Indication and interpretation of investigation in toxicology

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What is a Poison?

All substances are poisons;

there is none that is not a poison.

The right dose differentiates a poison and a remedy.

Paracelsus (1493-1541)

Toxicology

- Toxicology - study of poisons and their antidotes

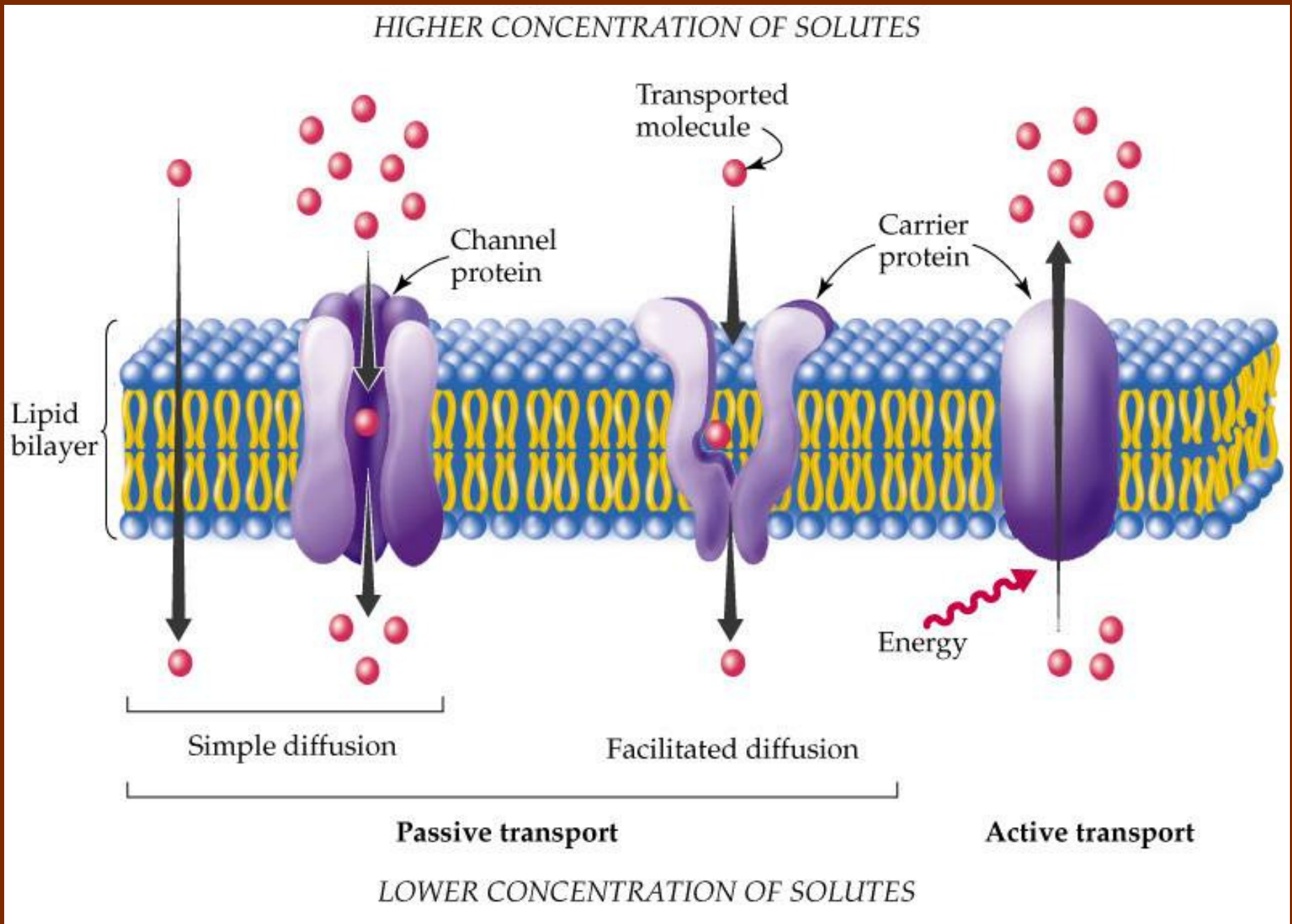
- Dose determines the response
- Pathway, Duration of Frequency of Exposure and Chemical determine Dose
- Absorption, Distribution, Metabolism & Excretion

Toxicology

- The extent of the effect is dependent upon the concentration of the active compound at its site of action over time
- Bioactivation: compounds to reactive metabolites
- Individual variation of the organism will affect ADME

ADME: Absorption, Distribution, Metabolism, and Excretion

- The body has defenses:
  - Membrane barriers
    - passive and facilitated diffusion, active transport
  - Biotransformation enzymes, antioxidants
  - Elimination mechanisms


HIGHER CONCENTRATION OF SOLUTES
Transported molecule
Channel protein
Carrier protein
Lipid bilayer
Energy
Simple diffusion
Facilitated diffusion
Passive transport
Active transport
LOWER CONCENTRATION OF SOLUTES

Absorption

ability of a chemical to enter the blood (blood is in equilibrium with tissues)

- **Inhalation** - readily absorb gases into the blood stream via the alveoli. (Large alveolar surface, high blood flow, and proximity of blood to alveolar air)

Absorption

- **Ingestion**-absorption through GI tract - stomach (acids), small intestine (long contact time, large surface area - villi; bases and transporters for others)
- **Dermal** - absorption through epidermis (stratum corneum), then dermis; site and condition of skin

Exposure

Injection

- intravenous, intramuscular, intraperitoneal

- Typical Effectiveness of Route of Exposure

  iv > inhale > ip > im > ingest > topical

Distribution

- the process in which a chemical agent translocates throughout the body
- Blood carries the agent to and from its site of action, storage depots, organs of transformation, and organs of elimination

Distribution

- Rate of distribution (rapid) dependent upon
  - blood flow
  - characteristics of toxicant (affinity for the tissue, and the partition coefficient)
- Distribution may change over time

Distribution

- Storage and Binding
- Storage in Adipose tissue - Very lipophylic compounds (DDT -synthetic fertilizer) will store in fat. Rapid mobilization of the fat (starvation) can rapidly increase blood concentration

Distribution

- Storage in Bone - Chemicals analogous to Calcium - Fluoride, Lead, Strontium
- Binding to Plasma proteins - can displace endogenous compounds. Only free is available for adverse effects or excretion

Lead poisoning

PbO was used like sweetener, water pipes,leaded petrol, accumulators, painter's colours…..

Pb has ability to replace other biological important elements (Ca, Fe, Zn) in binding groups -SH, -NH_2, -COOH,... in protein and other molecules.

Inhibition

d-ALA – dehydratase - haemoglobin synthesis damage

NMDA receptors in the brain – worsening of long-term memory

Ludwig van Beethoven

Francisco Goya

Sir John Franklin

Lead poisoning

Therapy – elimination of accumulated lead from the organism using chelation therapy, which releases Pb from deposit in bones and excretes it in urine.

Target Organs

- adverse effect is dependent upon the concentration of active compound at the target site for enough time
- Not all organs are affected equally
  - greater susceptibility of the target organ
  - higher concentration of active compound

Target Organs

- Liver - high blood flow, oxidative reactions
- Kidney - high blood flow, concentrates chemicals
- Lung - high blood flow, site of exposure
- Neurons - oxygen dependent, irreversible damage
- Myocardium - oxygen dependent
- Bone marrow, intestinal mucosa - rapid divide

Excretion

- Toxicants are eliminated from the body by several routes
- Urinary excretion
  - water soluble products are filtered out of the blood by the kidney and excreted into the urine
- Exhalation
  - Volatile compounds are exhaled by breathing

Excretion

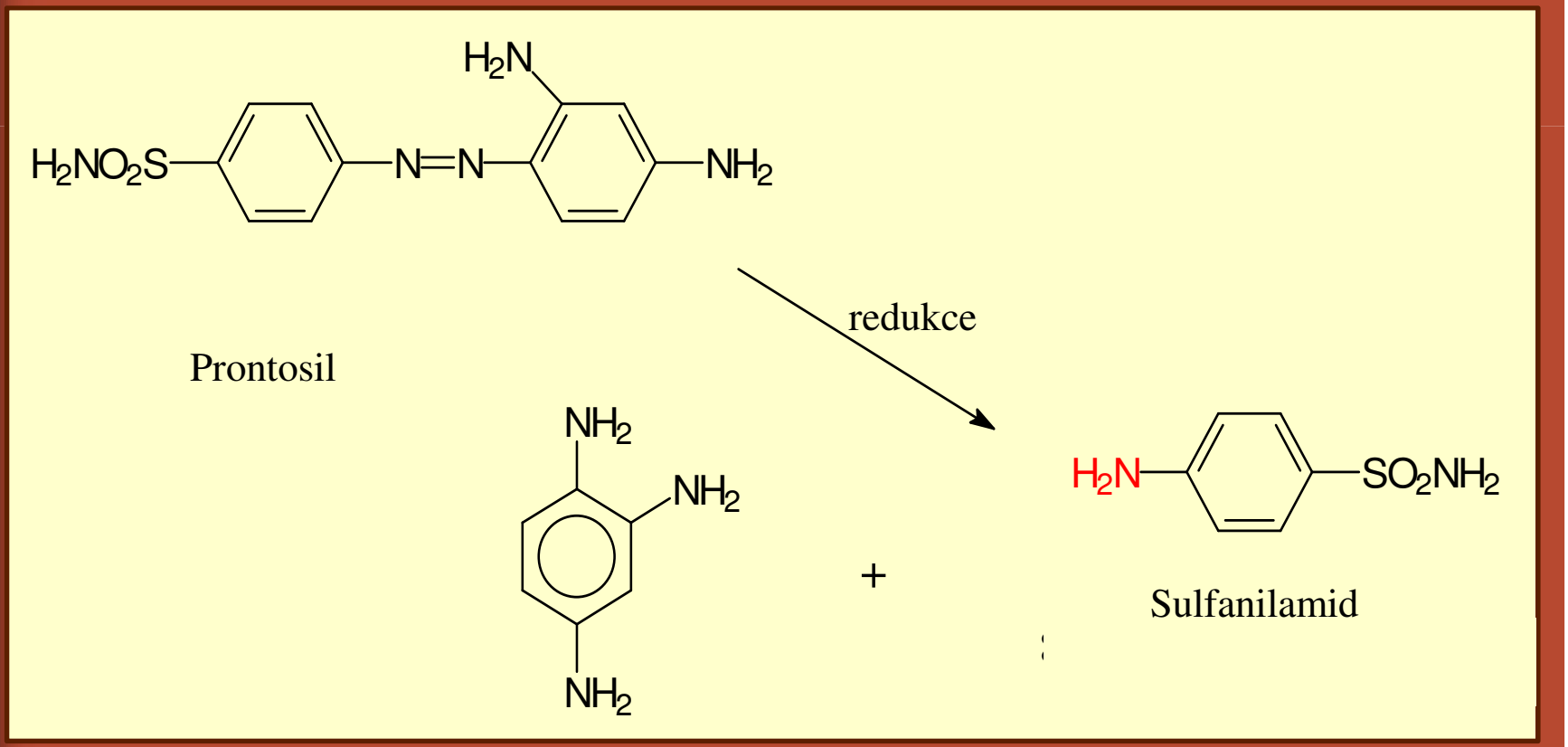
- Biliary Excretion via Fecal Excretion
  - Compounds can be extracted by the liver and excreted into the bile. The bile drains into the small intestine and is eliminated in the feces.
- Milk Sweat Saliva

Biotransformation

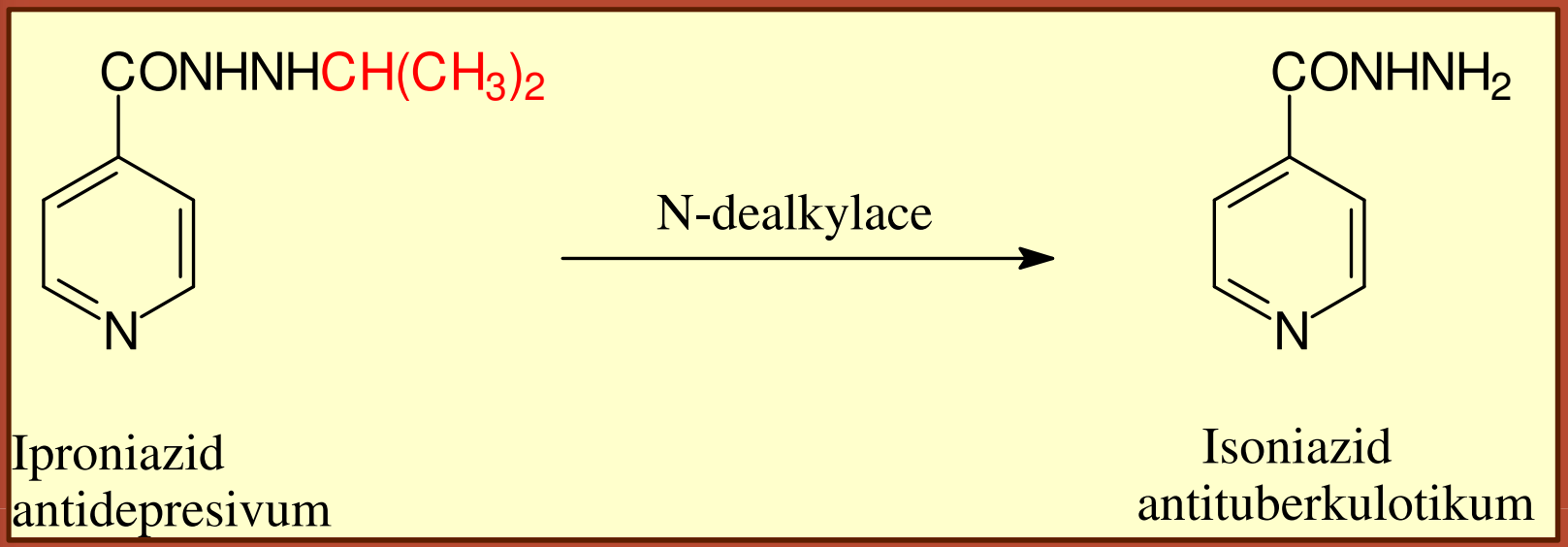
- Key organs in biotransformation
  - LIVER (high)
  - Lung, Kidney, Intestine (medium)
  - Others (low)
- Biotransformation Pathways
  - Phase I - make the toxicant more water soluble
  - Phase II - Links with a soluble endogenous agent (conjugation)

Metabolism

- Bioactivation -Biotransformation can result in the formation of reactive metabolites



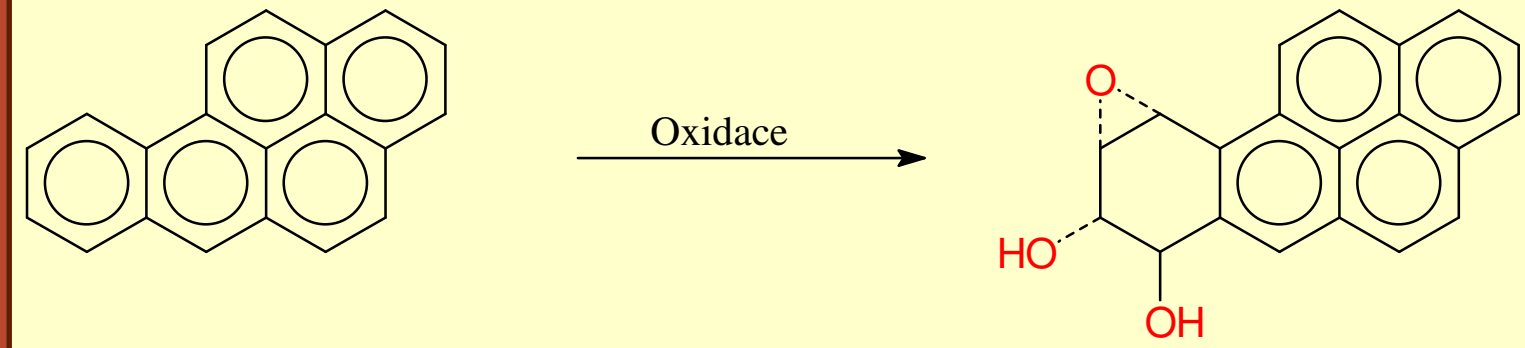
Change of activity



Iproniazid
antidepresivum

Isoniazid
antituberkulotikum

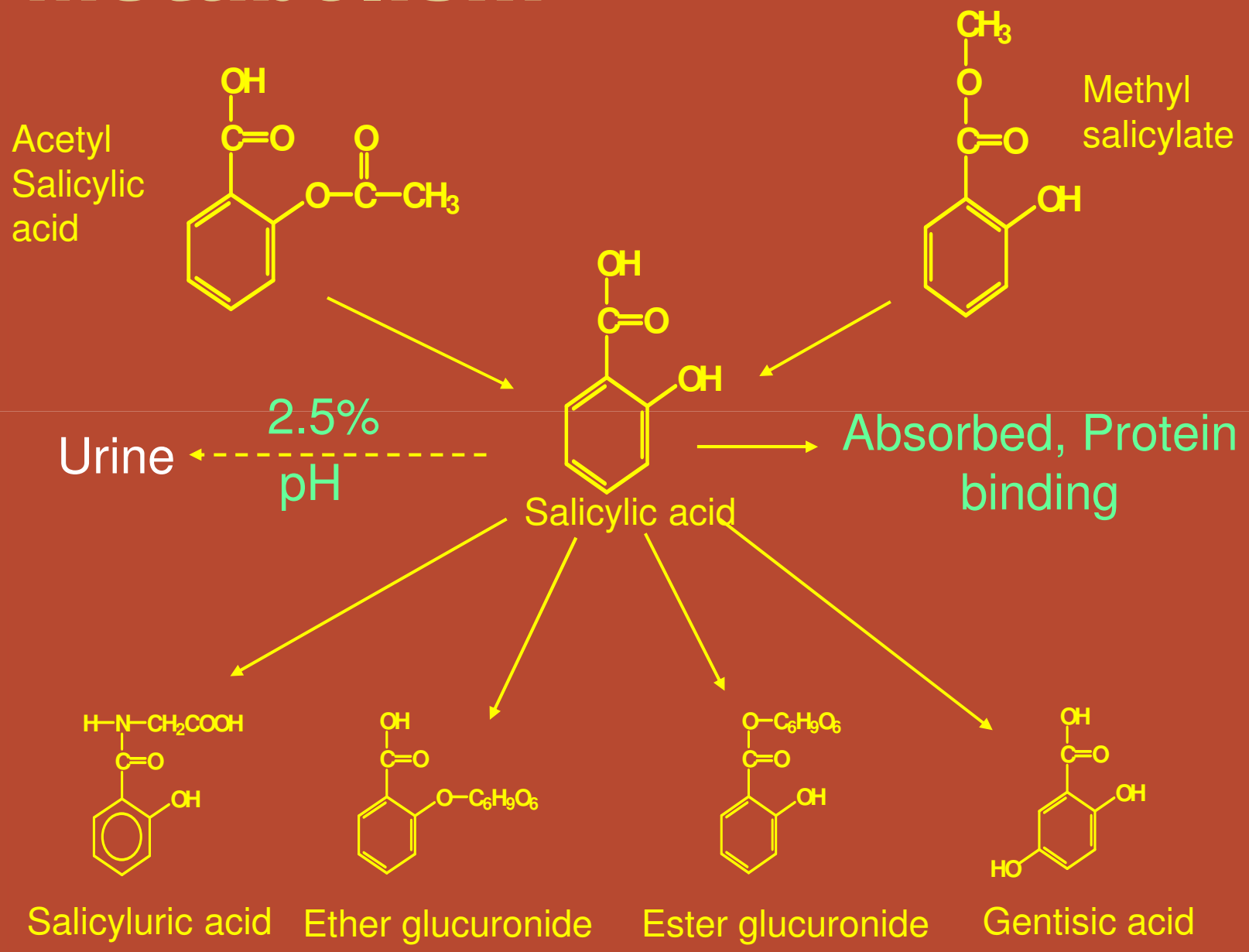
Toxication



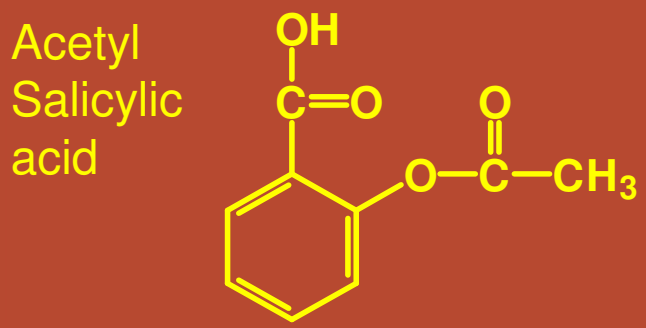
Benzpyren

7,8-Diol-9,10-epoxydy benz[a]pyrenu
silné kancerogeny

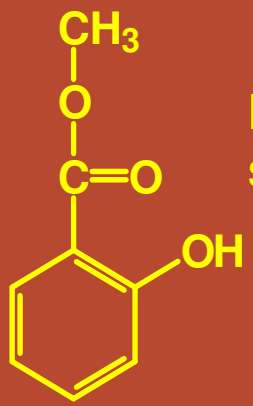
Metabolism


Acetyl Salicylic acid
Methyl salicylate
Urine
2.5%
pH
Salicylic acid
Absorbed, Protein binding
Salicyluric acid
Ether glucuronide
Ester glucuronide
Gentisic acid

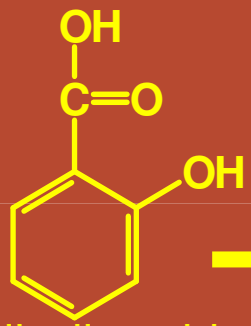
Overdose!



Acetyl Salicylic acid



Methyl salicylate



Salicylic acid

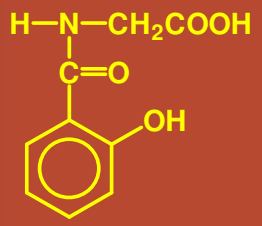
2.5%

Urine

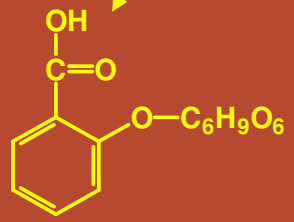
pH

More ASA Absorbed
Decreased Protein binding

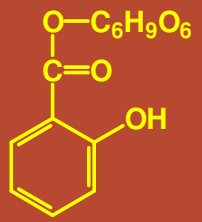
SATURATED



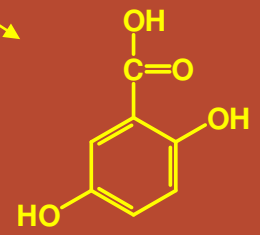
Salicyluric acid



Ether glucuronide



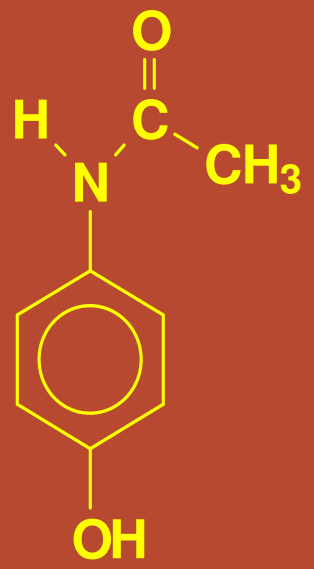
Ester glucuronide



Gentisic acid

Acetaminophen

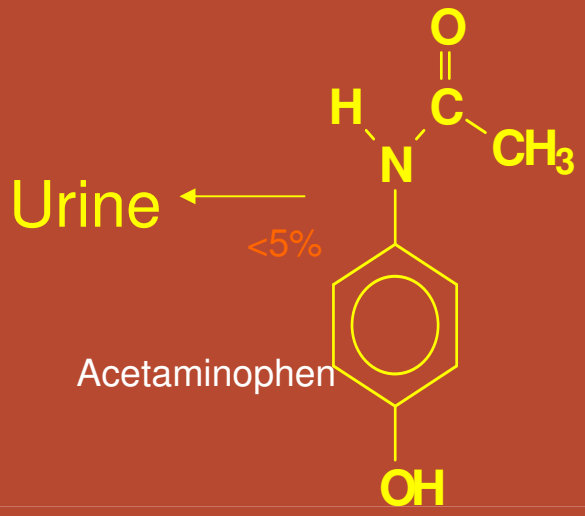
N – acetyl – *p* – aminophenol (APAP)



Acetaminophen

- First synthesized and used in the late 1800's
- "Rediscovered" in 1950
- A metabolite of phenacetin, it was not widely accepted in the medical community until the 1970's

Metabolism



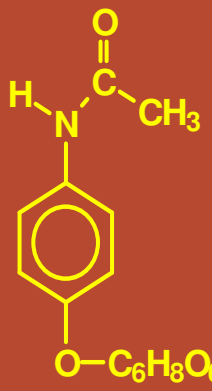
Acetaminophen

Urine

<5%

UDP-glucuronosyl-transferase

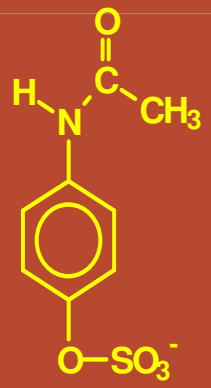
50%



Acetaminophen glucuronide

40%

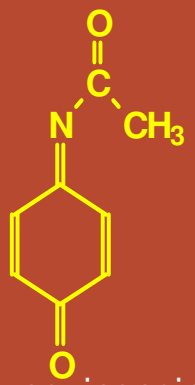
Phenosulfotransferase



Acetaminophen sulfate

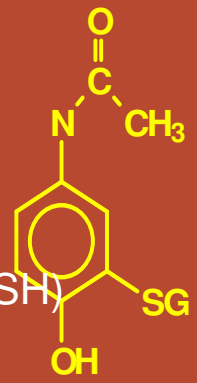
CytoP450

5-15%



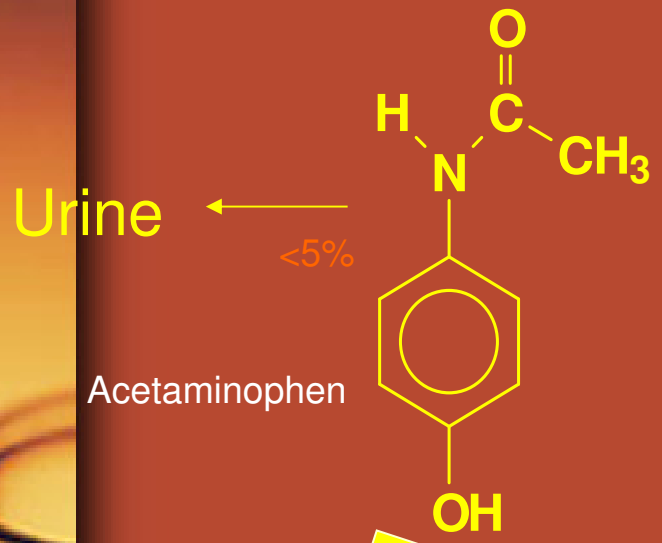
N-acetylparabenzoquinoneimine

Glutathione (GSH)



Acetaminophen glutathione conjugate

Overdose!



Urine

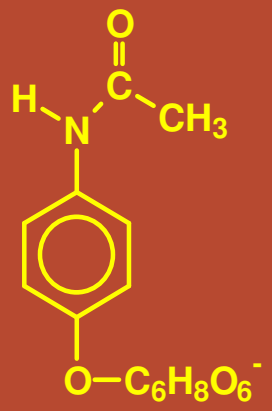
<5%

Acetaminophen

UDP-glucuronosyl-transferase

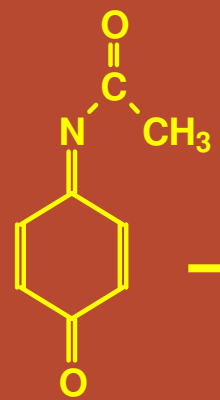
SATURATED

Phenosulfotransferase



CytoP450

39%

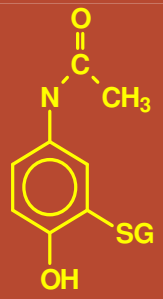


NAPQI

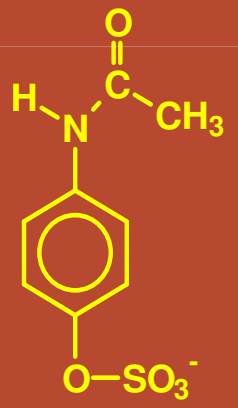
O

N-acetylparabenzoquinoneimine

Glutathione (GSH)



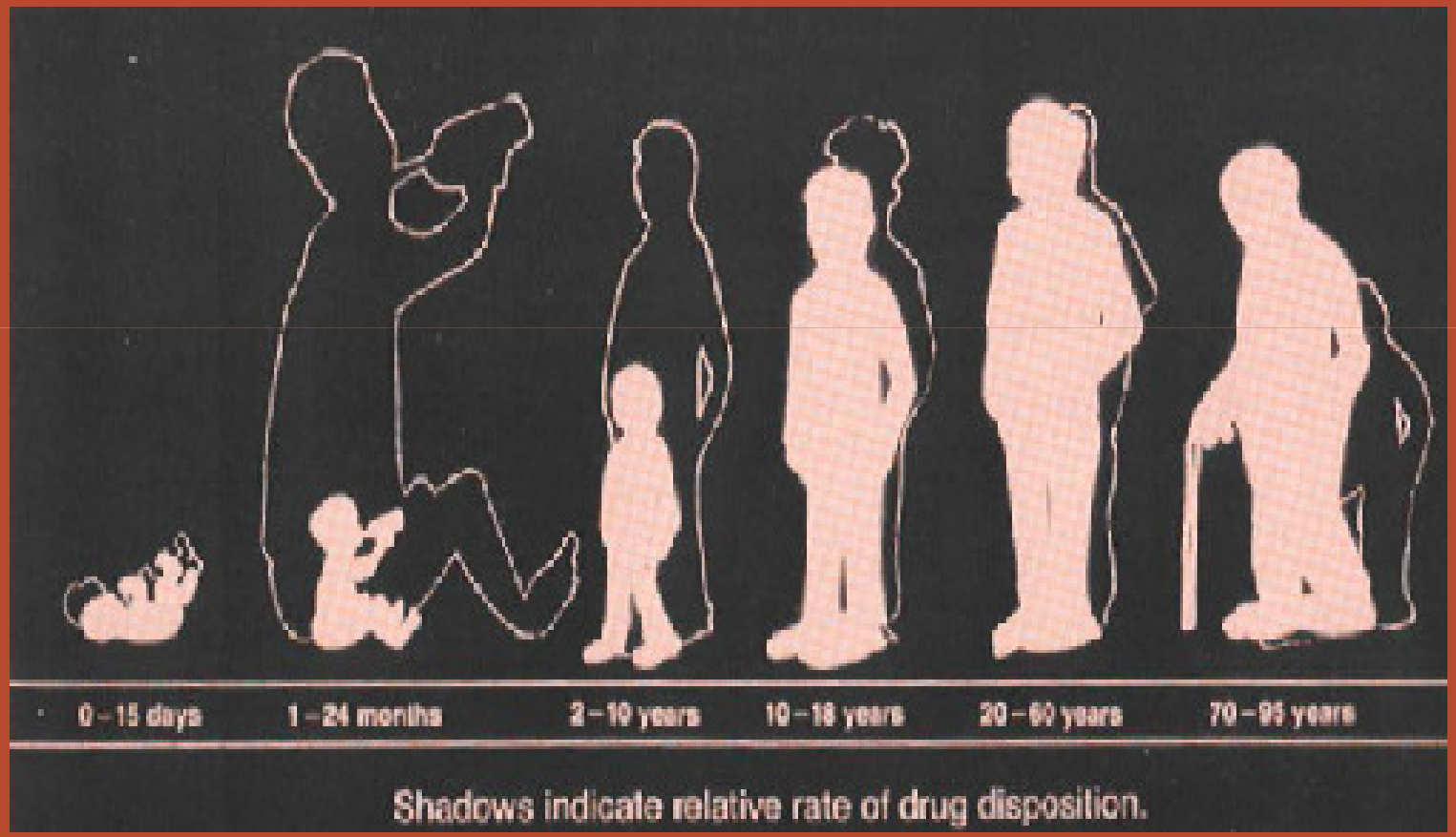
Acetaminophen glutathione conjugate



Acetaminophen sulfate

Binding to cellular proteins leading to hepatic and renal injury

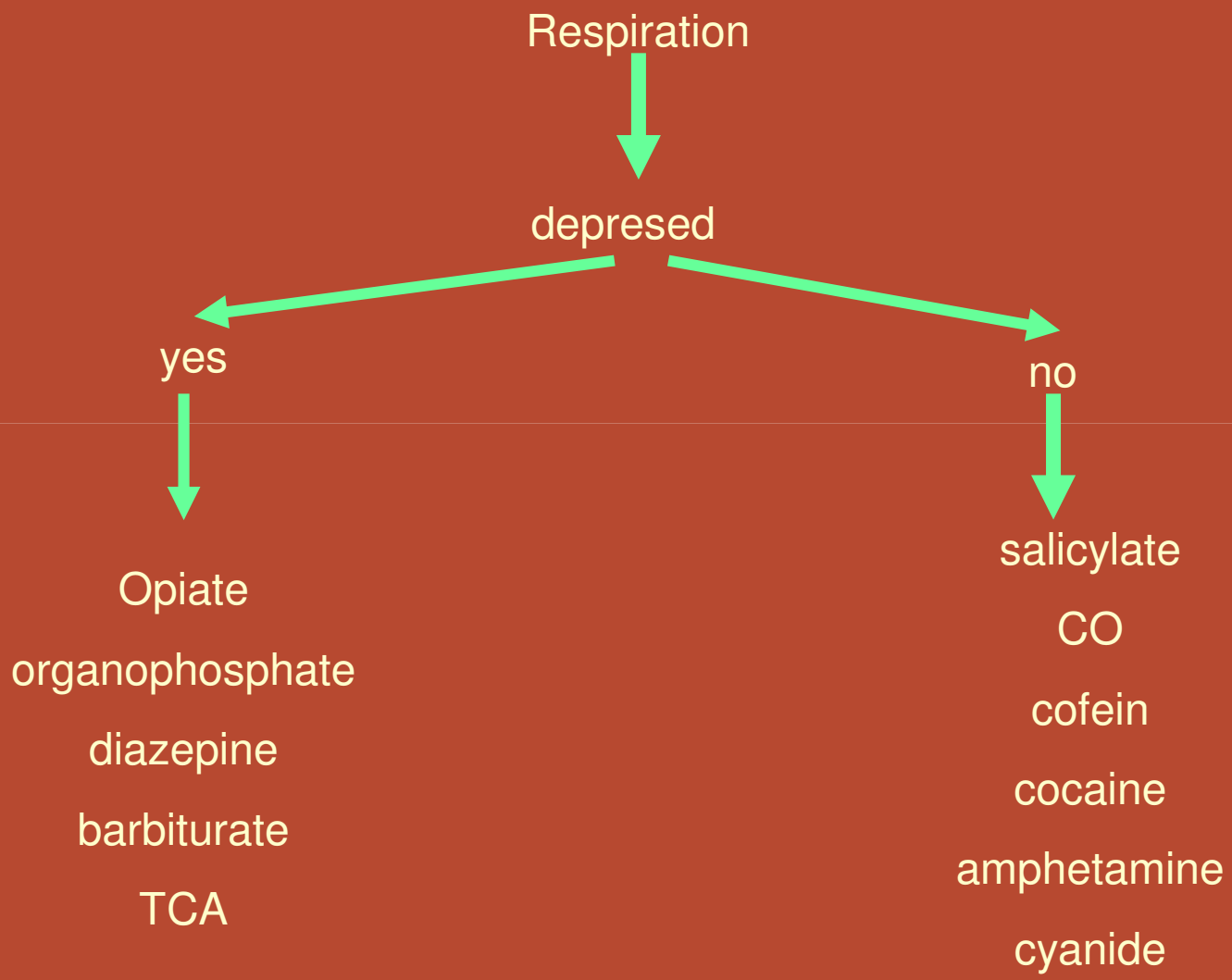
Drug disposition by age



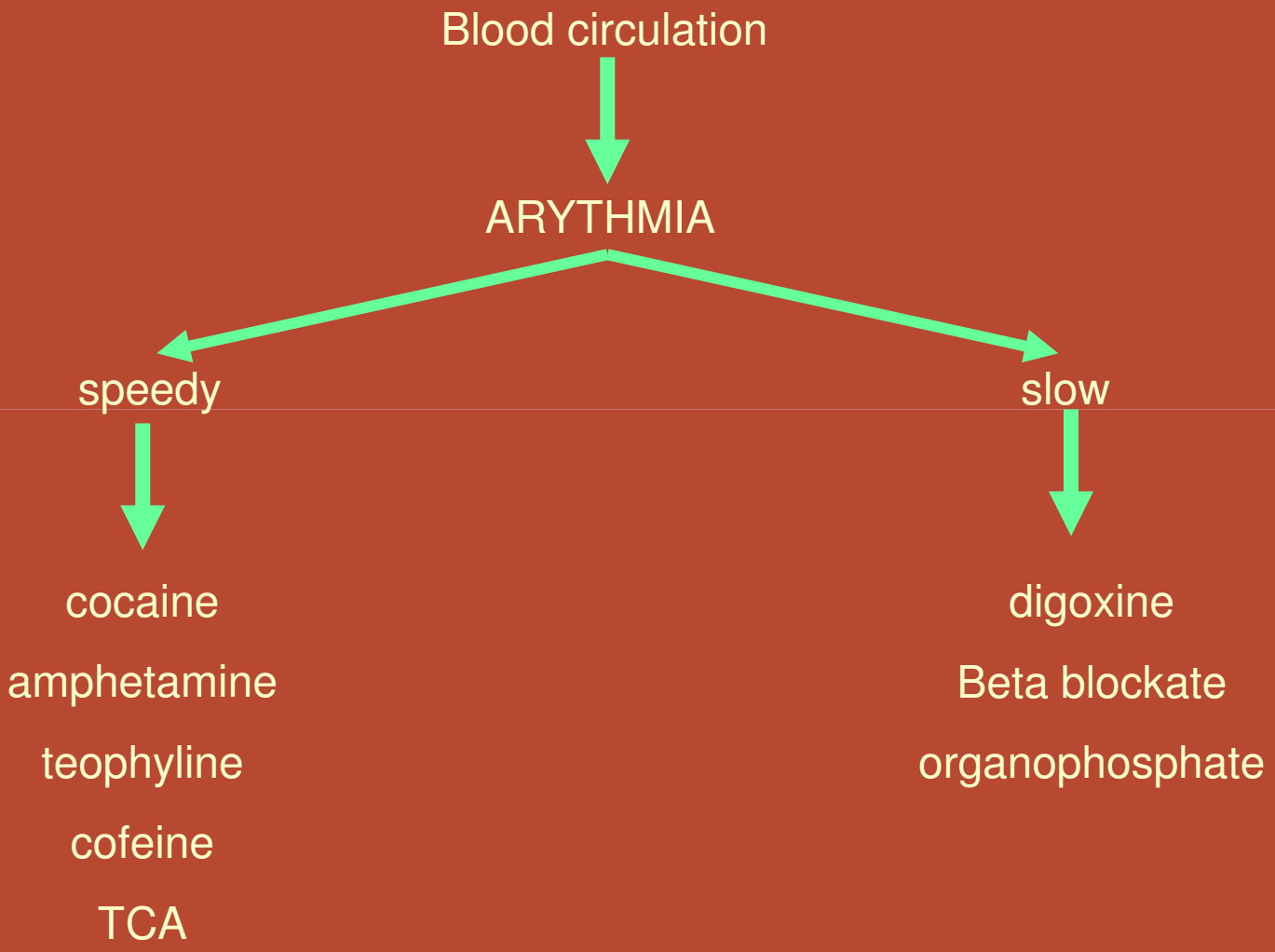
Individual Susceptibility

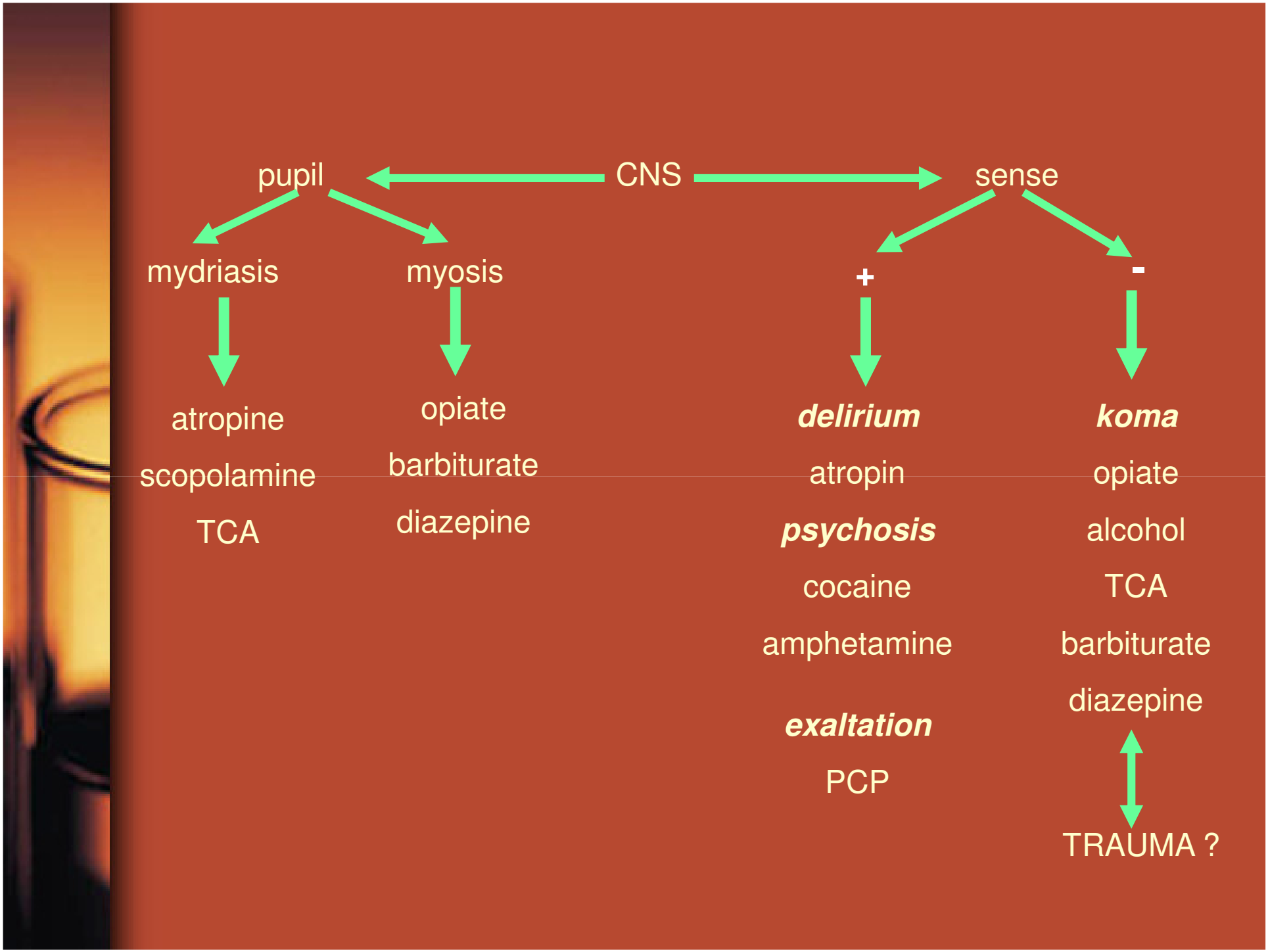
- Age
  - changes in excretion and metabolism rates, body fat
- Nutritional status
- Health conditions
- Previous or Concurrent Exposures
  - Additive –antagonistic -synergistic

Intoxication?



Intoxication?




pupil
CNS
sense
mydriasis
myosis
+
-
atropine
scopolamine
TCA
opiate
barbiturate
diazepine
delirium
atropin
psychosis
cocaine
amphetamine
exaltation
PCP
koma
opiate
alcohol
TCA
barbiturate
diazepine
TRAUMA ?

Commonest poisons on admission to hospital

- Paracetamol 60%
- Ethanol 35%
- Salicylate 30%
- Carbon monoxide 25%
- Tricyclics & phenothiazines 12%
- Others 30%

Acute intoxication natrium fluorosilicate (Na_2SiF_6)

- male 27 year after ingestion 3–4 spoons white powder Na_2SiF_6
- Hospitalization 1,5 h after ingestion
- During following 6 hour was developed organ dysfunction, which leads to death
- The amounth of poison refered by patient corresponds with tabulated letal dose for Na_2SiF_6 : over 5–10 g or 70–140 mg/kg.

Standard laboratory tests

- Arterial blood gases
  - Ventilation problems
  - Acid-base disturbances
- Urea & electrolytes (incl Cl, HCO_3, creat)
  - Hyper/hypo kalaemia
  - Anion gap
- Osmolality
  - Alcohols
- Calcium, albumin, Mg
  - Oxalate/fluorides

Osmolality

- Osmolality calculation
  - glucose + urea + Na (2x) in mmol/l
- Osmolality gap
  - diference between measured and calculated osmolality
  - ethanol, methanol and other alcohols, ethyleter, aceton, glykol a manitol

Anion gap

- **Anion gap** – the difference of kations and anions in serum, plasma or urine
- For finding out causation of metabolic acidosis
- The higher gap – more serious acidosis
- $([Na^+]+[K^+]) - ([Cl^-]+[HCO_3^-])$

Methanol intoxication

- **Methanol itself is not toxic**
- **metabolites – formic acid and formaldehyde – lead to metabolic acidosis**
- **Therapy:** blocation of alcoholdehydrogenase
  - **Ethanol**
  - **Fomepizol**

    hemodialysis

Standard laboratory tests

- Glucose
  - Differential diagnosis of coma
  - Hypoglycaemic agents/EtOH/salicylates
- LFTs (liver function tests)
  - Paracetamol
  - Iron salts
  - Halogenated hydrocarbons

Standard laboratory tests

- Creatine kinase
  - Rhabdomyolysis
- FBC/INR
  - Paracetamol
- Urine tests
  - Colour
  - Hb, (myoglobin)
  - Crystals

Emergency measurement of plasma drug concentration

- assessing severity of poisoning
  - if this is not possible clinically
- determining need for specific treatment
- monitoring efficacy of treatment
- guiding therapy in severely ill patients in rapidly changing circumstances

Toxicological testing in overdose

1. **Toxicity predictable based on serum levels. Drug-specific therapy can be instituted when levels dictate:**

Salicylate	Theophylline	Lithium
Digoxin	Paracetamol	
Methanol	Ethylene glycol	

2. **Toxicity correlates with serum level, but supportive care only required:**

Ethanol	Barbiturates	Phenytoin

Toxicological testing in overdose

3. **Toxicity and requirement for specific treatment depend on clinical parameters - testing only confirms:**

Tricyclics	Narcotics (naloxone)
Cyanide	Organophosphates
Benzodiazepines (flumazenil)	

4. **Toxicity poor correlation with serum level - supportive care only required:**

Neuroleptics	Cocaine
Hallucinogens	Phenylpropanolamine
Amphetamine	Phencyclidine

Reducing absorption

- ((emesis))
- (lavage)
- ORAL CHARCOAL

Increasing elimination

- (forced diuresis)
- Urine alkalinization
- Dialysis
- Charcoal/resin haemoperfusion
- Multiple-dose oral charcoal

Specific antidotes

- Paracetamol: N-acetylcysteine Methionine
- Methanol/ethylene glycol: Ethanol, fomepizole
- Opiates: Naloxone
- Metals: Chelators (DFO, EDTA, etc)

Intoxication

- Toxicological emergencies
  - 70% of accidental poisonings involve children
  - 80% of suicides involve overdose

Routes of Exposure

- Ingestion
- Inhalation
- Injection
- Surface absorption

Ingested Poisons

- Assessment
  - History
  - Physical Exam
- Management
  - ABC's, prevent aspiration
  - Decide if inducement of vomiting is needed
  - Fluid administration and meds

Specific Ingested Poisons

- Antiemetics
- Contaminated food
- Poisonous plants
- Niacin (nicotinic acid)
- Ethylene glycol/methanol

Inhaled Poisons

- Presentation
  - Respiratory problems
  - CNS problems
  - Cardiovascular problems

Specific Inhaled Poisons

- Cyanide gas
- Carbon monoxide
- Freon
- Ammonia
- Methyl chloride

Summary

- **Protect yourself** in all cases
- Protect patient
- Good primary and secondary survey
- O2, EKG
- Rapid transport

Poisoning by CO

- CO is poisonous colourless gas
- Closed rooms – imperfect burning
- CO has strong affinity to haemoglobin - carbonylhaemoglobin (CoHb), transfer O_2 in tissues is impossible
- CO bond to haemoglobin is 200x stronger than O_2 bond
- Remove CoHb from the blood takes about two days

Symtoms

- 10-25 % transformation of haemoglobin to carbonylhaemoglobin - headache, vertigo, weakness, dezorientation……
- 30-50 % COHb – confusion, hyperventilation, dysrytmie, vomiting, sleepiness, coma….
- Over 50 % - tissue hypoxy, cardiovascular dysfunction, serious acidosis, colvusions, shock, coma, death.
- In the serious and lethal condition have patients lips or cheeks unusual light red colour - COHb is carmine red

Poisoning by smoke gas with dominance of CO_2

- ABR, COHb, lactate, CK, LD, AST, myoglobin and cardiac enzymes (EKG!)
- The other components of fume usually don‘t determinated
- In reality prevale poisoning by **CO_2**, or **combined poisoning by CO/ CO_2**
- Many intoxications are wrong diagnose: alcohol, „pure“ CO poisoning, sedative intoxication, delirium,…)

Drog testing

Toxicological laboratory testing

Material

- Blood
- Urine
- Stom. Cont.
- Tissue
- Hair
- Saliva
- Sweat
- Meconium

Possibility of toxicological analysis

- Differencial diagnostic of acute intoxication
- Drug abuse
- Control of therapy
- Criminality:
- car accident
- Ilegal drug production
- breaking, violation
- Death investigation:
- homicide, suicide

Clinical

- ARD
- Internal
- Psychiatry…

Forensic

- Police
- Court

Detection of a drug

- Positive – above cut-off
- Negative – below cut-off
  - Doesn't mean nothing is there, just that it is below cutoff level
- Cut-off Levels
  - Determine what is positive/negative
- Calibrators and Controls
  - QA/QC

Drugs of Abuse Testing
Who / When to Test

- Pre-employment
- Reasonable Suspicion
- Routine Physicals
- Rehabilitation monitoring
- Random Testing (for safety & security)
- Department of Transportation
- Athletic Testing

Window of Detection

- Most drugs - 3 to 4 days (cocaine, heroin, methamphetamine)
- Marijuana - 10 days or more, depending on use
- Front Window – If sample is taken to early, drug may not be in person's system
- Take urine sample 3-5 hours later, if drug recently taken

Adulteration

- Things added to alter results – salt, bleach, acetic acid, Visine, hand soap, water – to dilute urine.
- Adding these things will change the adsorption – may not be able to read test.
- Lab can check pH, specific gravity, and temperature to see if it has been altered.
- This is why collection must be observed!
- These problems can be avoided

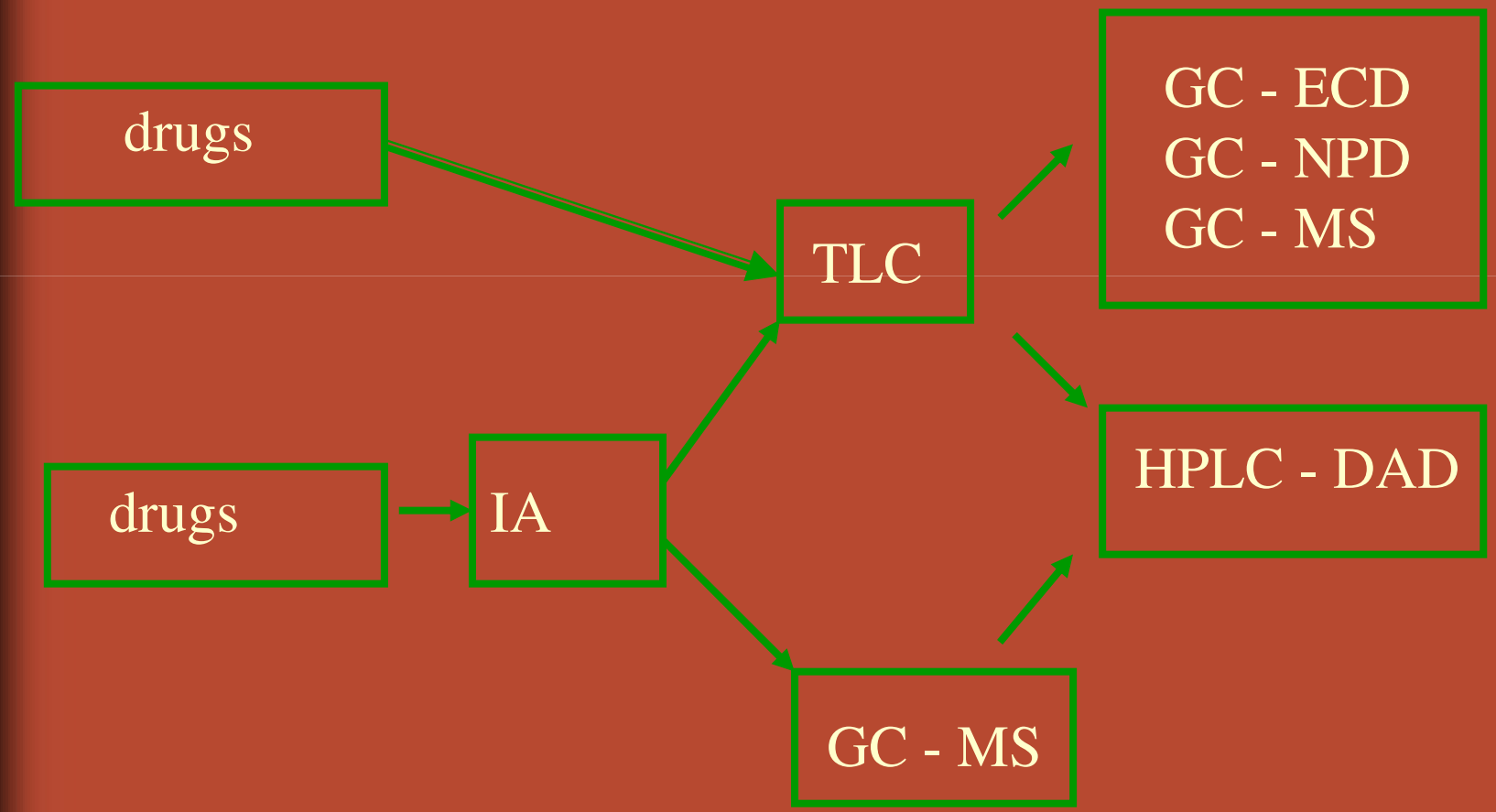
How is urine tested?

- Screening Tests
  - Immunoassay - Antigen/Antibody Test
  - Thin Layer Chromatography
- Confirmation Tests (cannot a repeat of the first test – must be a different test, e.g. Aph. vs. Methamph.
  - Gas Chromatograph/Mass Spectrometry
  - Thin Layer Chromatography
  - High Performance Liquid Chromatography

Quantitation

- BAC (blood alcohol level)
- – indicate intoxication at a certain level
- Drug levels – No studies have been done to determine if someone is intoxicated with a specific level
  - E.g. studies with cocaine or marijuana won't be allowed
  - If a level is in blood – shows more recent use

Systematic toxicology analysis STA

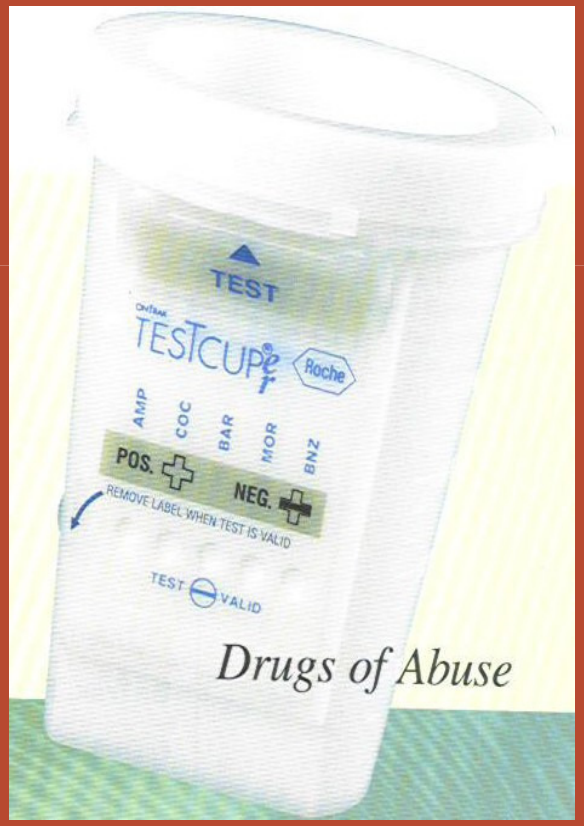


Tentative methods

Test stripes

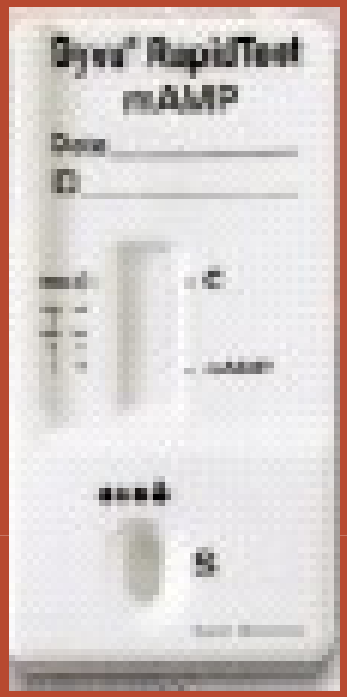
- **Quickly detection**
  - Amphetamine
  - Benzodiazepine
  - Cocaine
  - THC
  - Opiates

Test in urine cup

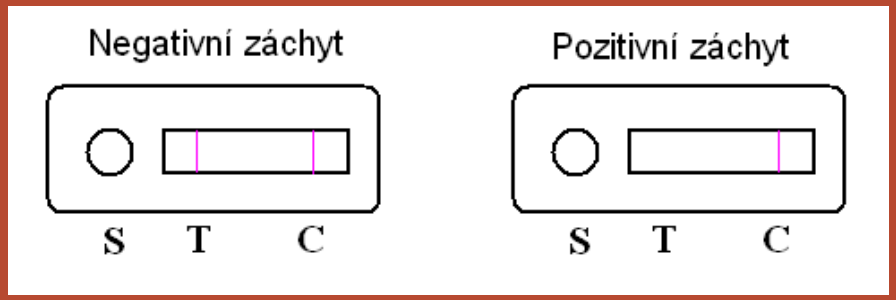


- **Detection of**
  - Amphetamine
  - Benzodiazepine
  - Cocaine
  - THC
  - Barbiturate
  - Morfine
  - PCP

Monotests



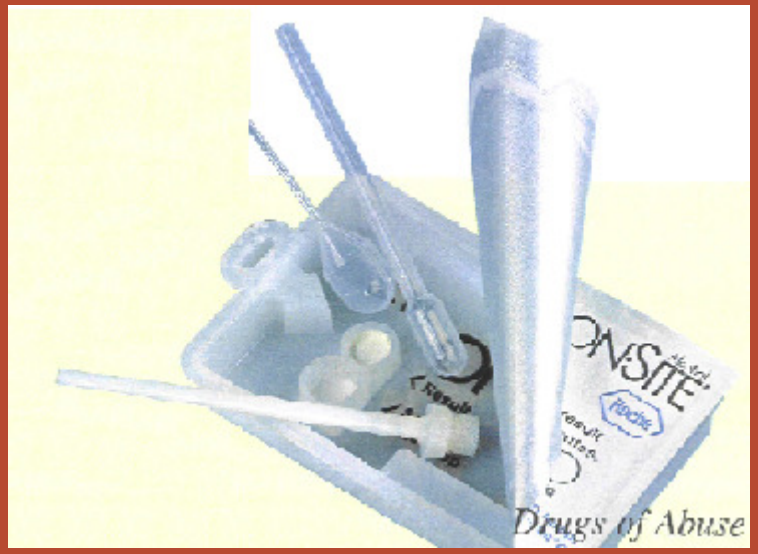
- simple
- Possibility of storage



- S – marked antibody
- T – fixed drug
- C – control of test

Saliva test

- Also for alcohol
- Sensitivity from 0,02% alcohol in blood



Immunoassay

Immunoassay

- EMIT, ELISA, EIA
- CEDIA
- RIA, IRMA
- FIA, MEIA
- CLIA

Immunoassay

Types of antibody:

• anti determinant group – only investigation of ph**enobarbital**

• anti chemical structure – group of similar substances - **barbiturates**

AxSYM ABBOTT

- FPIA

Immunoassay

Aplication:

- *terapeutic drug monitoring* – TDM
- rapid clinical action
- *differential diagnostic – acute intoxication*
- paracetamol – hepatotoxicity
- digoxin – kardiotoxicity
- theophylin
- carbamazepin, phenobarbital

- *differential diagnostic* - for screening of group of drugs – acute intoxication

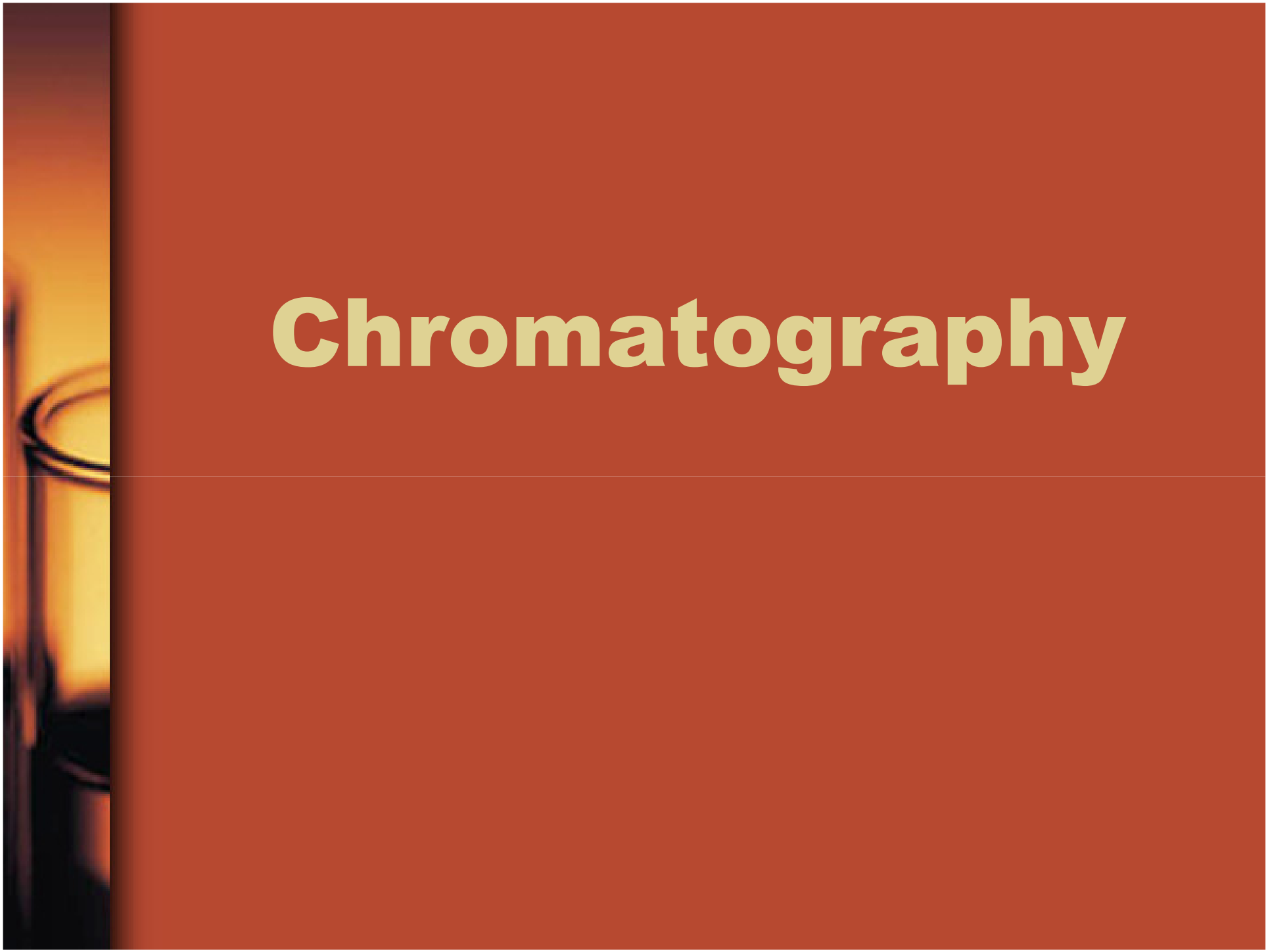
tricyclic antidepresives, barbiturates, benzodiazepins
canabinoids, amphetamins, opiate, cocaine

Immunoassay - advantage

Immunoassay for drugs in biological fluids

- no special isolation
- high sensitivity
- quick result
- simply
- automatization
-

Immunoassay is only for screening


Chromatography

Chromatography

- Chromatography is used to separate mixtures of substances into their components.
- All forms of chromatography work on the same principle.
- They all have a ***stationary phase*** (a solid, or a liquid supported on a solid) and a ***mobile phase*** (a liquid or a gas).
- The mobile phase flows through the stationary phase and carries the components of the mixture with it. Different components travel at different rates.

Screening - thin layer chromatography

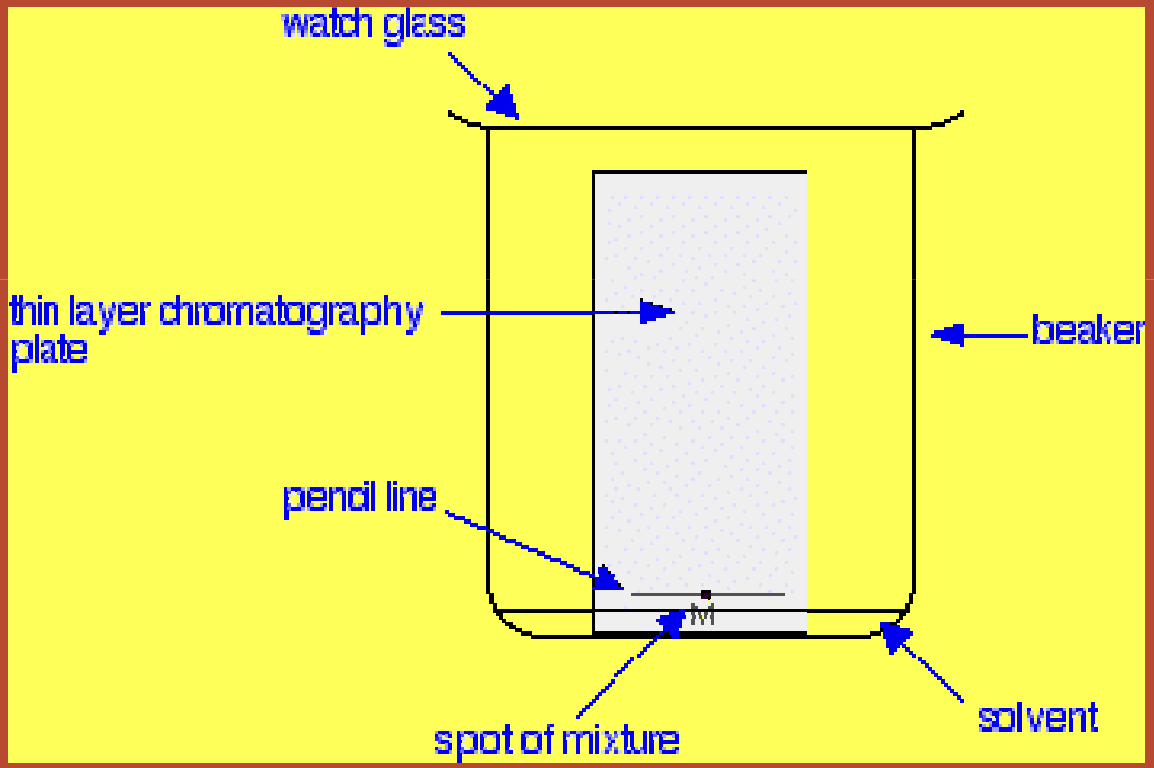
Thin layer chromatography is done exactly as it says - using a thin, uniform layer of silica gel or alumina coated onto a piece of glass, metal or rigid plastic.

The silica gel (or the alumina) is the stationary phase.

The stationary phase for thin layer chromatography also often contains a substance which fluoresces in UV light

The mobile phase is a suitable liquid solvent or mixture of solvents.

Schema of chromatography



Sample preparation

Isolation

- „general unknown“ components – isolation of broad group of toxicological significant components - lower extractive yield
- targeted isolation of drugs after identification of unknown components – optimalization of isolation with high extractive yield

Isolation of drugs from biological material

Extraction liquid - liquid
Standard fractional extraction of drugs

50 ml urine, stomach content
pH=3.0, 100 ml diethylether → acid and neutral analytes EA

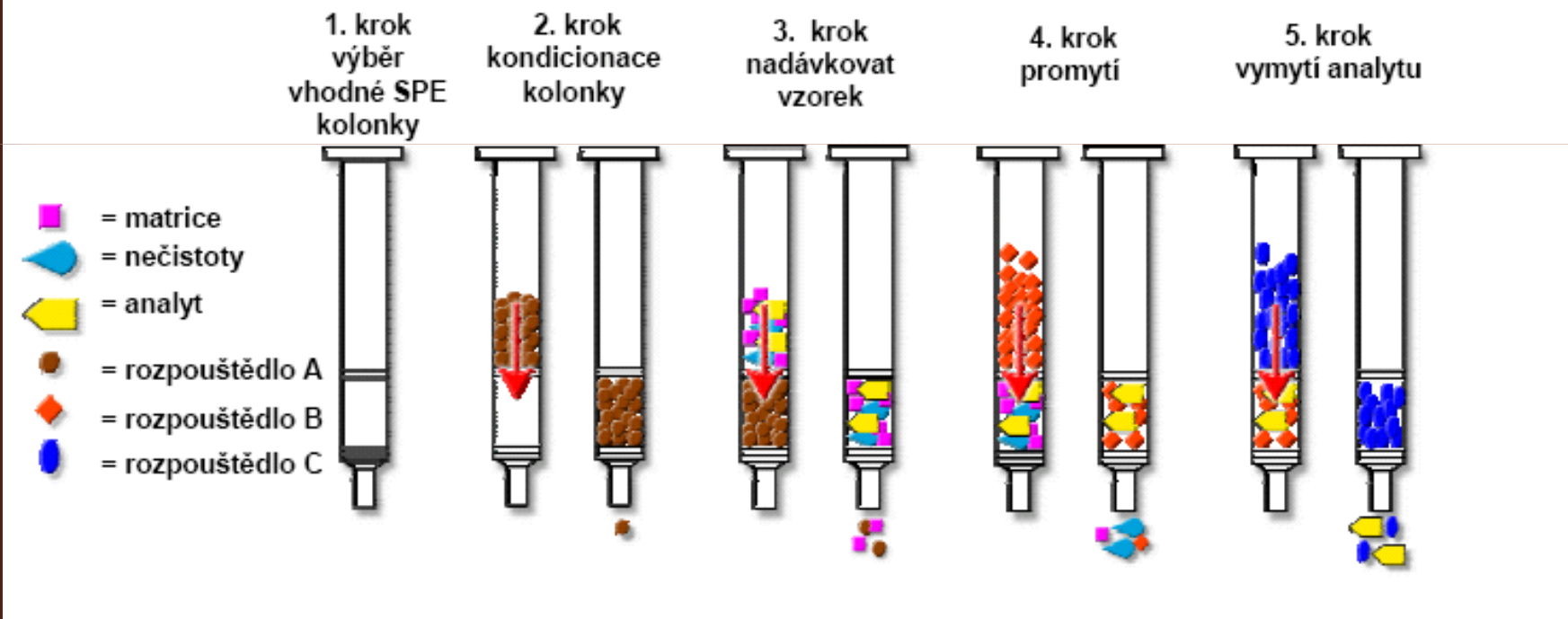
Rest of watter phase
pH=10.0, 100 ml diethylheter → bacic and neutral analytes EB

Rest of urine (20 ml)
hydrolytic degradation of conjugates

hydrolysatet, pH=7.0
100 ml diethylheter → conjugate metabolites EC

Isolation of drugs from biological material

SPE extraction
Polypropylen or glass tube, septum, sorbent



Isolation of drugs from biological material

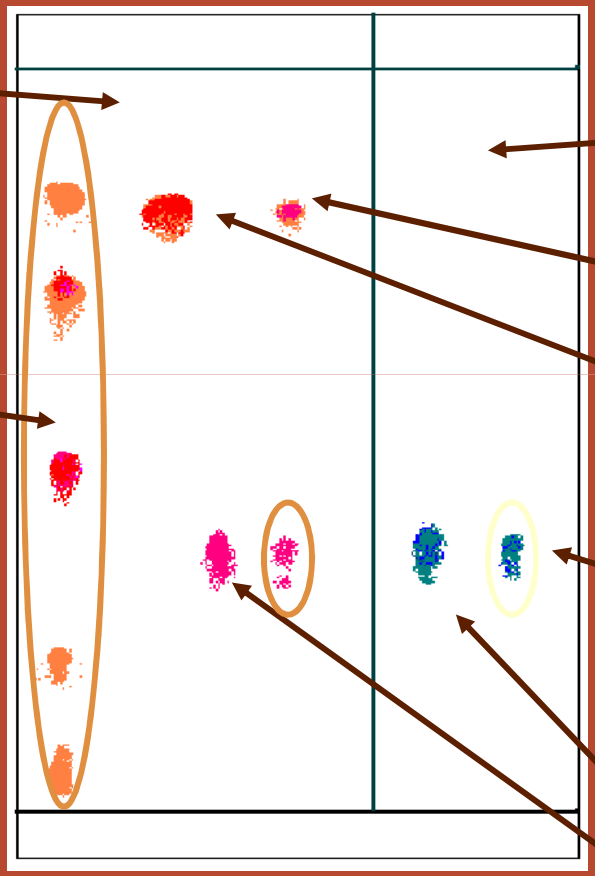
Derivatisation of analytes

- ✓ change of fyzical and chemical feature of analytes
- ✓ higher volatility
- ✓ higher stability
- ✓ better condition for chromatography (polarity)
- ✓ higher sensitivity (detekction rate)
- ✓ change of matrix

TLC intoxication cocaine and ecstasy

Part
by Dragendorf
reagent
detected
(KI and $Bi(NO_3)_3$)

AtKFAD
(atropin, codein,
phenmetrazin,
aminophenazon,
diazepam)



Part of chromatogram
by Marquis reagent
detected
(H_2SO_4 + formaldehyd)

cocaine - verification

cocaine - standard

ecstasy - verification

ecstasy - standard

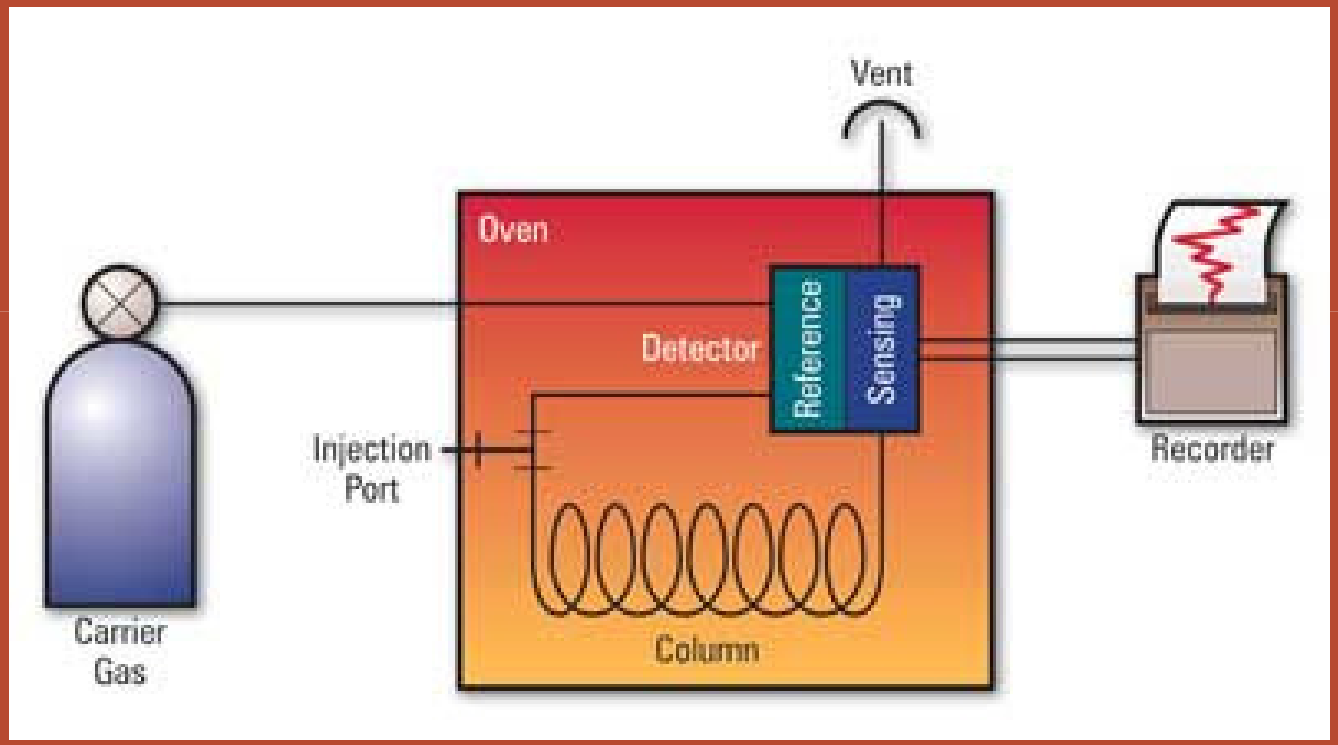
Mobile phase:
EtOAc-EtOH-NH_3 (36:2:2)

Gas chromatography

- **GC** is an analytical technique for separating compounds based primarily on their volatilities
- provides both qualitative and quantitative information for individual compounds present in a sample
- Compounds move through a column as gases, either because the compounds are normally gases or they can be heated and vaporized into a gaseous state
- The compounds partition between a stationary phase, which can be either solid or liquid, and a mobile phase (gas)
- The differential partitioning into the stationary phase allows the compounds to be separated in time and space

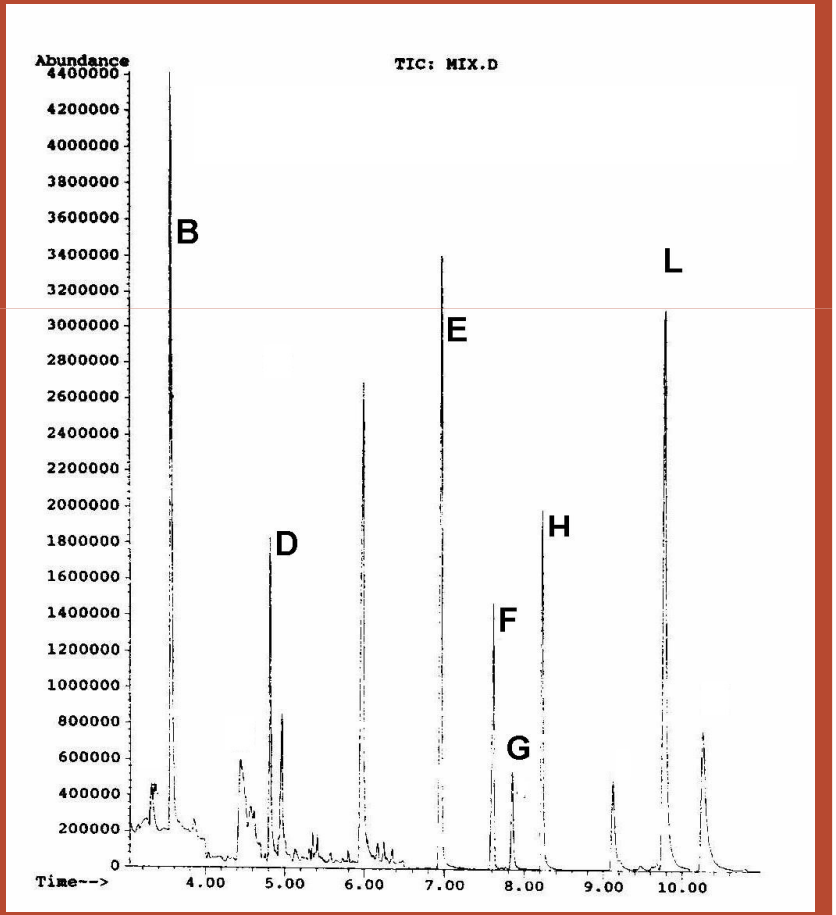
Gas Chromatography

- Sample (must contain stable, volatile compounds) is vaporized in a heated chamber
- Column is filled with silanized (silicon-coated) calcium silicate
- Column is kept hot (400 ^{o}C) in oven
- Sample is pushed through column using gas pressure (He or N_2)


Vent
Oven
Detector
Reference
Sensing
Injection
Port
Recorder
Carrier
Gas
Column

Chromatogram

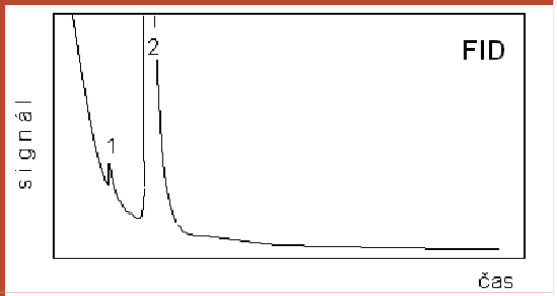
- B – Amphetamine
- D – Ecstasy
- E – EDDP (metabolite of methadone)
- F – Methadone
- G – Cocaine
- H – Cocaethylene
- L – THC



Gas chromatography with specific detection GC-NPD

Flame-ionisation detector

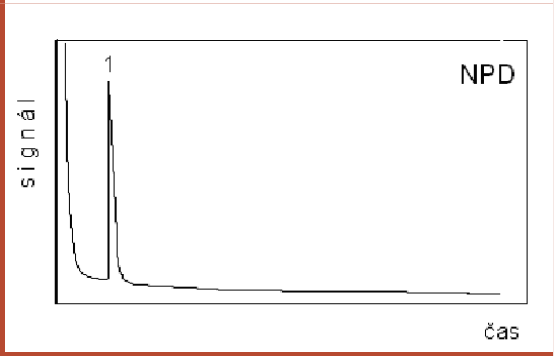
- GC – good separation
- less of samples than TLC
- purify of extracts



- <u>Specific detection NPD</u>:

analytes with nitrogen and phosphorus
Majority of drugs, alcaloides…

- screening method



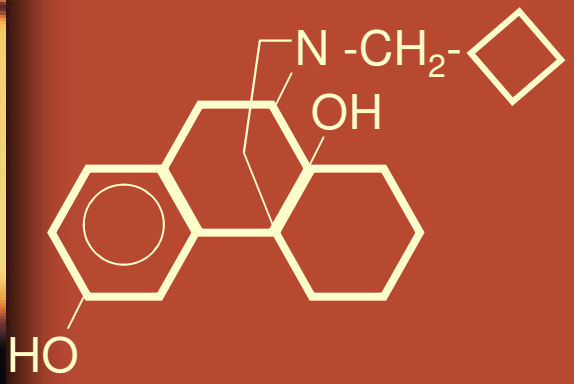
Mass Spectrometry

- Uses the interaction of electric and/or magnetic fields (i.e. eletromagnetic radiation) with matter to determine weight or mass
- Measures mass, not absorption or emission of electromagnetic radiation

MS Principles

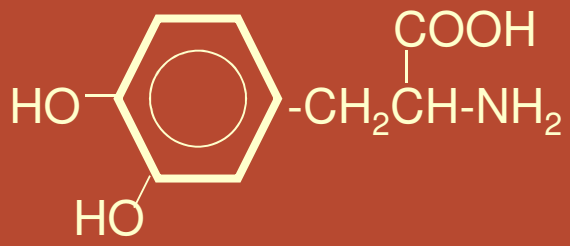
- Different compounds can be uniquely identified by their mass

Butorphanol



MW = 327.1

L-dopa



MW = 197.2

Ethanol

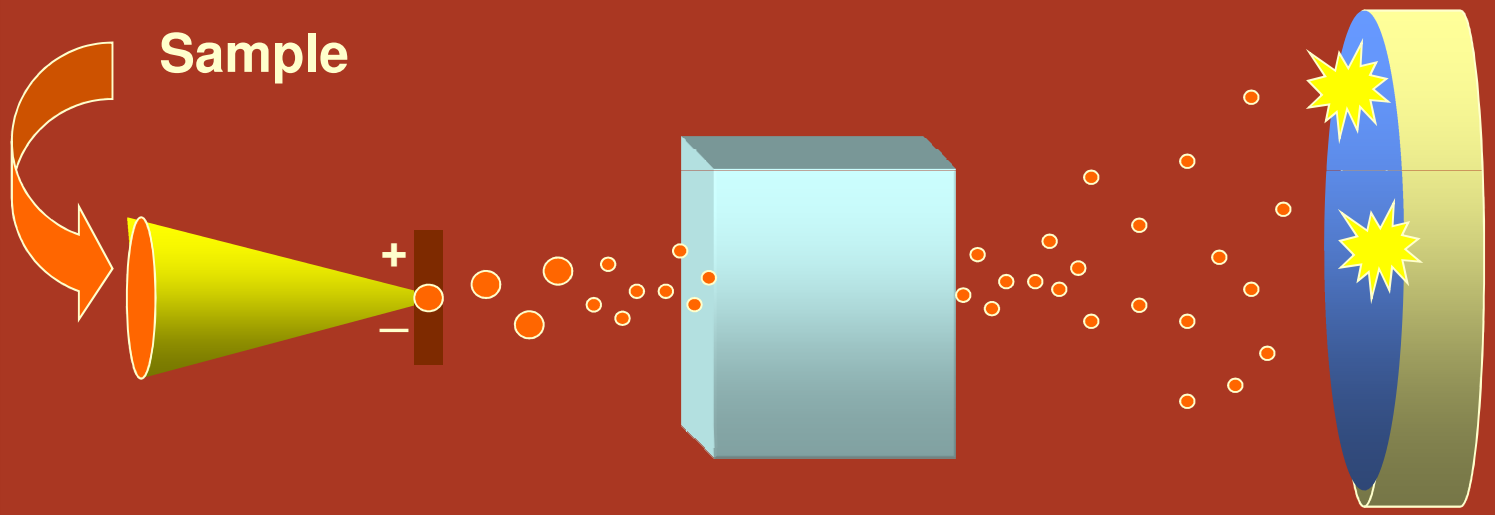
CH_3CH_2OH

MW = 46.1

MS Principles

- Find a way to “charge” an atom or molecule (ionization)
- Place charged atom or molecule in a magnetic field or subject it to an electric field and measure its speed or radius of curvature relative to its mass-to-charge ratio (mass analyzer)
- Detect ions using microchannel plate

Mass Spec Principles

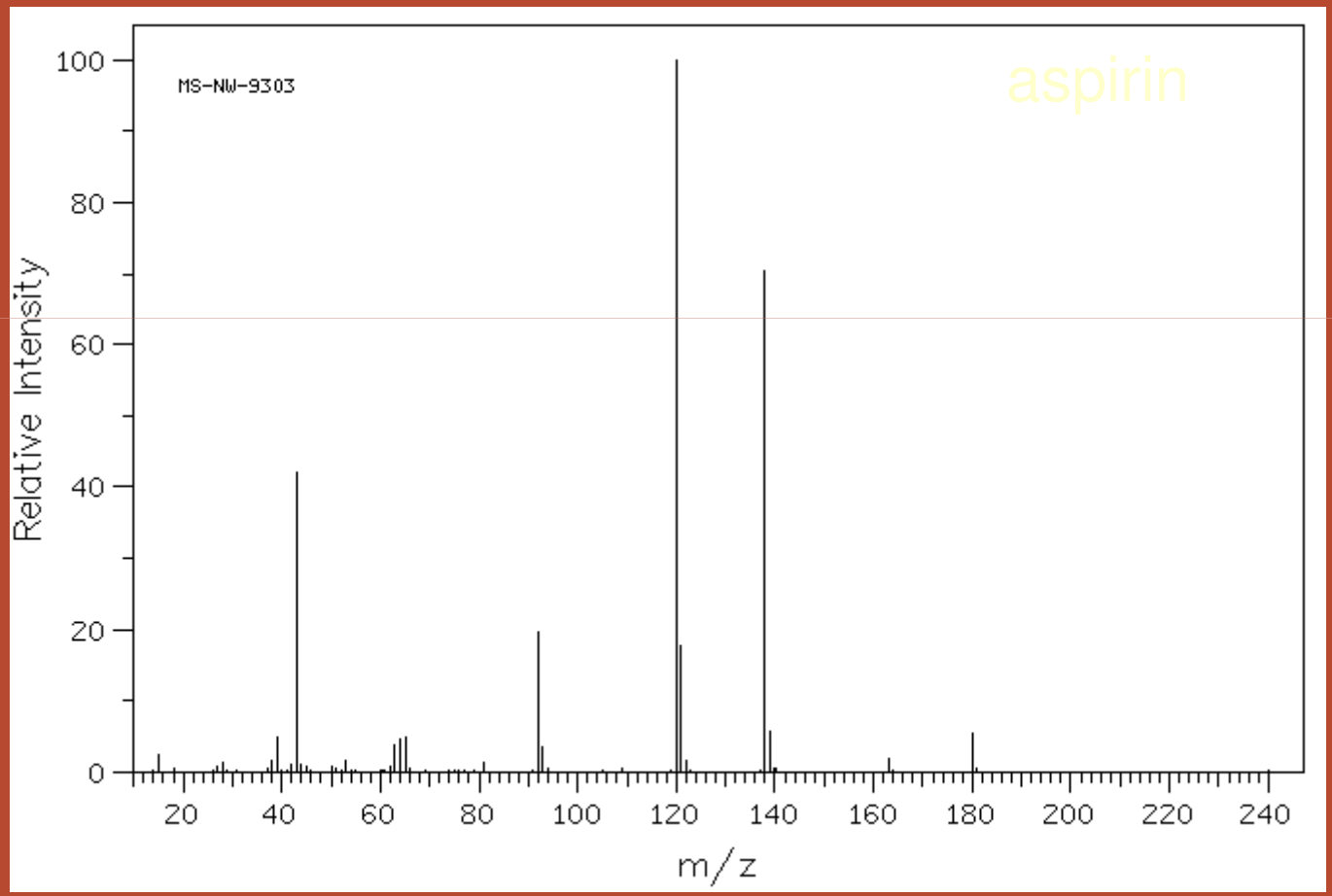


Ionizer

Mass Analyzer

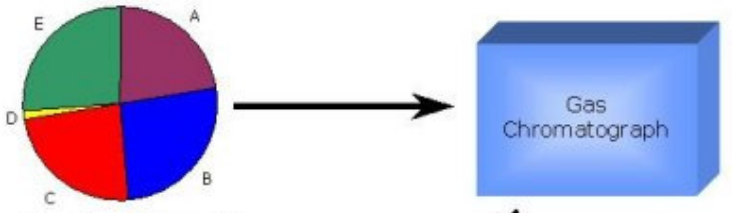
Detector

Typical Mass Spectrum

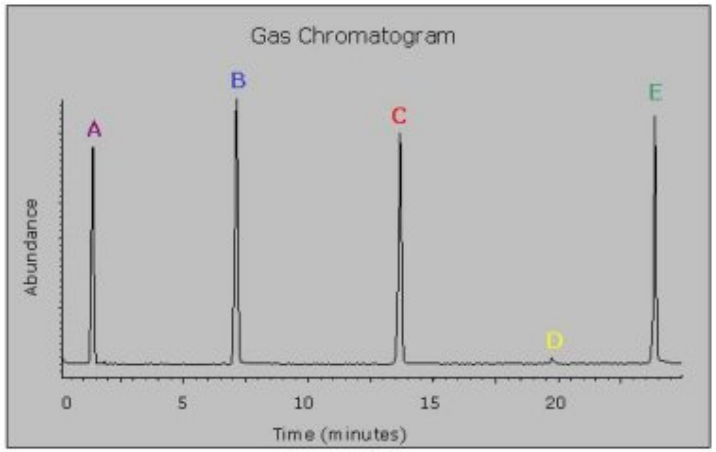


GC-MS

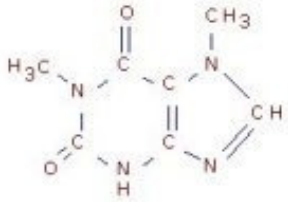
Gas Chromatography



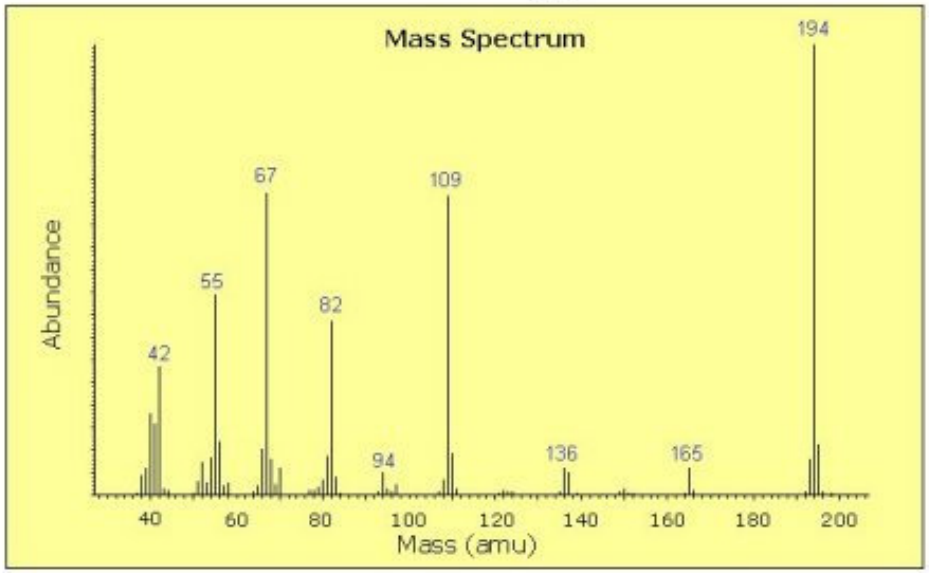
Sample: mixture of volatile liquids (~1μL)



Mass Spectrometry



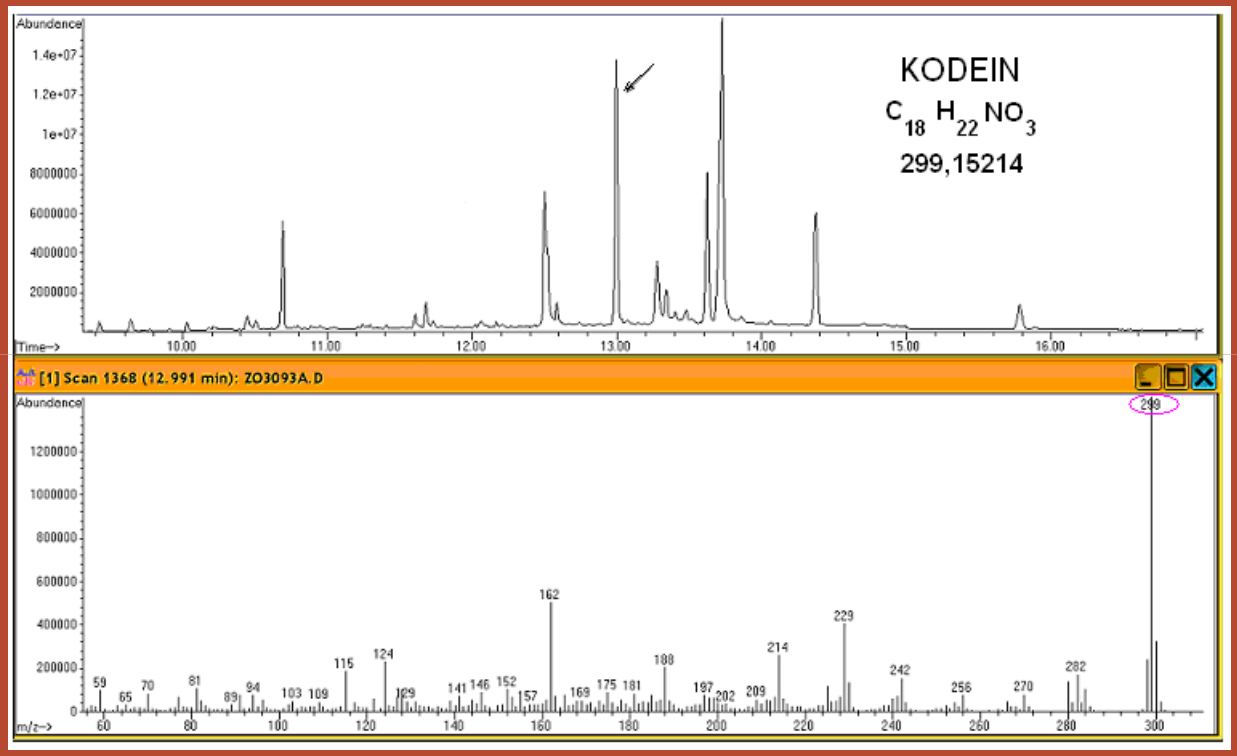
Typical sample: isolated compound (~1 nanogram)



Applications

- Determination or confirmation of chemical structure of drugs and drug metabolites (MS-MS)
- Detection/quantitation of impurities
- Detection/quantitation of drugs and their metabolites in biofluids and tissues
- High throughput drug screening
- Analysis of liquid mixtures (LC-MS)

GC-MS



Codeine: M+ (299)

Toxicology today

Combination of method:

- immunochemistry
- chromatography
- spectral method

Key stone in toxicology:

acknowledgement of results by independent methods

Forensic toxicology

- The qualitative and quantitative identification of drugs and chemical poisons in biological fluids and tissues as they relate to the purposes of the law

Toxicology

- Most crucial to the criminal investigator is the toxicologist's work of identifying a poison; then, there is the significant issue of quantity: was there or was there not a lethal amount present?
- The detection of poison may also allow the pathologist to rule out all other causes of death.

Looking for 3 things:

- What was there?
- How much was there?
- If something there, is it a lethal level?

Key points

- Laboratory support for drug-related emergencies consists of standard biochemical/haematological tests, measurement of specific substances and drug screens for unknown poisons.

- Standard laboratory tests are most important for determining immediate management in most patients.

Key points

- Emergency measurement of specific substances is indicated in a small number of cases where specific therapy may be instituted depending on the nature and quantity of the poison ingested.
- Forensic toxicological standard for organic samples: chromatography in tandem in MS

17th annual report on the state of the drugs problem in Europe 15.11.2012

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)

Established: 1993

Seat: Lisabon

Opioids

Problem opioid users: estimated at about 1.4 million Europeans
About 710 000 opioid users received substitution treatment in 2010
Principal drug in about 50 % of all drug treatment requests

Drug-induced deaths accounted for 4 % of all deaths of Europeans aged 15–39, with opioids being found in about three quarters of cases

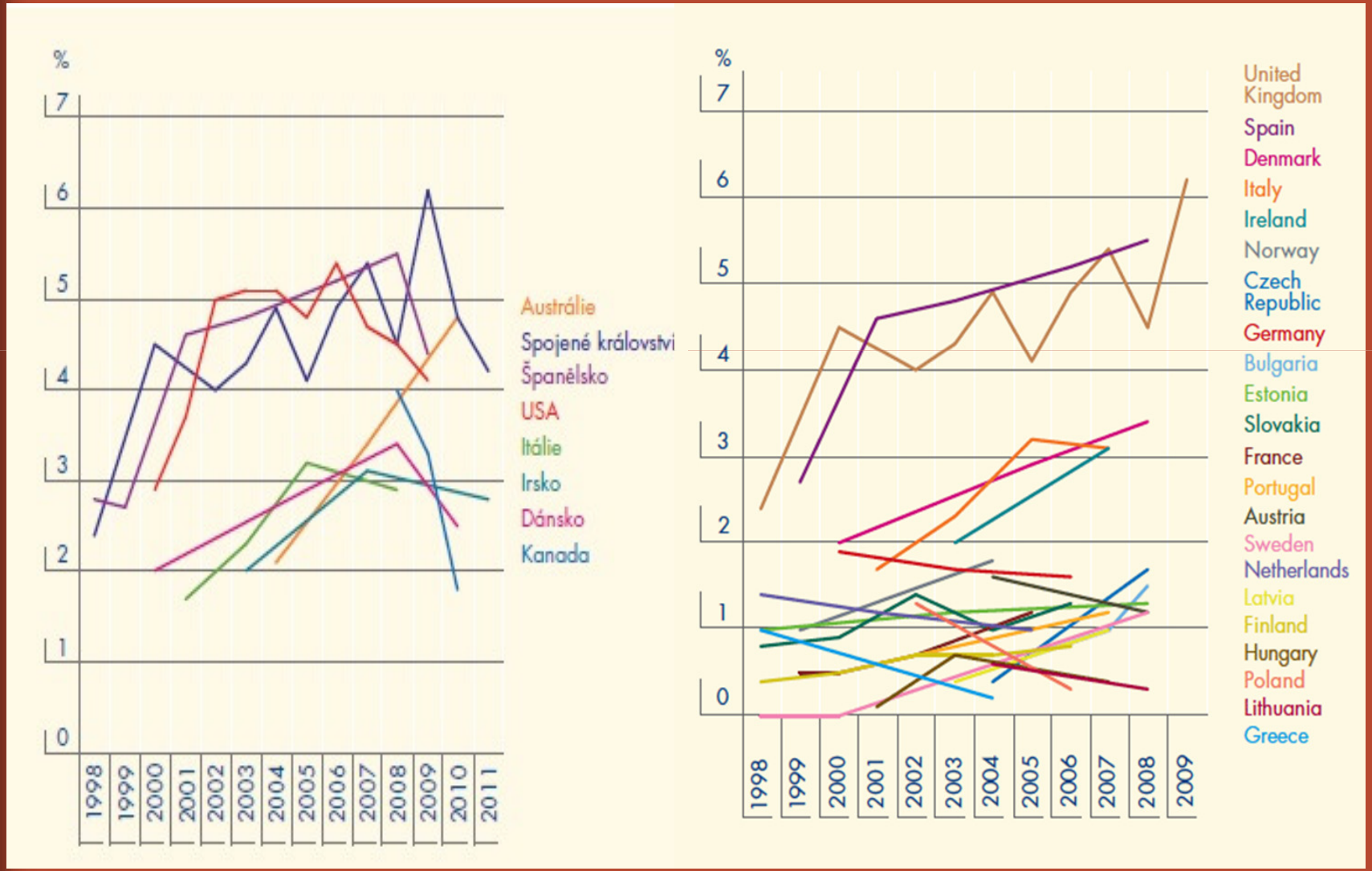
Injecting in decline, but still a serious public health risk

Drug injecting remains a major cause of avoidable health problems and death among young Europeans.

Injecting is particularly associated with drug overdose, as well as serious infections.

The outbreaks of HIV in Greece and Romania

Cocaine: young adult



Cocaine

Lifetime prevalence: about 15.5 million (4.6 % of European adults)

Last year use: about 4 million European adults (1.2 %) or one in four lifetime users

Last month use: about 1.5 million (0.5 %)

Country variation in last year use: overall range 0.1 % to 2.7 %

Increased number of mortal intoxication in Spain and UK

Ecstasy

Lifetime prevalence: about 11.5 million (3.4 % of European adults)

Last year use: about 2 million (0.6 %) or one in six lifetime users

Country variation in last year use: overall range 0.1 % to 1.6 %

Amphetamines

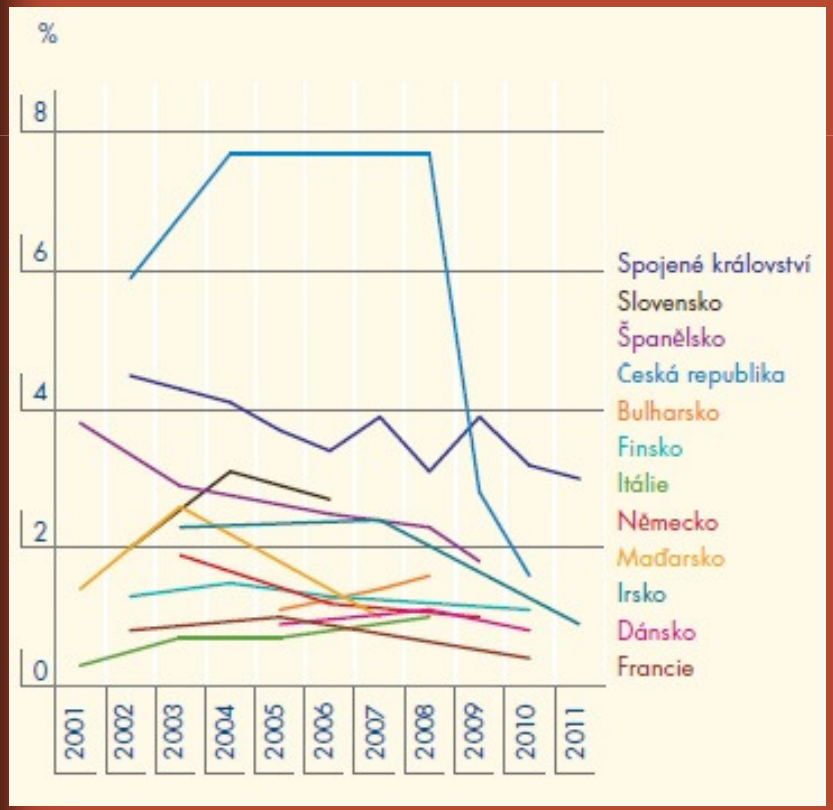
Lifetime prevalence: about 13 million (3.8 % of European adults)

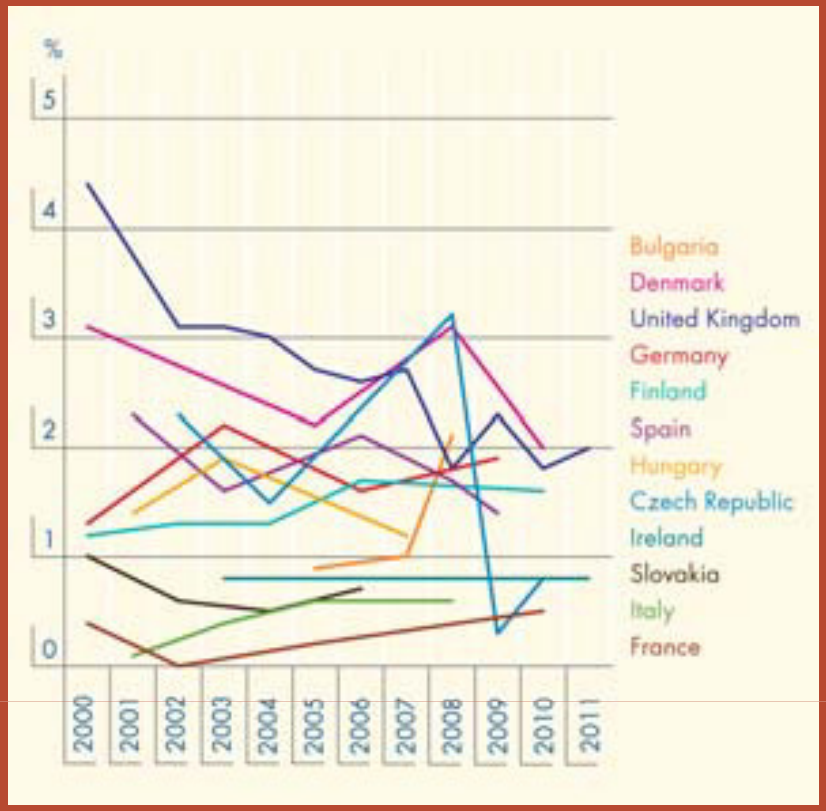
Last year use: about 2 million (0.6 %) or one in six lifetime users

Country variation in last year use: overall range 0.0 % to 1.1 %

Young adults

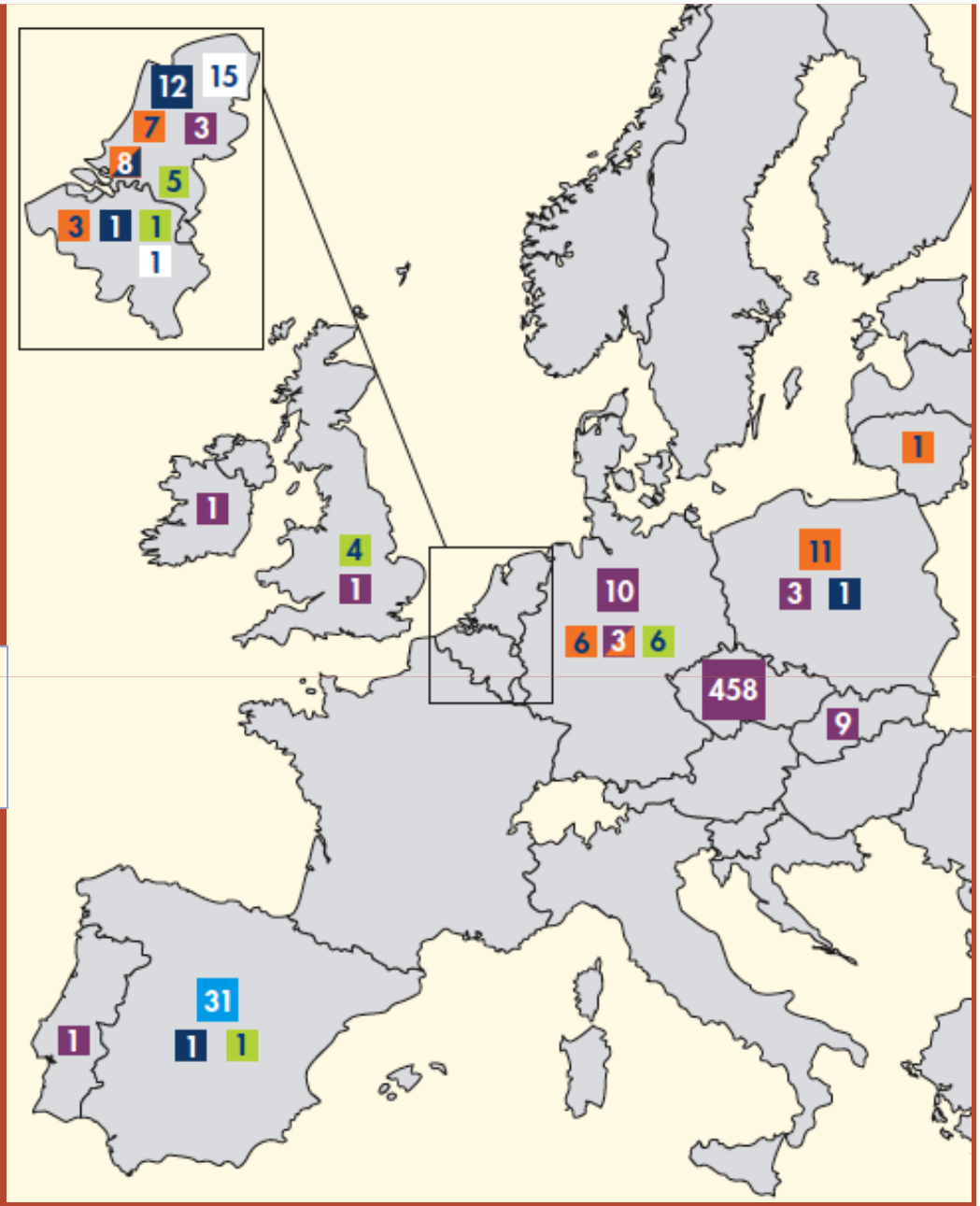
Ecstasy





Amphetamines

Nonlegal production of drogs liquidate in EU by Europol report (2010)



Amphetamine	x	Ecstasy	x
Methamphetamine	x	Other	x
Cocaine	x	Unknown	x

Cannabis

Lifetime prevalence: about 80.5 million (23.7 % of European adults)

Last year use: about 23 million European adults (6.8 %) or one in three lifetime users

Last month use: about 12 million (3.6 %)

Country variation in last year use: overall range 0.3 % to 14.3 %

Cannabis
prevalence among young adult

More diversity in synthetic drug use

While attention has largely been focused on either concerns about established stimulants or on the emergence of new uncontrolled psychoactive substances, a number of other synthetic drugs have entered and established themselves on the European drug market. Although the numbers of Europeans using drugs such as GHB (gamma-hydroxybutyrate), GBL (gamma-butyrolactone), ketamine and, more recently, mephedrone are low, high levels of use are found in some sub-populations, and these drugs appear to have the potential for more widespread diffusion.

New drog in internet shop

	01/2012	07/2011	01/2011
Kratom (natural)	179	128	92
Salvia (natural)	134	110	72
Hallucinogenic mushrooms (natural)	95	72	44
Methoxetamine (arylcyclohexylamine)	68	58	14
MDAI (aminoindane)	65	61	45
6-APB (benzofuran)	54	49	35
MDPV (cathinone)	44	32	25
4-MEC (cathinone)	43	32	11
Methiopropamine (thiophene)	39	28	5
5-IAI (aminoindane)	38	27	25

Source: EMCDDA.

THANK YOU FOR YOUR ATTENTION

Regionální rozdíly v míře a vzorcích problémového užívání amfetaminů v Evropě