

New Lethal Forms of Cocaine Driving the Emerging Stimulant Epidemic: Impact on Public Health Systems

Thom Browne Jr., MA

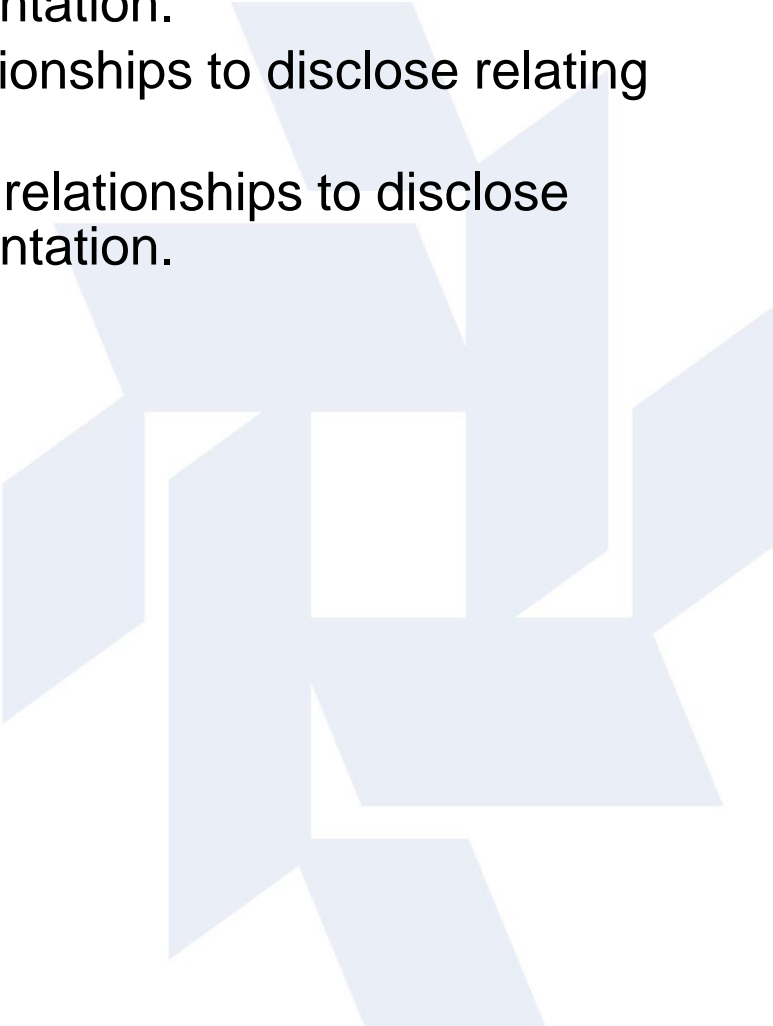
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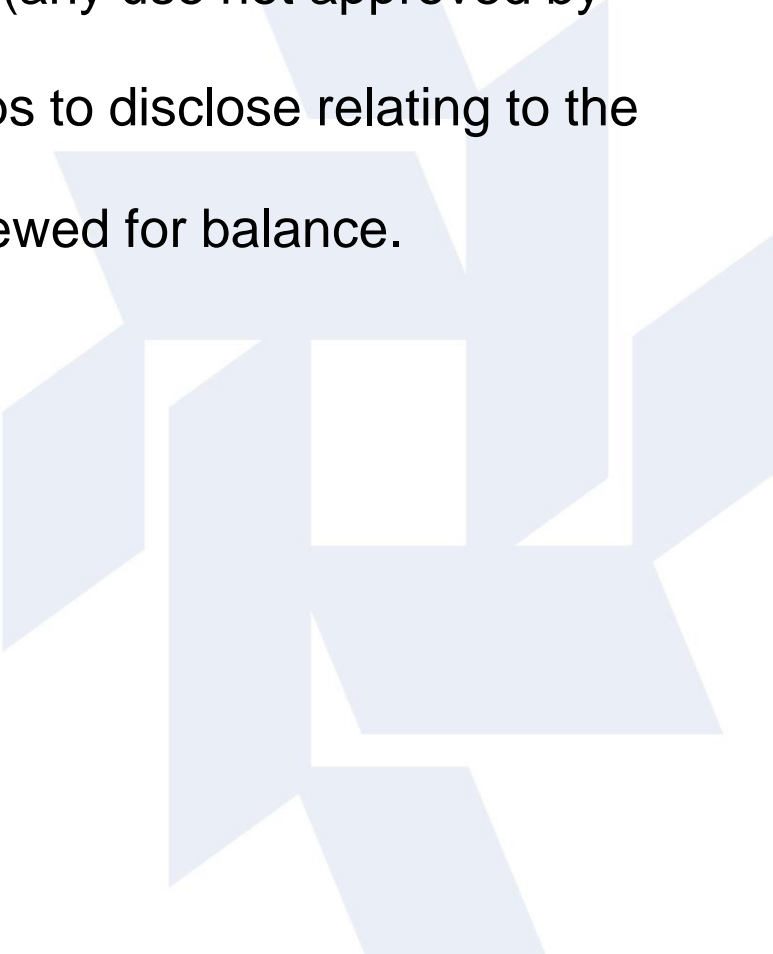
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Faculty Disclosure

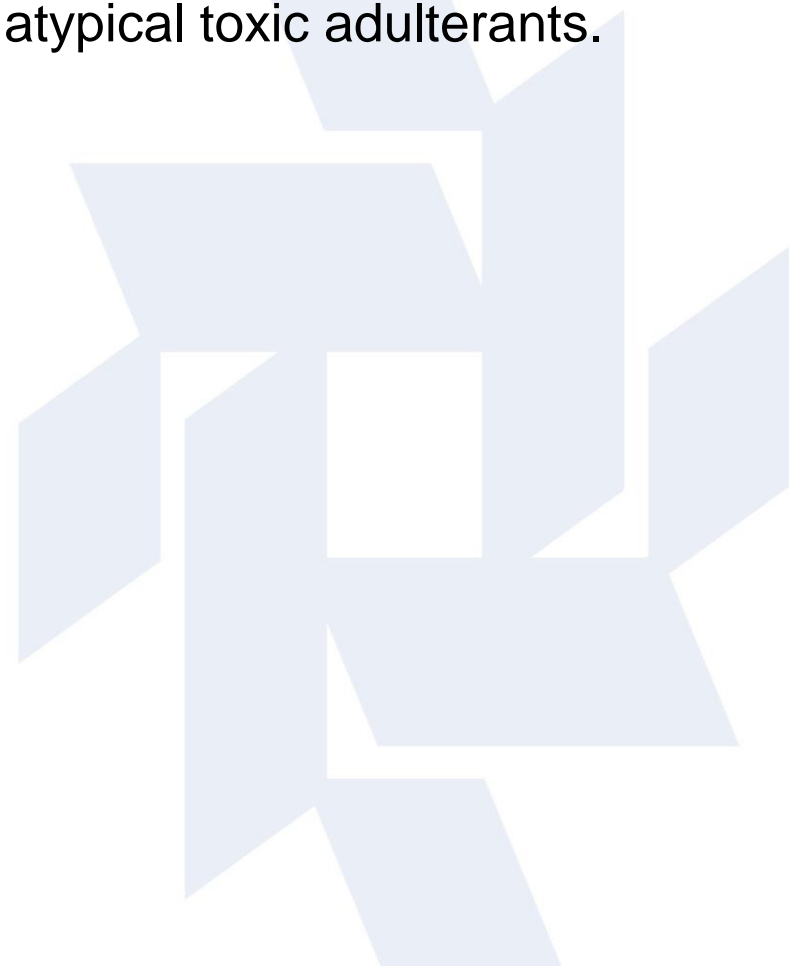
- **Thom Browne Jr., MA**, has no financial relationships to disclose relating to the subject matter of this presentation.
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Disclosure

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
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Learning Objectives

- Identify the major toxic adulterants appearing in cocaine.
- Explain the health-related effects of individual toxic adulterants.
- Apply existing technologies for detecting atypical toxic adulterants.



Genesis of Global Toxic Adulterant Project

- **In 2010, Brazil treatment centers at a national conference asked INL for assistance in finding the cause of unusual infections, diseases, and health problems among cocaine-using clients**
- **INL contacted Brazil Federal Police (DPF) National Institute of Criminalistics drug testing lab for information on composition of cocaine samples seized throughout Brazil**
- **DPF chemists had analyzed thousands of cocaine samples (HCl & Crack) and published numerous articles on cocaine composition in peer-reviewed journals**
- **Data showed that aminopyrine, phenacetin, and levamisole were new toxic adulterants being added to cocaine since 2010**
- **Adulterants which reduced white blood cells (aminopyrine & levamisole) explained infections & diseases due to compromised immune systems**

**Chemical Profile of Cocaine Samples
in Sao Paulo – Nov. 2014
(1144 samples)**

| Adulterants | Crack | HCl |
|--------------------|-------|-----|
| Phenacetin | 60% | 6% |
| Aminopyrine | 25% | 1% |
| Levamisole | 1% | 50% |

Chemical Profile of Cocaine Samples in the Southern Cone - 2012

| | Brazil | Chile | Paraguay | Uruguay | Argentina |
|------------------------------------|-----------------|-----------------|----------------|-----------------|-----------------|
| No. Samples Tested: | 40 | 20 | 20 | 9 | 15 |
| Average Purity (Range) | (29.7% - 89.6%) | (15.8% - 92.2%) | (4.6% - 84.6%) | (35.8% - 82.4%) | (17.4% - 18.4%) |
| Number (%) with Adulterants | 30 (75%) | 8 (40%) | 17 (85%) | 9 (100%) | 15 (100%) |
| Phenacetin | 26 (65%) | 1 (5%) | 13 (65%) | 2 (22%) | 15 (100%) |
| Levamisole | 1 (3%) | | 1 (5%) | 2 (22%) | |
| Other | 3 (7%) | 7 (35%) | 3 (15%) | 5 (55%) | |
| Aminopyrine + Phenacetin | 16 (40%) | - | 8 (40%) | 1 (11%) | |

April 2016 Drug Adulterant Testing Results

Peru

PCB (cocaine paste base): 1 combo

1. Phenacetin



May 2016 Drug Adulterant Testing Results

Argentina

Paco (cocaine paste base): 2 combos

1. Phenacetin and Metamizole
2. Phenacetin and Aminopyrine

Ecuador

New street drug called **"H"**

-- Heroin cut with diltiazem, phenacetin, and cocaine

-- Heroin cut with aminopyrine, diltiazem, tolycaine, noxiptiline, and diethyl phthalate

Cocaine HCl

-- cut with levamisole and lidocaine

**Chemical Profile of Drug Samples
in South Africa – May 2017
(50 samples each)**

| Adulterants | Cocaine | Heroin |
|----------------------|---------|--------|
| Phenacetin | 94% | 32% |
| Acetaminophen | -- | 18% |
| Levamisole | 16% | -- |

August 2017 Drug Adulterant Testing Results

- INL/Colombo Plan Drug Testing in **Tegucigalpa, Honduras** detected *Levamisole* Levels in Cocaine HCL samples between **60 – 80 %**
- Honduras is a Transit Country for U.S. Bound Cocaine
- *Levamisole* levels in U.S. Cocaine HCl samples were **13%** in July 2014*

*DEA Cocaine Signature Program Report. July 2014.

Health Consequences of Adulterants

| Adulterant | Classification | Country Detected | Health Consequences | Street Drug |
|-------------|-------------------------------------|--|--|---|
| Phenacetin | Analgesic | United States, Ecuador, Argentina, Peru, South Africa, Brazil | <ul style="list-style-type: none"> *Hemolytic anemia (reduction red blood cells) *Kidney Failure *Bladder/Kidney Cancer *Analgesic Nephropathy *Hematological disorders | Heroin, "H," Coca Paste, Paco, Cocaine HCl, Crack |
| Levamisole | Medication used for expelling worms | United States, Ecuador, Argentina, Brazil, South Africa, Sri Lanka, Honduras | <ul style="list-style-type: none"> *Fever *Agranulocytosis (reduction white blood cells) | Cocaine HCl, Heroin, Methamphetamine |
| Lidocaine | Local Anesthetic | United States, Ecuador, Brazil, South Africa | <ul style="list-style-type: none"> *CNS Problems *Nausea, *Vomiting *Dizziness *Tremors *Convulsions *Arrhythmia | Cocaine HCl, Heroin |
| Benzocaine | Local Anesthetic | United States, South Africa, Brazil | <ul style="list-style-type: none"> *Blood disorder (Methemoglobinemia: inability to release oxygen effectively to body tissues) | Crack, Heroin |
| Aminopyrine | Analgesic Anti-inflammatory | United States, Argentina, Brazil, Ecuador | <ul style="list-style-type: none"> *Agranulocytosis (reduction white blood cells) | Crack, Paco, Heroin, "H" |

Health Consequences of Adulterants

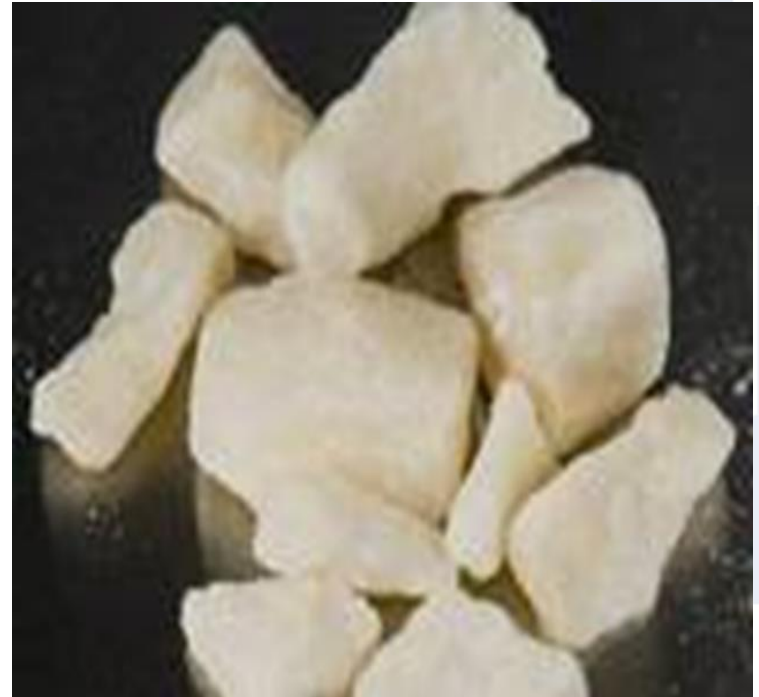
| Adulterant | Classification | Country Detected | Health Consequences | Street Drug |
|---------------------|--|---|--|--------------------------------------|
| Diltiazem | Calcium channel blocker Antihypertensive drug | United States, Ecuador | <ul style="list-style-type: none"> *Heroin laced with Diltiazem could cause users to overdose *Bradycardia *Hypotension *Potentiates cocaine toxicity & toxic cardiac effects | Heroin, "H" |
| Metamizole/Dipyrone | Pain killer Fever reliever Spasm reliever | United States, Argentina | <ul style="list-style-type: none"> *Agranulocytosis (reduction white blood cells) *Aplastic anemia | Heroin, Paco |
| Acetaminophen | Analgesic | United States, South Africa, Afghanistan, | <ul style="list-style-type: none"> *With heroin, dramatically depresses heart rate/breathing *Acute liver (hepatic) failure *Coma *Cocaine increases hepatotoxicity (liver damage) | Heroin, Cocaine HCl |
| Diphenhydramine | Antihistamine | United States | <ul style="list-style-type: none"> *With heroin, dramatically depresses heart rate/breathing *Tachycardia *Torsade de Pointes *Encephalitis *Seizures | Heroin, Cocaine HCl, Methamphetamine |

Severe Health Problems Accelerated with Adulterated Drugs versus Adulterated Aspirin

**Health Problems from Aspirin Containing
Phenacetin Took Years to Appear. Aspirin was
Taken as needed for Pain in the 1960s**



**Crack Used 15 X day X 7 days/week X 6 months
Today Health Problems Appear within Months**



Expansion of Toxic Adulterant Project to the U.S. (2017)

- Realizing that the same source countries for Latin America, Asia, and Africa also supplied the United States with drugs, INL and Colombo teamed with JMJ Technologies and NMS Labs to test U.S. street-level drug samples for the same toxic adulterants detected worldwide
- NMS Labs obtained over 500 street-level drug samples from state-level drug testing labs in Vermont and Kentucky
- Analysis showed that opioids, cocaine, and other drugs are adulterated with multiple, highly toxic adulterants like other countries worldwide
- Results of this analysis indicated a **'hidden' adulterant epidemic** that adds a new, unforeseen dimension to the U.S. opioid overdose crisis

- The general narrative today is that fentanyl-laced heroin and cocaine, and overprescribing of opioid pain medicines are driving the nation's overdose epidemic.
- This narrative ***“fails to capture the full dimensions of the problem and leads to inadequate and even confounding solutions.”*** *
- The current drug problem is **far more complex.**

*DuPont, R.L. (2017). The opioid epidemic is an historic opportunity to improve both prevention and treatment. Brain Research Bulletin, pii:S0361-9230(17), 3092-3097.

- A 2016 CDC study found that fentanyl was detected in over half (**56%**) of the 5,512 opioid overdose deaths in ten states between July – December 2016.*
- However, in 2017 there were an estimated 72,306 drug overdose deaths according to CDC, of which 29,406 (**41%**) were due to synthetic opioids such as fentanyl.**
- Thus, fentanyl is undoubtedly contributing to overdose rates, but it is far from their only cause.

*O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016. MMWR Morb Mortal Wkly Rep 2017;66:1197–1202. DOI: <http://dx.doi.org/10.15585/mmwr.mm6643e1>

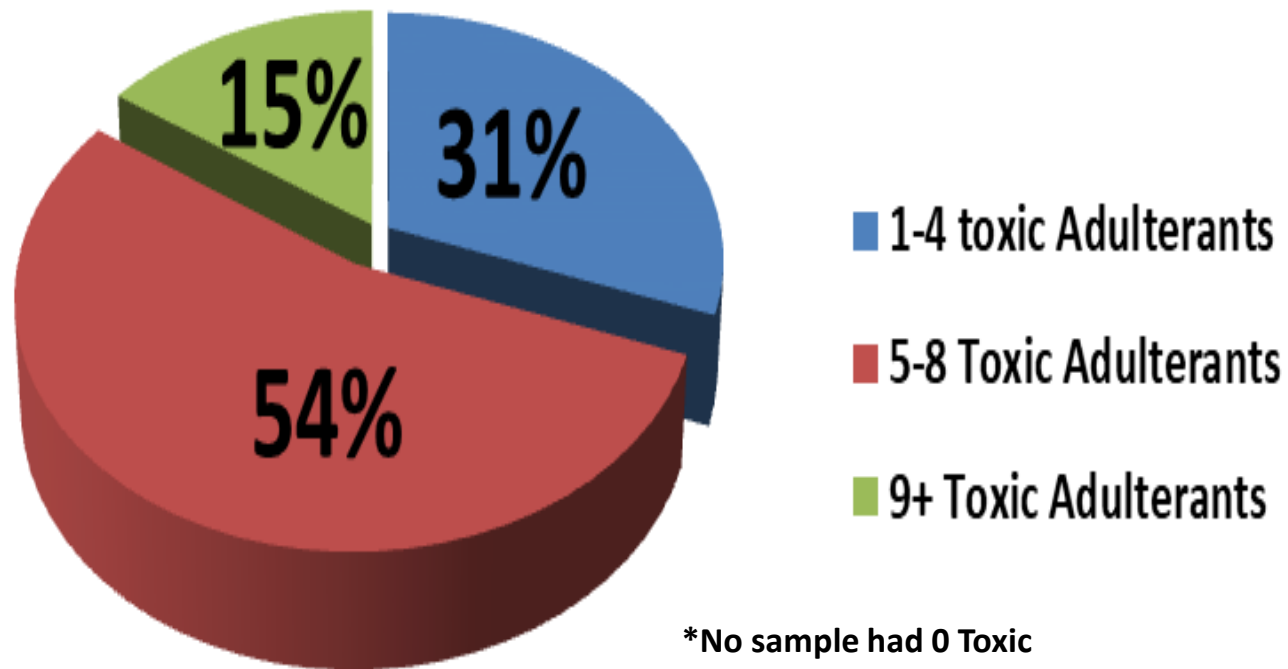
**NIDA, Overdose Death Rates, revised August 2018

Opioids, cocaine, and other drugs are now increasingly cut with multiple, highly toxic substances, in some cases as many as **ten (10)** adulterants, other controlled drugs, and impurities from the heroin manufacturing process, in addition to fentanyl.

U.S. drug samples analysis shows that fentanyl was not the only toxic adulterant in seized materials tested by Quadrupole Time of Flight (QTOF) Mass Spectroscopy, a technology not routinely available in analysis of seized materials or biological samples.

This novel U.S. data suggest that absent fentanyl, overdose and severe near-term health problems, even death, could occur due to a **synergistic and poisonous effect of multiple toxic adulterants, other controlled substances, and heroin impurities now routinely added to street drugs.**

TOTAL KY & VT DRUG SAMPLES (n=431)



*No sample had 0 Toxic Adulterants

Vermont & Kentucky Street-level Drug Samples (2016 - 2017)

| VT #156 | VT #160 | KY #26 | KY #105 |
|---------------|---------------|-----------------|-----------------|
| Cocaine | Cocaine | Cocaine | Cocaine |
| Heroin | Heroin | Heroin | Heroin |
| Tramadol | Fentanyl | Tramadol | Fentanyl |
| Ketamine | Levamisole | Fentanyl | 4-ANPP |
| Fentanyl | Acetaminophen | 4-ANPP | Acetaminophen |
| Aminopyrine | Quinine | Aminopyrine | Diphenhydramine |
| Diltiazem | Lidocaine | Diphenhydramine | Levamisole |
| Quinine | Procaine | Quinine | Phenacetin |
| Quetiapine | Caffeine | Lidocaine | Quinine |
| Caffeine | Acetylcodeine | Dipyron | Caffeine |
| Acetylcodeine | 6-MAM | Caffeine | Acetylcodeine |
| 6-MAM | Papaverine | Acetylcodeine | 6-MAM |
| Noscapine | Noscapine | 6-MAM | Papaverine |
| Papaverine | | Papaverine | Noscapine |
| Morphine | | Noscapine | |

Legend:

Black = controlled drugs

Purple = fentanyls

Red = adulterants

Green = impurities from heroin manufacturing process

Kentucky Drug Sample Containing Fentanyl

| | | | |
|------|---------|----------|--|
| KY26 | Fayette | 4/4/2017 | <p>Caffeine (0.73, 39687) Diphenhydramine (2.04, 723315) Lidocaine (0.63, 33334) Aminopyrine (0.63, 3296) Tramadol (0.78, 4107) Cocaine (1.07, 1923) 4-ANPP (1.96, 11284) Acetylcodeine (0.71, 5834) 6-MAM (0.56, 881) Heroin (0.72, 100970) Fentanyl (1.99, 494025) Quinine/Quinidine (0.84, 21406) Papaverine (1.5, 7189) Noscapine (1.6, 757897) Dipyrone Breakdown Products</p> |
|------|---------|----------|--|

Kentucky Drug Sample without Fentanyl

KY159

Jessamine

5/3/2017

Acetaminophen (0.55, 50242)

Caffeine (0.59, 105451)

Diphenhydramine (2.04, 225665)

Cocaine (1.11, 11312)

Quinine/Quinidine (0.88, 421766)

6-MAM (0.56, 12828)

Papaverine (1.55, 21837)

Heroin (0.17, 958644)

Noscapine (1.64, 334002)

Acetylcodeine (0.73, 23106)

Methamphetamine (0.57, 10477)

Amphetamine (0.58, 23824)

Super Speedball Effect

[Quintuple Depressant / Double Stimulant]

| | | | |
|-------|----------|-----------|---|
| KY100 | Franklin | 3/20/2017 | Methamphetamine (0.57, 21175) Cocaine (1.12, 2315) Morphine (0.57, 181) Acetylcodeine (0.75, 32444) 6-MAM (0.56, 15581) Heroin (0.78, 933919) Papaverine (1.55, 8458) |
|-------|----------|-----------|---|

- The VT and KY adulterants include, but are not limited to, **banned pharmaceuticals, veterinary products, analgesic pain relievers, sedatives, antihistamines, opioid pain medications, muscle relaxants, antiarrhythmics, and impurities from the heroin manufacturing process.**
- These compounds have been associated with severe health effects, including **decreased production of red and white blood cells due to bone marrow damage, multifocal inflammatory leukoencephalopathy, hemolytic uremic syndrome, renal failure, multiple malignancies, and life-threatening cardiac arrhythmias.***
- Variation in the substances used to adulterate street drugs and their concentrations contributes to the unpredictability of the drug's effects, and the potential for unknown, unexpected, and potentially life-threatening effects.**

*Mark Gold. Deadly Adulterants: New Dangers of Illicit Drugs. The Sober World Magazine – July 2017.

*Phillips et al. Cardiac complications of unwitting co-injection of quinine/quinidine with heroin in an intravenous drug user. J Gen Intern Med 27(12): 1722-5.

**Cole et al. Adulterants in illicit drugs: a review of empirical evidence. Drug Testing Analysis 2011, 3, 89 – 96.

These toxic adulterants can cause numerous medical consequences including death.

However, these adulterants are not routinely tested by forensic laboratories on seized materials, medical examiners, or emergency rooms.

Emerging Cocaine Threat to the U.S.

The composition of street-level cocaine has changed significantly over the last decade, posing a greater public health threat

- Cocaine availability and use in the United States increased between 2015 and 2016, with some indicators (including past year cocaine initiates, and cocaine-involved poisoning deaths) reaching levels equal to or greater than 2007 availability levels, and are likely to continue increasing in the near term.*
- The CDC reported cocaine-involved drug poisoning deaths in 2015 increased for the third straight year, with more cocaine deaths recorded in 2015 (6,784) than any other year in the prior decade except 2006. This represents a 25.2 percent increase in cocaine-related overdose deaths from 2014 to 2015.*

* U.S. Department of Justice, Drug Enforcement Administration. (2017). 2017 National Drug Threat. DEA-DCT-DIR-040-17. Washington, DC: DEA. Available: https://www.dea.gov/docs/DIR-040-17_2017-NDTA.pdf

Multiple threats include:

1. Higher levels of levamisole in street samples
2. Cardiovascular threat of phenacetin/levamisole combinations
3. Adulteration with multiple, toxic adulterants like heroin (with and without fentanyl)
4. Pink cocaine in the form of the powerful stimulant/hallucinogenic 2C-B
5. Dragonfly cocaine: a cocaine, ketamine, and MDMA mixture
6. New toxic cocaine in the form of translucent flakes or fly wings

Cocaine is Toxic

- Cocaine greatly influences the cardiovascular system and is a well known trigger of acute coronary syndromes*
- Toxic effects of cocaine include arterial vasoconstriction**
- Cocaine causes transient increases in blood pressure, respiratory rate, and heart rate**

*Kloner RA & Rezkalla SH. Cocaine and the Heart. New Engl J Med 2003;348(6):487-8.

**Katarzyna M, et al, Acute coronary syndrome after levamisole-adulterated cocaine abuse. Journal of Forensic & Legal Medicine, 21 (2014) 48-52.

Levamisole is Toxic

- An accumulating body of literature has described a clear link between levamisole-adulterated cocaine use and the occurrence of **neutropenia** and **agranulocytosis**, **vasculitis**, **retiform purpura** and other forms of **skin necrosis**, **vasculopathy**, **arthralgia**, and **leukoencephalopathy***
- Chronic exposure to levamisole-contaminated cocaine is associated with **broad cognitive and neuroanatomical impairments** (e.g., executive function deficits and pronounced thinning of the lateral prefrontal cortex)**
- Levamisole is also linked to **neurotoxic effects** with regular use of levamisole-contaminated cocaine**

*Brunt TM, et al, Adverse effects of levamisole in cocaine users: a review and risk assessment. Arch. Toxicol. 91, 2303-2313 (2017).

*Lee KC, et al, Complications associated with use of levamisole-contaminated cocaine: an emerging public health challenge. Mayo Clin. Proc. 87, 581-586 (2012).

**Vonmoos M, et al, Cognitive and neuroanatomical impairments associated with chronic exposure to levamisole-contaminated cocaine. Translational Psychiatry (2018)8:235.

Levamisole: Role as an Adulterant

- It is suggested that levamisole increases the number of D1 dopamine receptors in the brain and potentiates the intense “high” of cocaine*

*Hofmaier T, et al, Aminorex, a metabolite of the cocaine adulterant levamisole, exerts amphetamine like actions at monoamine transporters. *Neurochem Int* (2014) Jul; 73(100): 32-41.

*Tallarida CS, et al, Levamisole and cocaine synergism: a prevalent adulterant enhances cocaine’s action in vivo. *Neuropharmacology*, 2014 Apr;79:590-5.

*Katarzyna M, et al, Acute coronary syndrome after levamisole-adulterated cocaine abuse. *Journal of Forensic & Legal Medicine*, 21 (2014) 48-52.

*Larocque A & Hoffman RS, Levamisole in cocaine: Unexpected news from an old acquaintance. *Clin Toxicol*, 2012 Apr;50(4):231-41.

Levamisole: Role as an Adulterant

- The neurobiological effects of levamisole combined with cocaine have been the subject of many studies over last decade*
- Levamisole potentiates the euphoria and psychostimulant effects of cocaine*
- From a neurobiological standpoint, levamisole has a psychostimulant effect that is synergic with that of cocaine, which means greater addictive potential and greater risk of dependence**

*Larocque & Hoffman (2012); Lee, Ladizinski, & Federman (2102); Auffenberg, Rosenthal, & Dresner (2013); Tallardia, Tallardia, & Rawls (2015); Brunet et al (2017); Kudlacek et al (2017)

**Raymon & Isenschmid (2009); Dube (2010), Tallardia et al (2014)

Levamisole Metabolized into Aminorex

- A metabolite (aminorex) of levamisole acts to prolonged the high and enhance the stimulant effects associated with cocaine*
- Recent research reveals levamisole may be partially metabolized into an amphetamine-like compound (aminorex) which could increase dopamine concentration in the reward pathway and thus activate endogenous opioids**
- After the cocaine effect “fades out” the levamisole/aminorex effects “kicks in”*
- Humans & horses metabolize levamisole to aminorex, an amphetamine-like drug***
- In conclusion, levamisole/aminorex can mimic the effects of cocaine at a fraction of the cost**

*Hofmaier T, et al, Aminorex, a metabolite of the cocaine adulterant levamisole, exerts amphetamine like actions at monoamine transporters. *Neurochem Int* (2014) Jul; 73(100): 32-41.

*Hess C, et al, Metabolism of levamisole and kinetics of levamisole and aminorex in urine by means of LC-QTOF-HRMS and LC-QqQ-MS. *Anal Bioanal Chem*. 2013 May;405(12):4077-88.

**Mark Gold. Deadly Adulterants: New Dangers of Illicit Drugs. *The Sober World Magazine* – July 2017.

***Karch SB, et al, Aminorex poisoning in cocaine abusers. *Int J Cardiol*. 2012 Jul 26;158(3):344-6.

Aminorex

- Aminorex is an amphetamine derivative developed in 1960s as an appetite suppressant by pharmaceutical industry*
- It was withdrawn from the market and sales were banned in 1972*
- Aminorex has a psychostimulant effect significantly greater than cocaine**

*Kudlacek O, et al, (2017). Cocaine adulterants and effects on monoamine transporters. The Neuroscience of Cocaine. Elsevier Inc.
<https://doi.org/10.1016/B978-0-12-803750-8.00007-5>

**Chang A, et al, (2010). Levamisole: A dangerous new cocaine adulterant. Clinical Pharmacology and Therapeutics, 88(3), 408-411.

Aminorex and Idiopathic Pulmonary Hypertension

- Aminorex is a proven cause of potentially fatal Idiopathic Pulmonary Hypertension (IPH)*
- Aminorex ingestion was responsible for a 5-year epidemic (1969 – 1972) of Idiopathic Pulmonary Hypertension (IPH) in Switzerland, Austria, and Germany**
 - IPH: arteries in the lungs become blocked or narrowed, making it harder for the heart to pump blood through them
 - Raises blood pressure in the lungs and causes heart to weaken, which may eventually lead to heart failure

*Karch SB, et al, Aminorex associated with possible idiopathic pulmonary hypertension in a cocaine user. Forensic Sci Int. 2014 Jul;240:e7-10.

**Karch SB, et al, Aminorex poisoning in cocaine abusers. Int J Cardiol. 2012 Jul 26;158(3):344-6.

Combined Levamisole/Aminorex Effect on Cocaine

- It has been suggested that the modulating effects of aminorex on the dopamine transporters are independent of those produced by levamisole*
- Both effects are more long-lasting than those induced by cocaine*
- Therefore, both levamisole and aminorex may prolong the psychostimulant effect*

*Hofmaier T, et al, Aminorex, a metabolite of the cocaine adulterant levamisole, exerts amphetamine like actions at monoamine transporters. *Neurochemistry International*, 73(1), 32-41.

Nationwide Public Health Alert Issued Concerning Life-Threatening Risk Posed by Cocaine Laced with Veterinary Anti-Parasite Drug

Monday, September 21, 2009

The Substance Abuse and Mental Health Services Administration (SAMHSA) is alerting medical professionals, substance abuse treatment centers and other public health authorities about the risk that substantial levels of cocaine may be adulterated with levamisole – a veterinary anti-parasitic drug. Ingesting cocaine mixed with levamisole can seriously reduce a person's white blood cells, suppressing immune function and the body's ability to fight off even minor infections. People who snort, smoke, or inject crack or powder cocaine contaminated by levamisole can experience overwhelming, rapidly-developing, life threatening infections. Other serious side effects can also occur.

According to the Drug Enforcement Administration and State testing laboratories, the percentage of cocaine specimens containing levamisole has increased steadily since 2002, with levamisole now found in over 70 percent of the illicit cocaine analyzed in July. Levamisole can severely reduce the number of white blood cells, a problem called agranulocytosis. THIS IS A VERY SERIOUS ILLNESS THAT NEEDS TO BE TREATED AT A HOSPITAL. **For more information, contact the SAMHSA Press Office at 240-276-2130.**

Levamisole Levels in Cocaine from 2014 – 2017 were Higher than in 2009 when Nationwide Health Alert Issued (per DEA Cocaine Signature Reports)

January 2014: *“Many South American cocaine laboratory operators add diluents to the finished product prior to pressing it into bricks. Of all CY 2013 bricks examined, **68% contained Levamisole.**”*

July 2014: *“Of all bricks examined, **72% contained Levamisole.** The average concentration of levamisole in cocaine bricks was 13% (130 grams per kilogram).”*

July 2016: *“Of all bricks examined, **93% contained Levamisole.**”*

April 2017: *“Of all bricks examined, **86% contained Levamisole.**”*

2018: *“Of all bricks examined, **40% contained Levamisole.**”*

Levamisole Levels in Individual Cocaine Samples Increasing (was **13%** in July 2014)*

Majority Compound in Some KY Cocaine HCl Samples in April/May 2017

| | | | |
|-------|---------|----------|--|
| KY7 | Fayette | 4/4/2017 | Levamisole (0.56, 287387) Cocaine |
| KY102 | Fayette | 5/2/2017 | Levamisole (0.56, 172243) Cocaine (0.95, 164908) |
| KY109 | Fayette | 5/2/2017 | Levamisole (2.09, 11705872 intensity) Cocaine (2053934 intensity) |

Majority Compound in Honduran Cocaine HCl Samples in August 2017

- INL/Colombo Plan Drug Testing in **Tegucigalpa, Honduras** detected *Levamisole* Levels in Cocaine HCL samples between **60 – 80 %**
- Honduras is a Transit Country for U.S. Bound Cocaine

*DEA Cocaine Signature Program Report. July 2014.

Cardiovascular Threat of Phenacetin/Levamisole Combinations

Phenacetin

- Phenacetin induces hemolytic anemia, a disorder in which red blood cells are destroyed prematurely, affecting oxygen transfer*

*Millar J, et al, Phenacetin-induced hemolytic anemia. Can Med Assoc J (1972) Apr 8; 106(7): 770–775

Levamisole

- Humans metabolize levamisole to aminorex*
- Aminorex ingestion responsible for Idiopathic Pulmonary Hypertension (IPH)**
 - IPH: arteries in the lungs become blocked or narrowed, making it harder for the heart to pump blood through them

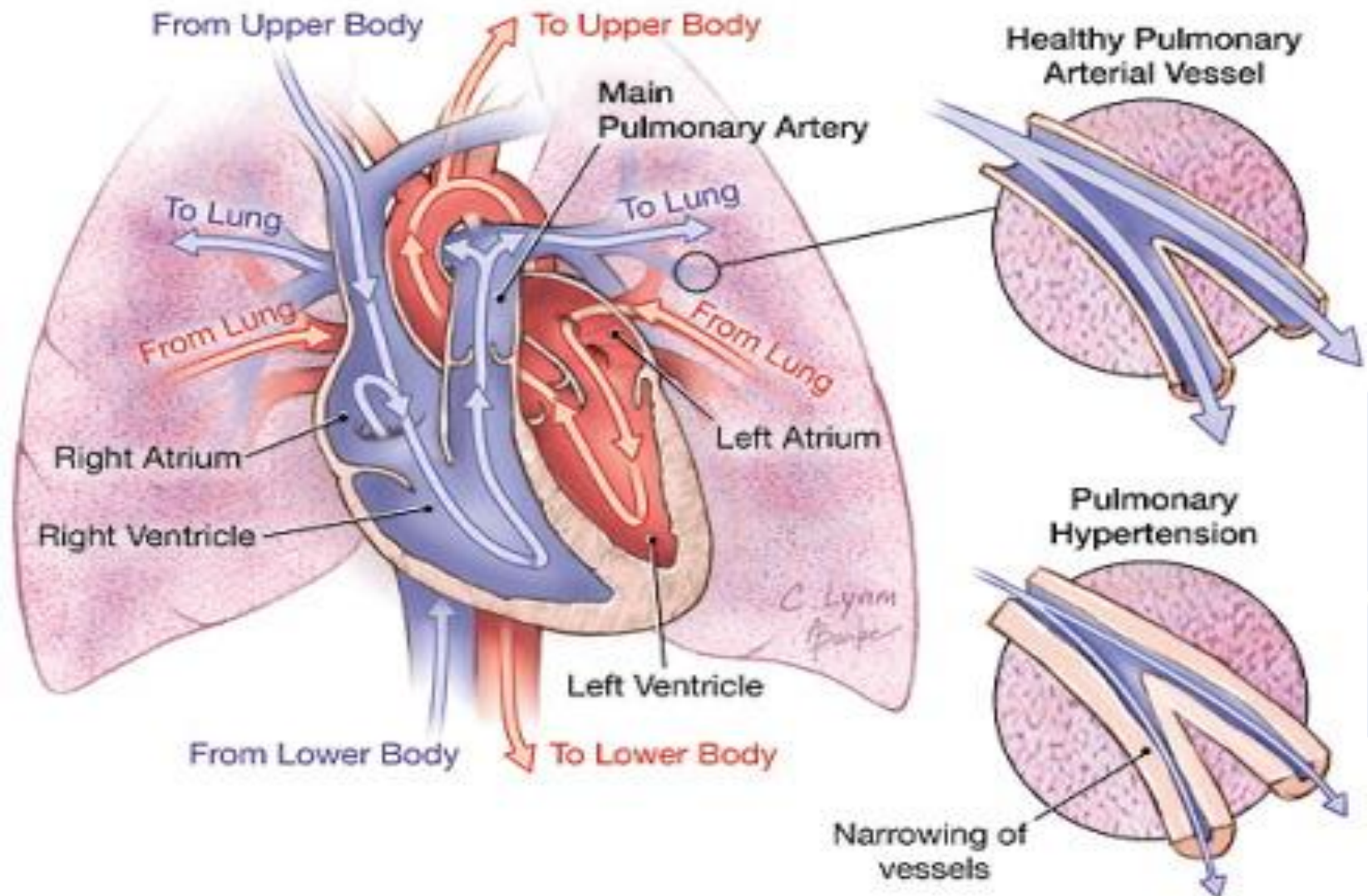
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**Karch SB, et al, Aminorex poisoning in cocaine abusers. Int J Cardiol (2011);158(3):344-6

Increased Phenacetin/Levamisole Combos Seen in the U.S.

| | | | |
|-------|-----------------|-----------|---|
| VT174 | Drug Task Force | 2/28/2017 | Levamisole (0.56, 441991) Phenacetin (1.83, 916049) Cocaine (1.19, 2837588) |
| VT175 | Drug Task Force | 2/28/2017 | Levamisole (0.57, 376319) Phenacetin (1.83, 576256) Cocaine (1.24, 2004025) |
| VT275 | Washington | 4/12/2017 | Levamisole (0.56, 247441) Phenacetin (1.82, 735535) Cocaine (1.19, 1526700) |
| VT147 | Washington | 2/3/2017 | Phenacetin (1.81, 709968) Cocaine (1.08, 1616122) Levamisole (0.56, 248922) |
| VT285 | Washington | 4/12/2017 | Levamisole (0.56, 305458) Heroin (0.93, 1588) Phenacetin (1.82, 807932) Cocaine (1.21, 1758522) |
| VT286 | Washington | 4/12/2017 | Levamisole (0.56, 293287) Cocaine (1.24, 1796324) Heroin (0.97, 1116) Hydroxyzine (2.21, 68643) Phenacetin (1.83, 195528) Lidocaine (0.71, 5391) |

Idiopathic Pulmonary Hypertension (IPH)



Cocaine Increasingly Cut Like Heroin with Fentanyl + Adulterants

| | | | |
|------|---------|-----------|---|
| KY76 | Fayette | 4/11/2017 | Caffeine (0.44, 69) Diphenhydramine (2.05, 1563) Levamisole (0.56, 455444) Cocaine (1.17, 4260945) Fentanyl (2.29, 153) Quinine/Quinidine (0.93, 933) |
| KY85 | Fayette | 4/11/2017 | Cocaine (1.16, 4243053) Levamisole (0.56, 438374) Fentanyl (2.01, 2104) |

Toxicological Results of Cocaine Adulterant Testing

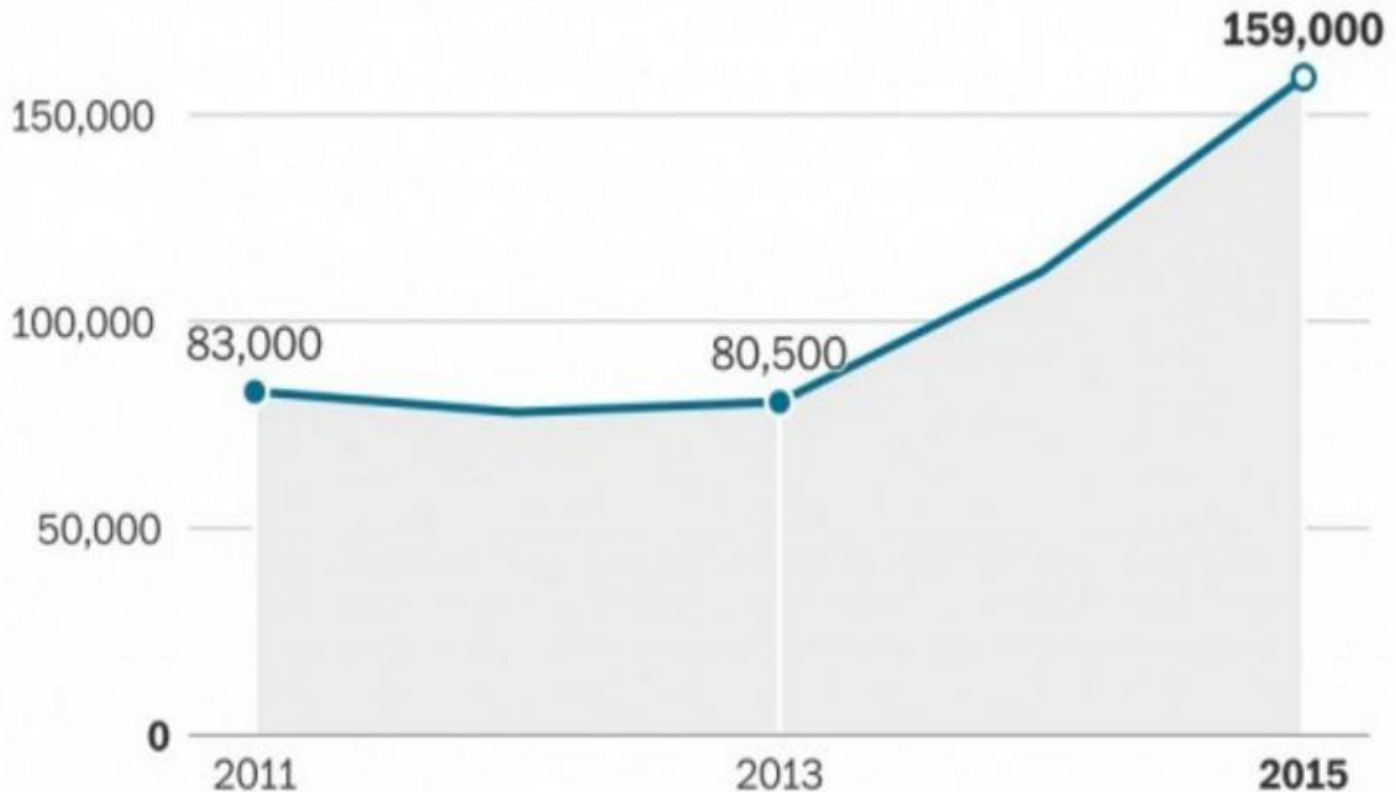
A Pilot Study in Sao Paulo, Brazil

An abstract graphic composed of several overlapping, semi-transparent light blue geometric shapes, including rectangles and trapezoids, arranged in a complex, layered pattern on the right side of the slide.

Increased Coca Cultivation in Colombia

Colombia's coca boom

Coca cultivation is on the rise in Colombia.



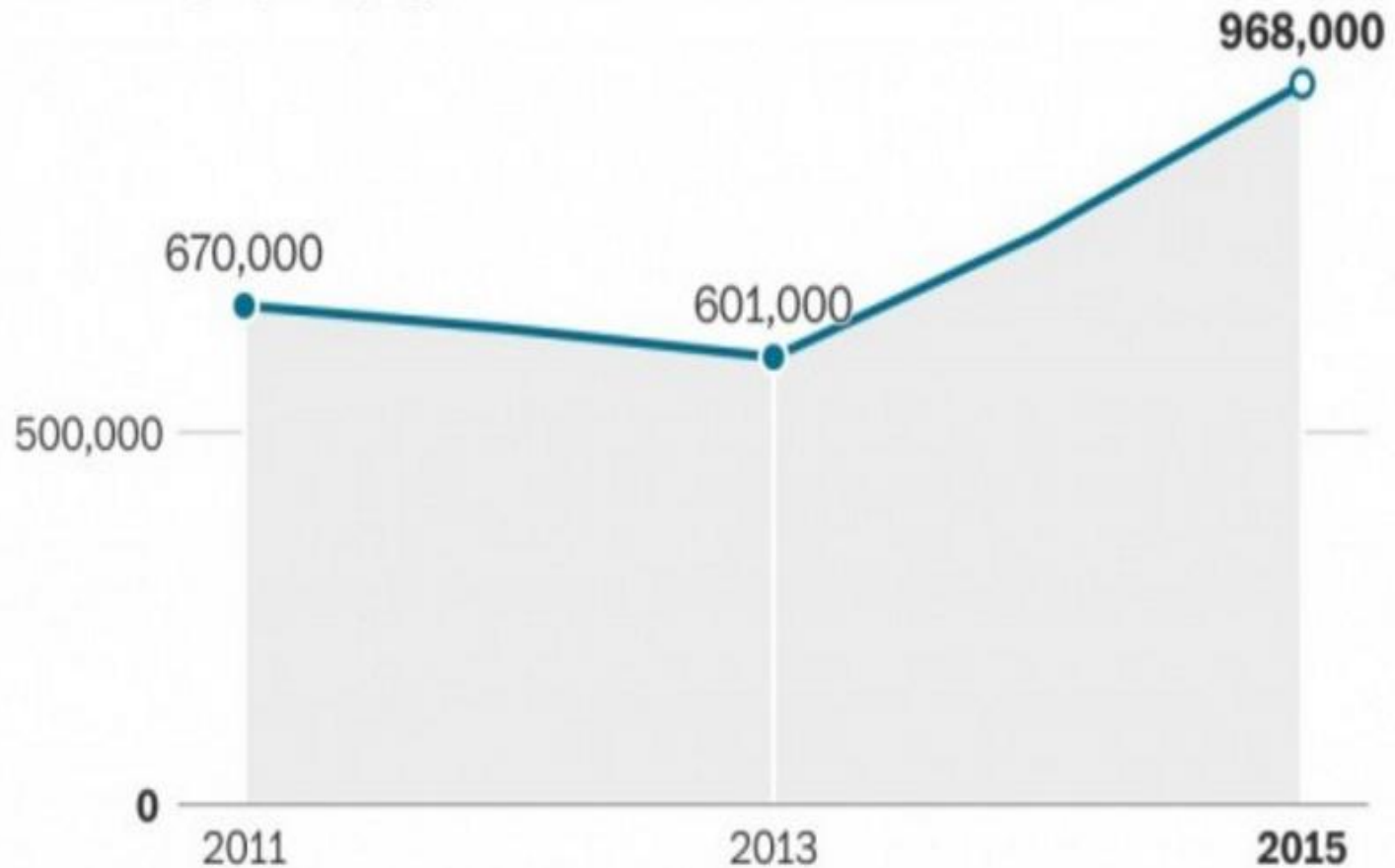
Figures are in hectares, an area equal to about 2.5 acres of land

Source: State Department

Increase in Cocaine Use

New cocaine users in U.S.

The number of people trying cocaine in the U.S. has increased.



Source: U.S. Substance Abuse and Mental Health Services Administration

Crackolandia, a Crack and Cocaine HCL Free Trade and Use Zone



Veja onde fica a Cracolândia em São Paulo

Segundo a PM, área é formada pelas avenidas Duque de Caxias, Rio Branco, Ipiranga, Casper Líbero e Rua Mauá, mas há outras vias como a Rua Helvética, onde também há viciados, de acordo com a Prefeitura

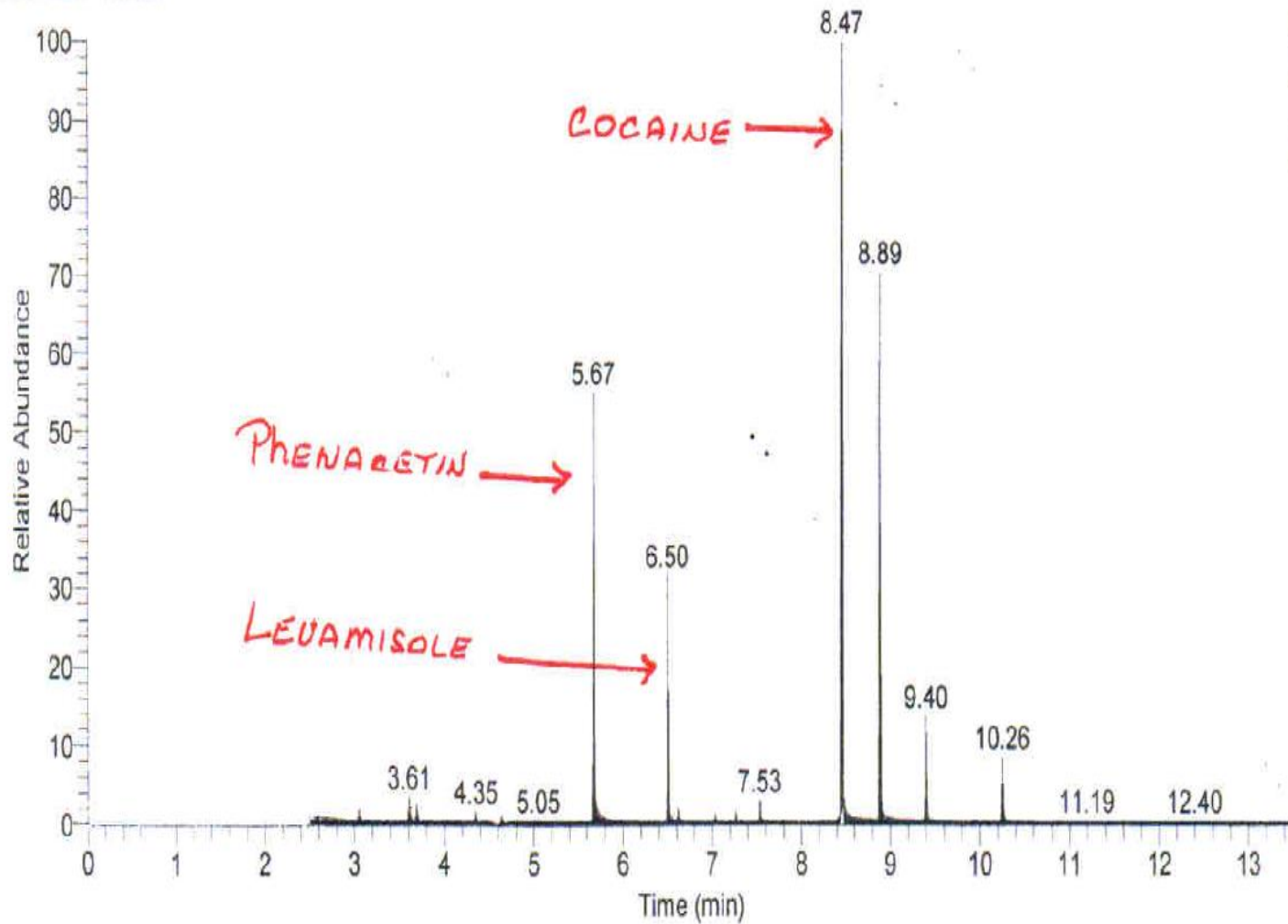


sky NEWS HD



Toxic Adulterants in the New Cocaine GC/MS

RT: 0.00 - 13.53



NL:
1.73E9
TIC MS
70-16-
b15amasa

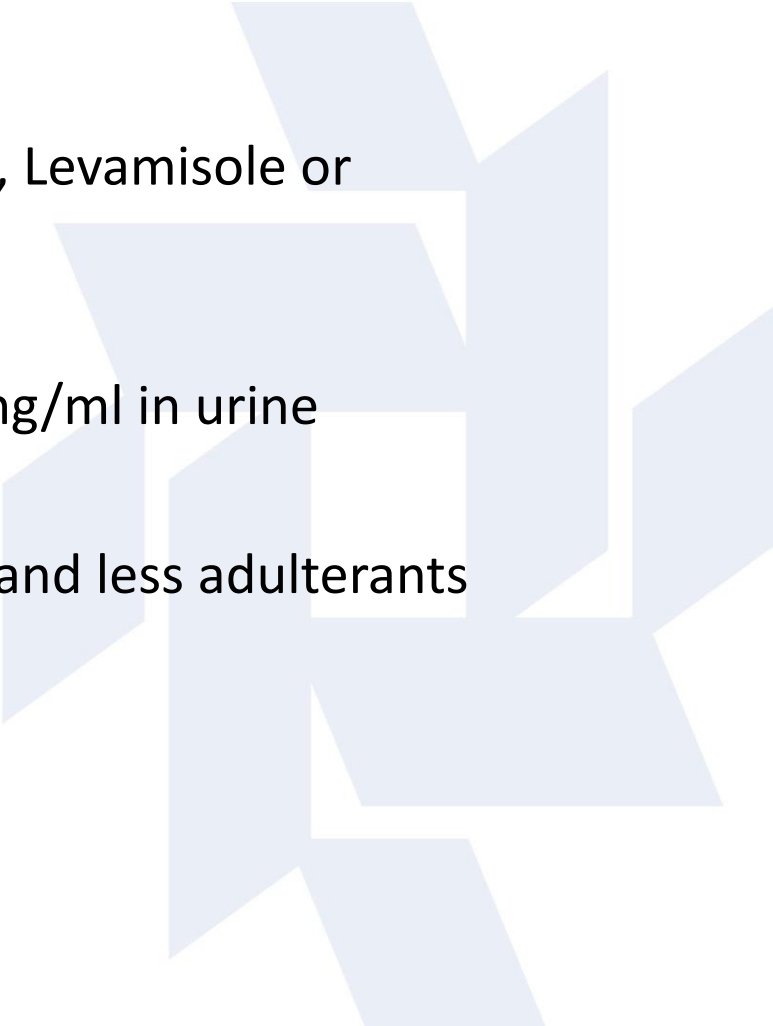
Toxic Adulterants Effects and Results of 2015 Crackolandia Samples

| Example DATA (ng/ml) Urine | | | | | |
|----------------------------|-------|-------|------|-------|-------|
| # | Phen | Lev | Amin | Benz | Coc |
| 6C | | 24 | | >5000 | |
| 7C | >1000 | 184 | 14 | >5000 | >5000 |
| 8C | 347 | | 11 | >5000 | >5000 |
| 10C | >1000 | 33 | 17 | >5000 | >5000 |
| 17C | 53 | 53 | | >5000 | 2115 |
| 21C | >1000 | 910 | | >5000 | >5000 |
| 23C | 519 | | 14 | >5000 | |
| 29C | >1000 | 72 | 33 | >5000 | >5000 |
| 30C | 941 | 980 | | >5000 | >5000 |
| 35C | >1000 | 123 | 14 | >5000 | >5000 |
| 40C | | >1000 | | >5000 | 956 |
| 42C | >1000 | 11 | 19 | >5000 | >5000 |
| 44C | >1000 | 164 | 33 | >5000 | >5000 |
| 45C | 34 | 35 | | >5000 | 715 |
| 47C | 22 | | 12 | >5000 | |
| 54C | 937 | | 152 | >5000 | |
| 55C | >1000 | 235 | 132 | >5000 | >5000 |



Urine samples of Brazil crack cocaine users were 77% positive for Phenacetin, a banned carcinogen; 54% for Aminopyrine; and 26% for Levamisole (the last two cause agranulocytosis).

Toxic Adulterants Effects and Results of 2019 Crackolandia Samples

- 114 urine samples collected from crack and cocaine HCL abusers who had used within the last 24 hours
 - 66 % had detectable levels of Phenacetin, Levamisole or Aminopyrine.
 - Concentrations ranged as high as 5000+ ng/ml in urine
 - 2015 vs 2019 samples had more cocaine and less adulterants
- 

Recommendations

- These findings highlight the urgent need to make adulterant testing of cocaine and other drugs a part of standard drug toxicology panels used by public health departments, health care providers, emergency departments, medical examiners, crime laboratories, and substance abuse treatment centers to identify emerging drug/adulterant trends and better inform public health responses.
- Targeted public health alerts in communities, cities, states, etc. where toxic adulterants have been identified in street-level cocaine or toxicological samples.
- Additional research to better understand patterns of adulterant use and their potential contribution to morbidity and mortality when combined with cocaine.
- A comprehensive *Toxic Adulterants Health Risk Assessment* that identifies the combined interactive effects of multiple controlled drugs and toxic adulterants found in individual street drug samples to better guide clinical and medical practice.



Rx Drug Abuse & Heroin Summit

AN NCAD MEETING



New Lethal Forms of Cocaine Driving the Emerging Stimulant Epidemic: Impact on Public Health Systems

Thom Browne Jr., MA

CEO, Colombo Plan Secretariat

David Martin, PhD

President, JMJ Technologies

Moderator: Melynda Benjamin, JD, *Executive Officer Department of Specialty Courts, Kentucky Administrative Office of the Courts, and Member, Operation UNITE Board of Directors*