Chapter 14
NeuroAIDS in Drug Abusers: Associations with Oral Manifestations

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Keywords Drug use • Cocaine • Methamphetaminhe • Cannabis • Maijuana • Oral health • Dental disease • Xerostomia • Oral ulceration • Dry mouth

Core Message
Both HIV infection and illicit drug use have significant oral health implications. While certain illicit compounds like cocaine, cannabis, and betel nut have the potential to directly cause oral soft tissue pathologies, most others including opioid agents and methamphetamine affect salivary flow and enhance the rate of dental decay and periodontal disease. Because immunologic deficiency caused by HIV infection leads to unique head and neck pathologic manifestations, among patients with HIV infection who are also users of illicit substances, special attention should be paid to recognizing the signs of oral diseases to help preserve their oral and general health.

Illicit drug use and dependence are major global health issues. It is estimated that 1 in 20 adults or a quarter of a billion people between the ages of 15 and 64 years used at least one drug in 2014, about 29 million are current problem drug users, and 0.2 million die each year from overdose or medical complications from heroin, cocaine, and other drugs [1]. Dependence on illicit drugs has major global and local economic and social impacts and contributes to crime, political instability, and the spread of communicable diseases such as HIV [1]. Cannabis remains the most widely used illicit substance globally. In 2014, some 3.8 percent of the global population, 183 million people, had used cannabis in the past year, a proportion that has remained stable since 1998 [1]. This was followed by opiates and cocaine at 0.4% or about 18 million people for each, amphetamine-type stimulants at 0.8% or 36

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million people, and "ecstasy" at 0.5% or 19 million users [1]. Some 10–13% of the drug users continue to be problem users afflicted with drug dependence and/or drug-use disorders, and among these, the prevalence of medical conditions such as HIV infection at approximately 14%, hepatitis C infection at almost 52%, and hepatitis B infection at 9% continues to add to the global burden of disease and death [1]. A recent systematic review of the published data on illicit drug use expanded on the information previously published from the Global Burden of Disease (GBD) study [2, 3] by demonstrating specific health outcomes associated with each major drug of abuse [4]. This analysis showed cannabis as a risk factor for schizophrenia (triggering an earlier onset of schizophrenia among those who would develop the disorder regardless); opioids, cocaine, and amphetamine dependence as risk factors for suicide; and injecting drug use (IDU) as a risk factor for HIV and hepatitis B and C viruses. Other studies have shown HIV prevalence to be almost 28 times higher among people who inject drugs [5]. In fact, in 2006, the HIV prevalence among IDUs in China, the United States, and Russia, the three leading countries for injecting drug use, was 12%, 16%, and 37%, respectively. In addition to contributing to higher infection rates, the use of many drugs of abuse by people receiving antiretroviral agents leads to both nonadherence and drug interactions that result in poorer virologic response to HIV treatments [6–9].

In the United States, the 2013 data provided by the National Survey on Drug Use and Health (NSDUH) has estimated 24.6 million individuals aged 12 and older or 9.4% of the US population are current illicit drug users (having used an illicit drug during the month prior to the survey interview) [10]. Among them, 2.2 million are aged 12 to 17 accounting for 8.8% of the US adolescents. According to this report, marijuana is the most commonly used illicit drug (7.5% of the population), followed by the nonmedical use of prescription-type drugs (2.5%), cocaine (0.6%), hallucinogens (0.5%), inhalants (0.2%), and heroin (0.1%), while nearly one quarter of adults (58.5 million) and 6.2% of the adolescents (1.6 million) are binge alcohol users. It is important to note that of the 22.7 million individuals 12 years or older who met the criteria for dependence and abuse for an illicit drug or alcohol,[1] only an estimated 2.5 million received treatment at a specialty facility for an illicit drug or alcohol problem [11]. The main barriers to receiving the appropriate treatment include not having appropriate health coverage, not being ready to stop, not knowing where to go for treatment, not having transportation and inconvenient hours [10].

Worldwide, a myriad of prescription drugs, over-the-counter preparations, and chemical compounds prepared from naturally occurring, semisynthetic, or synthetic compounds are used illicitly and are associated with significant medical consequences including conditions manifested in the head and neck region [12] (Table 14.1).

Naturally occurring opiates such as morphine and codeine, the semisynthetic opiates like heroin, and the synthetic opioids like methadone are all central nervous system (CNS) depressants and, because of their euphoric properties, are among the

[1] NSDUH defines dependence on and abuse of alcohol or illicit drugs using the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), which include such symptoms as withdrawal, tolerance, the use in dangerous situations, trouble with the law, and interference with major obligations at work, school, or home during the past year.

Table 14.1 Categories of illicit drugs discussed in the chapter

Main drug categories	Class	Examples
CNS depressants	Naturally occurring Opiates	Morphine and codeine
	Semisynthetic opiates	Heroin, fentanyl, and oxycodone
	Synthetic opioids	Methadone
	Other depressants	Barbiturates, benzodiazepines, and GHB
CNS stimulants	Naturally occurring Stimulants	Coca, khat, and betel nut
		Cocaine and crack cocaine
	Synthetic stimulants	Methamphetamine, methcathinone, and methylenedioxy-methamphetamine
	Other stimulants	Cannabis

widely abused drugs; their repeated use, in addition to their serious physical and mental health complications, is associated with abnormalities in orofacial structures. Similarly, the nonmedical use of other CNS depressants like barbiturates, nonbarbiturate depressants, and benzodiazepines can have adverse consequences for the cognitive functions as well as the user's dentition. Naturally occurring central nervous system stimulants such as coca, khat, and betel nuts; products extracted from these plants like cocaine and crack cocaine; as well as fully synthetic forms like amphetamine and amphetamine-type compounds, illegally used for their strong hallucinogenic effects, can have significant health effects both systemically and also in the intra- and extraoral tissues. Cannabis, used for its sedative and hallucinogenic effects, is often mixed with tobacco for smoking purposes and for that has implications in the development of oral dysplasia and malignancy. Although HIV infection during its advanced stages and profound immunologic deficiency can be associated with a number of unique head and neck manifestations that have been well described over the past three decades, among illicit drug users, the intra- and extra-oral pathologies encountered are not specific to HIV infection. This chapter provides a comprehensive review of the oral health consequences of some of the most commonly used illicit substances and examines each drug of abuse for its harmful effects on the orofacial tissues.

14.1 CNS Depressants: Opiates

Opiates are the naturally occurring alkaloids derived from the opium poppy, *Papaver somniferum*. Members of this category of drugs include "opium," the coagulated juice of the opium poppy; "morphine," which is extracted from opium poppy straw; and "codeine," a methylated form of morphine [13]. There are many methods to abuse for these agents ranging from ingesting (raw opium and prescription codeine), chewing (raw opium), smoking (prepared opium) to injecting (morphine) [13]. Another member of this category is the semisynthetic drug "heroin" that is synthesized from morphine. It is illegally available in several forms from crude to different

grades of purified form and in these forms can be injected, inhaled, sniffed, snorted, or smoked [13]. Other semisynthetic opiates synthesized for medical use include oxycodone (OxyContin), hydrocodone (Vicodin), and buprenorphine (Suboxone) [13]. The final members of the opiate family are the fully synthetic opiate analogs referred to as opioids or opiate-like drugs that include methadone and fentanyl [12, 13]. Several types of fentanyl have been synthesized specifically for sale on the illicit market, and they can be either smoked or snorted and even injected [13]. Methadone, legally used to treat addiction to narcotics, is available in tablet, liquid suspension, and sterile solution forms and unfortunately has emerged as a drug of abuse in recent years [14].

Opiates and opioids are central nervous system depressants, and their main medical use is for their strong analgesic properties, but some are also prescribed as cough suppressants and in treatment of diarrhea [15]. Their nonmedical use is for their euphoric effect and also for reducing anxiety, boredom, or physical or emotional pain [12]. Based on the 2010 National Survey on Drug Use and Health, public health experts estimate that more than 35 million Americans age 12 and older used an opioid analgesic for nonmedical use some time in their life—an increase from about 30 million in 2002 [16]. Improper use of any opioid can result in serious side effects including overdose, respiratory depression, and death. In 2009, there were nearly 343,000 emergency department visits involving nonmedical use of opioid analgesics [17]; in 2008, nearly 36,500 Americans died from drug poisonings; and, of these, nearly 14,800 deaths involved opioid analgesics [18]. Despite these serious risks, ironically, some of the most severe health effects of injectable opioids like heroin is less related to the drug itself and more due to the unhygienic and needle-sharing practices which lead to the transmission of hepatitis viruses and HIV. One out of every ten new HIV infections is caused by injecting drug use, and currently 3 million injection drug users are living with HIV worldwide [19]. In fact, in parts of Eastern Europe and Central Asia, over 80% of all HIV infections is related to drug use [19].

The oral effects of opiate and opioid narcotics are both direct (causing pathological changes in the salivary, oral, and dental tissues) and indirect (lifestyle related). The most common self- reported and clinical finding among long-term users of narcotic drugs, including methadone, is high levels of dental decay and breakdown (Fig. 14.1).

The first reports of high rate of dental disease among opiate users were published in the 1940s [20]. Since then, both typical (interproximal and occlusal) and atypical (smooth surface and cervical) caries have been described among opioid and methadone users [21–30]. In one recent study of 41 heroin users in San Francisco, the decayed-missing-filled surfaces (DMFS) index[2] was determined to be very high and more skewed toward decayed surfaces [31, 32]. Although the xerostomic effect (inducing hyposecretion of saliva) of narcotic analgesics is a known property of these compounds and most likely a contributing factor in the development of tooth

[2] An index of past caries experience based on the number of decayed, missing, and filled surfaces of deciduous (indicated by lowercase letters) or permanent (indicated by capital letters) teeth.

decay among long-term users, other factors such as a taste preference for sweets [33–37], craving for carbohydrates [38, 39], poor self-care and oral hygiene practices [22, 30, 32, 39], and inadequate access to dental care [29, 40, 41] may all be influential in the high rates of tooth decay in this population. Long-term opioid use has also been reported to be associated with higher rates of periodontal disease including adult periodontitis [22, 42, 43] and necrotizing gingivitis [44] (Fig. 14.2).

Furthermore, opportunistic fungal and viral infections may also occur, [30, 44, 45] most likely due to an underlying immunological suppression reported to occur with drugs of abuse and independent of HIV infection [46–48]. In addition, there is at least one case report of tongue mucosa pigmented lesion attributed to a fixed-drug reaction to heroin pyrolysate vapors [49].

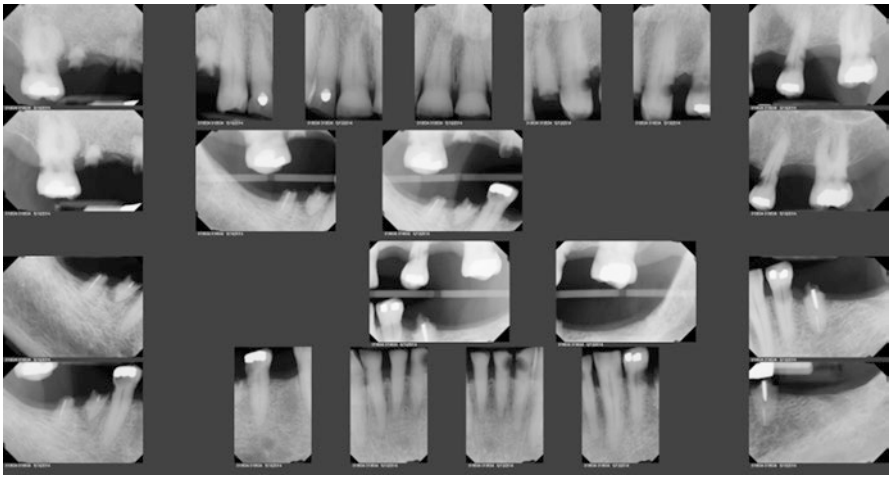

Fig. 14.1 Periapical radiographs of a patient with multiple interproximal and cervical tooth decay. Note teeth that have broken off because of advanced decay

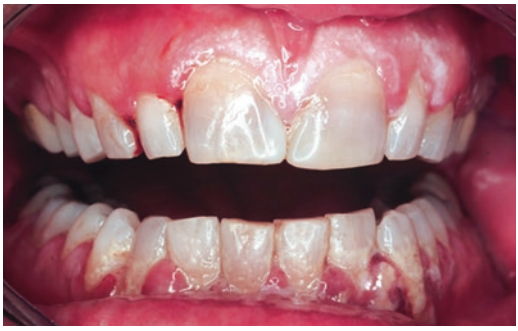

Fig. 14.2 Necrotizing gingivitis in an HIV-positive patient. Note areas of necrosis in the interdental papillae and the pseudomembrane in the gingivae of the maxillary central incisors

14.2 Other CNS Depressants

In this chapter, three members of this category are discussed: benzodiazepines, barbiturates, and *gamma* hydroxybutyric acid. They are available in a variety of forms, most as orally ingested tablets and suspensions and some as injectable solutions and even suppositories.

Benzodiazepines are a group of CNS depressants and among the most frequently prescribed medications worldwide as anxiolytic and sedative-hypnotic agents. About 2000 benzodiazepines have been synthesized by the pharmaceutical industry, and their illicit use is driven by diverting the legally synthesized preparations into illegal markets; they are mostly used for the enhancement of the "high" induced by other drugs or relief of side effects associated with overstimulation or withdrawal of other drugs [13].

Barbiturates are also CNS depressant compounds, but they have been largely replaced on both the licit and illicit markets by benzodiazepines. While they were formerly used as hypnotics/sedatives, their medical use today is limited to the treatment of seizure disorders as long-acting antiepileptics and as adjuncts to anesthesia as short-acting agents [13].

Sedatives/ hypnotics like benzodiazepines and barbiturates cause xerostomia, especially among long-term users, and tooth decay is the most important dental effect of chronic dry mouth [50].

Gamma hydroxybutyric (GHB) acid is a naturally occurring analog of gamma-aminobutyric acid (GABA) with CNS depressant properties. In medicine, it has been used as an adjunct in anesthesia and as an aid to alcohol/opiate withdrawal, but currently it is only legally available in the United States for the investigational treatment of narcolepsy [51]. GHB has become a major club drug over the past decade and has been implicated in a number of crime types, most notably in drug-facilitated sexual assault [52]. In its illicit use, it can quickly lead to systemic toxicity causing strong hallucinations and very erratic behaviors like self-mutilation; oral self-extractions have been reported in several case reports [53–57].

14.3 CNS Stimulants

Central nervous system stimulants include naturally occurring plants such as "coca," "khat," and "betel nuts"; products extracted from the leaf of the coca bush like "coca paste," "cocaine hydrochloride," and "crack cocaine"; and wholly synthetic substances such as "amphetamine," "amphetamine-type compounds," "MDA" (3,4-methylenedioxy-amphetamine), and "MDMA" (3,4-methylenedioxy-methamphetaime) [12].

For its euphoric effect, the leaves from the coca plant (*Erythroxylum coca*) can be chewed, brewed in form of tea, or transformed into coca paste that can be ingested or smoked [13].

Cocaine is the main alkaloid synthesized from coca leaves as a hydrochloride salt, and in this form it can be snorted. Crack cocaine is a smokeable form of cocaine made by processing cocaine with sodium bicarbonate into small rocks. Cocaine freebase is also obtained from cocaine hydrochloride by using a solvent or a process that converts it into its base form, which is no longer water soluble and can only be smoked.

The biological effect of cocaine is through blocking voltage-gated sodium channels and prevention of action potential; therefore, its medical use is in anesthesia as a topical anesthetic in eye and nasal surgery [13]. It is also a serotonin-norepinephrine-dopamine reuptake inhibitor and leads to an increase in these neurotransmitters, hence its euphoric properties [58]. The sympathomimetic effects of cocaine are responsible for significant cardiovascular effects including increased heart rate, coronary and systemic vasoconstriction, reduced myocardial perfusion and ischemia, and elevated systemic arterial pressure [59]. In the orofacial tissues, the use of cocaine is associated with a number of intra- and extraoral findings that seem to be related to its sympathomimetic effect. In the nose, chronic snorting leads to recurrent epistaxis, intranasal irritation and ulceration, and sinusitis and nasal septum perforation, referred to as cocaine-induced midline destructive lesions (CIMDL) [60–62]. CIMDL is reported to affect 4.5% of the users and mimic systemic conditions such as Wegener's granulomatosis by featuring positive antineutrophil cytoplasmic antibodies (ANCA), suggesting a complex inflammatory and autoimmune etiology [63–65]. The destruction of the sinonasal structures causes a loss of height of the nose and a broadening of its base, referred to as a saddle nose deformity. In the mouth, chronic use has a similar effect on the palate, causing palatal sialometaplasia or perforation [66–70].

Cocaine use has also been reported to be associated with oral leukoplakia, oral and gingival ulcers, and manifestations in the periodontal tissues including necrosis and recession. Finally, cocaine use can lead to bruxism and temporomandibular joint pain and dysfunction [71–78] (Fig. 14.3).

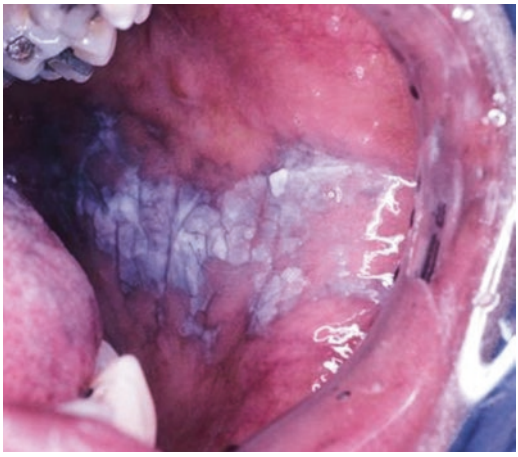

Fig. 14.3 An area of leukoplakia in the buccal mucosa of an HIV-positive woman with a habit of smoking cocaine-laced cigarettes

Khat (*Catha edulis*) is a flowering bush indigenous to East Africa and southern Arabia [79]. In North Yemen, khat is chewed on a daily basis and is restricted to men [80]. Leaves of the khat shrub are typically chewed and held in the cheek, like chewing tobacco, to release their stimulant chemicals. The main psychoactive ingredients in khat are cathinone and cathine [79]. These chemicals are structurally similar to amphetamine and result in similar stimulant effects in the brain and body, although they are less potent. Like other stimulants, cathinone and cathine stimulate the release of the stress hormone and neurotransmitter norepinephrine and raise the level of the neurotransmitter dopamine in brain circuits regulating pleasure and movement [79]. Oral leukoplakia, oral mucosal pigmentation, and oral dryness have been reported in individuals who chew khat [81].

Betel nut (areca nut), the seed of the areca palm (*Areca catechu*), grows in much of the tropical Pacific, Asia, and parts of east Africa [82]. The term "betel quid" (synonymous with "pan" or "paan") generally contains betel leaf, areca nut, and slaked lime and may contain tobacco along with other substances for flavoring (cardamom, saffron, cloves, aniseed, turmeric, mustard, or sweeteners) [82]. Arecoline is the primary active ingredient responsible for the central nervous system effects of the areca nut and has properties similar to nicotine [82].

One significant oral lesion seen among people who use betel quid regularly is submucous fibrosis (Figs. 14.4 and 14.5).

Lesions of submucous fibrosis start as blanched or marble-like pale mucosa and progress to fibrous bands in the buccal and labial mucosa which cause a restriction in opening the mouth [83]. It has been suggested that in a genetically proposed individual, areca alkaloids cause fibroblast proliferation, increased collagen synthesis, and inhibition of collagen phagocytosis [84]. Submucous fibrosis is considered a premalignant oral lesion [83]. Oral lichenoid reaction and excessive tooth abrasion and fracture have also been reported to occur with areca nut use [85].

The synthetic amphetamine and amphetamine-like compounds have been used medically for nasal decongestion and bronchial dilation, the promotion of weight loss, and also in the treatment of attention deficit disorder, narcolepsy, and depression [86, 87]. These include dextroamphetamine (Dexedrine), methamphetamine (Desoxyn), and methylphenidate (Ritalin) [87]. They are not only abused in their pharmaceutically available forms, but they are also illegally produced as methamphetamine, methcathinone ("bath salts"), and methylenedioxy-methamphetamine (MDMA, "ecstasy") [87]. Worldwide, common street names for methamphetamine are black beauties, chalk, crack meth, crystal meth, meth, ice, crystal, crank, glass, shabu, and yaba. "Speed" is a common street name for both methamphetamine (in the United States/North America) and amphetamine (in Europe) [13, 87]. Like cocaine, amphetamines result in an accumulation of the neurotransmitter dopamine. While in therapeutic doses they improve alertness, attention, and performance on various cognitive and motor tasks, when abused, their desired effect is increased alertness and energy, postponement of hunger and fatigue, exhilaration, and euphoria [13]. Globally, it is estimated that 36 million adults use amphetamines, including methamphetamine, amphetamine, and ethcathinone, and about 19 million use substances sold as "ecstasy" (MDMA) [1].

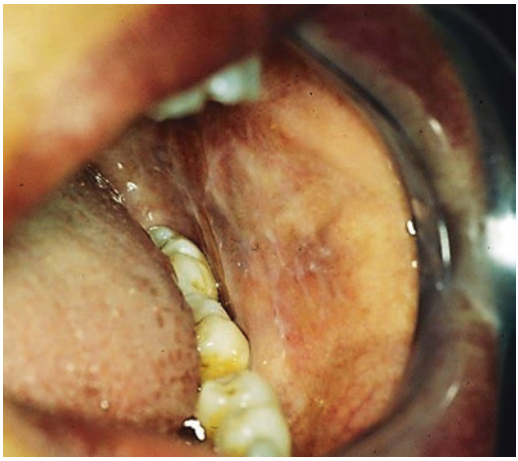

Fig. 14.4 Oral submucous fibrosis in the buccal mucosa of a man with betel nut chewing habit. Note the areas of tissue fibrosis

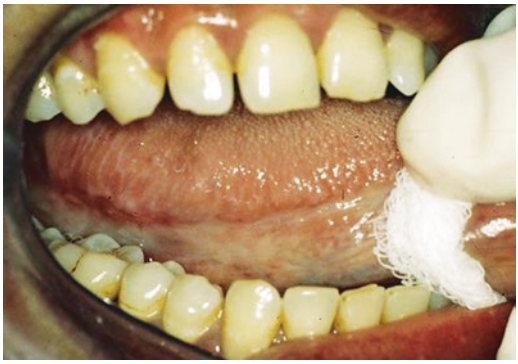

Fig. 14.5 Oral submucous fibrosis in the lateral and ventral aspects of the tongue of a man with betel nut chewing habit. Note the areas of tissue fibrosis

Methamphetamine was first synthesized in Japan in 1893, and its pharmaceutical form was heavily used during World War II by the British, German, American, and Japanese military personnel for its performance-enhancing properties; after the war, this drug penetrated the civilian market in Japan and led to its first epidemic in that country [88, 89]. In the United States, the epidemic gained a foothold, first, in Hawaii and California, and then it spread eastward with clandestine production by the "do-it-yourselfers" throughout the country, particularly in rural areas [90]. Methamphetamine is produced in a variety of forms that can be injected, orally ingested, sniffed/snorted, and smoked. Dependence on these drugs has significant neurologic, cardiovascular, and metabolic consequences including memory loss, aggression, hyperexcitability, paranoid and psychotic behavior, increased heart rate, hypertension, and malnutrition; in addition, it has been shown to contribute to increased transmission of infectious diseases, such as hepatitis and HIV [91]. Methamphetamine use has been reported to be associated with severe oral health problems such to the extent that the term "meth-mouth" started to gain popularity in

the late 1990s among the users and the professionals working in the field of addiction medicine and in the mid-2000s began appearing in the news media [92]. Since then, despite a paucity of evidence for methamphetamine-specific oral damage [32, 93], the term continues to be used, by both the dental professionals and the lay public, to convey an image of blackened, rotting, crumbling teeth and the associated soft tissue breakdown with gingival abscesses (Fig. 14.6).

It is more accurate to consider the specific oral conditions seen among methamphetamine users which include xerostomia and bad taste [94–96], rampant tooth decay [97–99], and bruxism and tooth wear [100, 101] (Figs. 14.7 and 14.8).

In one pilot study of 18 long-term methamphetamine users (average length of use of 8 years) in 1999, 50% of the participants reported severe dry mouth (22% had reduced salivary flow by clinical assessment) and 60% reported oral ulcer and irritation right after use [102] (Fig. 14.9).

Among the mechanisms suggested for the development of xerostomia are amphetamine-induced vasoconstriction in the vasculature of salivary glands [96] and stimulation of the inhibitory alpha-2 receptors in salivary secretory cells [103]. In one small pilot study of 28 subjects, no differences were observed in the rate of salivary flow between methamphetamine users and the control subjects, but there was a trend toward lower pH and decreased buffering capacity of saliva among the using group [104]. This reduction in salivary pH had previously been reported to be relatively small and among a small group of individuals who only smoked MDMA, raising doubt about the significance of its role in enamel erosion and the risk for tooth decay [105]. The pattern of dental caries among methamphetamine users is similar to that observed among patients with severe xerostomia (like those with a history of radiation to the head and neck region) and affects the cervical and the smooth tooth surfaces as well as the interproximal surfaces of the anterior teeth. Although the corrosive effects of the methamphetamine constituents such as anhydrous ammonia (found in fertilizers), red phosphorus (found on matchboxes), and lithium (found in batteries) on the tooth enamel have been suspected as etiologic factors in enamel erosion, the extent of tooth decay among some users and its rate of progression appear to be more related to lifestyle factors such as oral hygiene and the level of consumption of sugary food [106, 107]. Furthermore, a recent cohort study of adult methamphetamine users found the intravenous administration was associated with significantly more missing teeth in the cohort than the smoking

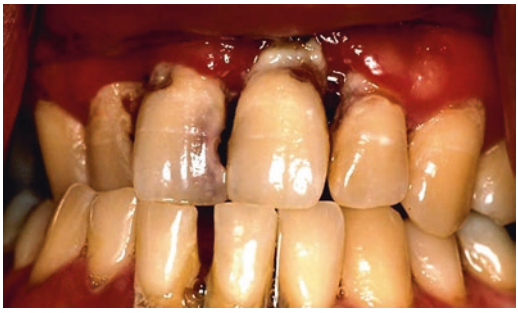

Fig. 14.6 Rampant decay, severe gingival recession, and purulence from a periodontal abscess in an HIV-positive man with a history of heavy crystal methamphetamine use

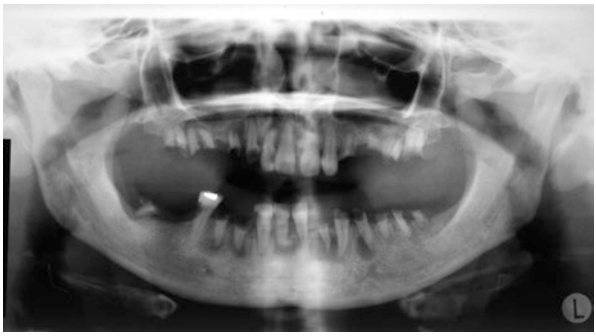

Fig. 14.7 The panoramic radiograph of an HIV-positive woman with a 4-year history of meth use. Note the number of dental abscesses

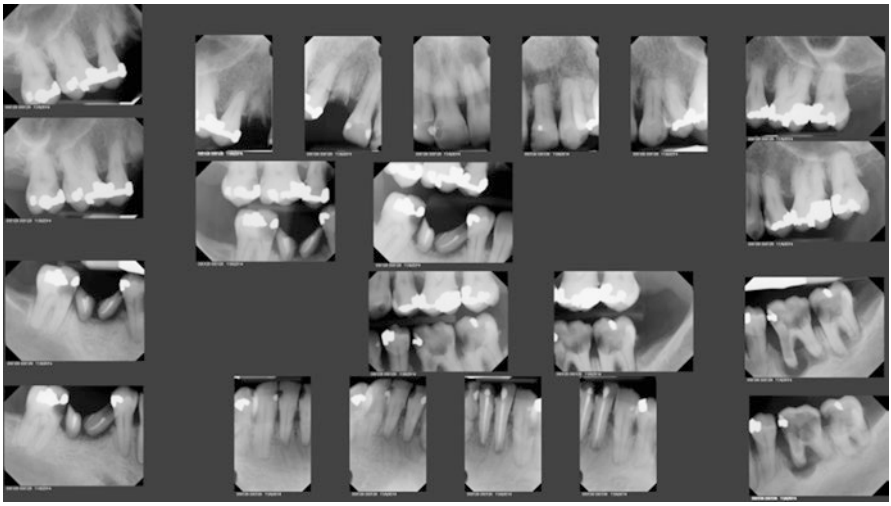

Fig. 14.8 The periapical radiograph of a person with a 10-year history of meth use (4–5 times daily). Note the level of tooth decay activity and broken teeth

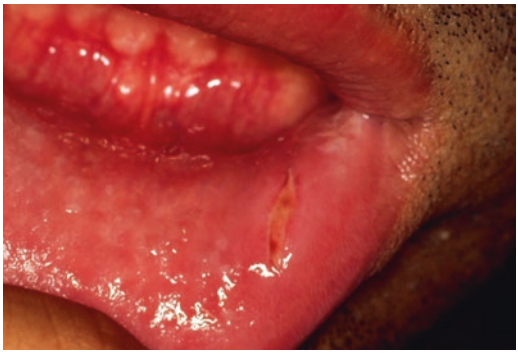

Fig. 14.9 An ulcer in the labial mucosa of an active crystal methamphetamine user

route [99]. Among other contributing factors are also forgoing dental care, grinding or clenching teeth, and the concomitant use of other substances such as alcohol and tobacco [106, 107]. In addition, increased neuromuscular activity in methamphetamine users may be responsible for bruxism, tooth grinding, and temporomandibular joint tenderness among methamphetamine users [100, 101, 108]. In one recent report of the osteonecrosis of the jaw (ONJ) in a chronic methamphetamine user, the authors suggest an etiologic correlation between ONJ and exposure to the toxic phosphorus vapor generated through heating and smoking this drug [109], a possibility that must be explored by future studies.

The oral effects of the designer amphetamine-like drugs, methylenedioxymethamphetamine (MDMA "ecstasy"), and methcathinone ("bath salts") are similar to those described for methamphetamine users. Ecstasy use is reported to cause significant dry mouth lasting up to 48 h after consumption, oral ulceration 1–2 days after use, and bruxism during use [110]. Bath salts have been reported to cause severe bruxism and grinding that can lead to tooth wear and fractures [40].

14.4 Cannabis

Cannabis remains the world's most widely used illicit substance with estimated annual prevalence ranging from 3.8 percent of the world adult population (183 million individuals aged 15–64) [1]. Cannabis preparations, marijuana, hashish, and hash oil, are obtained from the plant *Cannabis sativa* that contains over 60 types of cannabinoids [111]. Δ^9-Tetrahydrocannabinol (THC) is the plant's main psychoactive constituent, and several other cannabinoids such as Δ^8-THC, cannabinol, and cannabidiol have additive, synergistic, and antagonistic effects on THC [112]. THC is found in its highest concentration in the resin produced by the female flower heads, followed by the plant's flowers, leaves, stems, and seeds [111]. Marijuana is made from the plant's dry flowers and seeds and consists of 0.5–5% THC, while hashish, made from the resin produced by the flower heads, consists of 25% THC and hash oil, the liquid extracted from hashish, consists of 15–50% THC [111]. It is important to note that much of the cannabis used today comes from *Cannabis sativa* subspecies such as skunkweed and netherweed, developed through selective breeding techniques over the past 20 years, with THC contents in the magnitudes of 15 to 30 times higher than the old generations of cannabis used in the 1970s, the period of time when much of the research on the health effects of THC was performed [112]. In a 2001 review article, Ashton Gold is quoted from his paper in 1991: "This single fact has made obsolete much of what we once knew about the risks and consequences of marijuana use" [112, 113].

Some of the common street names for cannabis are bongo, buddha sticks, and ganja [12]. Cannabis can be smoked as hand-rolled cigarettes ("a joint") or from a variety of pipes including the water pump ("a bong"); hashish can be eaten when baked in cookies and cakes or be mixed with tobacco and smoked; hash oil is spread on the paper wrapping of cigarettes and smoked; yet, because of water insolubility,

cannabis is not suitable for intravenous use [111]. Cannabis exerts its mind-altering effects by interaction with endogenous neuronal receptor CB_1 located in the CNS, the cerebral cortex, the limbic areas, the basal ganglia, the cerebellum, the thalamus, and the brain stem; cannabis also has an endogenous ligand called anandamide with a high affinity for the CB_1 receptor [114–116]. Additionally, cannabis has immunosuppressive properties because of its interaction with another receptor, CB_2, found on immune cells such as macrophages in the spleen and also the B- and T-cell lymphocytes [117]. Medically, cannabis is used as an antiemetic, an appetite stimulant, and a pain reliever in the treatment of cancer and AIDS and in the management of glaucoma and neurologic conditions such as epilepsy, migraine, and bipolar disorder [116]. The nonmedical use of cannabis leads to a wide range of mood changes such as euphoria, relaxation, hallucination, confusion, and disorientation—effects that may be attributed to an additional interaction of THC on dopamine release from the nucleus accumbens and prefrontal cortex [112].

There is evidence for a potential relationship between cannabis and cancer development in the lungs and the oropharyngeal tissues. Other than nicotine and along with carbon monoxides and other bronchial irritants, the smoke from the herbal cannabis preparations contains the same carcinogens, the polycyclic aromatic hydrocarbons benzanthracenes and benzopyrenes, as the smoke from tobacco cigarettes [112]. The THC in cannabis has tumorigenic properties through promoting the transcription of P4501A1 (CYP1A1), an enzyme capable of converting the polycyclic aromatic hydrocarbons into carcinogens, as well as the formation of reactive oxygen species and also immunologic suppression [118]. On the other hand, laboratory studies have shown that THC may also possess protective antitumor properties by inducing apoptosis in several different human cancer-cell lines [119]. Taken together, the net effect of cannabis use on cancer development appears to be quite complex.

Compared to smoking tobacco cigarettes and because of the way it is inhaled, smoking cannabis exposes the person to a greater volume and a longer period of exposure to the smoke. In fact, smoking 3–4 cannabis cigarettes per day is associated with the same level of bronchial damage as 20 tobacco cigarettes per day [120]. Moreover, bronchial biopsies of marijuana smokers show more molecular abnormalities in Ki-67, EGFR, and p53 than nonsmokers [121], suggesting field cancerization effects on the bronchial epithelium and possibly the entire aerodigestive tract [119].

Studies of patients with head and neck cancers have shown marijuana use to be prevalent [122–124], and oral premalignant lesions such as leukoplakia and erythroplakia have also been reported among regular marijuana users [125]. One case-control study of 173 subjects with oral squamous carcinoma of the head and neck and 176 cancer-free controls showed the risk of cancer to be 2.6 times higher among marijuana users [126]. This positive association was refuted by a population-based case-control study of 407 individuals with head and neck cancer and 615 control subject where the use of marijuana did not show any association with oral cancer diagnosis or the molecular abnormalities in glutathione S-transferase genes (known to be involved in biotransformation of polycyclic aromatic hydrocarbons), while a

combined effect was observed with cigarette smoking and alcohol use [127]. In the latter study, however, the subjects were not long-term marijuana users. A pooled analysis of nine case-control studies from the United States and Latin America showed the association of marijuana use with head and neck cancer to differ by tumor site, with an increased risk for oropharyngeal cancer and a reduced risk for tongue cancer [128]. A recent review of 11 epidemiologic studies on all cancers confirmed the conflicting results among these studies for the effect of marijuana use and aerodigestive tract cancers [129]. It is clear that well-designed longitudinal studies of long-term cannabis users, separating the impact of smoking tobacco, alcohol use, and HPV infection, are necessary to show the true impact of cannabis use on oral cancer development at the population level.

Other oral health implications of cannabis use are xerostomia and poor oral hygiene [94, 117, 125, 130, 131] that may increase the risk of caries and periodontal disease. Other reported findings include multiple oral papillomas [132] and oral candidiasis [131, 133], both of which most likely related to the immunologic suppression effects of cannabis and also the hydrocarbons in cannabis acting as an energy source for candida growth [133].

Cases of gingival hyperplasia have also been reported with cannabis use [134] (Figs. 14.10 and 14.11).

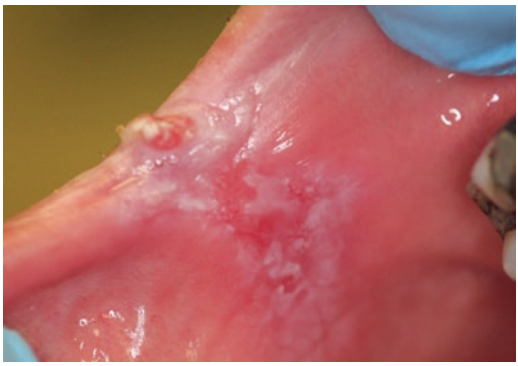

Fig. 14.10 Papillomatous lesion and leukoplakia in the inner aspect of the labial commissure in a man with a 30–40 per day cannabis cigarettes use

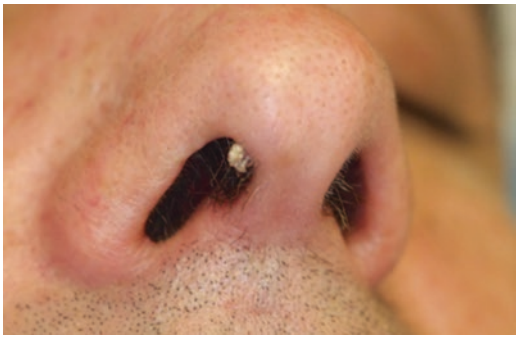

Fig. 14.11 Papillomatous lesion nasal mucosa in a man with a 30–40 per day cannabis cigarettes use

14.5 Summary

Illicit drug use and dependence are associated with significant systemic and oral sequelae. Oral presentations are mostly seen in the dentition with very high caries activity and/or periodontal disease. Dental breakdown in most instances is due to drug-induced xerostomia, but other factors such as diet and especially the high use of carbohydrates also play major roles. Other oral presentations of concern are pre-malignant and dysplastic lesions that occur with certain drugs such as cannabis. Patients who enter recovery programs for their drug dependence should not only be screened for HIV infection and other STDs, they should also receive an assessment by a dental professional for the diagnosis and treatment of drug-related dental and soft tissue pathologies and also instructions for appropriate oral hygiene practices and home care.

Conflict of interest The authors report no conflicts of interest.

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