MedLinkNeurology

UPDATED 03.04.2021 RELEASED 09.23.1996 EXPIRES FOR CME 03.04.2024

Stroke associated with drug abuse

AUTHOR

Michael T Mullen MD

EDITOR

Steven R Levine MD

Introduction

Overview

Drugs of abuse are frequently associated with **stroke**, especially in the young. In this article, the author reviews the clinical features and pathophysiology of stroke related to drug abuse.

Key points

- Drugs of abuse increase the risk of both **ischemic stroke** and intracerebral hemorrhage.
- Stimulants such as amphetamines, cocaine, and phencyclidine cause a sympathetic surge with elevated blood pressure and vasospasm.

• Heroin-associated strokes are most often attributed to infectious complications such as endocarditis or ruptured **mycotic aneurysm**.

• Cannabis use may be associated with an increased risk of ischemic stroke, although data are limited.

Historical note and terminology

Although often considered a peculiarly modern problem, the use of drugs for their psychoactive effects dates back thousands of years. Drugs derived from the ingestion of plants have the longest history of abuse. Abuse of synthetic and semi-synthetic drugs date to the pharmaceutical development of these substances in the early 20th century. The major classes of drugs of abuse include opiates, stimulants (cocaine, amphetamine and related agents), hallucinogens (LSD, phencyclidine, etc.), marijuana, barbiturates and other sedatives, and inhalants. Alcohol and tobacco, the 2 most widespread drugs of abuse, will not be discussed in this article. This certainly should not be taken as minimizing their addictive potential or clear impact on stroke risk. Each of the broad classes of drugs of abuse produces a distinct clinical intoxication and is associated with a limited spectrum of cerebrovascular disease. Familiarity with these patterns is important to the evaluation and treatment of patients with stroke. Several difficulties arise in any discussion about drugs of abuse. First, a variety of common street names exist to describe various drugs. As no standard definitions of these terms exist, they may at times mean different things to different people. Second, given the illicit nature of most drugs of abuse, patients' perception of the drug ingested must be considered of limited reliability. Tainted and substituted compounds are common, and only toxicological confirmation or direct testing of the substance itself can confirm the true identity of the ingested drug. Finally, a variety of different means of administration of individual drugs exist, and the effects of the drug, both desired and undesired, vary considerably based on this fact.

Table 1. Street Names and Methods of Administration for Drugs of Abuse

Agent	Administration	Common name(s)
Methampheta mine	Orally, intravenously, intranasally	Meth, speed, dexies, crystal, ice

Amphetamine derivatives	Orally, intranasally	MDMA, Ecstasy, X, molly, bath salts, plant food, jewelry cleaner, ivory wave, purple wave, zoom, cloud nine
Cocaine hydrochloride	Intranasally	Blow, nose candy, snow, dust, coke
Cocaine, alkaloidal	Inhaled or smoked; intravenously	Crack, rock, base, white pipe
Phencyclidine	Orally	PCP, angel dust, trank, DOA
Heroin	Intravenously, inhaled, or smoked	Smack, junk, skag, black tar
Cannabis	Inhaled, smoked, or ingested	Marijuana, hashish, pot, grass, weed
Synthetic cannabis	Inhaled, smoked, or ingested	Spice, K2, black mamba, Bombay blue, bliss, blaze

Amphetamines are synthetic sympathomimetics whose anorectic action led to their initial use as diet pills. They have also been used as mental stimulants by long-distance drivers, students, and others trying to preserve cognitive performance in the face of **sleep deprivation**. Athletes have used them to enhance physical performance. The euphoriant effect of higher doses has broadened their abuse potential. Methamphetamine is typically taken orally, although it can be smoked and injected. Intravenous users crush tablets of "speed," dissolve them in a liquid, filter them through cotton, and then inject them. Cerebrovascular complications arise from the more rapid onset of sympathomimetic action, and from foreign body reactions to "diluents" or filler substances like talc or cornstarch.

Amphetamine derivatives encompass a broad range of drugs with sympathomimetic action. Methylenedioxymethamphetamine or “ecstasy” is used both for its stimulant and euphoric properties. Other synthetic amphetamine-like substances, such as mephedrone, pyrovalerone, and methylenedioxypyrovalerone, are gaining popularity as well. These drugs can be purchased online or in drug paraphernalia stores. They are variably labeled as “bath salts,” or “plant food,” and there has been a dramatic increase in calls to United States poison control centers related to these substances (35). Ephedrine is used for the treatment of asthma and nasal decongestion (28) and is contained in the form of ephedra

in the Chinese herbal preparation *ma huang*, frequently sold as an herbal stimulant. Over-the-counter sympathomimetics, such as phenylpropanolamine and pseudoephedrine, have been used to treat nasal congestion or facilitate weight loss (08; 28). The abuse potential and link to cerebrovascular disease associated with these drugs has been recognized since the 1980s (72; 08). Phenylpropanolamine was voluntarily withdrawn from the market in 2000 after the FDA reviewed a number of reports of hemorrhagic stroke associated with its therapeutic use (41). Amphetamines and **methylphenidate** are increasingly used to treat hyperactivity and attention deficit disorder in children and adults.

Cocaine is derived from the leaves of the shrub *Erythroxylon coca*, which grows in the Peruvian and Bolivian Andes. For many centuries, the leaves of this plant were chewed or sucked by inhabitants to decrease hunger, increase endurance, and generate a sense of well-being. Addiction was not described until more concentrated forms of cocaine became available. Alkaloidal cocaine was first purified in 1860 by Niemann. Sigmund Freud and Hans Koller explored the physiological actions of cocaine. Freud first successfully employed the euphoriant effects of cocaine to wean a patient addicted to morphine. The unforeseen result was to create the first person addicted to cocaine (28).

Phencyclidine was popular in the 1980s as a stimulant that heightened sensory perception. Strokes were reported in several users (04; 08). The risk of psychosis and violent behavior with higher doses or chronic use decreased its popularity.

Opium is derived from the unripe seed capsules of the poppy plant, *Papaver somniferum*. Opium addiction is recorded as early as the third century BC, and during the early part of the 20th century it was estimated that 1 out of every 400 Americans was addicted to opium or related agents. Heroin (diacetylmorphine) is a semisynthetic derivative of morphine, which is 1 of the substances contained in opium. Heroin abuse did not develop until the advent of hypodermic needles (28). Although it is frequently injected intravenously, increases in purity have allowed for intranasal use. The increase of prescribing opioid medications has contributed to increased abuse of both prescription opioids and heroin.

Cannabis, from the plant *Cannabis sativa*, is the most widely used recreational drug in the world. It is most often prepared as marijuana or hashish, which are subsequently smoked, inhaled, or ingested. Cannabis has been legalized in a number of states in the U.S. and in Canada. The psychoactive ingredient in cannabis is delta-9-tetrahydrocannabinol (THC). Potency can vary widely across preparations based on the THC content, which is generally higher in hashish than in marijuana (78). Synthetic drugs that bind to the same cannabinoid receptors as THC have been developed. These drugs are sold as synthetic cannabis under brand names such as spice or K2. Similar to synthetic

amphetamines, synthetic cannabis can be purchased online or in drug paraphernalia stores (09).

Clinical manifestations

Presentation and course

Stroke can occur during the first minutes of acute intoxication with a drug, in the hours following ingestion, or weeks (rarely months) following intoxication. Recognition of the role of drug use in the pathogenesis of stroke requires familiarity with the acute effects of commonly used recreational drugs and a high index of suspicion. The signs and symptoms of a stroke are not different in the user of recreational drugs unless the user is acutely intoxicated. Rather, the physician must probe for a history of substance abuse from the patient, friends, and family. Given the fact that drugs of abuse are typically produced illegally, there is little assurance that the patient has consumed the agent described and not some substituted alternative drug of abuse. Thus, the clinical history alone must be considered of limited reliability. Identifying agents via toxicology screens or, rarely, analysis of drug samples themselves is of great importance. Suspicion can be confirmed in many cases through prompt urine toxicology screening in a patient who presents during or soon after acute intoxication. Confirmation of the role of drug abuse as the cause of symptoms weeks and months after acute intoxication depends on a complete history and plausible mechanism of action, for example, a stroke caused by a **necrotizing vasculitis** due to chronic use of an amphetamine, or **infective endocarditis** with **cardioembolic stroke** in an intravenous drug user who does not use sterile needles.

Identification of a stroke secondary to ingestion of a specific drug permits a directed stroke work-up. For example, angiography may be indicated in patients taking drugs associated with vasculopathy or to search for vascular malformations in certain drug users with intracranial hemorrhage. Recognition that angiographic vasculopathy is due to abuse of a certain agent will prevent initiation of unnecessary treatments with possible morbidity, eg, long-term immunosuppression, which is appropriate for autoimmune but not drug-induced vasculopathy. Thus, familiarity with the cerebrovascular complications of drug abuse guides the diagnostic evaluation of the patient and determines long-term stroke prophylaxis.

Sympathomimetic drugs cause a common profile of acute intoxication. Users of amphetamines, amphetamine derivatives (MDMA, ephedrine, phenylpropanolamine, methylphenidate, etc.), and cocaine experience elation and increased alertness; motor activity, coordination, and physical endurance are increased. Orgasm is reportedly delayed and heightened. Pupils are dilated, systolic blood pressure is elevated, and reflex bradycardia is noted. Blood pressure might be normal in patients by the time they arrive for medical attention unless they are still intoxicated. Higher doses cause agitation, suspiciousness verging on paranoia, and violent acts. Palpitations and stereotyped motor behavior may be present. Chronic use causes labile mood, paranoia, and a frank psychosis resembling **schizophrenia**. Some users engage in "runs" of iterative drug use for several days, finally stopping because of insurmountable exhaustion, lack of funds, or because they are too disorganized to continue ingesting the drug (usually by injection) (08).

Intoxication with phencyclidine varies with the dose ingested. Lower doses heighten sensory perception and cause euphoria or dysphoria and mood lability. Higher doses increase agitation and induce a state of excited **catatonia** or frank paranoid psychosis with auditory hallucinations. Bizarre, potentially violent behaviors are seen. Analgesia occurs with higher doses. Phencyclidine intoxication is also associated with elevated systolic pressure, sweating, hypersalivation, miosis, burst-like **nystagmus**, and **ataxia** (04; 08).

Acute heroin intoxication causes a pleasant, dream-like euphoria with impaired concentration. Some users experience anxiety rather than drowsiness, and **nausea and vomiting** may occur. Pupils are small but reactive. Tone is decreased in the face and neck muscles. A dry mouth, difficulty urinating, constipation, and respiratory depression can be seen. Chronic users are often irritable and dysphoric, having developed tolerance to many of the acute effects of heroin use (08).

Cannabis and synthetic cannabis intoxication cause an increased sense of well-being, mild euphoria, and feelings of relaxation. High doses can cause hallucinations and paranoia. Systemic effects include mild reductions in blood pressure, increased heart rate, dry mouth, and dilation of corneal blood vessels.

Prognosis and complications

Patients who use methamphetamine are at risk for systemic vasculopathy. Screening for other organ system dysfunction is warranted. Patients who use cocaine may have myocardial ischemia, cardiac arrhythmias, or sudden death. Screening evaluation is warranted.

The systemic complications of stroke in the setting of acute heroin intoxication include hypotension, increased risk for pulmonary edema, and respiratory depression with possible hypoxia.

Prognosis is largely determined by whether or not the individual user continues to use these drugs. Many of the reported patients are "lost to follow-up," presumably because they have returned to drug use. Users of methamphetamine appear at risk for recurrent stroke due to ongoing vasculopathy.

Biological basis

Etiology and pathogenesis

Cocaine. Cocaine acts as a CNS stimulant by blocking the reuptake of norepinephrine and epinephrine after sympathetic stimulation, thus, potentiating the actions of the sympathetic nervous system. Cocaine reinforces its own use by inhibiting the reuptake of dopamine in the ventral tegmental area of the mesocorticolimbic system. The prolongation of the actions of dopamine in this area "rewards" cocaine use and encourages its reuse. It also acts as a local anesthetic by blocking the initiation or conduction of nerve impulses following local administration (28). Cocaine is ingested in 2 forms. Cocaine hydrochloride is injected intravenously or snorted intranasally. Alkaloidal (freebase or crack) cocaine is smoked.

Amphetamines. Amphetamines are the most potent CNS stimulants among sympathomimetic drugs. Methamphetamine has the most potent CNS effects of the amphetamines. These drugs act by facilitating the release of central norepinephrine and dopamine stored in synaptic vesicles. Wakefulness, attention, and the ability to perform simple but not complex mental tasks are improved in sleep-deprived subjects. Athletic performance is enhanced. At higher doses, dopamine is released in the neostriatum, leading to stereotyped behaviors. Release of dopamine in the mesolimbic cortex rewards amphetamine use and encourages its reuse. At highest doses, they trigger the release of 5-hydroxytryptamine in the mesolimbic cortex, disturbing perception and causing frank psychosis. They may also directly stimulate 5-hydroxytryptamine receptors. They are also anorectic through their actions on the lateral hypothalamic feeding center (28). Amphetamines are taken orally, intravenously, or smoked (crystal methamphetamine). Intravenous formulations may be diluted with talc or cornstarch.

Amphetamine derivatives. Methylphenidate is structurally related to amphetamine but has greater stimulation of mental rather than physical activities. It has the same mechanism of action as the amphetamines. Higher doses are associated with increased risk of convulsions. Like amphetamines, it is a polar molecule that achieves higher levels in the CNS (28). Methylphenidate is ingested orally; tablets are sometimes crushed and injected intravenously.

Several synthetic sympathomimetics have been employed to treat nasal congestion. Their alpha-agonist activity causes hypertension, and this effect has been invoked to explain acute stroke occurring in some patients using these agents. Ephedrine has both alpha- and beta-adrenergic agonist activity and also enhances the release of norepinephrine from sympathetic neurons. It is a CNS stimulant, although it is less potent than the amphetamines. Pseudoephedrine is a stereoisomer of ephedrine that is used as a nasal decongestant. Phenylpropanolamine is another synthetic sympathomimetic used to treat nasal congestion, but it causes less CNS stimulation (28). These drugs are primarily ingested orally.

Heroin. Heroin binds to mu opioid receptors in the brain. The proscription against legal use of heroin makes access to sterile needles and syringes difficult. Ignorance regarding sterile technique and the temporal exigencies of physical addiction combine to increase the risk of infective endocarditis and its complications, which includes ischemic stroke via embolism, mycotic cerebral aneurysms, and intracranial hemorrhage.

Cannabis. Cannabis contains greater than 100 different cannabinoid substances, the 2 most notable being delta-9-tetrahydrocannabinol (THC) and cannabidiol (**CBD**). THC is the main psychoactive component of cannabis, and CBD is the main nonpsychoactive component. There are 2 known cannabinoid receptors: CB1R, which is located in the central nervous system, and CB2R, which is found peripherally, and in particular, within immune system tissues. The amount of THC and CBD vary based on the plant, although studies have suggested increasing THC content and decreasing CBD content in recent decades (15). Cannabis can be smoked or ingested orally. It causes a euphoric sensation with reduced anxiety and alertness and altered perception; however, anxiety or dysphoria can occur in some individuals. Synthetic cannabinoids are a heterogeneous group of compounds but generally act at the CB1R receptor and have similar effects as cannabis. Because they can be much more potent than cannabis, they likely have a greater risk of adverse events including agitated psychosis, hallucinations, and seizures.

The mechanisms by which drug abuse causes stroke are not fully understood but are likely heterogeneous. In this regard, it is useful to distinguish between stroke as a direct or an indirect medical complication of drug abuse. Direct medical complications result from the physiological action of the drug or its toxic effects. For example, it has been proposed

that hemorrhagic stroke may be due to the sympathomimetic and hypertensive action of drugs like cocaine, methamphetamine, or the amphetamine derivatives. The abrupt rise in sympathetic activity causes a sharp increase in blood pressure, which ruptures an intracerebral artery, causing a "hypertensive" hemorrhage or a vascular malformation or aneurysm, causing lobar or **subarachnoid hemorrhage**. It is likely that this explanation is too simplistic and that additional poorly understood factors are involved. In general, the mechanisms of ischemic stroke are even less clearly defined.

Indirect complications are not immediately linked to a specific drug or its mechanism of action, but rather to the means of its administration or to contaminants mixed in with the drug. For example, cardioembolic stroke can be secondary to bacterial endocarditis in an intravenous drug user who employs nonsterile needles. The drug injected is not relevant to the pathogenesis of endocarditis. Additionally, cocaine has been reported to cause myocardial infarctions and cardiomyopathies, creating the potential for cardioembolic stroke (17; 69; 06). Similarly, several drugs intended for intravenous use are mixed with talc or cornstarch, which have been found to occlude arteries causing stroke. On autopsy, deposits of talc were found occluding the small vessels in the medulla of a young woman who crushed and injected tablets of methylphenidate and suffered a medial medullary stroke (54).

The cerebrovascular complications and specific proposed mechanisms by which they occur for the most commonly implicated drugs are described below.

Cocaine. Stroke following cocaine use typically occurs in the first minutes or hours after ingestion, rarely up to a week later. Headache is common, and seizures have been reported in 20% of patients. Approximately 80% of strokes attributed to use of cocaine hydrochloride are hemorrhagic (45). Among those undergoing angiographic evaluation, roughly 50% are found to have an underlying aneurysm or arteriovenous malformation (46). Among patients with aneurysmal subarachnoid hemorrhage, 1 study reported a higher re-rupture rate (7.7% vs. 2.7%, $p< 0.05$) and a higher rate of in-hospital mortality (26% vs. 17%, $p< 0.05$) among cocaine users (11). Many of the hemorrhages seen in patients without vascular malformations are deep, similar to hypertensive hemorrhages. In patients using alkaloidal cocaine, approximately half of strokes are ischemic and 50% are hemorrhagic (46; 26). In a large, population-based case control study of adults less than 50 years of age, acute cocaine use, defined as use within 24 hours, was strongly associated with ischemic stroke (age, sex, and race adjusted odds ratio = 6.4, 95% CI 2.2) (14). This study did not report suspected etiology of these infarcts, but a different small study suggested that large artery atherosclerosis is common, occurring in 44% (75). Several mechanisms have been proposed:

(1) Acute hypertension during the sudden surge of sympathetic activity plausibly explains the rupture of small penetrating arterioles in patients with deep hemorrhages or with ischemic strokes in the territories of small penetrating arteries. This would also explain the rupture of saccular aneurysms or arteriovenous malformations.

(2) Vasospasm has been observed in several angiographic studies done both acutely and subacutely (27; 31; 45; 43) and strongly suggested pathologically in 1 case (43). The vasospasm has been attributed to the direct effect of noradrenergic innervation of these vessels, but vasospasm has also been documented in vessels with sparse innervation (64). Cocaine-induced vasospasm has been shown to be mediated by endothelin-1 (24). It has been postulated that vasospasm may be associated with hemorrhage by causing ischemia of the distal vessel wall as well as the cerebral parenchyma, resulting in a sudden rise in blood flow causing vessel rupture when the vasospasm is relieved (10).

(3) **Vasculitis** has been suggested in a few cases (40; 47; 56; 51) and generally appears as a non-necrotizing small vessel **angiitis** involving arterioles and venules without granuloma formation or fibrinous degeneration. Controversy exists as to whether this represents a hypersensitivity angiitis or a true **arteritis** (08; 56; 51) or even diapedesis of leukocytes through the vessel wall. As a rule, these cases have not fulfilled rigorous pathological criteria for vasculitis. It should be noted that it is usually not seen on angiography because it affects vessels too small to be seen.

(4) Cocaine directly enhances platelet aggregation through increased synthesis of thromboxane A2 and increased responsiveness to arachidonic acid (74); a procoagulant effect via depletion of protein C and antithrombin III has also been proposed (32). This may increase the likelihood of thrombus formation at the site of vasospasm (43).

(5) A moyamoya-type vasculopathy occurring in 2 chronic cocaine users has been reported. One patient presented with aneurysmal subarachnoid hemorrhage, the other with bilateral ischemic stroke. Both patients had extensive collateral development with lenticulostriate networks (73). Patients with pseudocholinesterase deficiency may be especially vulnerable to cerebrovascular complications of cocaine because they are unable to metabolize the drug efficiently (34).

Methamphetamine. Stroke following methamphetamine use can occur after oral, intravenous, or inhalational use. Stroke occurs within minutes to hours after last use in many cases, but has been reported weeks and even months after last use (58; 44). Hemorrhagic stroke, including both intraparenchymal and subarachnoid hemorrhage, is more common than ischemic stroke, although both are possible (16; 50; 20; 67; 44).

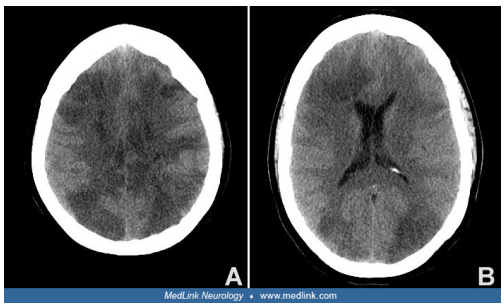
Methamphetamine may cause stroke through several mechanisms. As a sympathomimetic, methamphetamine can cause acute hypertension and chronic use may cause long-term hypertension. Hypertension is a major risk factor for both ischemic and hemorrhagic stroke. Vasospasm with superimposed thrombosis has also been proposed (63). Chronic administration of methamphetamine has been associated with a **necrotizing angiitis** involving arterioles and capillaries, which has been likened to polyarteritis nodosa and hypersensitivity angiitis (65; 66; 16; 05; 08). It is also possible that methamphetamine use may lead to accelerated atherosclerosis (30). Affected vessels have been described as beaded with segmental narrowing and aneurysm formation. These abnormalities are not restricted to the central nervous system (16). Finally, there is an increased risk of severe dilated cardiomyopathy in methamphetamine users, which may represent a cardioembolic source of ischemic stroke (33).

Amphetamine derivatives. Intracerebral hemorrhage has been described in patients using "ecstasy", or methylenedioxymethamphetamine, and a vascular malformation was identified in at least 1 patient (18). Ischemic stroke due to MDMA has also been described (49). Phenylpropanolamine and pseudoephedrine have been linked to deep and lobar hemorrhages occurring a few hours after ingestion (72; 39; 71). Angiography in 3 cases showed the beading classically associated with amphetamine use (72; 39). A large, case-control study confirmed an association between a first-use of phenylpropanolamine and hemorrhagic stroke in women; however, no association was identified with a first-use of pseudoephedrine (41). Chronic abusers of these substances may be at higher risk. Ephedrine use has been linked to subarachnoid and intracranial hemorrhage as well as, less commonly, ischemic stroke (79; 72; 07). Angiography disclosed an aneurysm in 1 patient with subarachnoid hemorrhage, and vasculitic changes in 2 patients with intracerebral hematomas. There have been a number of reports of stroke associated with the use of herbal remedies containing ephedra (68). A case-control study did not confirm an association with ephedra use and hemorrhagic stroke, except possibly with consumption of high doses of ephedra (55).

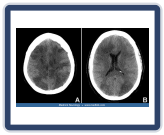
Ischemic stroke has been reported in users of prescription amphetamines and methylphenidate for **attention deficit hyperactivity disorder** (70). Large population studies, however, have failed to detect an increased risk of stroke in patients receiving pharmacotherapy for attention deficit hyperactivity disorder (29; 48). These studies may be limited by healthy user bias, but nonetheless, they are reassuring that these medications appear safe when used at typical doses in otherwise healthy subjects. Similarly, case reports of ischemic stroke possibly associated with phentermine have been described (42), but a large case-control study of an obese population did not identify an association between phentermine and stroke (21). These data highlight that there may be

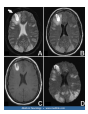
important differences across amphetamine derivative drugs that impact whether or not they present a risk for stroke.

Heroin. Heroin use most commonly causes stroke through complications of its intravenous injection. The use of nonsterile needles causes infective endocarditis and septic embolization. The mitral, aortic, and tricuspid valves are involved with varying frequencies (08; 53). Septic embolization and the rupture of mycotic aneurysms have been associated with ischemic stroke, subarachnoid hemorrhage, and diffuse vasculitis.



Stroke associated with heroin use (CT)
Axial noncontrast CT imaging through the brain at 2 different levels demonstrates multiple watershed areas of infarction throughout the brain in a young female having taken heroin. (Contributed by Dr. Gomez-Hassan.)





Peripheral thrombophlebitis secondary to repeated use of nonsterile needles may cause stroke through paradoxical embolism in a patient with a right-to-left intracardiac shunt. Foreign body embolization of talc and cornstarch admixed with heroin has also been documented. Rare cases of what is presumed to be a hypersensitivity angiitis have been reported in heroin users. Angiography in these cases demonstrated a small vessel arteritis or diffuse angiitis (08).

Cannabis and synthetic cannabinoids. There are case reports of stroke temporally associated with the use of both cannabis and synthetic cannabinoids (25; 03). Topical reviews have concluded that cannabis may increase stroke risk (78; 37), and proposed stroke mechanisms include cardiac arrhythmia, systemic hypotension, cerebral vasospasm, platelet aggregation, and/or oxidative stress (80; 02; 77; 15). Both cannabis and synthetic cannabis have also been suggested as causes of reversible cerebral vasoconstriction syndrome, which can present with subarachnoid hemorrhage, intraparenchymal hemorrhage, and ischemic stroke (22; 62). Data from the Behavioral Risk Factor Surveillance System, from the U.S. Centers for Disease Control, found that among adults 18 to 44 years of age, marijuana users (N=43,860) had higher odds of stroke compared to nonusers (adjusted OR 1.82, 95% CI 1.08-3.10). Furthermore, they found that the odds of stroke were greater among frequent users, defined as greater than 10 days per month (adjusted OR 3.12, 95% CI 1.4-6.97) and among marijuana users who also smoked tobacco (adjusted odds ratio 2.63, 95% CI 1.07-6.46) (61).

A statement by the American Heart Association indicated that "overall, evidence is still inconclusive for cannabis use and adverse cardiovascular outcomes, resulting in an urgent need for carefully designed, prospective short- and long-term studies. Ideally, controlled trials of various forms and routes of administration would be tested, but rigorous study of recreational drugs remains a challenge."

Given the wide use of cannabis and the methodologic limitations of existing literature, it is difficult to establish a causal link between cannabis use and stroke. There have been several large studies that have failed to detect an association between cannabis and stroke. A case-control study failed to find a significant association between cannabis use and stroke after adjusting for age, sex, ethnicity, and tobacco use (OR 1.59, 95% CI: 0.71-3.70) (01; 78). Another large population-based cohort study from Sweden did not find an association between cannabis use and stroke before 45 years of age (23). A scientific statement from the American Heart Association published in 2020 found that "overall, evidence is still inconclusive for cannabis use and adverse cardiovascular outcomes" (60).

Hallucinogens. As mentioned earlier, there are several case reports linking PCP to hemorrhagic stroke (04; 08). Data associating other hallucinogens (eg, LSD) with stroke are limited.

Barbiturates, other sedatives, and inhalants. There are no clear data associating these agents with stroke.

Epidemiology

The peak ages of patients with stroke related to drug abuse are in the third and fourth decades. The relative risk of stroke in drug users is 6.5 (95% confidence interval: 3.1 to 13.6) relative to nonusers, after controlling for other stroke risk factors. When restricted to those under 35, it is 11.7 (confidence interval: 3.2 to 42.5) (38). Epidemiologic evidence suggests that stroke associated with drug abuse has been increasing and that this is contributing to the increasing incidence of **stroke in young adults** (19). Little data are available regarding risk of stroke related to specific drugs of abuse; however, a study of hospital discharges in the United States found that there has been an increase in stroke related to infective endocarditis, from 2.4 to 18.8 hospitalizations per 10 million United States residents from 1993 to 2015 (59). The data in table 2 summarize estimates (%) of drug use in the past month during 2008 in different age categories (US Department of Health and Human Services 2008).

Table 2. Types of Illicit Drug Use in the Past Month (Percentages) 2008

Drug	12 to 17 years	18 to 25 years	26 years or older
Cocaine	0.4	1.5	0.7
Crack cocaine	0.0	0.2	0.2
Stimulant	0.5	1.1	0.2
Phencyclidine	0.1	0.0	*
Heroin	0.1	0.2	0.1

* Low precision; no estimate reported.

Prevention

Illicit drug use appears to wax and wane in cycles as a function of many factors, including availability, perceived risk to personal health, psychosocial status of the individual drug, and treatment efficacy.

Availability refers both to accessibility within a given geographical location and actual cost as a percentage of disposable income. Geographic availability means that the users can easily purchase a drug within their neighborhood. Theoretically, this can be reduced by interdicting drug transportation before local delivery and sale. Successful interdiction may reduce drug use through the resulting increase in cost passed on by distributors to consumers to cover losses. Popularity is also affected by the cost per dose, which may rise with reduce availability. Attempted interdiction has been stymied in many cases because drug production is ubiquitous; arresting 1 trafficker or destroying 1 region of cultivation does not sufficiently reduce availability.

Perceived risk refers to the health risks associated with drug use. The clearest example is the decline in intravenous drug use after it was linked to the intravenous transmission of HIV and AIDS. The popularity of heroin subsequently fell until the purity of street heroin was sufficient to afford a "high" with inhalational ingestion.

Psychosocial status refers to the perception of the ill effects of single or chronic use of an individual drug within the community. Crack cocaine use fell when communities saw the disastrous effects it had on users due to its addictive potential. Crack users seemed willing to sacrifice anything to obtain their next dose. Phencyclidine use fell when people noted the prevalence of "bad highs" characterized by paranoia and violence. Psychosocial status also refers to whether a community tolerates drug use among its members. Social stigmatization may reduce the likelihood of initial experimentation in the individual user. This is only effective when the attitudes of the community are conveyed to the potential drug user. Initial experimentation appears to begin among preadolescents and adolescents. Community attitudes have less effect when this age group has little parental or adult supervision. When illicit drug use is assigned low psychosocial status among all age groups, the demand for these substances will decline.

Treatment efficacy refers to the availability of treatment to help illicit drug users break their habit. It entails both medical care through the withdrawal syndrome (if present) and psychological counseling to deal with factors underlying psychological addiction.

Differential diagnosis

Stroke related to drug use should be considered in all young patients with stroke, particularly in the absence of traditional vascular risk factors. **Stroke in the young** has many mechanisms, including premature atherosclerosis, arterial dissection,

cardioembolism, **prothrombotic** states, and infection, and these should also be considered.

Diagnostic workup

Drug use should be suspected in any young person (under 55 years of age) who presents with a stroke. It should be remembered that drug use encompasses not only illegal substances like cocaine, methamphetamine, and heroin, but also diet pills, over-the-counter decongestants, prescription drugs, synthetic cannabinoids, and amphetamine derivatives. A detailed history should be sought from the patient, friends, and family. Urine toxicology screens should be sent immediately. They can be positive as early as 1 hour after ingestion and remain positive for 2 days to 3 days. Chronic users may have positive toxicology screens for longer periods. Importantly, synthetic cannabinoids and amphetamine derivatives are not tested for in routine urine toxicology screens.

In general, evaluation of the **young stroke** patient in the setting of drug abuse is similar to that of a patient without a history of drug use. In particular, it should be noted that patients with intracranial or subarachnoid hemorrhage associated with drug abuse are no less likely to harbor underlying vascular lesions than other patients. Head CT is done in all patients. A lumbar puncture is needed in patients with suspected subarachnoid hemorrhage when the CT scan is negative. MRI may be helpful to identify patterns of ischemic stroke. MR angiography or CT angiography may be helpful in identifying underlying vascular abnormalities (vasospasm, stenosis, occlusion, vascular malformations, aneurysms). Transcranial Doppler may also be useful in identifying vasospasm. Conventional angiography may be necessary to exclude the presence of aneurysms or vascular malformations in patients with subarachnoid or intracranial hemorrhage and may reveal evidence of vasculitis or vasospasm in patients with ischemic stroke due to cocaine, amphetamine, or amphetamine-like agents. Blood cultures and transesophageal echocardiography should be performed to exclude endocarditis in stroke patients who have used drugs intravenously. Finally, as drug abusers represent a high-risk population, patients should be tested for HIV, syphilis, and other infectious diseases for which clinical suspicion exists. In 1 series of 42 patients with cocaine-related stroke, 3 had HIV, 3 had hepatitis, 2 had syphilis, and 1 had **tuberculosis** (57).

Management

Acute therapy of stroke in patients with suspected drug abuse should be generally similar to the care provided to all stroke patients, including adequate hydration, close neurologic monitoring, and attention to preventing medical complications. The role of **tissue plasminogen activator** in ischemic stroke due to drug abuse likely depends on the presumed mechanism. In the case of stroke associated with cocaine use, there is evidence to suggest that a combination of vasospasm and superimposed thrombosis may occur; in such cases, thrombolysis may be a reasonable therapeutic option. A small cohort study of acute ischemic stroke patients treated with thrombolysis comparing 29 cocaine-positive to 75 cocaine-negative patients found no increased risk of treatment complications in the cocaine-positive group and similar outcomes between the 2 groups (52). Ischemic stroke due to infective endocarditis, on the other hand, is associated with a high risk of **hemorrhagic transformation** and tissue plasminogen activator is not recommended in this setting. Mechanical thrombectomy should be considered in acute stroke due to drug abuse when a large vessel occlusion is present.

In hemorrhagic stroke associated with acutely elevated blood pressure due to drug use, it may be reasonable to be somewhat more aggressive than usual in reducing blood pressure. Ideal therapy for ongoing vasculitis among users of methamphetamine has not been identified, in part because the pathogenesis of the vasculitis is unclear. Steroid therapy has been used in some patients on a short-term basis, but there is little evidence to suggest if this is beneficial. Calcium channel blockers, in particular the dihydropyridine agents (nifedipine, amlodipine, isradipine), have been advocated for the treatment of stroke in cocaine users, but no formal data exist regarding efficacy (36). Vascular malformations and aneurysms should be treated similarly to those occurring in patients without a history of drug abuse.

Patients should be closely monitored for symptoms of drug withdrawal and appropriate therapy instituted if necessary (eg, methadone in opiate addiction). As many abusers of illicit drugs also abuse alcohol, a low threshold should exist for initiating **benzodiazepines** for symptoms suggestive of alcohol withdrawal.

Long-term **secondary stroke prevention** strategies should obviously include cessation of the identified abused drug. Hypertension should be identified and treated. Antiplatelet therapy is probably indicated for patients with ischemic stroke, though there are limited data specifically applicable to stroke in the setting of drug abuse.

Special considerations

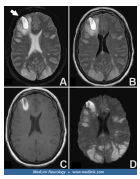
Pregnancy

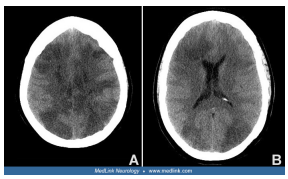
Neonatal **cerebral infarction**, both ischemic and hemorrhagic, has been reported in infants born to mothers who had used cocaine within 2 days to 3 days of delivery (12; 13). Elevated blood pressure and cerebral blood flow during the first 24 hours of life in these neonates may increase the risk of intracerebral hemorrhage.

Anesthesia

Anesthetic risks vary depending on the drug ingested and the cumulative effects of chronic drug use on health in general. Acute intoxication requires identification of the responsible agent before anesthesia or invasive procedures can be safely undertaken. A persistent prothrombotic state has been reported in some users of cocaine, methamphetamine, amphetamine derivatives, or other sympathomimetics. Angiography in these patients has been complicated by spontaneous intra-arterial thrombosis and cerebral infarction (79).

Media





References

01 Barber PA, Pridmore HM, Krishnamurthy V, et al. Cannabis, ischemic stroke, and transient ischemic attack: a case-control study. Stroke 2013;44(8):2327-9. **PMID 23696547**

02 Barnes D, Palace J, O'Brien MD. Stroke following marijuana smoking. Stroke 1992;9:1381. **PMID 1519298**

03 Bernson-Leung ME, Leung LY, Kumar S. Synthetic cannabis and acute ischemic stroke. J Stroke Cerebrovasc Dis 2014;23(5):1239-41. **PMID 24119618**

04 Bessen HA. Intracranial hemorrhage associated with phencyclidine abuse. JAMA 1982;248:585. **PMID 7097906**

05 Bostwick DG. Amphetamine induced cerebral vasculitis. Hum Pathol 1981;12(11):1031-3. **PMID 7319490**

06 Brown E, Prager J, Lee HY, Ramsey RG. CNS complications of cocaine abuse: prevalence, pathophysiology, and neuroradiology. AJR Am J Roentgenol 1992;159:137-47. **PMID 1609688**

07 Bruno A, Nolte KB, Chapin J. Stroke associated with ephedrine use. Neurology 1993;43:1313-6. **PMID 8327131**

08 Brust JC. Drug dependence. In: Baker AB, editor. Clinical neurology. Philadelphia: Harper & Row, 1986.

09 Brust JC. Spice, pot, and stroke. Neurology 2013;81(24):2064-5. **PMID 24212392**

10 Caplan L. Intracerebral hemorrhage revisited. Neurology 1988;38:624-7. **PMID 3352921**

11 Chang TR, Kowalski RG, Caserta F, Carhuapoma JR, Tamargo RJ, Naval NS. Impact of acute cocaine use on aneurysmal subarachnoid hemorrhage. Stroke 2013;44(7):1825-9. **PMID 23652270**

12 Chasnoff IJ, Bussey ME, Savich R, Stack CM. Perinatal cerebral infarction and maternal cocaine use. J Pediatr 1986;108:456-9. **PMID 3950828**

13 Chasnoff IJ, Griffith DR, MacGregor S, Dirkes K, Burns KA. Temporal patterns of cocaine use in pregnancy. Perinatal outcome. JAMA 1989;261:1741-4. **PMID 2918671**

14 Cheng YC, Ryan KA, Qadwai SA, et al. Cocaine use and risk of ischemic stroke in young adults. Stroke 2016;47(4):918-22. **PMID 26965853**

15 Choi SH, Mou Y, Silva AC. Cannabis and cannabinoid biology in stroke: controversies, risks, and promises. Stroke 2019;50(9):2640-5. **PMID 31366312**

16 Citron BP, Halpern M, McCarron M, et al. Necrotizing angiitis associated with drug abuse. N Engl J Med 1970;283:1003-11. **PMID 4394271**

17 Cregler LL, Mark H. Medical complications of cocaine abuse. N Engl J Med 1986;315:1495-9. **PMID 3537786**

18 De Silva RN, Harries DP. Ecstasy [letter]. BMJ 1992;305:310. **PMID 1356545**

19 de los Ríos F, Kleindorfer DO, Khoury J, et al. Trends in substance abuse preceding stroke among young adults: a population based study. Stroke 2012;43:3179-83. **PMID 23160887**

20 Delaney P, Estes M. Intracranial hemorrhage with amphetamine abuse. Neurology 1980;30:1125-8. **PMID 7191505**

21 Derby LE, Myers MW, Jick H. Use of dexfenfluramine, fenfluramine, and phentermine and the risk of stroke. Br J Clin Pharmacol 1999;47(5):565-9. **PMID 10336582**

22 Ducros A, Boukobza M, Porcher R, Sarov M, Valade D, Bousser MG. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 cases. Brain 2007;130(Pt 12):3091-101. **PMID 18025032**

23 Falkstedt D, Wolff V, Allebeck P, Hemmingsson T, Danielsson AK. Cannabis, tobacco, alcohol use, and the risk of early stroke: a population based cohort study of 45,000 Swedish men. Stroke 2017;48(2):265-70. **PMID 28028147**

24 Fandino J, Sherman JD, Zuccarello M, Rapoport RM. Cocaine-induced endothelin-1-dependent spasm in rabbit basilar artery in vivo. J Cardiovasc Pharmacol 2003;41(2):158-61. **PMID 12548074**

25 Freeman MJ, Rose DZ, Myers MA, Gooch CL, Bozeman AC, Burgin WS. Ischemic stroke after use of the synthetic marijuana "spice." Neurology 2013;81(24):2090-3. **PMID 24212384**

26 Giraldo EA, Taqi MA, Vaidean GD. A case-control study of stroke risk factors and outcomes in African American stroke patients with and without crack-cocaine abuse. Neurocrit Care 2012;16(2):273-9. **PMID 20645024**

27 Golbe LI, Merkin MD. Cerebral infarction in a user of free-base cocaine ("crack"). Neurology 1986;36:1602-4. **PMID 3785675**

28 Goodman Gilman A, Rall TW, Nies AS, Taylor P. Goodman and Gilman's the pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press, 1990.

29 Habel LA, Cooper WO, Sox CM, et al. ADHD medications and risk of serious cardiovascular events in young and middle-aged adults. JAMA 2011;306(24):2673-83. **PMID 22161946**

30 Ho EL, Josephson SA, Lee HS, Smith WS. Cerebrovascular complications of methamphetamine abuse. Neurocrit Care 2009;10(3):295-305. **PMID 19132558**

31 Huang QF, Gebrewold A, Altura BT, Altura BM. Cocaine-induced cerebral vascular damage can be ameliorated by Mg2+ in rat brain. Neurosci Lett 1990;109:113-6. **PMID 2314626**

32 Isner JM, Chokshi SK. Cocaine and vasospasm. N Engl J Med 1989;321:1604-6. **PMID 2586556**

33 Ito H, Yeo KK, Wijetunga M, Seto TB, Tay K, Schatz IJ. A comparison of echocardiographic findings in young adults with cardiomyopathy: with and without a history of methamphetamine abuse. Clin Cardiol 2009;32:E18-22. **PMID 19330818**

34 Jatlow P, Barash PL, van Dyke C, Byck F. Impaired hydrolysis of cocaine in plasma from succinylcholine sensitive patients. AFCR Clin Pharm 1976;24:255A.

35 Jerry J, Collins G, Streem D. Synthetic legal intoxicating drugs: the emerging 'incense' and 'bath salt' phenomenon. Clev Clin J Med 2012;79(4):258-64. **PMID 22473725**

36 Johnson BA, Devous MD Sr, Ruiz P, Ait-Daoud N. Treatment advances for cocaine-induced ischemic stroke: focus on dihydropyridine-class calcium channel antagonists. Am J Psychiatry 2001;158(8):1191-8. **PMID 11481148**

37 Jouanjus E, Raymond V, Lapeyre-Mestre M, Wolff V. What is the current knowledge about the cardiovascular risk for users of cannabis-based products? A systemic review. Curr Atheroscler Rep 2017;19(6):26. **PMID 28432636**

38 Kaku DA, Lowenstein DH. Emergence of recreational drug abuse as a major risk factor for stroke in young adults. Ann Intern Med 1990;113:821-7. **PMID 2240897**

39 Kase CS, Foster TE, Reed JE, Spatz EL, Girgis GN. Intracerebral hemorrhage and phenylpropanolamine use. Neurology 1987;37:399-404. **PMID 3822132**

40 Kaye BR, Fainstat M. Cerebral vasculitis associated with cocaine abuse. JAMA 1987;258:2104-6. **PMID 3656626**

41 Kernan WN, Viscoli CM, Brass LM, et al. Phenylpropanolamine and the risk of hemorrhagic stroke. N Engl J Med 2000;343:1826-32. **PMID 11117973**

42 Kokkinos J, Levine SR. Possible association of ischemic stroke with phentermine. Stroke 1993;24:310-3. **PMID 8421834**

43 Konzen JP, Levine SR, Garcia JH. Vasospasm and thrombus formation as possible mechanisms of stroke related to alkaloidal cocaine. Stroke 1995;26:1114-8. **PMID 7762031**

44 Lappin JM, Darke S, Farrell M. Stroke and methamphetamine use in young adults: a review. J Neurol Neurosurg Psychiatry 2017;88(12):1079-91. **PMID 28835475**

45 Levine SR, Brust JC, Futrell N, et al. Cerebrovascular complications of the use of the "crack" form of alkaloidal cocaine [comment]. New Engl J Med 1990;323(11):699-704. **PMID 2388668**

46 Levine SR, Brust JC, Futrell N, et al. A comparative study of the cerebrovascular complications of cocaine: alkaloidal vs. hydrochloride: a review. Neurology 1991;41:1173-7. **PMID 1866000**

47 Levine SR, Welch KM, Brust JC. Cerebral vasculitis associated with cocaine abuse or subarachnoid hemorrhage. (letter to the editor). JAMA 1988;259:1648.

48 Liu H, Feng W, Zhang D. Association of ADHD medications with the risk of cardiovascular disease: a meta-analysis. Eur Child Adolesc Psychiatry 2019;28(10):1283-93. **PMID 30143889**

49 Manchanda S, Connolly MJ. Cerebral infarction in association with ecstasy abuse. Postgrad Med J 1993;69:874. **PMID 7904748**

50 Margolis MT, Newton TH. Methamphetamine ("speed") arteritis. Neuroradiology 1971;2:179-82. **PMID 5164222**

51 Martin K, Rogers T, Kavanaugh A. Central nervous system angiopathy associated with cocaine abuse. J Rheumatol 1995;22:780-2. **PMID 7791183**

52 Martin-Schild S, Albright KC, Misra V, et al. Intravenous tissue plasminogen activator in patients with cocaine-associated acute ischemic stroke. Stroke 2009;40:3635-7. **PMID 19745181**

53 Mathew J, Addai T, Arnand A, Morrobel A, Maheshwari P, Freels S. Clinical features, site of involvement, bacteriologic findings, and outcome of infective endocarditis in intravenous drug users. Arch Intern Med 1995;155:1641-8. **PMID 7618988**

54 Mizutani T, Lewis RA, Gonatas NK. Medial medullary syndrome in a drug abuser. Arch Neurol 1980;37:425-8. **PMID 7387487**

55 Morgenstern LB, Viscoli CM, Kernan WN, et al. Use of Ephedra-containing products and risk for hemorrhagic stroke. Neurology 2003;60(1):132-5. **PMID 12525737**

56 Morrow PL, McQuillen JB. Cerebral vasculitis associated with cocaine abuse. J Forensic Sci 1993;38:732-8. **PMID 8515225**

57 Nanda A, Vannemreddy P, Willis B, Kelley R. Stroke in the young: relationship of active cocaine use with stroke mechanism and outcome. Acta Neurochir Suppl 2006;96:91-6. **PMID 16671433**

58 Ohta K, Mori M, Youritaka A, et al. Delayed ischemic stroke associated with methamphetamine use. J Emerg Med 2005;28:165-7. **PMID 15707812**

59 Omran SS, Chatterjee A, Chen ML, Lerario MP, Merkler AE, Kamel H. National trends in hospitalizations for stroke associated with infective endocarditis and opioid use between 1993 and 2015. Stroke 2019;50(3):577-82. **PMID 30699043**

60 Page RL, Allen LA, Kloner RA, et al. Medical marijuana, recreational cannabis, and cardiovascular health: a scientific statement from the American Heart Association. Circulation 2020;142(10):e131-52. **PMID 32752884**

61 Parekh T, Pemmasani S, Desai R. Marijuana use among young adults (18-44 years of age) and risk of stroke: a Behavioral Risk Factor Surveillance System Survey analysis. Stroke 2020;51(1):308-10. **PMID 31707926**

62 Rose DZ, Guerrero WR, Mokin MV, et al. Hemorrhagic stroke following use of the synthetic marijuana "spice". Neurology 2015;85(13):1177-9. **PMID 26320200**

63 Rothrock JF, Rubenstein R, Lyden PD. Ischemic stroke associated with methamphetamine inhalation. Neurology 1988;38:589-92. **PMID 3352918**

64 Rowley HA, Lowenstein DH, Rowbotham MC, Simon RP. Thalamomesencephalic strokes after cocaine abuse. Neurology 1989;39:428-30. **PMID 2927656**

65 Rumbaugh CL, Bergeron RT, Scanlan RL, et al. Cerebral vascular changes secondary amphetamine abuse in the experimental animal. Radiology 1971;101:345. **PMID 5000427**

66 Rumbaugh CL, Fang HC, Higgins RE, et al. Cerebral microvascular injury in experimental drug abuse. Invest Radiol 1976;11:282-94. **PMID 821897**

67 Sachdeva K, Woodward KG. Caudal thalamic infarction following intranasal methamphetamine use. Neurology 1989;39:305-6. **PMID 2915804**

68 Samenuk D, Link MS, Homoud MK, et al. Adverse cardiovascular events temporally associated with ma huang, an herbal source of ephedrine. Mayo Clin Proc 2002;77(1):12-6. **PMID 11795249**

69 Sauer CM. Recurrent embolic stroke and cocaine-related cardiomyopathy. Stroke 1991;22:1203-5. **PMID 1926265**

70 Schteinschnaider A, Plaghos LL, Garbugino S, et al. Cerebral arteritis following methylphenidate use. J Child Neurol 2000;15:265-7. **PMID 10805196**

71 Sloan MA, Kittner SJ, Rigamonti D, Price TR. Occurrence of stroke associated with use/abuse of drugs. Neurology 1991;41:1358-64. **PMID 1891081**

72 Stoessl AJ, Young GB, Feasby TE. Intracerebral haemorrhage and angiographic beading following ingestion of catecholaminergics. Stroke 1985;16:734-6. **PMID 4024187**

73 Storen EC, Wijdicks EF, Crum BA, Schultz G. Moyamoya-like vasculopathy from cocaine dependency. AJNR 2000;21:1008-10. **PMID 10871003**

74 Togna G, Tempesta E, Togna AR, Dolci N, Cebo B, Caprino L. Platelet responsiveness and biosynthesis of thromboxane and prostacyclin in response to in vitro cocaine treatment. Haemostasis 1985;15:100-7. **PMID 3924789**

75 Toossi S, Hess CP, Hills NK, Josephson SA. Neurovascular complications of cocaine use at a tertiary stroke center. J Stroke Cerebrovasc Dis 2010;19(4):273-8. **PMID 20444626**

76 US Department of Health and Human Services. Substance Abuse and Mental Health Services Administration. Results from the 2008 National Survey on Drug Use and Health: National Findings. http://www.oas.samhsa.gov/nsduh/2k8nsduh/2k8Results.cfm#Ch2. Accessed March 4, 2010.

77 White D, Martin D, Geller T, Pittman T. Stroke associated with marijuana abuse. Pediatr Neurosurg 2000;32:92-4. **PMID 10838508**

78 Wolff V, Armspach JP, Lauer V, et al. Cannabis-related stroke: myth or reality. Stroke 2013;44:558-63. **PMID 23271508**

79 Wooten MR, Khangure MS, Murphy MJ. Intracerebral hemorrhage and vasculitis related to ephedrine abuse. Ann Neurol 1983;13:337-40. **PMID 6342508**

80 Zachariah SB. Stroke after heavy marijuana smoking. Stroke 1991;22:406. **PMID 2003312**

Contributors

Author

Michael T Mullen MD

Dr. Mullen of the Hospital of the University of Pennsylvania has no relevant financial relationships to disclose.

SEE PROFILE

Editor

Steven R Levine MD

Dr. Levine of the SUNY Health Science Center at Brooklyn has no relevant financial relationships to disclose.

SEE PROFILE

Former Authors

Birgitte H Bendixen MD PhD (original author), Scott Eric Kasner MD, and Brett Cucchiara MD

Patient Profile

Age range of presentation

0-01 month, 6-65+ years

Sex preponderance

male>female, >1:1

Heredity

none

Population groups selectively affected

none selectively affected

Occupation groups selectively affected

none selectively affected

ICD & OMIM codes

ICD-9

Drug dependence: 304

Nondependent abuse of drugs: 305

Cerebral thrombosis: 434.0

Cerebral embolism: 434.1

Cerebral artery occlusion, unspecified: 434.9

Cerebral atherosclerosis: 437.0

Intracerebral hemorrhage: 431

Subarachnoid hemorrhage: 430

Transient cerebral ischemia: 435

Acute, but ill-defined, cerebrovascular disease: 436

ICD-10

Drug dependence syndrome: F11.2, F13.2, F14.2

Harmful use of drugs: F11.1, F13.1, F14.1

Occlusion and stenosis of other cerebral artery: I66.8

Occlusion and stenosis of unspecified cerebral artery: I66.9

Cerebral atherosclerosis: I67.2

Intracerebral haemorrhage, unspecified: I61.9

Subarachnoid haemorrhage, unspecified: I60.9

Vertebro-basilar artery syndrome: G45.0

Cerebrovascular accident NOS: I64

Questions or Comment?

MedLink, LLC
3525 Del Mar Heights Rd, Ste 304
San Diego, CA 92130-2122

Toll Free (U.S. + Canada): 800-452-2400
US Number: +1-619-640-4660
Support: service@medlink.com
Editor: editor@medlink.com