Clinical & Experimental Dermatology Research

Raiker et al., J Clin Exp Dermatol Res 2016, 7:2
http://dx.doi.org/10.4172/2155-9554.1000337

Review Article Open Access

Dermatologic Signs and Symptoms of Substance Abuse

Nisha Raiker, Mouhammad Aouthmany and Navid Ezra*

Department of Dermatology, Indiana University School of Medicine, Indianapolis, Indiana, USA

***Corresponding author:** Navid Ezra, Department of Dermatology, Indiana University School of Medicine, Indianapolis, Indiana, USA, Tel: 4193501579; E-mail: navid.ezra@gmail.com

Received date: January 11, 2016; **Accepted date:** March 07, 2016; **Published date:** March 12, 2016

Abstract

Various substances of abuse are known to cause specific cutaneous manifestations. In this review, we highlight the cutaneous manifestations associated with the use of cocaine, heroin, marijuana, methamphetamine, alcohol, and anabolic steroids. Cutaneous signs of tanning addiction are also discussed, as tanning bed use is a particularly relevant and growing problem in Dermatology. We also provide examples of general signs of drug abuse, including stigmata of injection drug use, vascular complications, and infectious complications. This review aims to make clinicians more aware of these signs in order to better recognize substance abuse disorders and guide effective treatment.

Keywords: Cutaneous signs of abuse; Dermatology; Survey

Introduction

A survey conducted in 2012 found that approximately 9.2% of the American population aged 12 and older had used an illicit substance in the last month [1]. Clinicians often find it difficult to detect these dangerous practices, likely from lack of self-reporting, which frequently stems from fear of discrimination and disdain by others. Consequently, clinicians should be able to recognize the cutaneous signs of substance abuse in order to more effectively diagnose and treat patients. In this review, we provide an overview of key dermatologic symptoms of various abusive and addictive substances.

General cutaneous signs of illicit drug use

Stigmata of injection drug use (IDU)

Perhaps the most notorious sign of intravenous drug abuse is injection marks, also called "track marks". These linear marks represent post-inflammatory hyperpigmentation at the injection site, resulting from damage and consequent sclerosis of the underlying veins [2,3]. The antecubital fossa of the non-dominant arm is the site that is most commonly affected, as it is easily accessible and often disguisable with long-sleeved clothing [4]. Nevertheless, drug abusers have been reported to inject into more obvious veins, such as those in the neck, as well as more concealed veins such as the popliteal vein, inguinal veins, and dorsal veins of the feet [3,4].

Once the veins become sclerotic and inaccessible, drug users often resort to intradermal, subcutaneous, and sometimes intramuscular drug administration, also known as "skin-popping." This method of drug administration usually results in deep, circular, punched-out looking atrophic scars; however, hypertrophic scars and keloids have also been reported. They are frequently indicative of scar formation from prior small abscesses, but abscess formation does not necessarily arise from skin-popping [2-4].

Eventually, drug users resort to injection of drugs with a hot needle. This results in "sooting" tattoos which are marks represent inadvertent entry and accumulation of carbon and soot into the dermis. Drug users will often acquire commercial tattoos in order to disguise these scars [3-5].

Infectious complications

Skin and soft tissue infections (SSTI) are among the most common infectious complications of injection drug abuse, comprising the majority of emergency department visits by injection drug users (IDU) [2,3,6]. Abscesses and cellulitis include the most common SSTI affecting IDU [4,7]. There are several independent risk factors for developing SSTI in injection drug abusers, the most important being skin-popping [8]. Skin-popping causes tissue trauma and introduces bacteria into the skin. It may also introduce adulterant substances, which can concentrate locally and irritate the skin. Injection drug users who skin-pop are five times more likely to develop an abscess or cellulitis [9]. Other independent risk factors include the use of non-sterile needles and injecting "speedball," a combination of cocaine and heroin [3,4,10]. The most common pathogens isolated are *Staphylococcus aureus*, streptococcal species, and oral bacteria, such as *Eikenella corrodens*. Inoculation with oral pathogens is usually the result of IDU "cleaning" their needles with saliva prior to injection [3,11-13].

SSTI with uncommon pathogens, such as the spore-forming Clostridium species, have been reported in IDU who skin-pop with black tar heroin [2,4]. Black tar heroin is often cut with dirt that may be contaminated with heat-resistant spores. It is often injected into the subcutaneous tissue or dermis, an anaerobic environment where the spores are able to germinate and release exotoxin into the surrounding tissues. Wound botulism, tetanus, and necrotizing fasciitis due to the toxins of *C. botulinum*, C. tetani, and *C. perfringens*, respectively, have reported in skin-poppers [2,4,8,14-19].

Vascular complications

A study conducted by Pieper et al. found that 88% of IDU in the study had chronic venous insufficiency (CVI) [4]. Important contributors to CVI in IDUs included venous damage from repeated needle-sticks, thrombophlebitis, and deep venous thrombosis. Repeated infections also lead to damage to lymphatic vessels, which impairs lymphatic drainage. Chronic lower extremity edema often results from the combination of lymphatic obstruction and venous insufficiency [4, 20,21].

Intra-arterial injection of drugs, unintentional or purposeful, frequently results in ischemic complications and is thought to be due to a combination of the effects of the drug and its adulterant, which is a non-specific term for an additive commonly included in drug preparations. For example, cocaine is a potent vasoconstrictor that can also induce vasospasm. Adulterant particles are often locally injurious, causing thromboembolism and vasospasm that may result in compartment syndrome. Acute, drug-induced thrombosis is marked by intense burning and pain immediately following intra-arterial injection of the drug. Ensuing edema develops, followed by cyanosis [4,22-24]. In severe cases, skin necrosis can develop, such as scrotal necrosis due to pudendal artery thrombosis [25,26]. A case of scalp necrosis was reported in a patient secondary to heroin injection into the external carotid artery [27]. Reports of penile ulcers following heroin injection into the dorsal penile vein have also been described [28,29]. Digital veins and the ventral tongue are other bizarre injection sites that have the potential to develop ulcerations. Necrotic ulcerations in unusual sites should prompt clinicians to consider IV drug use in the differential [30]. Intravenous cocaine use has also been associated with necrotic skin ulcers and digital necrosis in in addition to secondary Raynaud's phenomenon and infarction to end-organs, such as the liver and kidney [31-33].

Occasionally, *pseudoaneurysms* and mycotic aneurysms, can develop as a result of vascular injuries due to IDU and bacterial infection of the arterial wall, respectively. They are characterized by pulsatile masses in the distribution of major arteries. Non-pulsatile aneurysms may be mistaken for abscesses, which can lead to catastrophic outcomes if they are wrongfully incised [22,34,35]. Mycotic aneurysms are commonly caused by *S. aureus* and often involve the femoral artery due to drug injection in the groin. More unusual organisms, such as *Candida albicans*, have also been reported to cause mycotic aneurysms [36]. Management of *pseudoaneurysms* and mycotic aneurysms are challenging and may involve resection of the aneurysm or surgical debridement of the infected artery and revascularization by grafting or re-anastomosis [37-40].

Cocaine

Cocaine is an alkaloid compound extracted from the South American coca plant known to create euphoria, pleasure, and increased libido. In addition, a systemic "fight or flight" response, consisting of tachycardia, vasoconstriction, hypertension, and mydriasis may occur [3,8,41]. The stimulant effects of cocaine stem from its dual mechanisms: as a sympathomimetic and an inhibitor of norepinephrine, dopamine, and serotonin reuptake [8,42]. Cocaine increases dopamine concentrations in reward centers of the brain, creating sustained and dose-dependent feelings of euphoria [42]. Long-term alterations in the neuronal pathways in these reward centers ultimately leads to addiction [42,43].

Cocaine hydrochloride is a crystalline white powder produced by adding hydrochloric acid to coca leaf paste. Nasal inhalation of the powder can cause necrosis and midline perforation of the nasal septum and oral palate, secondary to vasoconstriction in mucus membranes [8,44,45]. "Snorter" warts, or intranasal human papillomavirus (HPV)-related warts, have also been reported in cocaine snorters, especially among those who share paraphernalia contaminated with HPV [3,46].

Crack cocaine is produced from neutralizing aqueous cocaine hydrochloride with baking soda or another alkaline compound and heating the mixture until rock-like pellets form [47]. Crack cocaine is cheaper and more potent than cocaine hydrochloride, and is subsequently more prevalent within lower socioeconomic groups [48]. Crack cocaine is often smoked through a glass pipe, and users may have burns and cuts on their hands from holding broken pipes [3,44]. Loss of lateral eyebrows, or madarosis, has also been noted in users as a result of hot fumes contacting the face [3,49]. "Crack hands" or black, hyperkeratotic, punctate lesions over the dorsal and palmar aspects of the hands are other indicators of crack cocaine use [47,50].

Cocaine use by various methods has been associated with end-organ damage secondary to vasoconstriction and ischemia. Caramelo et al. reported renal infarction in a cocaine "mule" secondary to systemic absorption from the intestines [51]. Lower extremity ischemic phenomenon similar to that of Buerger's disease was reported by Denegri et al. in a long-term user of cocaine via inhalation method [52].

Cocaine is also associated with vasculitides, such as urticarial vasculitis [53], retiform purpura [54], scleroderma [32,55], Raynaud's phenomenon [56], Churg-Strauss [57], and a P-ANCA positive Wegener granulomatosis-like syndrome [58,59]. P-ANCA specifically against human neutrophil elastase distinguishes cocaine-induced dermatologic and rheumatologic diseases from primary autoimmune diseases [59].

Levamisole is an adulterant particle commonly added to powder cocaine in order to minimize the proportion of cocaine in the drug mixture being sold [60]. Levamisole-related complications from cocaine are also becoming increasingly common with the rise in levamisole-contaminated cocaine in the United States. In 2009, the U.S. Drug Enforcement Administration estimated that nearly 70% of the cocaine entering the United States was contaminated with levamisole [61]. Hemorrhagic bullae or necrosis of the bilateral cheeks and helices of the ears are common vascular complications associated with levamisole. Similar lesions on the chest, back, abdomen, legs, and buttocks have also been reported [62]. The pathogenesis of cutaneous levamisole toxicity remains unclear and may involve a true or immune-mediated vasculitis [63-65].

General excoriations of the body can result from cocaine abuse as it is known to cause formication and delusions of parasitosis, in which the user reports tactile hallucinations of insects crawling under their skin [66].

Heroin

Heroin is the acetylated opioid product of morphine, a naturally occurring opiate extracted from poppy seeds. Acetylation increases lipid solubility, allowing the compound to rapidly penetrate the blood brain barrier. This property along with heroin's high potency at mu-opioid receptors gives users immediate euphoria and pain relief, making heroin a highly addictive drug [8,67]. The principal forms of

heroin sold in the US drug market are white powder and black tar heroin. Due to its purity, white powder heroin can be snorted, smoked, or injected. Black tar heroin is an impure, gummy substance that is typically dissolved and injected intravenously (IV) or intramuscularly [67]. While heroin abuse used to predominate in urban areas, there has been a upward trend of use in some suburban and rural areas of the Midwestern United States since 2007 [68].

A common dermatologic complaint among heroin users is a pruritic urticarial rash of the body or genitalia due to mast cell degranulation and histamine release. Intense pruritus occurs immediately following injection with duration lasting up to several days [3, 69,70]. Cases of morbilliform eruptions in users have also been described, although the etiology remains indistinguishable between an adulterant or heroin itself [71]. Less commonly, glucagonoma-like syndrome of necrolytic migratory erythema as well as acanthosis nigricans have also been associated with heroin use [70,72,73].

Marijuana (Cannabis)

Marijuana is a psychoactive drug derived from the hemp plant, Cannabis sativa. As of April 2015, cannabis remains illegal in the United States except in 23 states and Washington D.C. Marijuana remains the most popular illicit substance used in the United States with an increase in use [74]. Typically marijuana leaves are dried and rolled into cigarettes, or "joints," for smoking. The leaves can also be steeped into teas and added to foods for consumption [74,75]. Marijuana contains delta-9-tetrahydrocannabinol (THC) among other compounds, which target cannabinoid receptors in the brain to produce effects such as euphoria, heightened senses, and a slowed perception of time. Activation of cannabinoid receptors produces systemic vasoconstrictions secondary to decreased production of nitric oxide and is responsible for the cutaneous manifestations of marijuana [76].

Common skin manifestations include premature aging such as periorbital darkening, hair loss and graying of hair. Some other skin manifestations include cannabis induced arteritis. This is a serious condition affecting marijuana users and is often misdiagnosed as atherosclerosis. Similarities in clinical presentation and arteriography exist between cannabis arteritis and thromboangiitis obliterans (TOA); cannabis arteritis may be considered a subtype of TOA [77]. In a retrospective study of peripheral vascular disease (PVD) in under the age of 50%, 20% of cases were due to TOA and cannabis use was more frequent among these patients [76,78]. The condition may present as Raynaud's phenomenon, ulceration, or necrosis in distal extremities or digits. Cannabis arteritis can be discerned from atherosclerosis via Duplex ultrasonography showing patent arteries. Treatment involves cessation of marijuana and antiplatelet therapy with low-dose aspirin to promote revascularization [77,79]. It is imperative that clinicians consider cannabis use in young patients presenting with PVD.

A report of recurrent migratory superficial thrombophlebitis was also described in a chronic cannabis user in the lower extremities, hand, and groin. The patient's condition resolved after cessation of marijuana use [80].

Interestingly, marijuana may provide benefits to the skin. A recent study by Olah et al. showed that cannabidiol (CBD), a nonpsychotropic phytocannabinoid derived from Cannabis sativa might, in fact, improve acne vulgaris through a sebostatic mechanism, among others. [81]. The study found that CBD had antiproliferative effects on both keratinocytes and sebocytes, thus decreasing formation of comedones and production of sebum. Furthermore, CBD has demonstrated antimicrobial activity, although activity against Propionibacterium acnes has not yet been determined [82,83]. CBD also has anti-inflammatory properties, owing to its inhibition of NF-κB signaling. Collectively, the effects exerted by CBD exemplify its pharmacologic potential in the treatment of acne vulgaris [81,84].

Methamphetamine

Methamphetamine or "meth" is a CNS stimulant manufactured from pseudoephedrine and ephedrine (ingredients of common decongestants) in addition to toxic chemicals such as acetone, ammonia (fertilizer), battery acid, ethylene glycol (antifreeze), and ether. The resulting product can be smoked, inhaled, injected, or ingested. Smoking and injecting are the most common modes of abuse, as they produce rapid-onset euphoria. Chronic users may exhibit aggression, anxiety, mood instability, and psychosis [85].

Dental decay, also known as "meth mouth", is one of the most common findings among meth abusers, due to a combination of methamphetamine-mediated vasoconstriction of oral mucosal vasculature, poor hygiene of the user, and chemical properties of the drug. Furthermore, meth intoxication increases dopamine levels, which can decrease saliva production, increase sugar consumption, and cause bruxism [44,86]. Methamphetamine also causes xerostomia, or dry mouth, which contributes to dental decay in meth users similar to that in Sjögren's syndrome [87]. Malnutrition, weight loss, and premature aging are other notable effects of methamphetamine. Finally, users can develop neurotic excoriations with subsequent abscess formation over the extremities due to the intense pruritus caused by delusions of parasitosis, or "meth mites" [88,89].

Alcohol

Ethanol (ethyl alcohol) is the intoxicating agent found in alcoholic beverages produced through fermentation of sugars and starches using yeast. Alcohol is a CNS depressant, impairing motor function and coordination, decision-making and judgment, and memory. Highly intoxicating doses can lead to respiratory depression and death [90]. The DSM-V classifies alcohol abuse and dependence as an alcohol use disorder (AUD). In 2012, approximately 17 million US adults and more than 800,000 US youths (ages 12-17) suffered from an AUD [91,92]. Long-term alcohol abuse is often associated with dermatologic stigmata of liver disease. While some findings may be nonspecific to alcoholism, alcohol abuse is among one of the leading cause of cirrhosis and should be considered in patients with cutaneous findings of liver disease [93].

There are multiple cutaneous findings in alcoholic liver disease. Superficial erythematous macule with radiating arterioles called spider angiomas are common. They classically appear in the regions of the hands, upper chest, neck, and face. They are a nonspecific finding in alcoholic liver disease and found in pregnant women, alcoholics without liver disease, and healthy individuals. Alcohol-induced vasodilation or elevated estrogen levels have been implicated as cause of these lesions [94]. Additionally, caput medusa or dilated periumbilical veins may occur in alcoholics and is an indicator of severe liver disease and portal hypertension [88].

Jaundice is a yellow discoloration of the skin and mucus membranes due to elevated serum bilirubin. Scleral icterus, or yellowing of the sclera, results when bilirubin levels reach 2.5 mg/dL. Jaundice is a nonspecific indicator of many types of liver disease.

Hyperbilirubinemia seen in alcoholic liver disease is specifically caused by hepatocellular dysfunction in bilirubin conjugation and excretion [95].

Porphyria cutanea tarda (PCT) is a condition characterized by hemorrhagic bullae, crusting, and scarring in sun-exposed areas often accompanied by facial hypertrichosis. It is caused by a defect in uroporphyirinogen decarboxylase, an enzyme in the heme biosynthesis pathway, that leads to an accumulation of porphyrins, which cause photosensitivity [96]. Alcohol was shown to increase the activity of earlier enzymes in this pathway, which leads to further accumulation of porphyrins and worsens the condition in patients with preexisting PCT. Agents or conditions that adversely affect the liver, such as alcohol abuse and/or hepatitis C, can lead to acquired PCT [97]. New-onset PCT in patients with other stigmata of alcoholic liver disease should alert clinicians of possible alcohol abuse.

Psoriasis in alcohol abusers arises in a distinct distribution of flat, hyperkeratotic, erythematous plaques over the acral surfaces [88,94]. Increased skin-surface involvement and diminished treatment responsiveness in alcohol abusers may be evidence that alcohol exacerbates psoriasis [98,99]. Other dermatologic disorders associated with alcohol abuse include rosacea, nummular eczema [96], and seborrheic dermatitis [100].

Anabolic-Androgenic Steroids

Anabolic-androgenic steroids (AAS) are synthetic androgenic steroids similar to testosterone. As their name suggests, they stimulate growth of bone and skeletal muscle. Akin to male sex hormones, anabolic steroids produce virilization in abusers. Medical indications of these compounds include delayed puberty, impotence, and muscle wasting seen in HIV or malignancy [101]. Because of their growth stimulating properties, bodybuilders and athletes are known to abuse these steroids to improve athletic performance. Illicit anabolic steroids have been sold at competitions and gyms as well as smuggled into the US from countries in which prescriptions are not required to obtain steroids. They are typically injected intramuscularly, ingested orally, or applied to the skin with a topical creams or gels, and abusers have been known to use 10-100 times medically indicated dosages [102].

Physicians should be aware of the skin manifestations of steroid abuse in order to recognize the clinical signs of this unhealthy practice in athletic patients. AAS stimulate the sebaceous gland unit, causing it to enlarge. High doses lead to increases in sebum production, skin-surface lipids, and Propionibacterium acnes population [103,104]. This effect most commonly manifests in patients as acne vulgaris. The classic distribution is on the face, shoulders, upper chest, and back. AAS can cause new-onset acne vulgaris or exacerbate pre-existing acne vulgaris into severe forms that are resistant to treatment, such as acne conglobata. With continued steroid use, acne vulgaris can progress to acne fulminans [104,105]. Recalcitrant acne vulgaris in athletic patients should alert physicians to include anabolic steroid use in their differential diagnosis. Enlargement of the sebaceous gland also leads to increased incidence of rosacea, seborrheic dermatitis, and oily hair and skin [106]. AAS also cause rapid increases in muscle mass, which can lead to linear striae resulting from the disproportionate rate of expansion of the skin to the underlying skeletal muscle. Areas in which the striae are most pronounced include the neck, trunk, shoulders, and upper arms, as the upper body has the most substantial increase in muscle mass [107]. While discontinuation of steroid use causes reduction in muscle size, striae are permanent [106]. Hair growth is also affected by use of AAS, resulting in androgenic alopecia of the scalp and hirsutism of the face and body. These effects are most apparent in female users of AAS but can also be seen in male abusers [104,106].

Tanning as an Addiction

The incidence of melanoma and non-melanoma skin cancers continues to rise. Ultraviolet (UV) radiation accounts for up to 90% of these cancers and is the only known modifiable risk factor associated with skin cancers [108-110]. While the importance of sun-protection is well recognized, excessive sunbathing and the overuse of tanning beds remains in our society. Tanning addiction is a developing phenomenon, as many behaviors associated with addiction are consistent with those of many frequent tanners [111]. Such behaviors include continuing to sunbathe despite knowledge of negative consequences (example: development of skin cancer), failure to discontinue tanning despite previous attempts to quit, impairment of interpersonal relationships, and neglect of personal responsibilities. A study conducted by Harrington et al. reported that 41% of indoor tanners surveyed met DSM-IV criteria for addictive behavior [111,112]. There has been debate as to whether the etiology of tanning addiction is neurobiological or based on cosmetic desire for tanned skin [113]. Recent evidence supports a biological etiology. Fell et al. reported that mice repeatedly exposed to UV light developed an endogenous opioid-dependent state secondary to increased release of endogenous β-endorphins and opioid receptor signaling. Furthermore, opioid withdrawal was precipitated in these mice by treatment with naloxone, an opioid receptor antagonist [114].

It is important that dermatologists are able recognize the psychological as well as cutaneous signs of tanning addiction. Perhaps the most significant change resulting from chronic UV light exposure is premature aging, or photoaging of the skin, which is distinct from natural skin aging. Unlike photoaging, physiologic skin aging is characterized by fine lines and moderate skin laxity. Photoaging results in dry, leathery skin with deep wrinkles, blotchy pigmentation (resembling lentigines), and yellow hues known as solar elastosis. Telangiectasias and precancerous lesions, including actinic keratoses are also common [109,115]. In regards to the development of nonmelanoma skin cancer, a study conducted by Karagas et al. showed that tanning bed users were 2.5 more likely to develop SCC and 1.5 times more likely to develop BCC [116]. Another study showed that patients with early-onset BCC (onset prior to age 50) were 1.6 times more likely to report the use of indoor tanning beds. This study also noted a strong association between tanning bed usage and early-onset BCC of the trunk and extremities, sites that normally receive less exposure to natural UV light [117]. Thus, BCC in patients under the age of 50 or unusual sites should prompt physicians to question patients about UV exposure. Melanomas in normally non-sun exposed areas, such as the breast and genitals, may also be indicative of excessive tanning bed use [118]. An increased number of seborrheic keratoses in a sun-exposed distribution were noted in an Australian population, suggesting UV light might increase the frequency of seborrheic keratoses in chronically sun-exposed and predisposed individuals [119].

Conclusion

Drug abuse and addictive behavior are commonly encountered issues in clinical dermatology practice. These behaviors can often produce cutaneous manifestations. It is important that dermatologists

are able to recognize these presentations, as they provide clinical clues that are relevant to the diagnosis and management in this patient population. While this review is not exhaustive, it provides a concise and high-yield overview of the major addictive substances and their associated cutaneous findings.

References

1. National Institute on Drug Abuse. Nationwide Trends Retrieved from trends on February 15, 2015.
2. Fink B, Landthaler M, Hafner C (2011) Skin alterations due to illegal drug abuse. J Dtsch Dermatol Ges 9: 633-638.
3. Hennings C, Miller J (2013) Illicit drugs: What dermatologists need to know. J Am Acad Dermatol 69: 135-142.
4. Del Giudice P (2004) Cutaneous complications of intravenous drug abuse. Br J Dermatol 150: 1-10.
5. Rosen VJ (1985) Cutaneous manifestations of drug abuse by parenteral injections. Am J Dermatopathol 7: 79-83.
6. Lloyd-Smith E, Wood E, Zhang R, Tyndall MW, Montaner JS, et al. (2008) Risk factors for developing a cutaneous injection-related infection among injection drug users: a cohort study. BMC Public Health.8: 405.
7. Vollum DI (1970) Skin lesions in drug addicts. Br Med J 2: 647-650.
8. Gontijo B, Bittencourt FV, Lourenço LFS (2006) Skin manifestations of illicit drug use. Anais Brasileiros de Dermatologia 81: 307-317.
9. Binswanger IA, Kral AH, Bluthenthal RN, Rybold DJ, Edlin BR (2000) High prevalence of abscesses and cellulitis among community-recruited injection drug users in San Francisco. Clin Infect Dis 30: 579-581.
10. Murphy EL, DeVita D, Liu H, Vittinghoff E, Leung P, et al. (2001) Risk factors for skin and soft-tissue abscesses among injection drug users: a case-control study. Clin Infect Dis 33: 35-40.
11. Brown PD, Ebright JR (2002) Skin and Soft Tissue Infections in Injection Drug Users. Curr Infect Dis Rep 4: 415-419.
12. Swisher LA, Roberts JR, Glynn MJ (1994) Needle licker's osteomyelitis. Am J Emerg Med 12: 343-346.
13. Olopoenia LA, Mody V, Reynolds M (1994) Eikenella corrodens endocarditis in an intravenous drug user: case report and literature review. J Natl Med Assoc 86: 313-315.
14. Cooper JG, Spilke CE, Denton M, Jamieson S (2005) Clostridium botulinum: an increasing complication of heroin misuse. Eur J Emerg Med 12: 251-252.
15. Passaro DJ, Werner SB, McGee J, Mac Kenzie WR, Vugia DJ (1998) Wound botulism associated with black tar heroin among injecting drug users. JAMA 279: 859-863.
16. Brett MM, Hood J, Brazier JS, Duerden BI, Hahné SJ (2005) Soft tissue infections caused by spore-forming bacteria in injecting drug users in the United Kingdom. Epidemiol Infect 133: 575-582.
17. Werner SB, Passaro D, McGee J, Schechter R, Vugia DJ (2000) Wound botulism in California, 1951-1998: recent epidemic in heroin injectors. Clin Infect Dis 31: 1018-1024.
18. Callahan TE, Schecter WP, Horn JK (1998) Necrotizing soft tissue infection masquerading as cutaneous abcess following illicit drug injection. Arch Surg 133: 812-817.
19. MacDonald KL, Cohen ML, Blake PA (1986) The changing epidemiology of adult botulism in the United States. Am J Epidemiol 124: 794-799.
20. Pieper B, Kirsner RS, Templin TN, Birk TJ (2007) Chronic venous disease and injection drug use. Arch Intern Med 167: 1807.
21. Pieper B, Templin T (2001) Chronic venous insufficiency in persons with a history of injection drug use. Res Nurs Health 24: 423-432.
22. Woodburn KR, Murie JA (1996) Vascular complications of injecting drug misuse. Br J Surg 83: 1329-1334.
23. Lindell TD, Porter JM, Langston C (1972) Intra-arterial injections of oral medications. A complication of drug addiction. N Engl J Med 287: 1132-1133.
24. Maxwell TM, Olcott C 4th, Blaisdell FW (1972) Vascular complications of drug abuse. Arch Surg 105: 875-882.
25. Cunningham DL, Persky L (1989) Penile ecthyma gangrenosum. Complication of drug addiction. Urology 34: 109-110.
26. Somers WJ, Lowe FC (1986) Localized gangrene of the scrotum and penis: a complication of heroin injection into the femoral vessels. J Urol 136: 111-113.
27. Conde-Taboada A, De la Torre C, García-Doval I, Abalde MT, Mayo E, et al. (2006) Scalp necrosis and ulceration secondary to heroin injection. Int J Dermatol 45: 1135-1136.
28. Bennett RG, Leyden JJ, Decherd JW (1973) The heroin ulcer. New addition to the differential diagnosis of ulcers of the penis. Arch Dermatol 107: 121-122.
29. White WB, Barrett S (1982) Penile ulcer in heroin abuse: a case report. Cutis 29: 62-63, 69.
30. Moser RH (1974) Heroin addiction. JAMA 230: 728-731.
31. Kumar PD, Smith HR (2000) Cocaine-related vasculitis causing upper-limb peripheral vascular disease. Ann Intern Med 133: 923-924.
32. Attoussi S, Faulkner ML, Oso A, Umoru B (1998) Cocaine-induced scleroderma and scleroderma renal crisis. South Med J 91: 961-963.
33. Heng MC, Haberfeld G (1987) Thrombotic phenomena associated with intravenous cocaine. J Am Acad Dermatol 16: 462-468.
34. Cruz JS, Teixeira JF, Costa HM, Braga AR (1999) False aneurysm of an axillary artery in an intravenous drug misuser. Eur J Surg 165: 505-506.
35. Georgiadis GS, Bessias NC, Pavlidis PM, Pomoni M, Batakis N, et al. (2007) Infected false aneurysms of the limbs secondary to chronic intravenous drug abuse: analysis of perioperative considerations and operative outcomes. Surg Today 37 :837-844.
36. Kocovski L, Butany J, Nair V (2014) Femoral artery pseudoaneurysm due to *Candida albicans* in an injection drug user. Cardiovasc Pathol 23: 50-53.
37. Jayaraman S, Richardson D, Conrad M, Eichler C, Schecter W (2012) Mycotic pseudoaneurysms due to injection drug use: a ten-year experience. Ann Vasc Surg 26: 819-824.
38. Benjamin ME, Cohn EJ Jr, Purtill WA, Hanna DJ, Lilly MP, et al. (1999) Arterial reconstruction with deep leg veins for the treatment of mycotic aneurysms. J Vasc Surg 30: 1004-1015.
39. Zainal AA, Yusha AW (1998) A 3 year audit of infected pseudoaneurysms in intravenous drug users managed surgically in the Vascular Unit, Hospital Kuala Lumpur. Med J Malaysia 53: 372-375.
40. Arora S, Weber MA, Fox CJ, Neville R, Lidor A, et al. (2001) Common femoral artery ligation and local debridement: a safe treatment for infected femoral artery pseudoaneurysms. J Vasc Surg 33: 990-993.
41. Warner EA (1993) Cocaine abuse. Ann Intern Med 119: 226-235.
42. Einhorn LC, Johansen PA, White FJ (1988) Electrophysiological effects of cocaine in the mesoaccumbens dopamine system: studies in the ventral tegmental area. J Neurosci 8: 100-112.
43. National Institute on Drug Abuse. Cocaine
44. Bergstrom KG (2008) Cutaneous clues to drug addiction. J Drugs Dermatol 7: 303-305.
45. Goodger NM, Wang J, Pogrel MA (2005) Palatal and nasal necrosis resulting from cocaine misuse. Br Dent J 198: 333-334.
46. Schuster DS (1987) Snorters' warts. Arch Dermatol 123: 571.
47. Payne-James JJ, Munro MH, Rowland Payne CM (2007) Pseudosclerodermatous triad of perniosis, pulp atrophy and 'parrot-beaked' clawing of the nails-a newly recognized syndrome of chronic crack cocaine use. J Forensic Leg Med 14: 65-71.
48. Vasica G, Tennant CC (2002) Cocaine use and cardiovascular complications. Med J Aust 177: 260-262.
49. Tames SM, Goldenring JM (1986) Madarosis from cocaine use. N Engl J Med 314: 1324.
50. Feeney CM, Briggs S (1992) Crack hands: a dermatologic effect of smoking crack cocaine. Cutis 50: 193-194.

51. Caramelo C, López de Mendoza D, Ríos F, Corrales M, Urbano J, et al. (2007) [Renal infarction and kidney rupture: complication of a massive cocaine intoxication in an intestinal carrier]. Nefrologia 27: 374-377.
52. Denegri A, Ameri P, Paparo F, Murialdo G (2014) Lower limb ischemia due to long-term abuse of cocaine. J Cardiovasc Med (Hagerstown) .
53. Hofbauer GF, Hafner J, Trüeb RM (1999) Urticarial vasculitis following cocaine use. Br J Dermatol 141: 600-601.
54. Streicher JL, Swerlick RA, Stoff BK (2014) Cocaine abuse and confidentiality: a case of retiform purpura in an adolescent patient. J Am Acad Dermatol 70: 1127-1129.
55. Kerr HD (1989) Cocaine and scleroderma. South Med J 82: 1275-1276.
56. Balbir-Gurman A, Braun-Moscovici Y, Nahir AM (2001) Cocaine-induced Raynaud's phenomenon and ischaemic finger necrosis. Clinical Rheumatology 20: 376-378.
57. Orriols R, Muñoz X, Ferrer J, Huget P, Morell F (1996) Cocaine-induced Churg-Strauss vasculitis. Eur Respir J 9: 175-177.
58. Perez Alamino R, Espinoza LR (2013) Vasculitis mimics: cocaine-induced midline destructive lesions. Am J Med Sci 346: 430-431.
59. Jiménez-Gallo D, Albarrán-Planelles C, Linares-Barrios M, Rodríguez-Hernández C, Martínez-Rodríguez A, et al. (2013) Pyoderma gangrenosum and Wegener granulomatosis-like syndrome induced by cocaine. Clin Exp Dermatol 38: 878-882.
60. Lee KC, Ladizinski B, Federman DG (2012) Complications associated with use of levamisole-contaminated cocaine: an emerging public health challenge. Mayo Clin Proc 87: 581-586.
61. Casale JF, Colley VL, Legatt DF (2012) Determination of phenyltetrahydroimidazothiazole enantiomers (Levamisole/Dexamisole) in illicit cocaine seizures and in the urine of cocaine abusers via chiral capillary gas chromatography-flame-ionization detection: clinical and forensic perspectives. J Anal Toxicol 36: 130-135.
62. Lee KC, Culpepper K, Kessler M (2011) Levamisole-induced thrombosis: literature review and pertinent laboratory findings. J Am Acad Dermatol 65: e128-129.
63. 63. Jenkins J, Babu K, Hsu-Hung E, Robinson-Bostom L, Kroumpouzos G. ANCA-positive necrotizing vasculitis and thrombotic vasculopathy induced by levamisole-adulterated cocaine: a distinctive clinicopathologic presentation. J Am Acad Dermatol. 2011 Jul;65(1):e14-6.
64. Jacob RS, Silva CY, Powers JG, Schieke SM, Mendese G, et al. (2012) Levamisole-induced vasculopathy: a report of 2 cases and a novel histopathologic finding. Am J Dermatopathol 34: 208-213.
65. Chung C, Tumeh PC, Birnbaum R, Tan BH, Sharp L, et al. (2011) Characteristic purpura of the ears, vasculitis, and neutropenia--a potential public health epidemic associated with levamisole-adulterated cocaine. J Am Acad Dermatol 65: 722-725.
66. Elpern DJ (1988) Cocaine abuse and delusions of parasitosis. Cutis 42: 273-274.
67. Volkow ND (2014) Heroin abuse and addiction, in National Insititute on Drug Abuse Research Report series.
68. Epidemiologic Trends in Drug Abuse, in Proceesings of the Community Epidemiology Work Group. 2013, National Institutes of Health.
69. Weidman A, Fellner MJ (1971) Cutaneous manifestations of heroin and other addictive drugs. Study and analysis. N Y State J Med 71: 2643-2646.
70. Young AW Jr, Rosenberg FR (1971) Cutaneous stigmas of heroin addiction. Arch Dermatol 104: 80-86.
71. Redmond WJ (1979) Heroin adulterants and skin disease. Arch Dermatol 115: 111.
72. Bencini PL, Vigo GP, Caputo R (1994) Necrolytic migratory erythema without glucagonoma in a heroin-dependent patient. Dermatology 189: 72-74.
73. Muller FM, Arseculeratne G, Evans A, Fleming C (2008) Necrolytic migratory erythema in an opiate-dependent patient. Clin Exp Dermatol 33: 40-42.
74. National Institute on Drug Abuse. Marijuana.
75. Volkow ND (2012) Marijuana in National Institutes of Health Research Report Series. National Insititute on Drug Abuse.
76. Cottencin O, Karila L, Lambert M, Arveiller C, Benyamina A, et al. (2010) Cannabis arteritis: review of the literature. J Addict Med 4: 191-196.
77. Noël B, Ruf I, Panizzon RG (2008) Cannabis arteritis. J Am Acad Dermatol 58: S65-67.
78. Sauvanier M, Constans J, Skopinski S, Barcat D, Berard A, et al. (2002) [Lower limb occlusive arteriopathy: retrospective analysis of 73 patients with onset before the age of 50 years]. J Mal Vasc 27: 69-76.
79. Cazalets C, Laurat E, Cador B, Jan F, Rolland Y, et al. (2003) [Cannabis arteritis: four new cases]. Rev Med Interne 24: 127-130.
80. Lee C, Moll S (2014) Migratory superficial thrombophlebitis in a cannabis smoker. Circulation 130: 214-215.
81. Oláh A, Tóth BI, Borbíró I, Sugawara K, Szöllõsi AG, et al. (2014) Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes. J Clin Invest 124: 3713-3724.
82. Appendino G, Gibbons S, Giana A, Pagani A, Grassi G, et al. (2008) Antibacterial cannabinoids from Cannabis sativa: a structure-activity study. J Nat Prod 71: 1427-1430.
83. Dunn SL, Wilkinson JM, Crawford A, Le Maitre CL, Bunning RA (2014) Cannabinoid WIN-55,212-2 mesylate inhibits interleukin-1ß induced matrix metalloproteinase and tissue inhibitor of matrix metalloproteinase expression in human chondrocytes. Osteoarthritis Cartilage 22: 133-144.
84. Wilkinson JD, Williamson EM (2007) Cannabinoids inhibit human keratinocyte proliferation through a non-CB1/CB2 mechanism and have a potential therapeutic value in the treatment of psoriasis. Journal of Dermatological Science 45: 87-92.
85. Volkow ND (2013) Methamphetamine, in National Institutes of Health Research Report Series. National Institute on Drug Abuse.
86. Brown RE, Morisky DE, Silverstein SJ (2013) Meth mouth severity in response to drug-use patterns and dental access in methamphetamine users. J Calif Dent Assoc 41: 421-428.
87. Hamamoto DT, Rhodus NL (2009) Methamphetamine abuse and dentistry. Oral Dis 15: 27-37.
88. Liu SW, Lien MH, Fenske NA (2010) The effects of alcohol and drug abuse on the skin. Clin Dermatol 28: 391-399.
89. Winslow BT, Voorhees KI, Pehl KA (2007) Methamphetamine abuse. Am Fam Physician 76: 1169-1174.
90. National Institute on Drug Abuse. Alcohol
91. SAMHSA 2012 National Survey on Drug Use and Health (NSDUH). Table 5.8A-Substance Dependence or Abuse in the Past Year among Persons Aged 18 or Older.
92. SAMHSA 2012 National Survey on Drug Use and Health (NSDUH). Table 5.5A-Substance Dependence or Abuse in the Past Year among Persons Aged 12 to 17.
93. Heidelbaugh JJ, Bruderly M (2006) Cirrhosis and chronic liver failure: part I. Diagnosis and evaluation. Am Fam Physician 74: 756-762.
94. Smith KE, Fenske NA (2000) Cutaneous manifestations of alcohol abuse. J Am Acad Dermatol 43: 1-16.
95. Roche SP, Kobos R (2004) Jaundice in the adult patient. Am Fam Physician 69: 299-304.
96. Higgins EM, du Vivier AW (1992) Alcohol and the skin. Alcohol Alcohol 27: 595-602.
97. Ghosn SH, Kibbi AG (2008) Cutaneous manifestations of liver diseases. Clin Dermatol 26: 274-282.
98. Gupta MA, Schork NJ, Gupta AK, Ellis CN (1993) Alcohol intake and treatment responsiveness of psoriasis: a prospective study. J Am Acad Dermatol 28: 730-732.
99. Poikolainen K, Reunala T, Karvonen J (1994) Smoking, alcohol and life events related to psoriasis among women. Br J Dermatol 130: 473-477.
100. Rosset M, Oki G (1971) Skin diseases in alcoholics. Q J Stud Alcohol 32: 1017-1024.
101. Anabolic Steroids.

102. Volkow ND Anabolic Steroids in National Institute on Drug Abuse Research Report Series National Institutes of Health
103. Scott MJ, Scott AM (1992) Effects of anabolic-androgenic steroids on the pilosebaceous unit. Cutis 50: 113-116.
104. Walker J, Adams B (2009) Cutaneous manifestations of anabolic-androgenic steroid use in athletes. Int J Dermatol 48: 1044-1048.
105. Merkle T, Landthaler M, Braun-Falco O (1990) Acne conglobata-like exacerbation of acne vulgaris following administration of anabolic steroids and vitamin B complex-containing preparations. Hautarzt, 41: 280-282.
106. Scott MJ Jr, Scott MJ 3rd (1989) Dermatologists and anabolic-androgenic drug abuse. Cutis 44: 30-35.
107. Hartgens F, Kuipers H (2004) Effects of androgenic-anabolic steroids in athletes. Sports Med 34: 513-554.
108. Akamine KL, Gustafson CJ, Davis SA, Levender MM, Feldman SR (2014) Trends in sunscreen recommendation among US physicians. JAMA Dermatol 150: 51-55.
109. Polefka TG, Meyer TA, Agin PP, Bianchini RJ (2012) Effects of solar radiation on the skin. J Cosmet Dermatol 11: 134-143.
110. FDA. Indoor Tanning: The Risks of Ultraviolet Rays. 2014.
111. Harrington CR, Beswick TC, Leitenberger J, Minhajuddin A, Jacobe HT, et al. (2011) Addictive-like behaviours to ultraviolet light among frequent indoor tanners. Clin Exp Dermatol 36: 33-38.
112. Ashrafioun L, Bonar EE2 (2014) Development of a brief scale to assess frequency of symptoms and problems associated with tanning. J Am Acad Dermatol 70: 588-589.
113. Tejeda HA, Bonci A (2014) Shedding "UV" light on endogenous opioid dependence. Cell 157: 1500-1501.
114. Fell GL, Robinson KC, Mao J, Woolf CJ, Fisher DE (2014) Skin Î²-endorphin mediates addiction to UV light. Cell 157: 1527-1534.
115. Rabe JH, Mamelak AJ, McElgunn PJ, Morison WL, Sauder DN (2006) Photoaging: mechanisms and repair. J Am Acad Dermatol 55: 1-19.
116. Karagas MR, Stannard VA, Mott LA, Slattery MJ, Spencer SK, et al. (2002) Use of tanning devices and risk of basal cell and squamous cell skin cancers. J Natl Cancer Inst 94: 224-226.
117. Karagas MR, Zens MS, Li Z, Stukel TA, Perry AE, et al. (2014) Early-onset basal cell carcinoma and indoor tanning: a population-based study. Pediatrics 134: e4-12.
118. Lim HW, James WD, Rigel DS, Maloney ME, Spencer JM, et al. (2011) Adverse effects of ultraviolet radiation from the use of indoor tanning equipment: time to ban the tan. J Am Acad Dermatol 64: 893-902.
119. Yeatman JM, Kilkenny M, Marks R (1997) The prevalence of seborrhoeic keratoses in an Australian population: does exposure to sunlight play a part in their frequency? Br J Dermatol 137: 411-414.