Drug abuse and renal disease

Emerging global causes of kidney disease

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Major types of illicit drugs

- Cannabis
- Amphetamines
- Cocaine
- Opioids/Heroin
Drug abuse

- Cannabis is by far the most commonly used illicit drug worldwide.
- Heroin and amphetamine dependence are the two most common forms of illicit drug dependence in the world.
- Cocaine dependence has the lowest estimated prevalence.
- Ever-growing global burden of illicit drug use and dependence.
The Role of Science in Addressing the Opioid Crisis

Nora D. Volkow, M.D., and Francis S. Collins, M.D., Ph.D.

Figure 1. Scientific Strategies for Combating the Opioid Epidemic.
An asterisk denotes strategies that are largely based on preclinical findings, which therefore have more uncertain outcomes and timelines.
Far døde av heroinoverdose. Mor er ruset. Besteforeldrene har overtatt foreldreløsens vare.
Tre millioner amerikanske barn har det som Melina Crettier (7).
• An estimated 149-271 million people worldwide used an illicit drug in 2009, 11-21 million of those injected drugs.
• Levels of illicit drug use seem to be highest in high-income countries and in countries near major drug production areas. Data from low-income countries are poor.
• All forms of drug dependence and disease burden are highest in men.
Global burden of drug abuse

- Drug abuse is a recognized contributor to the global burden of disease.
- The most harmful forms of illicit drug use is injecting drug use.
Global burden of drug abuse

• Opioid dependence, accounts for the highest proportion of illicit drug burden in the world.

• Drug injection play a central role in the transmission of blood-born infections such as hepatitis B and C and HIV.
Nephrotoxic effects of illicit drugs

• The kidneys can be injured in diverse ways by illicit drugs, both directly and indirectly.  
• The kidneys high degree of filtration make them specially susceptible.  
• When taken in an overdose they all can cause coma followed by traumatic rhabdomyolysis.  
• Most/all illicit drugs or their adulterants can lead to interstitial nephritis.
Cannabis

• Cannabis is the most commonly used illegal substance worldwide.
• The drug is generally smoked.
• The major adverse health effects of cannabis use are dependence and mental disorders.
• There is no data on cannabis causing renal disease.
Amphetamines

• Natural amphetamine:
  – Khat

• Synthetic drugs:
  – Amphetamine
  – Metamphetamine
  – Ecstasy/MDMA

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Amphetamine/Methamphetamine

- 17 million users worldwide, highest prevalence in the north of Europe.
- Taken orally, nasally or smoked (seldom).
- Injection is common among high-risk users.
Ecstasy/MDMA

• Becoming more popular again.
• Commonly used in the form of ecstasy tablets or snorted as powder
• In 2013, over 17 million Americans and 13 million Europeans reported having ever used ecstasy.
• The Ecstasy/MDMA use is highest in young adults.
Amphetamines-Renal manifestations

• Direct nephrotoxic effect is uncertain.

• Acute renal injury.
  – Nontraumatic rhabdomyolysis caused by hyperthermia, extreme exertion and dehydration.

• Hyponatremia
  – Intake of excessive water.
  – Increased free water caused by elevated levels of antidiuretic hormone. Ecstasy is a potent inducer of secretion of antidiuretic hormone.
Cocaine

• Cocaine is extracted from the South American coca plant.
• One of the oldest and most addictive psychoactive substance in existence.
• 14-21 million users worldwide, highest prevalence in North America.
• Taken orally, nasally or smoked, by intravenous injection, or vaginal or anal suppository placement.
Cocaine- Renal manifestations

• Cocaine use may impair kidney function by a variety of mechanisms:
  – Hemodynamics/vasoconstriction.
  – Platelet aggregation.
  – Increased oxidative stress.
  – Induction of renal atherogenesis.

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Cocaine and kidney injury: a kaleidoscope of pathology
Narender Goel,1,2 James M. Pullman,3 and Maria Coco2
Cocaine-Renal manifestations

• Acute renal injury
  – Rhabdomyolysis.
  – Renal infarction.
  – Thrombotic microangiopathy and malignant hypertension.
  – Vasculitis.

• Chronic kidney disease
  – Evidence linking cocaine and chronic kidney disease is limited.

• Hypertension
• Rhabdomyolysis
  – Vasoconstriction causing muscle ischemia and necrosis.
  – Direct toxicity.
  – Increased muscle activity from agitation or seizure.
  – Hyperthermia.
• Renal infarction
  – Uncommon, thought to be underreported.
  – All routes of cocaine administration have been associated with renal infarction.
• Pathophysiology:
  – Enhanced platelet aggregation and increased tromboxane synthesis.
  – Vasoconstriction through diverse mechanisms involving catecholamines and endothelin.

• Treatment:
  – Conservative and pain management.
• No long term data on the risk of CKD related to renal infarction.

Cocaine-induced renal infarction: report of a case and review of the literature
Shahrooz Bemanian¹, Mazda Motallebi² and Saeid M Nosrati³

BMC Nephrology 2005, 6:10
• **Thrombotic microangiopathy and malignant hypertension**
  – Cocaine is a potent activator of the sympathetic nervous system leading to intense vasoconstriction in both cardiac and peripheral vasculature.
  – Acute cocaine intoxication can cause severe, hypertension even with thrombotic microangiopathy and end-organ damage.
  – Usually self-limited.
• **Hypertension**
  – Cocaine use is not usually associated with chronic hypertension.
  – Appears to enhance the progression of renal disease in patients with hypertension.
• **Vasculitis**

• Cutting cocaine with adulterants in an effort to increase profits is common.

• Levamisole has been used as an immunomodulator in humans but is now only used as an anti-helmintic medication in animals.

• About 70% of cocaine is adulterated with Levamisole.

• Levamisole is proposed to be the mediator of cocaine-induced vasculitis.
• Necrotizing pauci-immune glomerulonephritis.
  – neutropenia, high-titer MPO ANCA, PR3-ANCA, ANA and lupus anticoagulant.
• Characteristic necrotic skin lesions on face and ears.
• Urine toxicology screen positive for cocaine and Levamisole.
• Treatment
  – drug cessation, if possible.
  – supportive care.
  – most cases require immunosuppression.

• Increasing incidence, awareness is important.
• Little data on prognosis but case reports on progression to end stage renal disease.
Heroin

• Heroin is extracted from the opium poppy.
• Synthetic opioids: Methadone, Buprenorphine and Fentanyl.
• 12-21 million users worldwide.
• The mortality rates due to overdose is highest in Northern Europe.
Heroin

• Heroin can be smoked, snorted and injected.
• Injection is the most harmful way of use.
  – contaminated drugs and inadequately sterile technique with injection can lead to localized and systemic infections.
  – shared needles or syringes is associated with an increased risk of infection with HIV, hepatitis B, and hepatitis C.
Renal manifestations

- Heroin users have a dramatically increased risk for ESRD.
- Heroin nephropathy
- HIV-associated nephropathy – HIVAN
- Hepatitis B related renal disease.
- Hepatitis C related renal disease.
- AA-amyloidosis.
Heroin Nephropathy

• Described for the first time in the late 1970’s.
• Nephrotic syndrome with a progression to renal failure.
• Renal histological appearance of FSGS.
• Predilection for black patients.
• The pathogenesis of heroin nephropathy is uncertain.
• Heroin nephropathy has largely disappeared
  – purity of street heroin has increased.
  – drug abusers have become HIV positive and either die earlier or develop HIV nephropathy.
  – heroin nephropathy represented a variety of renal disorders that are now recognized to be associated with other conditions.
HIV-associated nephropathy – HIVAN

- HIV is highly prevalent in injecting drug users.
- Great geographical variance.
- HIVAN was described for the first time in 1984.
- Heavy proteinuria with fast progression to ESRD.

Figure: Estimated number of injecting drug users (IDUs) and regional prevalence of HIV in people who inject drugs


Associated Focal and Segmental Glomerulosclerosis in the Acquired Immunodeficiency Syndrome


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HIVAN

- Collapsing form of FSGS.
- Predilection for black patients.
- HIVAN as a leading cause of ESRD in young African-American adults.
- Potent antiretroviral therapy has reduced the incidence of ESRD attributed to HIVAN.
Hepatitis B

- Endemic in part of the world. Mother-to-child transmission is the predominant mode of transmission.
- In low-endemic areas (US, Canada, Western Europe) the prevalence is <2%, infection occurs mostly sexually or through injecting drug abuse.
Renal manifestations

- Membranous glomerulonephritis.
- Membranoproliferative glomerulonephritis.
- Polyarteritis nodosa.

- The widespread use of hepatitis B vaccination has decreased the incidence of HBV-related renal disease in the US and Western Europe.
Hepatitis C

- HCV prevalence among injecting drug abusers is higher than 50% in most countries.
- Most patients infected with HCV in the US and Europe acquired the disease through intravenous drug abuse.
Renal manifestations

• Mixed cryoglobulinemia syndrome.
• Polyarteritis nodosa.
• Membranoproliferative glomerulonephritis.
  – Reported as the most predominant renal disease in white injecting drug abusers.

In-Depth Review

Chronic Nephropathies of Cocaine and Heroin Abuse: A Critical Review

Jared A. Jaffe and Paul L. Kimmel
Division of Renal Diseases and Hypertension, Department of Medicine, George Washington University Medical Center, Washington, DC

• New direct-acting antiviral drugs will hopefully lead to better outcome and a lower incidence of hepatitis C related renal disease in the years to come.
AA-amyloidosis

• AA-amyloidosis is a potential complication to chronic inflammation and infection.
• In intravenous drug abusers it is thought to be related to chronic skin infections from ”skin popping”.
• The kidney is the organ most frequently affected.
• Characterized by nephrotic proteinuria and a progressive renal disease.
Erik Heyerdahl Strøm M.D.
Dept. of Pathology
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• The first case report was published in 1978 in New York.
• The prevalence seems to be increasing worldwide.
• Renal amyloidosis is now the most common chronic renal disease in injecting drug abusers in Norway.

**Article**

July 1978

**Amyloidosis Secondary to Drug Abuse and Chronic Skin Suppuration**

Harold Jacob, MD; Chaim Charytan, MD; Joel H. Rascoff, MD; et al

Author Affiliations


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**Renal amyloidosis in intravenous heroin addicts with nephrotic syndrome and renal failure**

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• As of today 20 % of our dialysis population are past and present injecting drug abusers.
• Since the year 2005 we have had 46 injecting drug abusers in treatment at our dialysis ward at Oslo University hospital, Ulleval.
• Renal biopsy was performed in 34 of these 46 patients (74%).
• AA-amyloidosis was confirmed in 33 of 34 (97%).
• Male predominance; 70/30.
• Mean age is 50.2 years
• They have been injecting drug abusers for 25 years in mean.
• They have all had recurrence of suppurative skin infections, and a high incidence of sepsis and endocarditis.
• All patients are HCV antibody positive.
• 4.3% are HIV positive.
• Challenging group of patients.
• Continuous drug abuse.
• Poor adherence to dialysis and other medical treatment.
• Chronic infections.
• Renal transplantations is therefore not an option.
• The prognosis is poor.
Preventive measures

• Ensure that people at risk of developing drug dependence are identified and helped at an early stage.
• Good rehabilitation opportunities.
• Easy access to medication-assisted therapies.
• Free syringe and needle distribution centers.
• Drug injecting rooms.
• Free treatment of sores.
• Testing for and treatment of hepatitis C, B and HIV.
Summary

• The prevalence of illicit drug use is increasing in developed countries.
• Amphetamines, Cocaine and Heroin can cause reduced renal function in different ways.
• Injecting drug abuse is the most harmful form of illicit drug use.
Summary

• The incidence of Cocaine-induced vasculitis seems to be increasing.
• HCV is highly prevalent in injecting drug abusers.
• HCV-related glomerulonephritis is reported to be the most prevalent renal disease in caucasian drug abusers.
• The incidence of AA-amyloidosis is increasing and it is now the most common renal disease in Norwegian drug abusers on dialysis.
Conclusion

• The global burden of renal disease related to abuse of illicit drugs is expected to rise in the years to come.
• Illicit drug use should be considered in the differential diagnosis of any patient with unexplained renal pathology.
• With an ageing population of injecting drug abusers we might be facing a new era in drug abuse-related renal diseases.
• This population of patients is complex and challenging, and will raise many medical and ethical questions.
• More focus on prevention and early intervention is needed.
Thank you