Illicit drugs: What dermatologists need to know

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We review the most common systemic and cutaneous signs of heroin, cocaine, methamphetamine, Ecstasy, and marijuana use. We also provide an overview of the skin and soft-tissue infections frequently found in intravenous drug users and the effects of the adulterants added to the drugs. (J Am Acad Dermatol 2013;69:135-42.)

Key words: adulterants; cutaneous manifestations; cocaine; cutting agents; dermatology; ecstasy; heroin; illicit drugs; intravenous drug users; levamisole; levamisole-induced purpura; marijuana; methamphetamine; puffy hand syndrome; skin and soft tissue infections; skin popping; track marks.

It has been estimated that 8% of the population aged 12 years or older are current users of illicit drugs.[1] Because drug abuse carries a societal stigma, patients may not immediately report their history of drug abuse to the physician. It is important for dermatologists to recognize cutaneous signs of drug abuse to properly treat the patient.

CUTANEOUS SIGNS OF DRUG ABUSE

Track marks

Track marks are caused by intravenous (IV) drug injection and occur as a result of venous damage and thrombosis with subsequent scarring of the veins and pigmentation of the overlying skin (Figs 1 and 2). They are the result of repeated injections, blunt needles, and irritation from the drug or the adulterants. The most common site is the medial vein in the antecubital fossa of the nondominant arm.[2,3] However, many people inject in unseen places such as the popliteal fossa, dorsal veins of the feet, and inguinal veins to avoid this stigmata. It is important to note that the lack of track marks does not preclude IV drug use.[4] Interestingly, IV use of cocaine usually does not induce track marks because it typically does not contain sclerosing chemicals that are added to other drugs such as heroin.[5]

Skin popping

Drug users may inject the drugs intradermally or subcutaneously. This is done accidentally or when veins are sclerosed from previous use, but some users do prefer this method of delivery. Skin popping leaves irregular, leukodermic, atrophic, punched-out scars caused by irreversible tissue injury (Fig 3). Hypertrophic scars or keloids can develop over these areas.[6,7]

Puffy hand syndrome

Puffy hand syndrome is also a sign of past or current drug addiction. It presents as nonpitting edema of the back of the hands and may spare the fingers.[8] Quinine, which is an adulterant that is added to heroin, is thought to be the cause as it induces lymphatic damage.[9-11]

Sooting tattoos

These are caused by cooking the drugs and flaming the needles with matches and then injecting the carbon and soot into the dermis.[6,12] Many times users will cover these lesions with commercial tattoos to make them less noticeable.[6]

Tourniquet hyperpigmentation

This occurs when users apply whatever is available for tourniquets (eg, belts, shoelaces) too tightly and leave it on for too long causing inflammation and subsequent postinflammatory hyperpigmentation.[7]

SPECIFIC DRUGS

Cocaine (coke, C, snow, flake, blow)

Cocaine is a sympathomimetic that causes feelings of euphoria, increased confidence, and well-being,

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and results in tachycardia, hypertension, altered mental status, and mydriasis. Cocaine is extracted in the form of a coca paste from the *Erythroxylum coca* plant. It is treated with numerous chemicals to purify it into a water-soluble powder that is close to 100% pure. However, by the time the user buys it, dealers have generally diluted it with inert or active substances that will be discussed later in this article. Cocaine sold on the streets is a fine, bitter-tasting, white crystalline powder that can be mixed with water and injected, inhaled (snorted), or ingested orally but cannot be smoked.[13,14]

The free-base form, also called "crack," is a hard/brittle substance that is produced by neutralizing the cocaine hydrochloride with sodium bicarbonate (baking soda) or ammonia mixed with water. It causes similar symptoms to powdered cocaine but is more intense and addictive. Smoking crack affects the system in seconds as opposed to snorting cocaine, which takes around 15 minutes. Crack cocaine can only be smoked and is much cheaper and more accessible; subsequently, the use of cocaine has increased dramatically over the years.[14]

There are many cutaneous signs of cocaine abuse including halitosis, frequent lip smacking, cuts and burns on the lips from broken/chipped crack pipes, madarosis (loss of the lateral eyebrow) from the hot steam rising from the crack pipe,[5,15] palmar and digital hyperkeratosis from holding the hot crack,[16] and midline destructive lesions of the nasal septum caused by ischemia from snorting the cocaine.[5,17,18]

"Snorter warts" are nasal verrucae that have been reported in cocaine abusers. They are caused by the transmission of the human papillomavirus on dollar bills. The dollar bills are used to snort the cocaine and are passed from one person to the next, which transmits the human papillomavirus infection.[19]

Many types of vasculitis have been described in cocaine abusers such as urticarial vasculitis,[20] Churg-Strauss vasculitis,[21] necrotizing granulomatous vasculitis,[22] palpable purpura, and Buerger disease.[23-25] Pseudovasculitis with aggressive nasal destruction can be misdiagnosed as Wegener granulomatosis especially when the perinuclear antineutrophil cytoplasmic antibodies are falsely positive.[5,26] The cause is thought to be a combination of vascular ischemia because of the cocaine, irritation caused by the adulterants added to the cocaine, and infections secondary to trauma.[17]

Adverse drug reactions have been reported in cocaine users. There is 1 case report of acute generalized exanthematous pustulosis,[27] and another report of a college student developing Stevens-Johnson syndrome twice because of cocaine use. The authors believed it was a result of an adulterant that was added to the cocaine, but it could not be confirmed.[28] Cocaine has also been reported to unmask or cause scleroderma.[29,30]

Cocaine abuse can cause formication, which is a tactile hallucination of insects crawling underneath the skin that leads to delusions of parasitosis and/or neurotic excoriations.[23,31]

CAPSULE SUMMARY

- The use of illicit drugs has become a major societal problem; many illicit drugs or the adulterants used with them can show cutaneous manifestations.
- Here we provide a comprehensive review of the major cutaneous signs of illicit drug use for the most commonly abused drugs.
- This review should enable dermatologists to recognize those signs and enable correct diagnosis and therapeutic planning.

Heroin (smack, H, ska, junk)

Heroin is an opiate that causes significant euphoria, addiction, respiratory depression, and miosis. It is synthesized from morphine, which is a naturally occurring substance extracted from the seed pod of the Asian opium poppy plant. The most common forms of heroin are a white powder or a black sticky substance called "black tar."[32] Heroin base (common in Europe) must be mixed with an acid such as lemon juice to dissolve in water. The hydrochloride salt (common in the United States) only requires water to dissolve. Heroin once dissolved is then heated, drawn into a syringe or eyedropper through cotton, and then injected. Historically, a bag of heroin had a purity of 1% to 10% but over the last 15 years, the purity has increased to an average of 40%. The higher purity has allowed the drug to be snorted and smoked, which has increased the appeal of heroin for many new users who are hesitant of injecting.[14]

There are many cutaneous signs of heroin abuse. Of addicts, 4% develop urticaria, which can last for days. They can develop a "high pruritus," which is intense itching especially on the genitals and face.[7] There is a reported case of penile ulcers after injection into the dorsal vein of the penis[33] and necrotizing cellulitis of the scrotum after injection into the left femoral artery.[34] Pemphigus vegetans,[35] fixed drug eruptions, toxic epidermal necrolysis, necrolytic migratory erythema not associated with glucagonoma, and acanthosis nigricans[7] have all been described with heroin abuse.

Abbreviations used:

IDUs: intravenous drug users
IV: intravenous
SSTIs: skin and soft-tissue infections

Methamphetamine (speed, meth, chalk, ice, crystal, crank, glass)

Methamphetamine causes euphoria, anxiety, increased energy, aggression, psychomotor agitation, hallucinations, and severe withdrawal. The availability of methamphetamine has increased over the years. It is made by the reduction of ephedrine or pseudoephedrine in "meth labs." It can now be made in a single 2-L bottle using batteries and fertilizer, which make meth labs more mobile. The process of making methamphetamine is very toxic and flammable. It may be injected, smoked, or snorted.[36]

Signs of methamphetamine abuse are xerosis, pruritus, intense body odor, weight loss, premature aging, and hyperhidrosis. Users can develop a severe form of dental disease called meth mouth, which consists of rampant caries and enamel erosions starting at the gum line (Fig 4).[37] It is caused by a combination of xerostomia, bruxism (clenching and grinding of the teeth), and poor dental hygiene. Users may also develop formication leading to excessive skin picking especially on the face and premature aging. Acne excoriee and lichenoid drug eruptions[38] have been reported.

Cannabis (marijuana, pot, weed)

Cannabis use results in an altered mood and is made from the dried buds and flowers of the *Cannabis sativa* plant. The psychoactive chemical compound is delta-9-tetrahydrocannabinol.[39] The potency of marijuana has also increased over the years, and marijuana today can be 5 times stronger than the marijuana of the 1970s.[14] Marijuana is smoked as hand-rolled cigarettes (joints), pipes (bongs), or marijuana cigars (blunts). It can also be mixed with other drugs such as cocaine.

Chronic cannabis abuse can lead to cannabis arteritis that presents as peripheral necrosis most often of the lower limbs. It is a subtype of thromboangiitis obliterans. It is thought to be caused by the vasoconstrictive effects of delta-9-tetrahydrocannabinol and/or a contaminant, such as arsenic, which is known to cause thromboangiitis obliterans in cigarette smokers.[40] A retrospective analysis cited it as one of the most frequent causes of peripheral arterial disease in adults younger than 50 years.[41] It may present with Raynaud phenomenon and digital necrosis. Claudication may be the presenting sign before the development of ulcers or gangrene.[42] Duplex ultrasound can differentiate between cannabis arteritis and atherosclerosis. Treatment is for the patient to stop cannabis use and start aspirin 81 mg daily. For severe cases, iloprost (0.5-2.0 ng/kg/min), a prostaglandin, can be given. Patients may have complete revascularization with treatment.[43] Cannabis arteritis should be included in the differential of all young adults with peripheral necrosis.

Ecstasy

Ecstasy use results in euphoria, feelings of intimacy, and enhancement of body sensation. It first became popular in the rave/club setting. The main ingredient of Ecstasy is 3,4-methylenedioxymetamphetamine, but other drugs, such as ephedrine and gamma-hydroxybutyrate, can also be mixed into the tablet.[44]

There are few cutaneous side effects of Ecstasy reported in the literature. An acneiform eruption called "Ecstasy pimples" has been described. It consists of papules and pustules on the face without comedones similar to perioral dermatitis. Hepatotoxicity was associated with the eruption in 1 patient.[45] A case of guttate psoriasis has been reported that occurred 4 days after Ecstasy ingestion and was thought to be caused by a rise in noradrenaline secondary to 3,4-methylenedioxymetamphetamine.[46]

SKIN AND SOFT-TISSUE INFECTIONS

Skin and soft-tissue infections (SSTIs) are very common among IV drug users (IDUs) (Fig 5). In fact, SSTIs are the most common disease for which users are admitted to the hospital.[47,48]

The increased risk of SSTIs in IDUs is a result of many risk factors. A case-control study found that the independent risk factors for developing SSTIs were skin popping, the use of nonsterile needles, speedball injections (mixture of heroin and cocaine), and booting (drawing back blood usually into a dirty syringe before injection).[49] In one study, it was found that skin popping had a 5-fold greater risk of infection when compared with IV injection.[50] SSTIs associated with skin popping are usually multilobulated, deeper, and have more extensive necrosis than those in non-IDUs.

There are many different pathogens responsible for SSTIs in IDUs. Most cases have negative blood cultures.[51,52] One pathogen is cultured in 50% of the cases whereas more than 1 is found in 33% to 50%.[48,52] Anaerobic bacterial infections also commonly cause infections in IDUs.[53]

Staphylococcus aureus is the most frequently cultured organism in SSTIs, followed by streptococcal species and other oral/skin pathogens.[12,51] Oral pathogens, including *Eikenella corrodens*, cause

Fig 1. Track marks. Linear erythematous crusting in early lesions.

Fig 2. Track marks. Hyperpigmentation of overlying skin along course of vein. Image courtesy of Larry Stack, MD.

Fig 3. Skin popping scars. Multiple irregular, circular, hypopigmented scars on back of forearm. Central area of hemorrhagic crusting from recent injection.

infections because IDUs sometimes "clean" their needle or skin with their saliva before injection.[12,54,55] Drug dealers have been known to hide drug containers in their mouths during police raids, which was speculated to be the source of an outbreak of a clonal strain of *Streptococcus pyogenes* in Switzerland.[56]

There have been numerous reports of SSTIs among IDUs as a result of uncommon pathogens, mainly caused by *Clostridium* species. *Clostridium tetani* and *Clostridium botulinum* are unusual

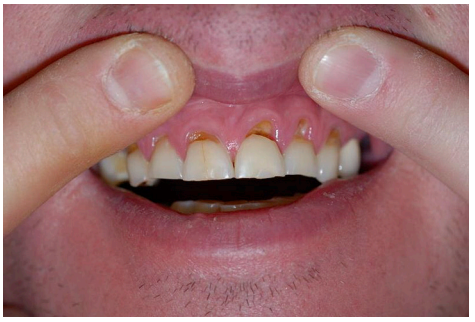

Fig 4. Meth mouth. Erosions of enamel starting at gum line. Image courtesy of R. Jason Thurman, MD, from Knoop et al, The Atlas of Emergency Medicine, Third Edition, (c) 2010, McGraw-Hill Education, New York, New York.

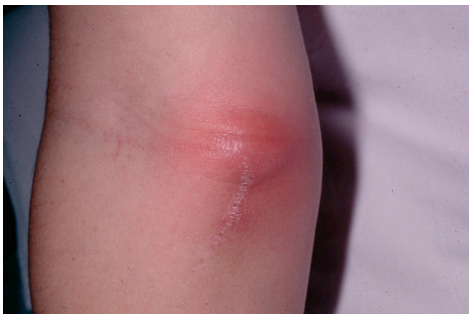

Fig 5. Skin abscess caused by intravenous drug use. There is also early track mark with erythema and crusting inferior to abscess. Image courtesy of Larry Stack, MD.

organisms except in IDUs who skin pop.[57-60] Infections are caused by black tar heroin, which is often cut with dirt that contains the spores. Unlike other microbials, the spores are not destroyed by heating the drug before injection. Actually, the heat stimulates the spores to germinate. Anaerobic bacterial spores injected IV cannot germinate and produce the toxins, but skin and muscle popping leads to an area where the spores can reproduce.[58,59]

Other *Clostridium* species, including *novyi*, *perfingens*, *sordellii*,[61] and *histolyticum*,[62] have been reported to be the cause of serious illness or death among IDUs. In the spring of 2000, there were 104 cases within 3 months in Europe with a fatality rate of 34%.[62] There were additional cases reported in the United States and Canada. Again, skin/muscle popping was a major risk factor, but the source of the bacteria is still unclear.[59] An investigation in San Francisco, Calif, isolated *Clostridium sordellii* from the injection paraphernalia in the home of a case patient.[63]

Necrotizing fasciitis is also more common among IDUs. Chen et al[64] reported that 55% of their 107 cases were in IDUs. IDUs with necrotizing fasciitis

most commonly present with pain out of proportion of examination (94%) or hyperthermia/hypothermia (88%).[65] They may not demonstrate the classic findings of hemorrhagic bullae, systemic toxicity, or palpable crepitance. The reports of pain may be mistaken as a drug-seeking behavior, which could be deadly if not taken seriously. Because of this, it is prudent to do surgical exploration in IDUs with cellulitis and unexplained severe pain.[66]

Fungal infections, including dermatophytosis, are commonly seen in IDUs. Disseminated candidiasis was reported among IV heroin users who used lemon juice to dissolve the heroin. The lemon juice contained an overgrowth of yeast. Patients developed high fevers, myalgias, and headaches, with later development of painful scalp nodules that resolved with alopecia. They also had ocular disease (*Candida endophthalmitis*), pleuritis, and costochondritis.[67-70] *Aspergillus* and zygomycosis has also been reported among IDUs.[71]

In addition to SSTIs, IDUs may develop pseudoaneurysms that may be mistaken for cutaneous abscesses especially when presenting as a nonpulsatile inflammatory mass. Development occurs when drugs are injected accidentally or purposefully into an artery.[72]

CUTTING AGENTS

Illicit street drugs often contain additional and unexpected substances that are intentionally added or may be unintentional contaminants of the manufacturing process. Diluents (eg, talc, mannitol, dirt, clay) are inert substances added by the dealer to expand the volume of the drug.[32,73] Injection of these substances, especially talc or starch, can form foreign body granulomas.[6,74] Adulterants are pharmacologically active additives that enhance the drugs effects. Some examples are quinine, lidocaine, amphetamine, caffeine, heroin, scopolamine, hydroxyzine, laxative, and diphenhydramine.[32,75]

Levamisole has recently been discovered to be a common adulterant added to cocaine. Unlike most cutting agents, levamisole is added at the onset of manufacturing in the countries of origin. The US Drug Enforcement Agency reported that 70% of the seized cocaine in 2009 contained levamisole, up from 30% in 2008.[76-78] It is thought that levamisole potentiates the effects of cocaine and increases dopamine levels.[79] Levamisole is also inexpensive, widely available, and has the right look, taste, and melting point to go unnoticed by cocaine users, which makes it an ideal adulterant.

Levamisole is an antiparasitic medication used for livestock. This medication was used in human beings as treatment for colon cancer, nephritic syndrome, and rheumatoid arthritis because of its immunomodulating effects, but it was voluntary withdrawn from the US market in 1999 because of neutropenia, agranulocytosis, and vasculitis.[80-82]

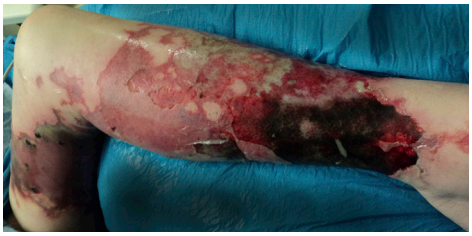

Fig 6. Levamisole-induced purpura in cocaine user. Necrotic and retiform purpura on lower extremity

Fig 7. Levamisole-induced purpura of ear in cocaine user.

In 2008, 5 patients with a history of cocaine use were found to have agranulocytosis and fever secondary to levamisole.[83] Recently, several additional cases have been reported of agranulocytosis with retiform purpura (Fig 6).[78,84-87] Vasculitis from the levamisole has a distinct presentation with purpuric lesions usually involving the external pinna and cheeks (Fig 7).[88] Biopsy specimen shows leukocytoclastic vasculitis, thrombotic vasculitis, vascular occlusion, or a combination of these. Lupus anticoagulant and/or cytoplasmic or perinuclear antineutrophil cytoplasmic antibodies are usually positive. The lesions typically resolve within 2 to 3 weeks of stopping cocaine and the serologies normalize. Unfortunately, levamisole is difficult to detect because it has a short half-life (5.6 hours) and requires specific testing using gas chromatography or mass spectrometry.[78] Because of this, the cause is suspected to be a result of levamisole but cannot be proven in many reports within the literature.

CONCLUSION

There are many cutaneous signs of drug abuse. Dermatologists need to recognize these signs to properly diagnose and treat these patients. Because illegal drugs are not regulated, new cutaneous manifestations are always emerging—whether they are from the adulterants that are added or from the drugs themselves. Because of this, dermatologists need to stay up to date with the literature regarding drug abuse and keep drug abuse on their differential diagnoses.

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