DW, Morrell JI, Vernotica EM. Focal necrotizing panniculitis and vascular necrosis in rats given subcutaneous injections of cocaine hydrochloride. J Cutan Pathol. 1997;24:25-9.
- 43. Posner DI, Guill MA. Cutaneous foreign body granulomas associated with intravenous drug abuse. J Am Acad Dermatol. 1985;13:869-72.
- 44. Hashibe M, Straif K, Tashkin DP, Morgenstern H, Greenland S, Zhang ZF. Epidemiologic review of marijuana use and cancer risk. Alcohol. 2005;35:265-75.
- 45. Combemale P, Consort T, Denis-Thelis L, Estival JL, Dupin M, Kanitakis J. Cannabis arteritis. Br J Dermatol. 2005;152:166-9.
- 46. Wollina U, Kammler HJ, Hesselbarth N, Mock B, Bosseckert H. Ecstasy pimple a new facial dermatosis. Dermatology. 1998;197:171-3.
- 47. Fisher AA, Brancaccio RR, Jelinek JE. Facial dermatitis in man due to inhalation of butyl nitrite. Cutis. 1981;27: 146-54.
- 48. Botella-Estrada R, Sanmartin O, Sanchez J, De La Quadra J. Dermatitis por "poppers". Urticária de contato y dermatitis de contato alérgica sumultáneas. Med Cutan Ibero Lat Am. 1993;23:117-20.

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- 1. According to the United Nations Organization, the annual prevalence of illicit drug use in age group 15-64 ammounts:
 - a) 1% of world population
 - b) 3% of world population
 - c) 5% of world population
 - d) 10% of world population
- 2. Based on his original work, Freud proposed that cocaine would be useful in the treatment of:
 - a) depression
 - b) morphine dependence
 - c) hysterical personality
 - d) monosymptomatic psychosis
- 3. Thinning of the eyebrows in crack users is secondary to:
 - a) a direct effect of the drug on hair follicles
 - b) thermal action of the vapors emanated
 - c) trychotillomania
 - d) intense vasoconstriction
- 4. Regarding pigmentation along venous paths (needle tracks), it is correct to state that:
 - a) it is found only in heroin users
 - b) it is more common in vessels of the dorsal aspect of the hands
 - c) it only occurs in afr individuals
 - d) it may be caused by soot accumulated on needles sterilized by flame
- 5. Cocaine has a mild euphorigenic effect when smoked. This is due to:
 - a) its high solubility in water
 - b) its low absorption by oral mucous membranes
 - c) its low absorption by lung mucous membranes
 - d) its vulnerability to pyrolysis
- 6. The highest concentration of THC (tetrahydrocannabinol) in *Cannabis* is found in:
 - a) the flowers (trichomes)
 - b) the green leaves
 - c) the dry leaves
 - d) the stem
- 7. The tongue pigmentation seen in heroin smokers is clinically and histologically similar to lesions of:
 - a) amyloidosis
 - b) fixed drug eruption
 - c) toxic melanoderma
 - d) ochronosis

- 8. Necrosis of the extremities is more frequent among users of:
 - a) amphetamines
 - b) cocaine
 - c) crack
 - d) heroine
- 9. The greatest risk factor for abscesses of soft tissues among injecting drug users is the use of:
 - a) pure cocaine
 - b) cocaine associated with heroin (speedball)
 - c) the intravenous route
 - d) the subcutaneous route (skin-popping)
- 10. In soft tissue infections among injecting drug users, which is the most common etiological agent?
 - a) Clostridium sp
 - b) Pseudomonas aeruginosa
 - d) Staphylococcus aureus
 - c) Streptococcus pyogenes
- 11. The primary mechanism of the euphorigenic action of cocaine is due to:
 - a) a block of catecholamine reuptake
 - b) a block of beta-adrenergic receptors
 - c) vasoconstriction effect
 - d) synergism with endorphins
- 12. Urticaria induced by opiates is triggered primarily by:
 - a) direct degranulation of mast cells
 - b) immediate IgE-dependent allergic mechanism
 - c) Arthus phenomenon-like mechanism
 - d) delayed hypersensitivity
- 13. The main cause for hospitalization in injecting drug users is:
 - a) seizures
 - b) skin and soft tissue infections
 - c) suicide attempts
 - d) acute thromboembolic phenomena
- 14. Folliculitis by *Candida* in heroin users is characterized by:
 - a) cultures also positive for S. aureus
 - b) painful lesions
 - c) lesions restricted to injection site
 - d) good response to antibiotics

- 15. This folliculitis represents:
 - a) the direct inoculation of the yeast into the hair follicle
 - b) a superposition of mycotic and bacterial folliculitis
 - c) an exclusive manifestation of immunosuppressed individuals
 - d) a manifestation secondary to systemic candidiasis
- 16. Among contaminants commonly added to injecting drugs, which has the highest vasoconstriction potential?
 - a) Starch
 - b) Dextrose
 - c) Quinine
 - d) Talc
- 17. Which is a characteristic of the scars from subcutaneous use (skin-popping) of illicit drugs?
 - a) preference for forearms
 - b) bizarre shapes
 - c) hypertrophic lesions
 - d) large dimensions (>5 cm)

- 18. Alkyl nitrites are characterized by:
 - a) euphorigenic action
 - b) high volatility
 - c) intense vasoconstriction action
 - d) intense muscle contraction action
- 19. Acneiform dermatitis in ecstasy users presents:
 - a) preferential involvement of the trunk
 - b) absence of comedones
 - c) late development
 - d) preference for females
- 20. Heroine is a derivative of morphine obtained by acetylation. This characteristic gives the molecule:
 - a) a high nephrotoxicity
 - b) a rapid transposition of the blood-CSF barrier
 - c) a potent vasoconstriction action
 - d) a rapid hepatic metabolization

ANSWERS

Primary cutaneous sarcomas. An Bras Dermatol. 2006;81(3):207-21.

1. d	11. d
2. b	12. c
3. b	13. c
4. b	14. b
5. d	15. a
6. c	16. b
7. a	17. d
8. b	18. d
9. c	19. d
10. b	20. c