#### PSYC1022: The Psychology of Addiction

Topic 1: Origins & Manufacture of addictive drugs (II)

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#### **Outline**

- Stimulants:
  - Tobacco
  - Cocaine
  - Amphetamine
  - Methamphetamine







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### Tobacco (nicotine)

- Smoked by tribes across the Americas
- 1492: discovered by Christopher Columbus
  - Scouts reported tribes people smoking "halfburned wood in their hands"



Christopher Columbus



San Salvidor, Bahamas

### Tobacco (nicotine)

- 1492: Rodrigo de Jerez
  - First European smoker
  - Introduced tobacco to Ayamonte, Spain
  - · Imprisoned for his "sinful & infernal habits"
  - Released 7 years later, during which time smoking had caught on
- 1523: official documentation of a tobacco merchant in Lisbon
  - Trade established in 30 years



Tobacco plant

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### Tobacco (nicotine)

- 1604: Stuart King James I
  - Denounced tobacco use, "harmful to the brain, dangerous to the lungs"
- 1604: English introduce heavy tariffs on imports
- 1609: commercial production began in Jamestown, Virginia from tobacco imported from Bermuda
- Until 1883: tobacco excise tax accounted for 1/3 of internal revenue collected by the U.S. government



Jamestown, Virginia (USA)

### Tobacco (nicotine)

- 1962: Britain's Royal College of Physicians
  - causal link between smoking & lung cancer, bronchitis & cardiovascular disease
- It is now broadly recognised by governments that quit smoking interventions yield substantial long term profits resulting from reduced health care expenditure & more productive economic activity.
  - Thus, the short term reduction in tax revenues are more than compensated for by long term profits.

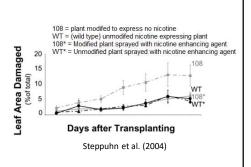


Harold Macmillan

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### Tobacco (nicotine)

- Nicotine constitutes approx. 0.6-3% of the dry weight of tobacco leaf
- Neurotoxic (particularly to insects) and functions as an antiherbivore chemical
- Nicotine derivative compounds widely used as pesticides in agriculture
  - removing nicotine from tobacco plants results in a 5% (approx.) increase in herbivore damage to leaf material.



- Alkaloid (like nicotine & the opiate alkaloids)
- Derived from the leaves of the coca plant
  - acts an antiherbivore chemical
- Grows naturally in abundance in South America



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### Cocaine

- Coca leaves were consumed by many South American native groups
  - 1000 BC: Mummies found in Northern Chile showed the presence of cocaine

(Rivera et. al., 2005)

 6000 BC: Evidence of coca leaf & lime production & distribution in Nanchoc Valley, Peru

(Dillehay et. al., 2010)



- Tea infusions or chewed leaves were consumed by South American natives
  - Practice still legal in Peru & Bolivia
  - Widely practiced by natives in other South American countries despite prohibition.





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#### Cocaine

- 1500s: Spanish conquistadors landed in South America
  - initially dismissed coca leaf consumption as the 'Devils work'
  - soon came to commercialise & tax its distribution when they discovered that the enslaved native population worked harder under its influence.
- 1600s: introduced to Spain
- 1858: gained popularity following research published by Paolo Mantegazza, an Italian neurologist, which highlighted the cognitive enhancing effects of coca leaf infusions.
- 1886: US state of Georgia introduced alcohol prohibition
  - John Pemberton, US Pharmacist, developed a non-alcoholic recipe with sweet syrup & coca infusion, coca-cola.
- 1904: Cocaine is extracted from coca-cola following prohibition of cocaine.



Paolo Mantegazza



John Pemberton



- 1855: cocaine alkaloid first isolated by German chemist, Friedrich Gaedcke
  - named it "erythroxyline".
- 1860: Albert Niemann's PhD
  - published & described a better extraction process, which is the basis of the contemporary technique
  - described its local anaesthetic effects & named it cocaine
    - The suffix "-caine" is now commonly used to name local anaesthetics.



Albert Niemann

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#### Cocaine

- 3 steps of Niemann's technique are used by South American drug cartels for illicit production:
- Coca paste: Place macerated leaves in a 55-gallon drum & cover with water. Add kerosene (a solvent) & mix vigorously by hand or place in washing machine or cement mixer to dissolve the water insoluble cocaine alkaloid, then filter off leaf waste & retain the solution. Add dilute sulfuric acid to turn the cocaine into water soluble cocaine sulfate, then add lime to precipitate coca paste as a yellow solid. Remove & package the paste.
- Coke base: Dissolve coca paste in dilute sulfuric acid. Carefully add the oxidizing agent potassium permanganate & stir vigorously to precipitate remaining impurities as a black sludge leaving overlying solution clear. Filter & add ammonia to precipitate pure coke base.
- Cocaine hydrochloride: Dissolve coke base in diethyl ether to precipitate remaining impurities. Filter solution & stir in an equal volume of acetone & hydrochloric acid which immediately precipitates cocaine hydrochloride as shiny white, flaky crystals. Filter & dry under heat-lamps and/or microwave ovens, press, package & ship.

Casale & Klein (1993)



Pablo Escobar

- Cocaine hydrochloride:
  - · injected, snorted, or taken orally
  - is not smoked because it will not vaporize until about 197°c. This burns & destroys the alkaloid giving a weak high plus a foul taste.
- Freebase cocaine:
  - made by dissolving cocaine hydrochloride in water, diethyl ether & ammonia, then extracting the precipitate.
  - Freebase vaporizes at 98°c, so it can be smoked, giving this form a faster high. However, diethyl ether is highly flammable in production & residual ammonia is damaging to the lungs.
- · Crack cocaine:
  - Crack is made by dissolving cocaine hydrochloride in water & sodium bicarbonate to form the crystalized precipitate.
  - · It crackles when smoked giving its name.
  - This is a potently addictive substance.







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### **Amphetamine**

- Derived from the plant *Ephedra* which grows throughout the world.
  - has long been used in Chinese medicine for the treatment of asthma, hay fever & colds.
- 1885: Japanese organic chemist, Nagai Nagayoshi, extracted the *ephedrine*, from ephedra.
  - used as a decongestant & to stop asthma attacks.
- 1887: Amphetamine was first synthesized by Romanian chemist, Lazăr Edeleanu, in an attempt to make a synthetic ephedrine.
  - Named phenylisopropylamine because the starting compound was phenyl-2-propanone (P2P) rather than plant derived ephedrine



Nagai Nagayoshi



Lazăr Edeleanu

### **Amphetamine**

- 1920s: shortage of ephedrine due to a civil war in China
  - 1927: the allergist, Gordon Alles, resynthesised amphetamine.
- 1933: Smith, Kline & French released amphetamine in an inhaler under the trade name Benzedrine, as a decongestant for blocked nose & asthma.
  - Studies of Benzedrine followed whereupon its mood enhancing & energising properties became increasingly apparent.
- Benzedrine & amphetamine tablets were widely used in WWII
  to increase alertness. But it became increasingly clear that
  performance enhancing effects were largely in the mind of the
  users, whereas objectively, their performance was impaired.
  This combined with the addictive properties led amphetamine
  to be used less as the war continued.





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# **Amphetamine**

- 1960s: epidemic of amphetamine use
  - gave rise to a moral panic, raising the problem of drug addiction up the political agenda.
  - Benzedrine inhalers were banned & regulation of prescription amphetamine came into force in both the US & UK at the end of that era.
    - US military had used amphetamine with its personnel in every war since WWII (e.g. Vietnam).



Jimi Hendrix

### Methamphetamine

- 1885: Nagai Nagayoshi, extracted ephedrine from ephedra
  - Further research into chemical manipulation of ephedrine led to creation of meth powder
- 1919: Akira Ogata, developed crystal form
  - Simpler to produce than amphetamine
  - Similar chemical structure to amphetamine with the addition of the methyl group





Crystalline form





Tablet form

Methamphetamine crystals

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# Methamphetamine

- 1939–1945: during WWII Germany manufactured & distributed more than 35 million tablets of meth
  - contributed to the rapid invasion of Europe
    - AKA Blitzkrieg or "lightning war"
  - 1941: production halted following recognition of its dangerous addictive potential.
- Japanese provided meth throughout the war, particularly to Kamikaze pilots.
- Civilian meth abuse multiplied at the end of the war when military supplies were opened for sale to the public.



