

Investigating Poisoning

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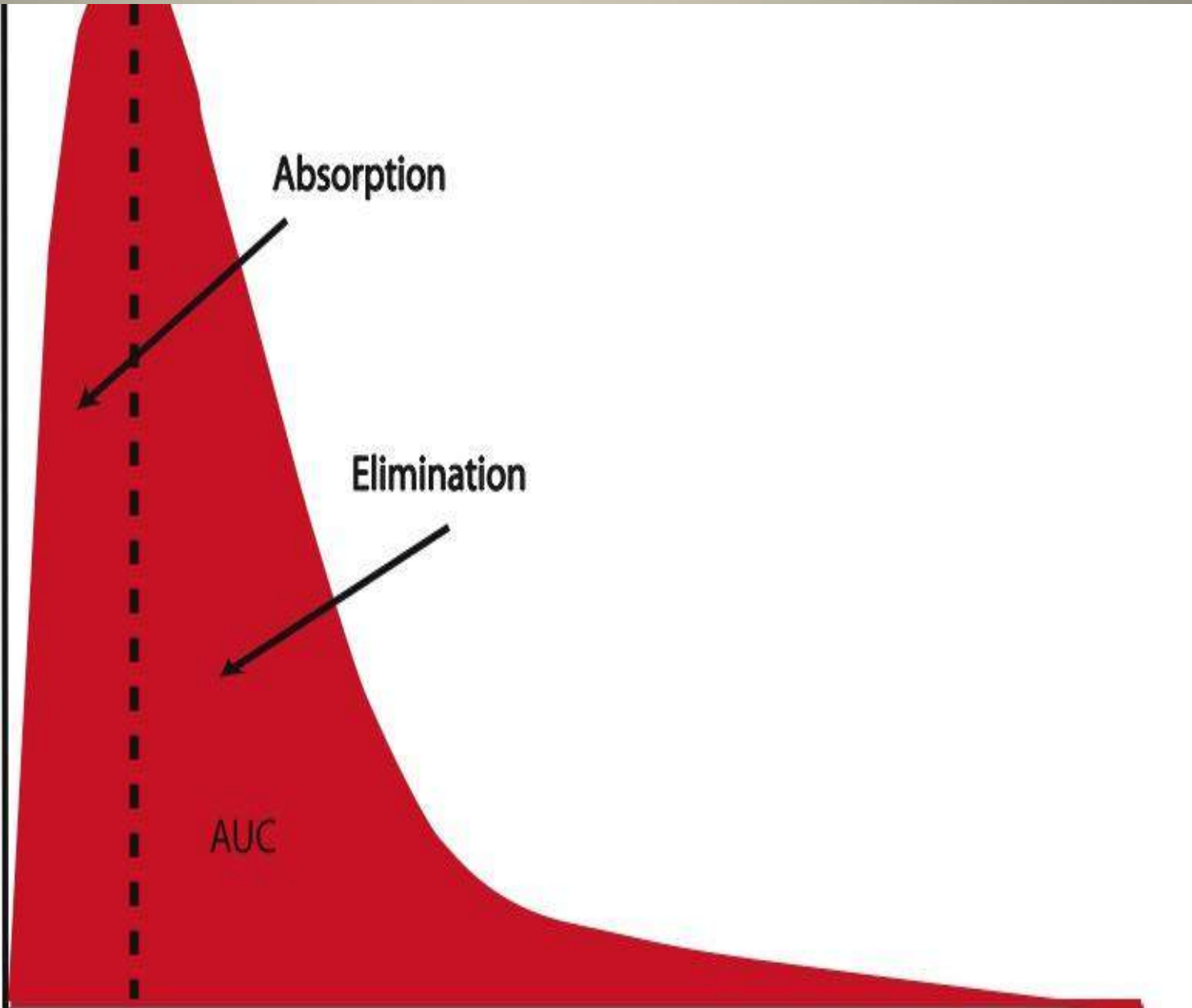
Poisoning

- Presentation
 - Clinical signs and symptoms
- Toxicokinetics
- Toxicodynamics
- Investigation
 - Methodologies for analysis
- Information
 - NPIS
- Intervention

Toxicokinetics

- Route
- Absorption from exposure site
- Distribution around the body
- Metabolism, typically liver
- Kidney role
- Active intervention
 - Minimise absorption/exposure
 - Maximise excretion

Concentration of drug in plasma



Absorption

Elimination

AUC

Kinetics

dc/dt is the rate ($c = \text{concentration}$; $t = \text{time}$) = k

k_a is the absorption rate from exposure site

k_e is the elimination rate from the body.

Elimination is an exponential decline

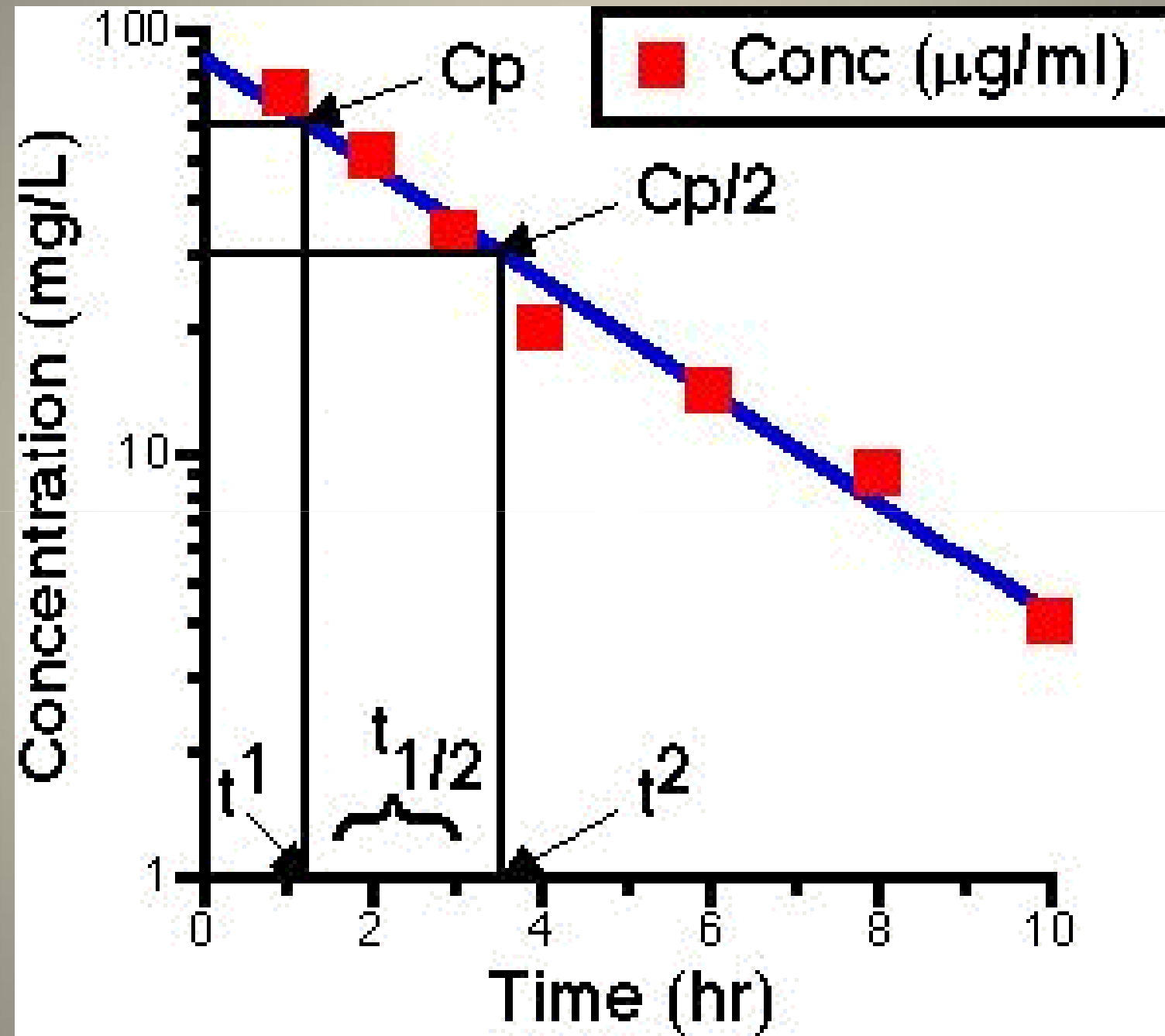
Kinetics

Half-life: time to reduce C_{p1} by 50%

i.e. $C_{p2} = (0.5) C_{p1}$

$k_e = 0.693/t_{1/2}$ i.e. $t_{1/2} = 0.693/k_e$

Half-life useful to assess how long before drug concentrations no longer likely to be toxic



Presentation

- Breathing
- Pulse/BP
- Pupil size
- Gait
- Level of Consciousness
- GCS

Glasgow Coma Scale (GCS)

	1	2	3	4	5	6
Eye	Does not open eyes	Open eyes Painful stimuli	Open eyes in response to voice	Open eyes spontaneously	N/A	N/A
Verbal	Makes no sounds	Incomprehensible sounds	Utters incoherent words	Confused Disorientated	Oriented converses normally	N/A
Motor	Makes no movements	Extension to painful stimuli (decerebrate)	Abnormal flexion to painful stimuli (decorticate)	Flexion/withdrawal to painful stimuli	Localises painful stimuli	Obeys commands

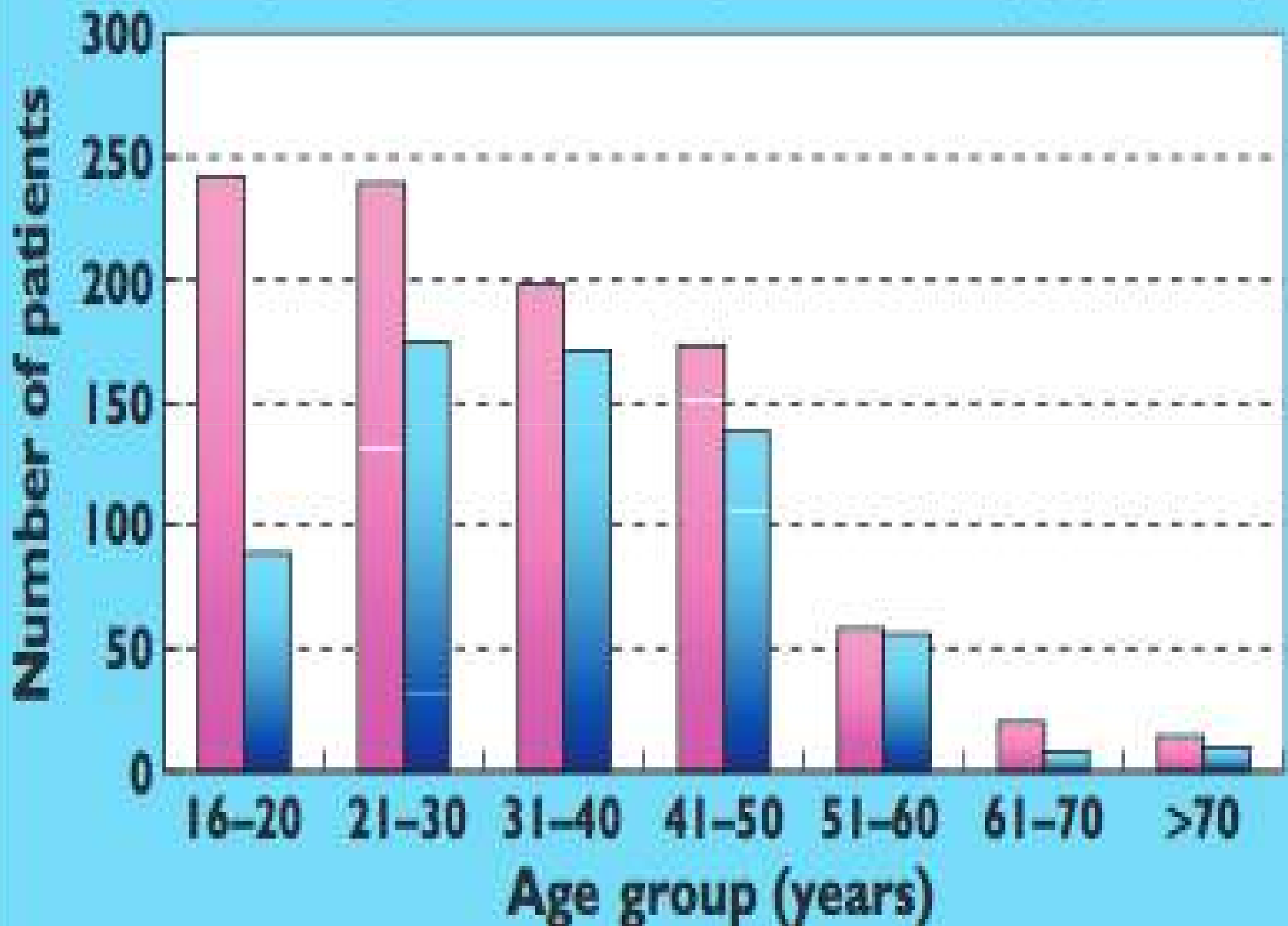
GCS

- 3-15
- Lower the score the worse the brain damage
- < 8 severe
- > 13 minor

Incidence of Poisoning

- 170,000 pa presentations are suspected overdose
- ~ 60% admitted (~ 40% of these discharged from admissions ward)
- 0.7% die
- 3674 poisoning deaths (2015)
 - Misuse: 67%
 - 3M:F
 - Commonest age 30-39y

Age of patients taking overdoses (by gender)



Investigation Historical 18th Century

Most poisons were plants or minerals

Arsenic mimicked symptoms of cholera, so homicidal use: Mary Blandy gave her father 'a white powder'

Investigators scraped some from the gruel pan

Tests: white, gritty, insoluble in cold water; thick white garlic smelling fumes when thrown on a hot iron as did arsenic

18th Century Poisoning Case

Mary Blandy 31y female



Suitor Capt Cranstoun son of Lord Cranstoun

BUT.....already married

Francis Blandy (father) furious!

18th Century Poisoning

- In 1751 Capt Cranstoun gave Mary 'a white 'forgiveness' powder' to put in father's food to make him 'more amenable'
- Francis Blandy (prosperous solicitor & Town Clerk) became very ill (vomiting, abdominal pain, diarrhoea teeth lost), died on 14th August .
- Mary admitted guilt and father forgave her
- Cranstoun fled the country.

18th Century Poisoning

- Dr Addington, symptoms consistent with poisoning.
- Examined powder: white, gritty, insoluble in cold water; thick white fumes smelling of garlic when heated and precipitation tests as did a known sample of arsenic.
- Mary was Hanged on 6th April 1752

Investigation 19th Century

Reinsch Test: Arsenic on copper = black copper
arsenate: qualitative

Reinsch Test

Qualitative test



Cu mesh
clean in
 HNO_3

Rinse the
Cu with
D.W.



Add 10 ml
conc. HCl and
20 ml test
solution



Fume
cupboard

For one
hour

Cool and wash with
D.W.



1 - Clean Copper
2 - Bismuth
3 - Arsenic
4 - Antimony
5 - Mercury

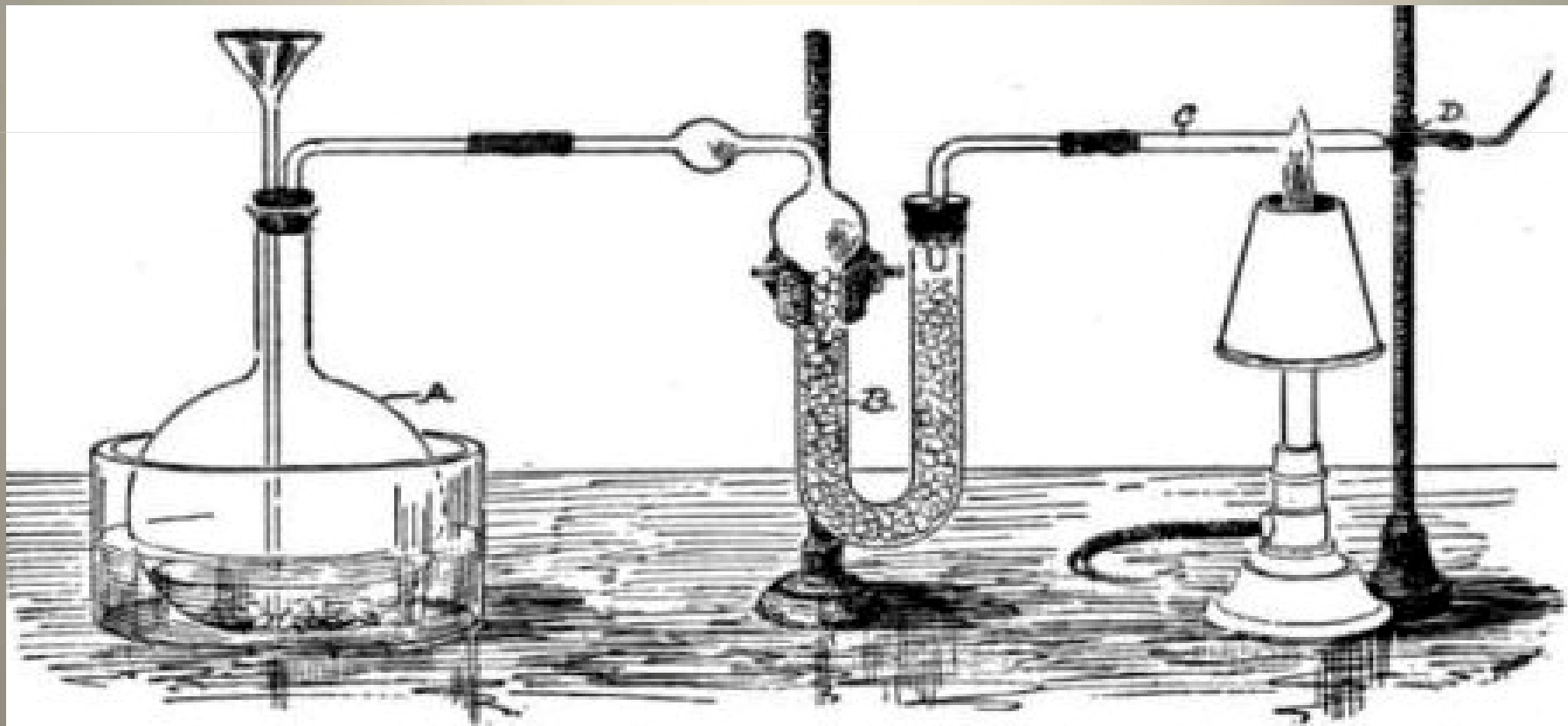
Results
Dull black-
Arsenic
Silvery- Mercury

Investigation 19th Century

- Increase specificity by sublimation and exposing to AgNO_3 (Ag_3AsO_4 : yellow),
 H_2S (As_2S_3 : yellow), CuSO_4 (AsCuHO_3 : green)
- Discriminates from other heavy metals:
mercury, Antimony, Bismuth

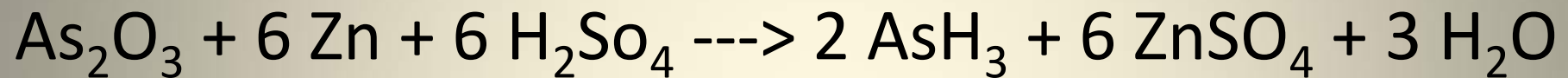
Early 19th Century

- Marsh Test: quantitative



Early 19th century

Arsenic sample in H_2SO_4 & Zn reduced to As^{3+} to form Arsine gas:



Igniting the gas i.e. oxidising the arsine, on a cold ceramic bowl will yield a silvery-black film; intensity related to amount present

Early 19th century

Mineral acids demonstrated by litmus paper, cloth oxidation differentiated by colour: HNO₃ (yellow), H₂SO₄ (red-brown), HCl (reddish) also precipitate and resolution tests:

H₂SO₄ + BaCl → BaSO₄ insoluble in HCl

HCl + AgNO₃ → AgCl insoluble in HNO₃, but soluble in NH₃

HNO₃ determined by yellow fumes on heating

19th Century Poisoning

- 14th September 1849: 7 people, had a lunch of bread, cucumber, boiled meat and apple dumplings. The lodger, Emanuel Barnett provided the flour for the dumplings
- Soon 2 or 3 ill: vomiting, diarrhoea: all stopped eating
- Gradually worse: one daughter, Elizabeth Gregory (21y) and son Sam (14y) died; others 'dying'
- Emanuel Barnett threw dumplings into the privy

19th Century Poisoning

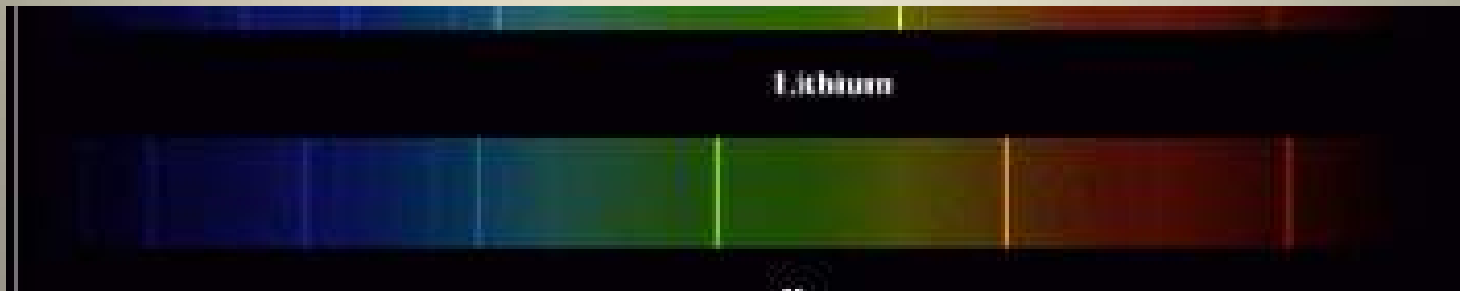
- Drs excluded cholera and police retrieved puddings, flour, sugar and vomit.
- Dr Herapath (analytical chemist) was called in
- Examination:
 - Microscopy: 3 crystals in Elizabeth's stomach: arsenic
 - Reinsch Test on stomach contents and uncooked dumpling dough: positive for **As**
 - Precipitant tests on stomach contents and uncooked dumpling dough: positive for **As**
 - Flour had NO **As** in it

19th Century Poisoning

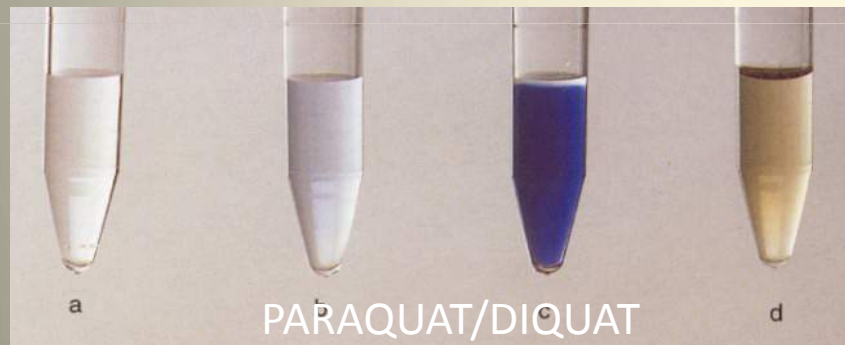
- Barnett stood trial in April 1850
- His claim that ‘there had been accidental contamination of the flour’ was believed by the jury
- He was acquitted.

Colour Tests

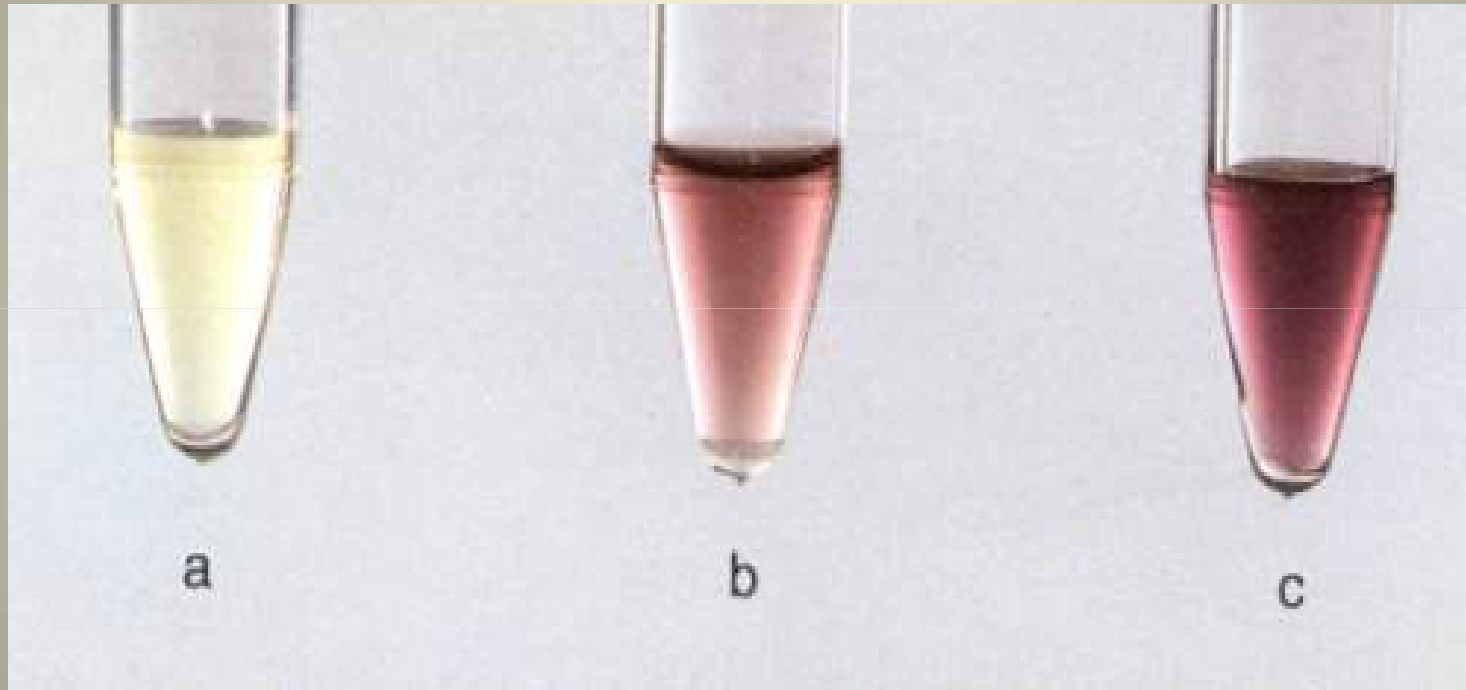
Spectroscopes: characteristic absorbance lines



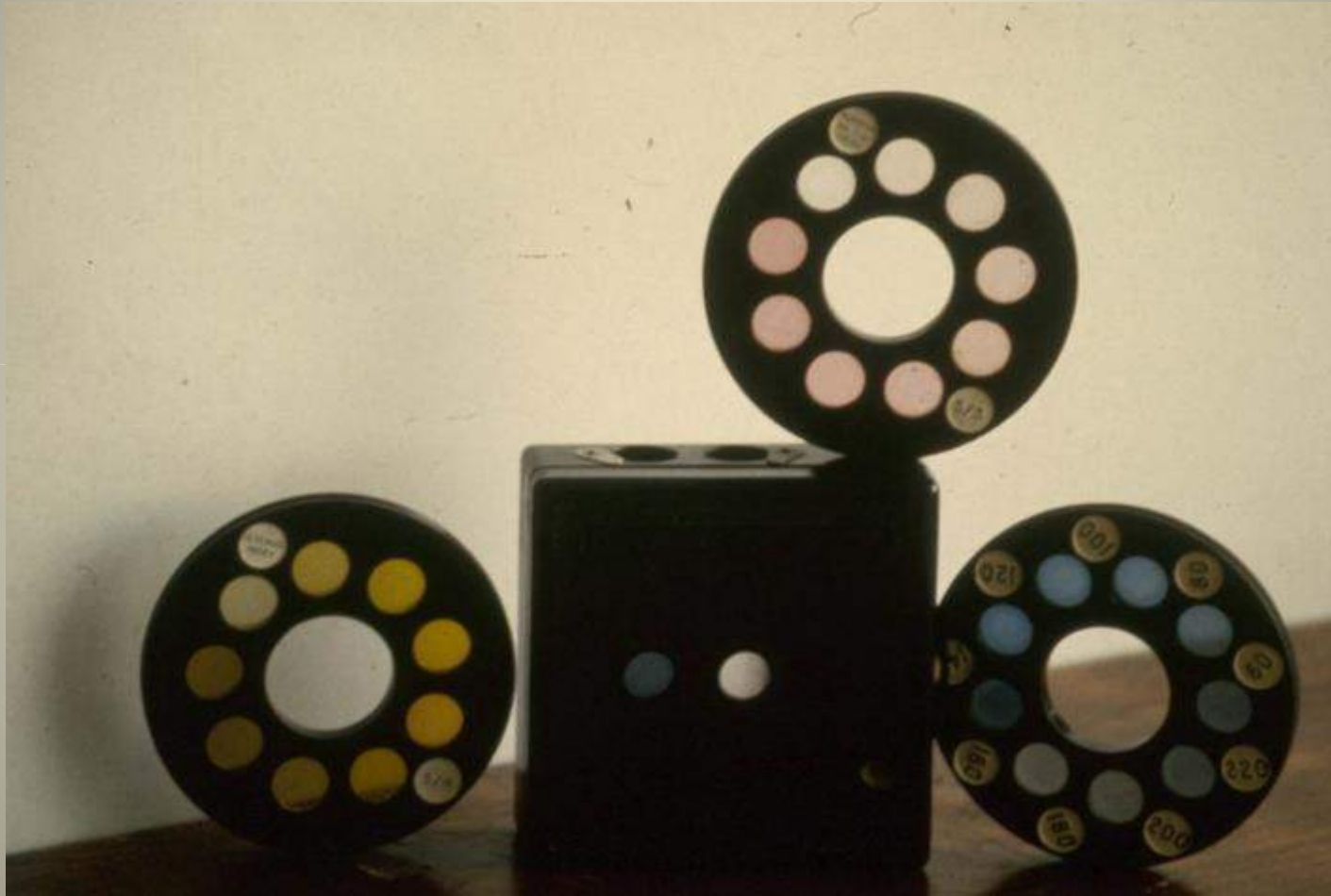
Urine Colour Tests



Serum Colour Tests



Semi-quantitation



Improving Specificity

Background interference: blank

Better end-point: chemical properties

Sample types: Urine, Blood, Vomit

Liquid-Liquid Extraction

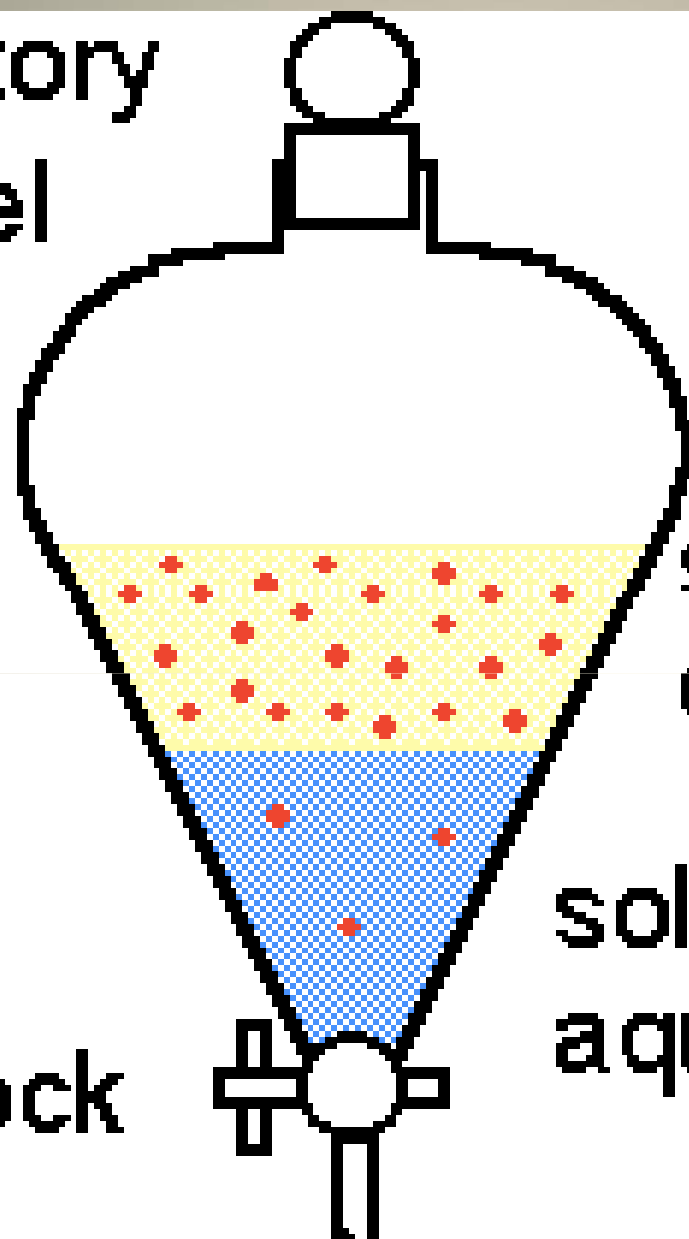
Lipophilic substance: organic solvent

Charged molecules: suppress ionisation to extract into solvent

Back-extract by changing charge into aqueous phase, improving specificity by appropriate choice of pH, solvent strength and volume ratios

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separatory
funnel



solute in
organic phase

solute in
aqueous phase

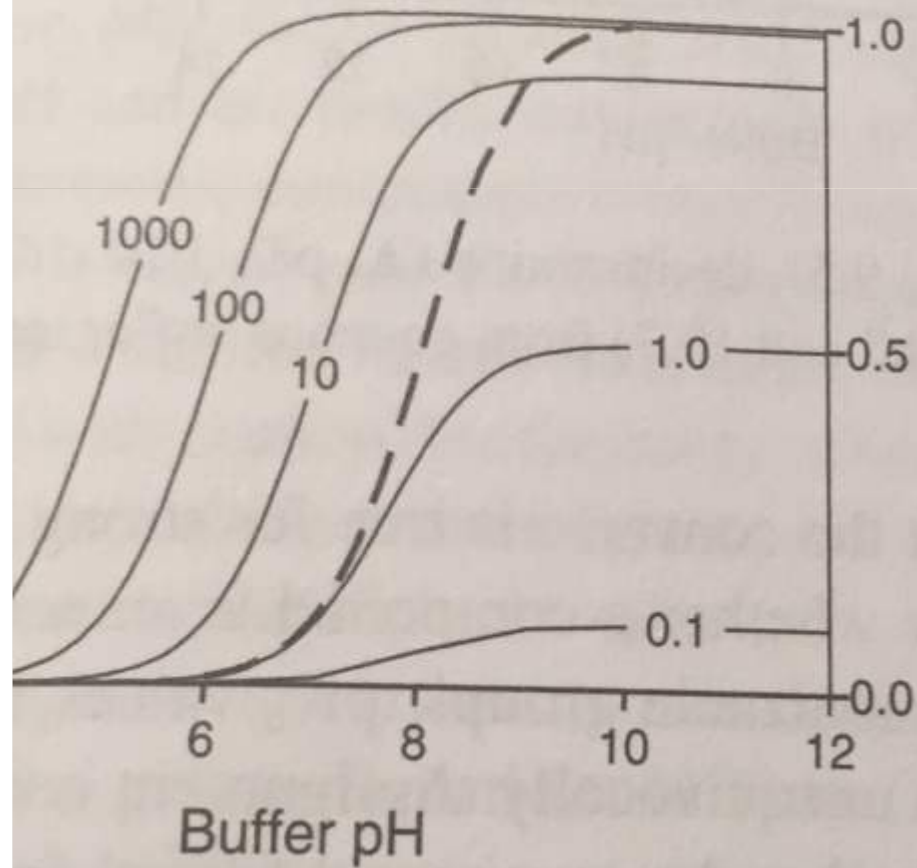
stopcock

Extraction: Liquid-Liquid

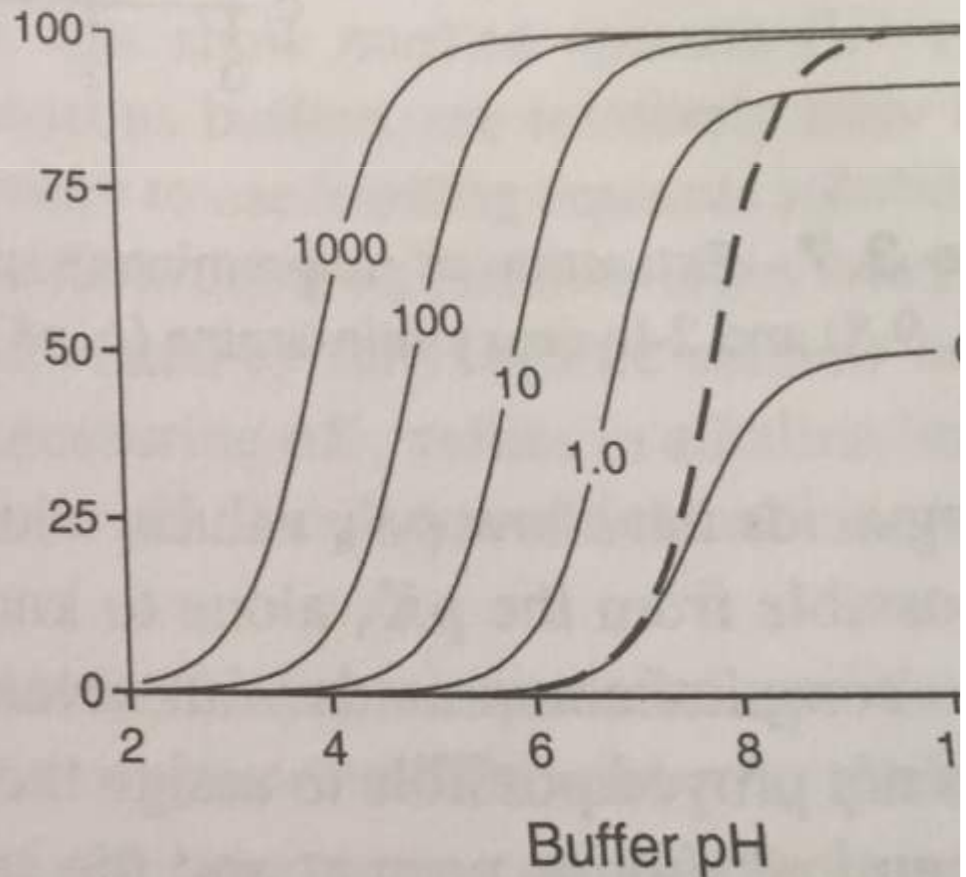


LLE: pH & organic phase volume

aqueous 1 + 1



(b) Organic:aqueous 10 + 1



Fraction Ionized

Henderson-Hasselbalch Equation

$$\text{pH} = \text{pK}_a + \log[\text{acid}/\text{base}]$$

Problems with liquid-liquid extraction

Emulsion formation/purity/disposal/eco

Hazards

Carcinogenic solvents: e.g. Benzene

Flammable solvents e.g. Diethyl Ether

Explosion Risk e.g. Di-isopropyl Ether

Metabolic Disruption e.g. Dichloromethane
(Carboxyhaemoglobin)

Liquid-Solid Extraction

Typically Silica Gel based

Commonest form C8 or C18 material

Condition column:

Suppress ionization to absorb

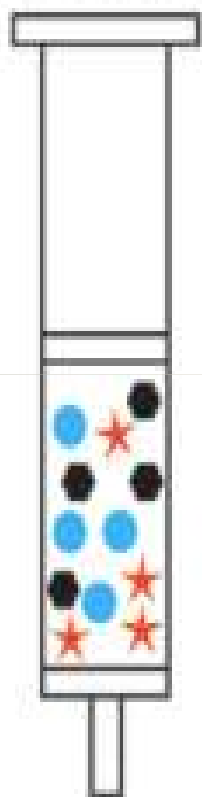
Apply sample

Rinse,

Elute compound of interest

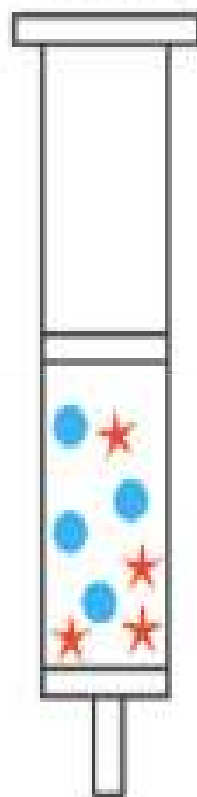
interferent ● analyte ●★

Add the Sample



(a)

Wash the Sample
to Remove Interferents



(b)

Elute the Analytes



(c)

Analysis

Spectrophotometric

Immunoassay

Chromatographic

Mass spectroscopic



20th Century Poisoning

- 17th September 1970 Jimi Hendrix, Samarkand Hotel, Notting Hill.
- Had a meal with his girlfriend, some wine, she took him to see a friend and they returned at 3am.
- Went to bed at 7am, having talked for 4 hours, she awoke at 11am, Jimi was unconscious and breathing

20th Century Poisoning

- Ambulance called arrived 11:18, left 11:27, transferred to St Mary Abbot's Hospital
- Pronounced dead 12:45pm
- Coroner asked Prof Teare to perform a Post Mortem
- Death by Aspiration of his own vomit
- Had taken Vasparax (brallo- and seco-barbital with hydroxyzine): Sedative
- Took 18x the dose

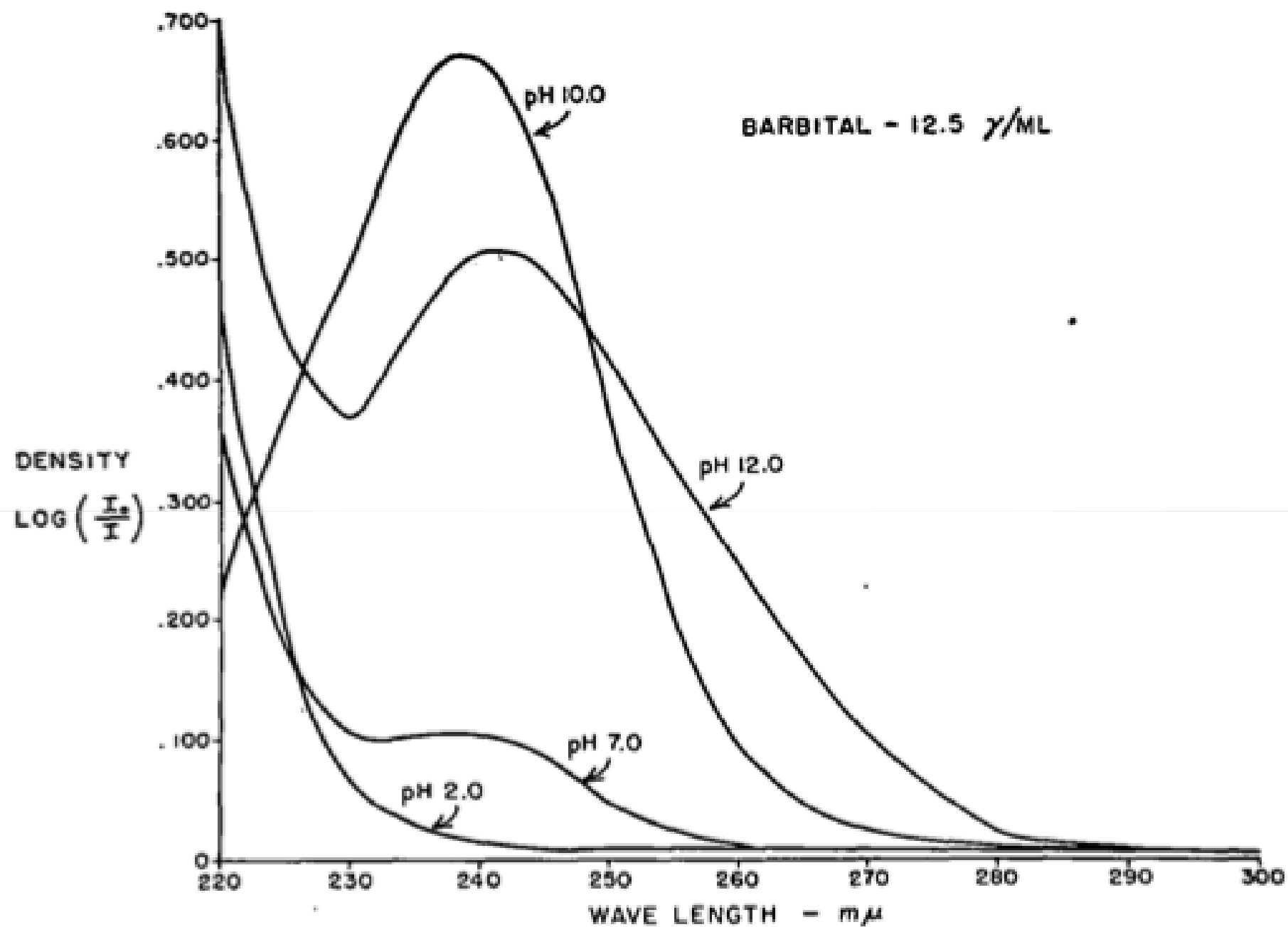


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA OF BARBITAL IN AQUEOUS SOLUTION OF VARIOUS DEGREES OF pH

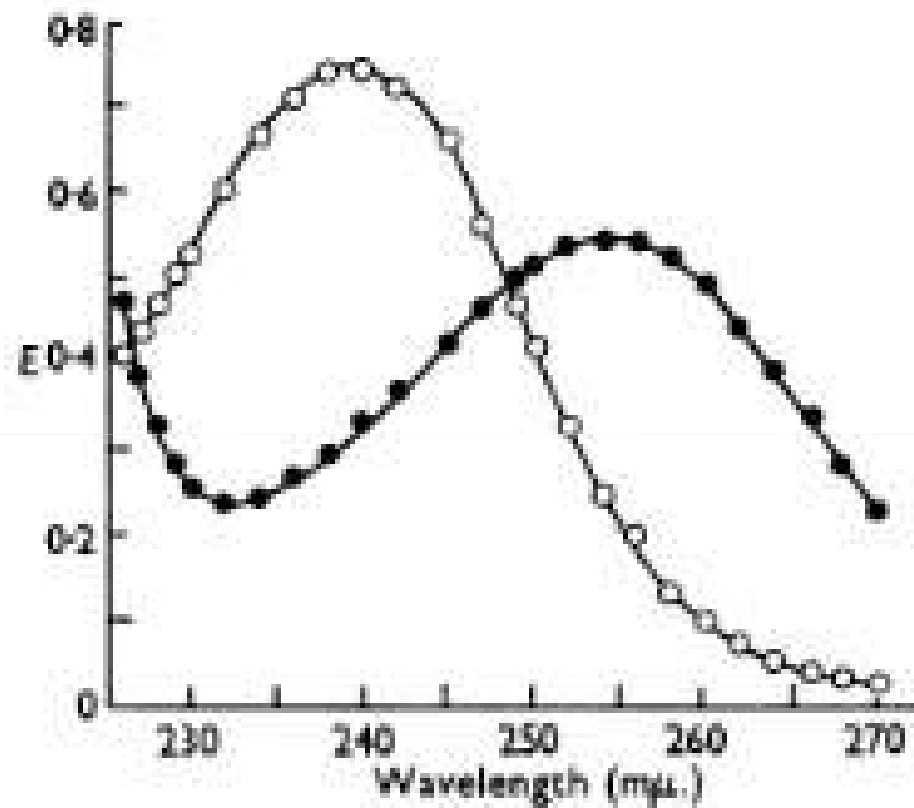


Fig. 1. Absorption spectra of a barbitone solution (13.5 μg./ml.). ●, In 0.45 N-NaOH; ○, in borate.

Table II.8 UV maxima of barbiturates at pH 9 and 13

Barbiturates	pH 9.2^a	pH 13.0^b
Allobarbital	241	256
Amobarbital	240	255
Barbital	239	254
Butalbital	240	255
Butobarbital	239	254
Cyclobarbital	239	256
Methylphenobarbital	244	243
Pentobarbital	239	255
Phenobarbital	239	254
Secbutabarbital	239	254
Secobarbital	239	254
Vinylbital	-	247

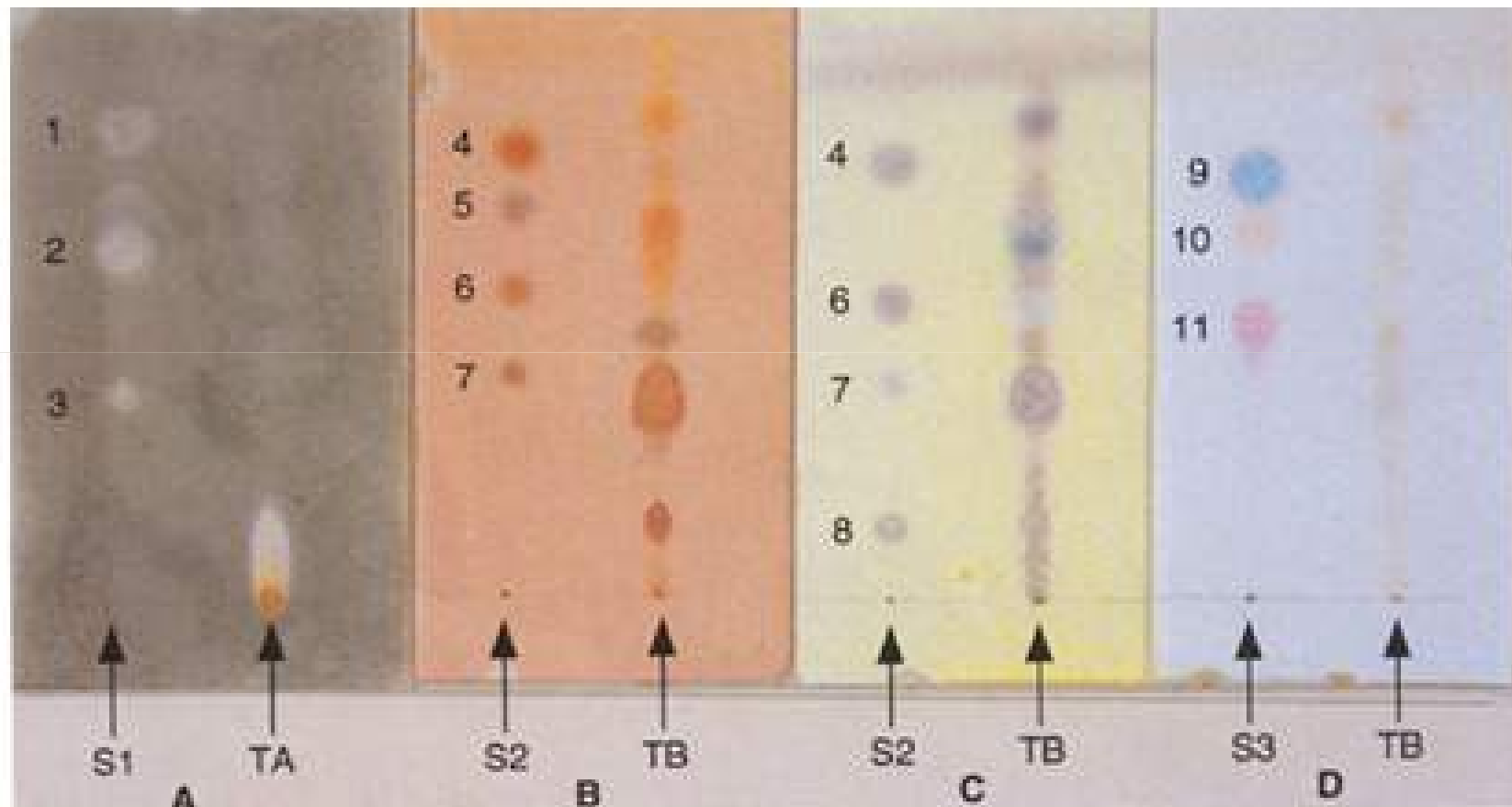
^a = 0.05 M borax buffer, pH 9.2

^b = 1.0 M sodium hydroxide solution, pH 13.0

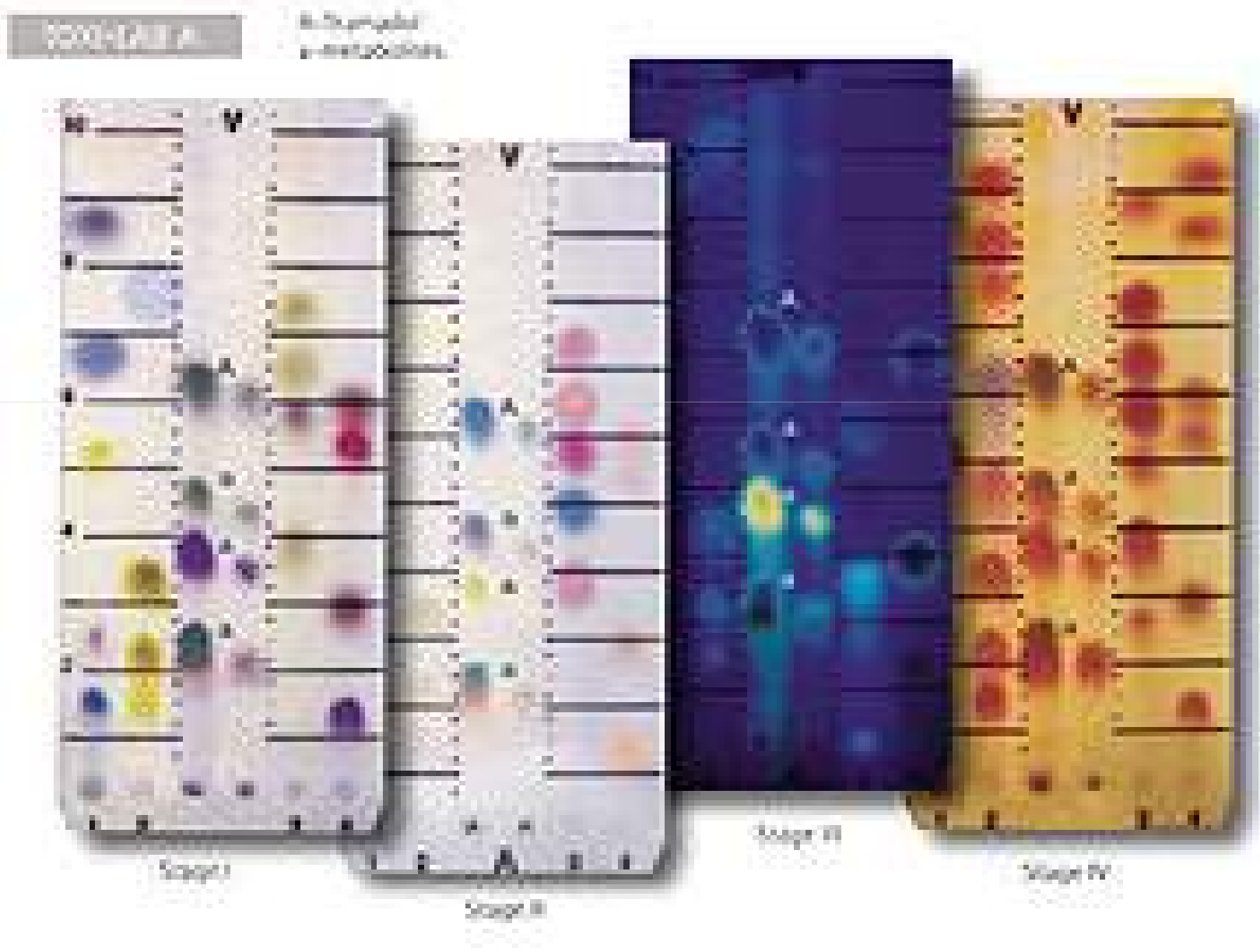
Thin-Layer Chromatography

- Silica Gel on a glass plate
- Apply extracted sample to origin
- Develop with selective solvents by capillary attraction
- Dry and react substances with a location agent

TLC: Acidic & Basic Extracts of Urine



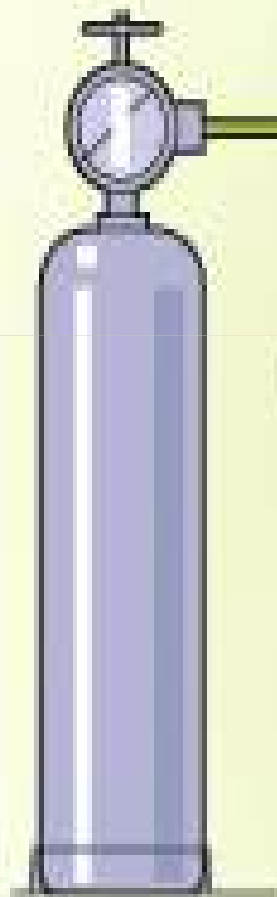
Commercialised TLC



Gas-Liquid Chromatography

- Extract sample
- If not volatile, derivatize to make it so
- Inject into flowing gas (H_2 , He or N_2)
- Separation by interaction with a selective wax coated onto an inert material
- Detection by physical property (flame ionisation, N_2 detector, Electron Capture etc)
- Record response as a chromatogram
- Peak height (area) proportional to concentration

Carrier
gas



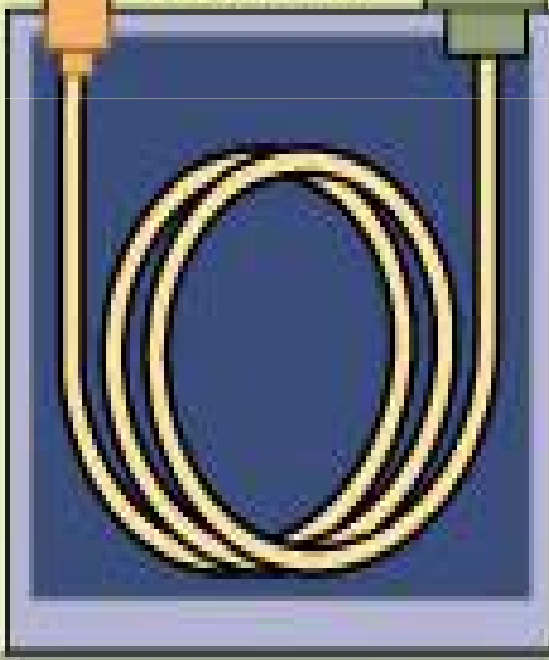
Flow/
pressure
control



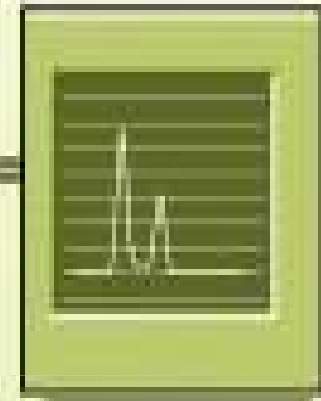
Injector



Column

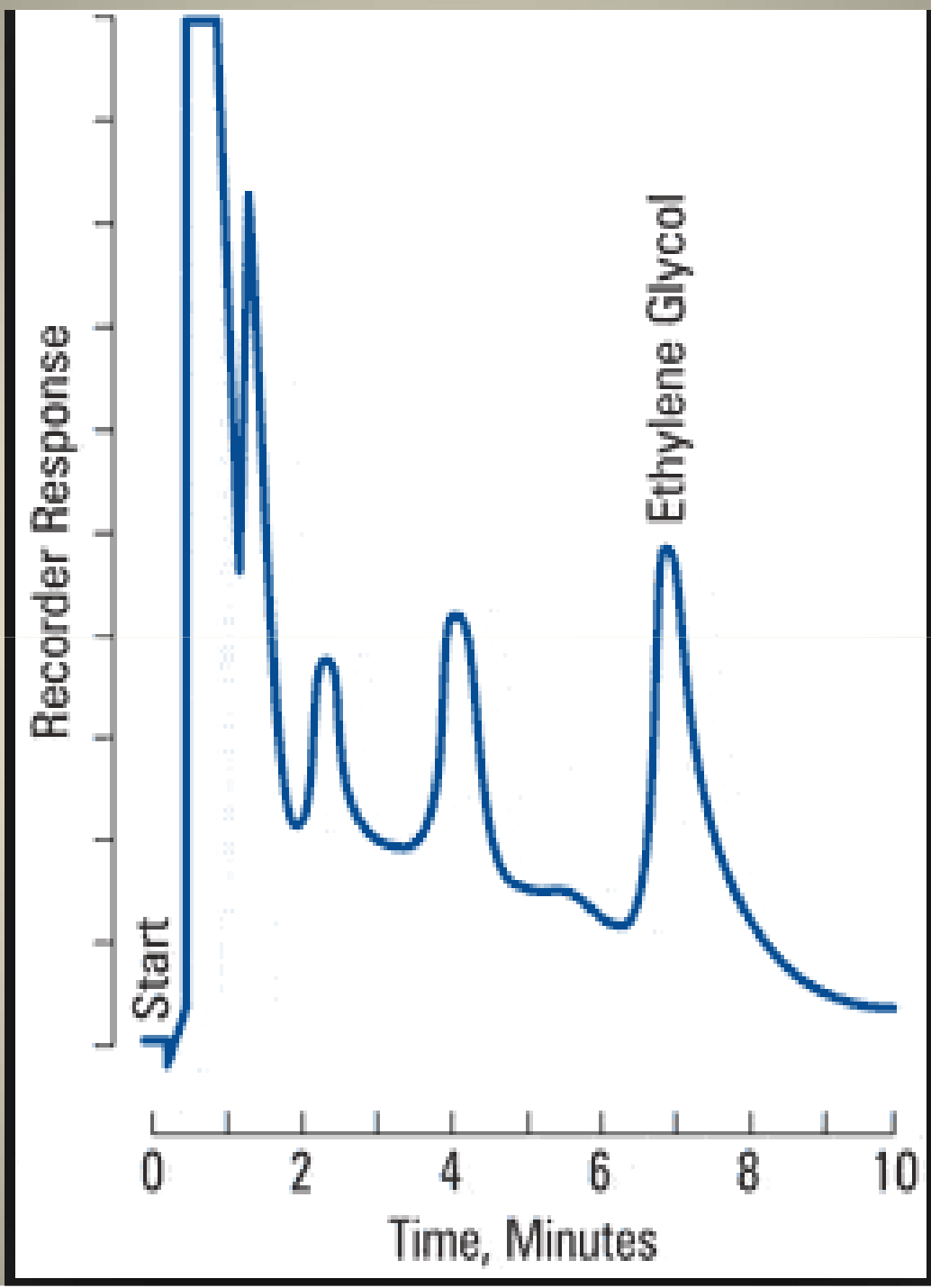


Detector



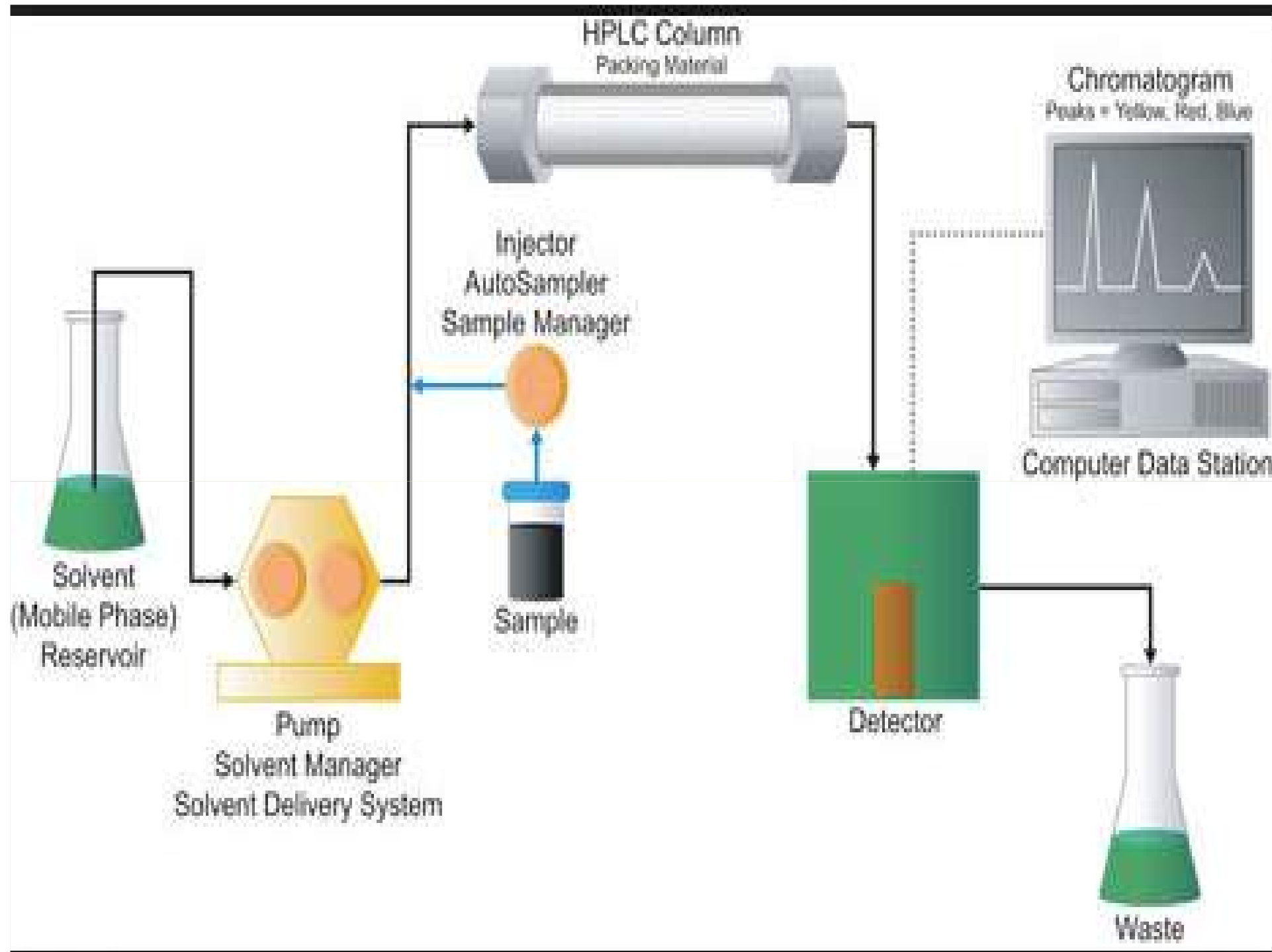
Data
system

© CHROMEDIA



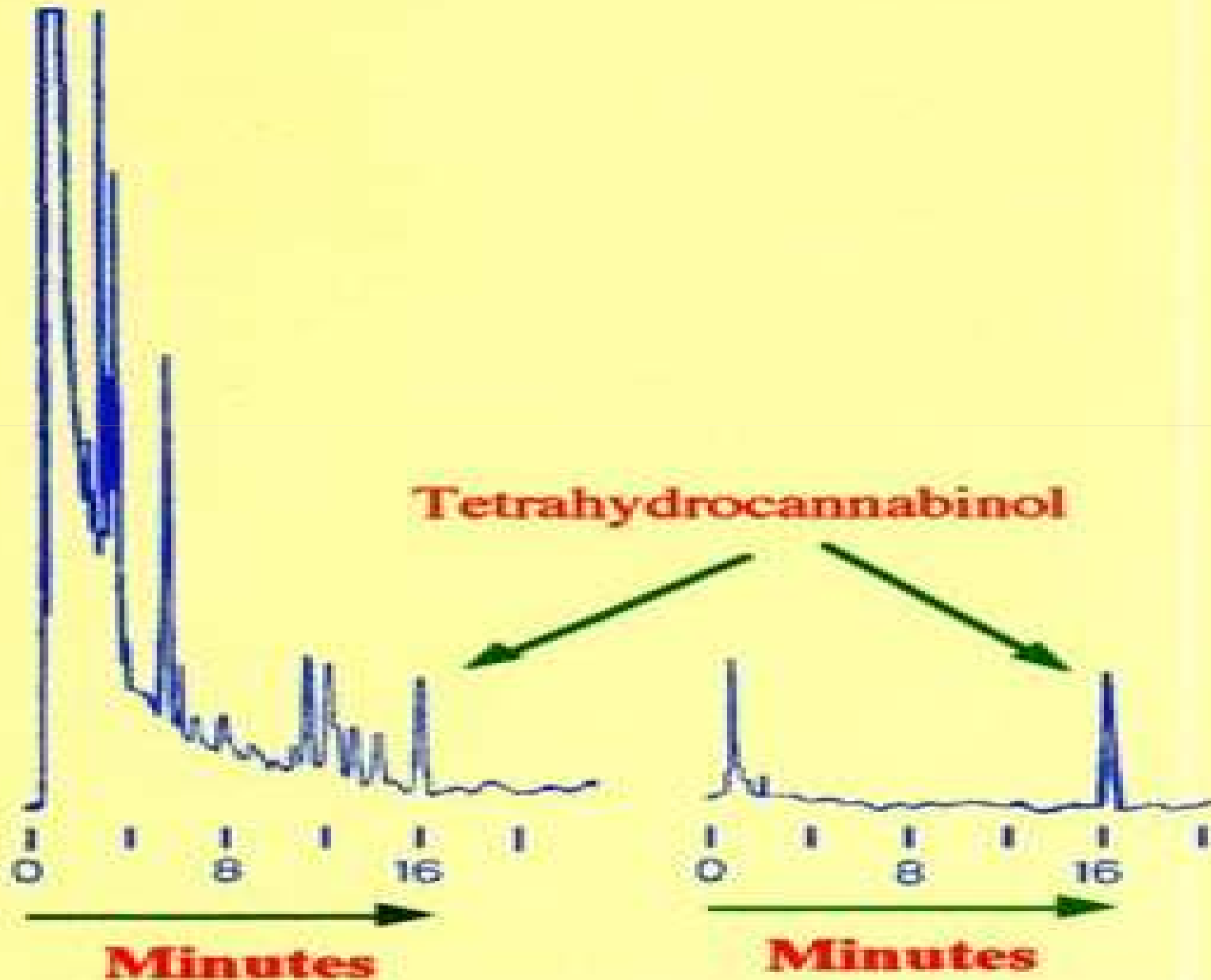
High Performance Liquid Chromatography

- Extract substances, concentrate if necessary
- Inject into flowing liquid typically aqueous with organic and pH modifiers
- Substances partition against a typically lipophilic stationary phase
- Detect by physical property (UV absorption, fluorescence, amperometry, etc)
- Chromatogram peak height (area) proportional to concentration



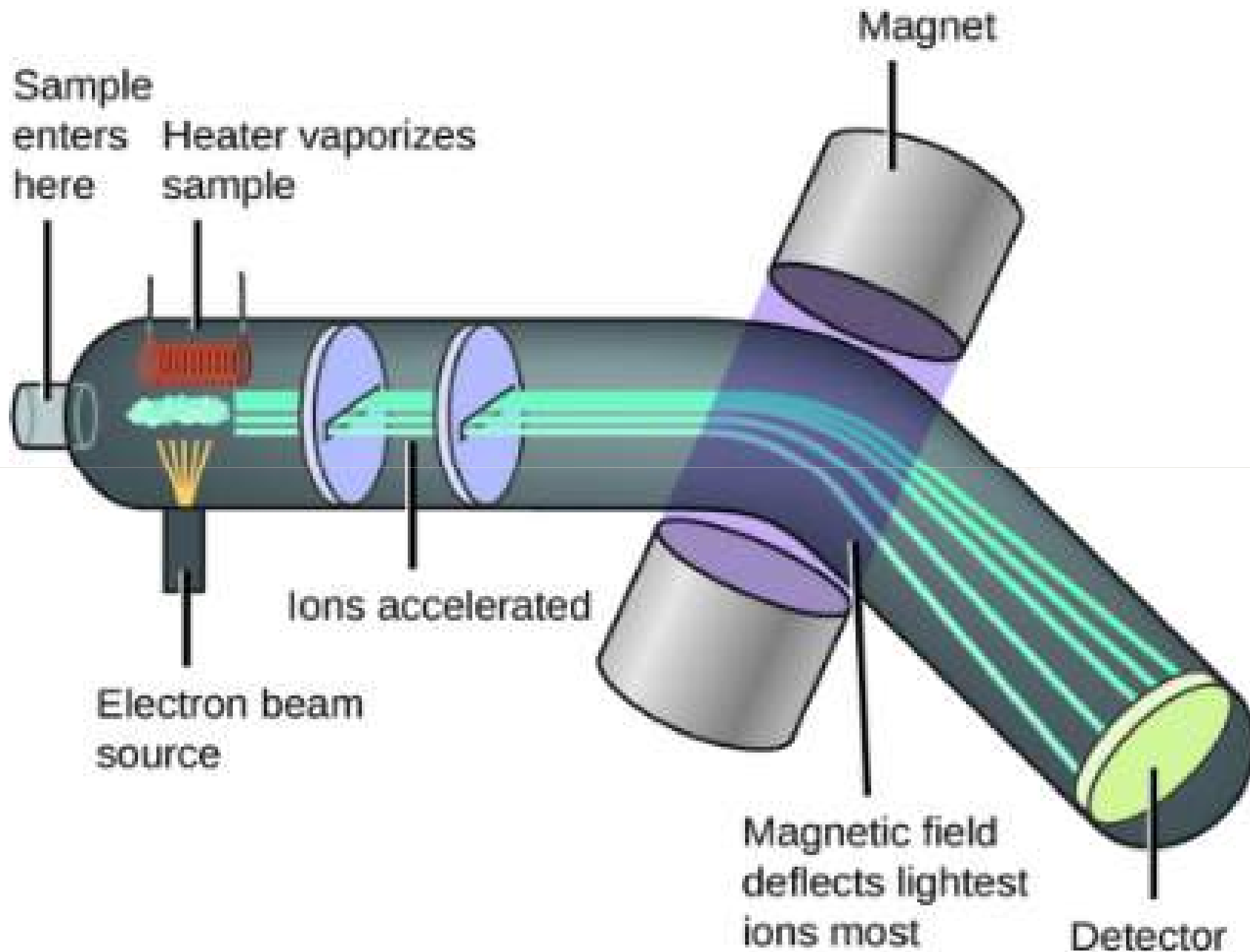
**Urine Extract
(50ng/ml of drug)**

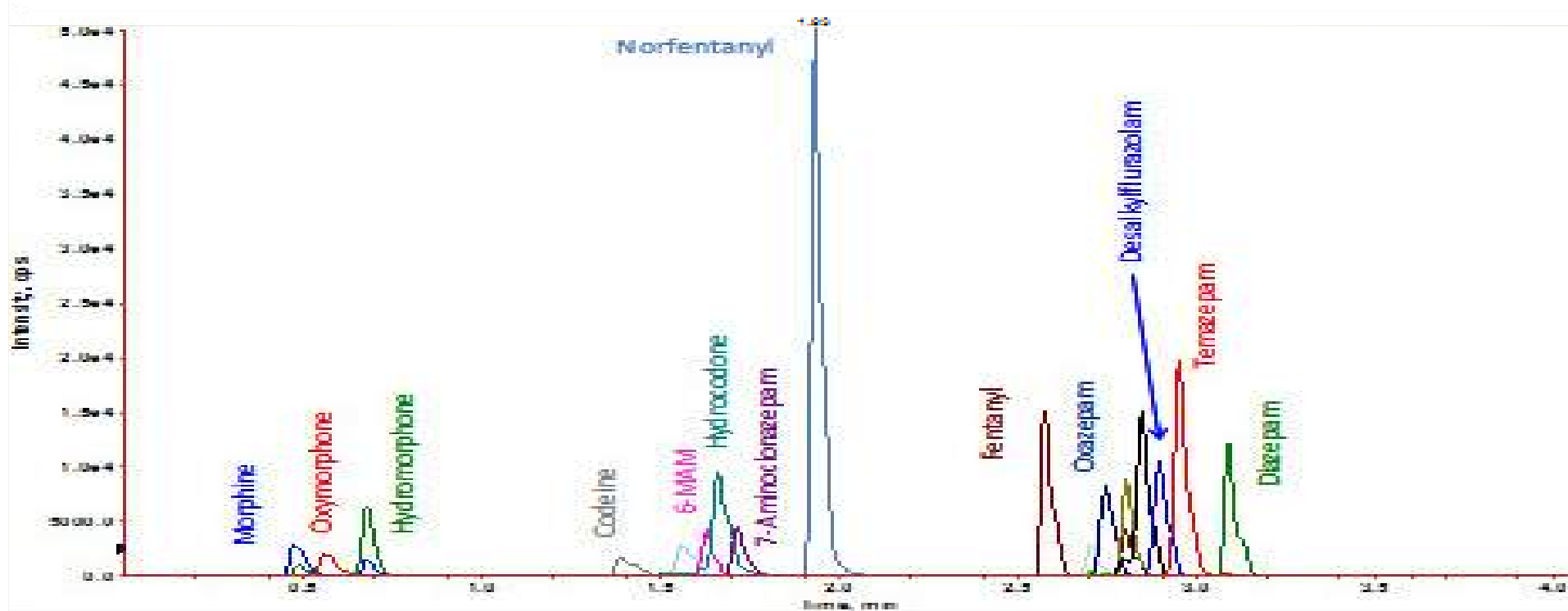
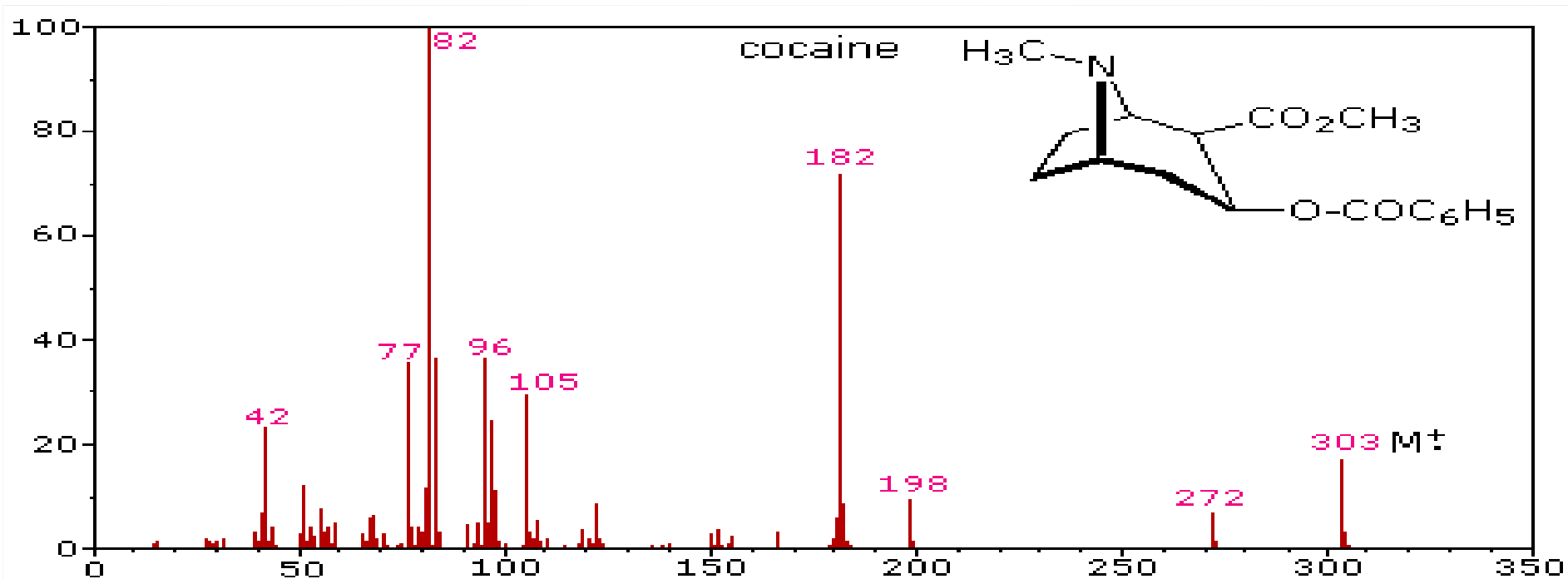
**Calibration
Standard**



Mass Spectrometry

- Detector for GC and HPLC
- Molecules accelerated through magnets and distance to select fragments of interest
- Molecular fragments enable identification (against a known library)
- Response proportional to concentration
- Can link MSs to enhance selectivity
- High sensitivity





Interpretation

Context /History

Clinical presentation

Analyses

Temporal relationships (Toxicokinetics/dynamics)

Collation of all information

Decision / intervention

Specialist Advice

The screenshot shows a web browser window displaying the TOXBASE website. The browser's address bar shows the URL <http://www.spib.axl.co.uk/toxbaseindex.htm>. The website header features the NPIS logo (National Poisons Information Service) and the TOXBASE® logo. Below the logo is a search bar with a 'Search:' label and buttons for 'Keyword', 'Sound', 'Dosage Calculator', and 'Factsheet'. A yellow navigation bar contains links for 'Chemicals', 'Specialist areas', 'Poisons index A-Z', 'General info', and 'News'. The main content area is divided into several sections: a left sidebar with links for 'Contributors', 'About the NPIS', 'TOXBASE', 'Telephone system', and 'Assays and antidotes'; a central 'Welcome To TOXBASE®' section with a date 'Updated 1 October 2007' and a disclaimer; a 'Newsflashes' section with two entries dated 9/2007; and a right sidebar with a 'REMEMBER' box about a backup site. The footer contains 'Contact', 'Site Index', and copyright information '© Crown copyright 1983-2007'.

NPIS
National Poisons Information Service

TOXBASE®

Search: Keyword Sound Dosage Calculator Factsheet

Chemicals Specialist areas Poisons index A-Z General info News

Contributors
NPIS centres in:
Birmingham
Cardiff
Edinburgh
Newcastle upon Tyne

NTIS Newcastle upon Tyne
Northern Ireland Regional
Medicines and Poison
Information Service
NPIC Dublin

About the NPIS
TOXBASE
Telephone system
Assays and antidotes

A service
commissioned by the
 Health Protection Agency

Welcome To TOXBASE®
The Primary Clinical Toxicology Database
of the National Poisons Information Service

Updated 1 October 2007

Every effort has been made to ensure that this database is accurate and up-to-date. However it cannot cover every eventuality and the information providers cannot be held responsible for any adverse effects of the measures recommended.

The information on TOXBASE is designed for healthcare professionals and may require expert clinical interpretation in the case with your local Poisons Centre or the Northern Ireland NPIC.

REMEMBER the TOXBASE backup site on www.toxbasebackup.org
If you cannot find the information you require on TOXBASE or if you need further advice contact your nearest centre in the UK NPIS

Newsflashes

9/2007 Risk of confusion between non-lipid and lipid formulations of injectable amphotericin. [Click for alert from NPSA](#)

9/2007 Following a judgement by the European Court of First Instance **paraquat** products have been withdrawn.
The Pesticides Safety Directorate (PSD) is issuing Notices for products containing paraquat, which means that from **12 September 2007** authorisation holders and their agents cannot

Contact Site Index © Crown copyright 1983-2007

Case

- 64y male
- GCS 13
- AED
- Worsened: visual impairment
- GCS 4
- pH 6.7 (normal 7.4)
- GC & GCMS: Methanol >3000 mg/L Very High!
Formic Acid 675 mg/L

Case

- Treated with sodium bicarbonate, haemofiltration and ethanol (ethanol competes with methanol for metabolism reducing the production of toxic formic acid)
- Repeated measurements of ethanol, methanol, formic acid to manage treatment
- Unable to reverse damage
- Patient died 5 days later

Substance Abuse and Musicians....

.....of my Era..!

Drugs, Death and Rock n' Roll

Composed by: Prof Larry Broussard

LSU Health Sciences Center

New Orleans LA 70112

USA

Performed and Re-arranged by: Dr Ian Watson

University Hospital Aintree

Liverpool

UK

Objective

- To use the deaths of famous rock and roll musicians as case studies to review the laboratory's role in the detection of drugs contributing to the cause of death.



Why rock and roll stars die young


- Elvis died in his early 40s in August 1977 **They say rock and pop stars live life in the fast lane and now researchers have proved it.**
- A Liverpool John Moores University study of 1,050 US and European artists found they are twice as likely to die early than the rest of the population.
- In all, 100 stars died between 1956 and 2005 with US stars dying at 42 on average and those from Europe at 35.

Where/How To Start?

- Isolated Case Studies
- Connect Performers
- Group by similar causes of death
- Artists from my era!

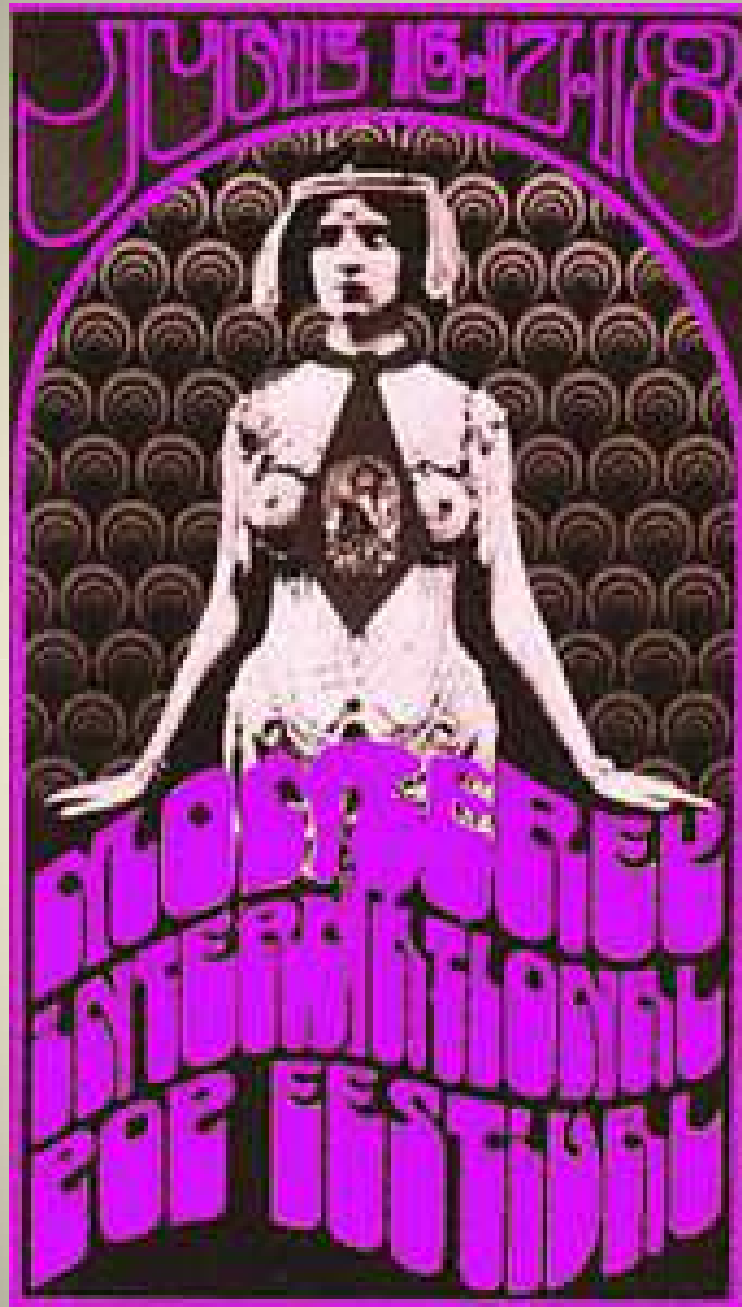
Connect Performers by Participation in a Landmark Festival

- 1967 Monterey Pop Festival
- First major rock and roll festival
- June 16, 17, 18
- More than 30 bands



**The
Monterey
International
Pop Festival**

June 16-17-18 1967



Performers Now Dead

- **Jimi Hendrix** **Janis Joplin**
- **Otis Redding** **Keith Moon (the Who)**
- **Mama Cass** **Papa John**
- **Jerry Garcia and Ron “Pig Pen” McKernan**
 - **(the Grateful Dead)**
- **Paul Butterfield and Mike Bloomfield**
 - **(Butterfield Blues Band)**
- **Brian Cole (Association)**

Attended But Did Not Perform

- Jim Morrison (the Doors)
- Brian Jones (Rolling Stones)

One-time Members of The Byrds Who Died

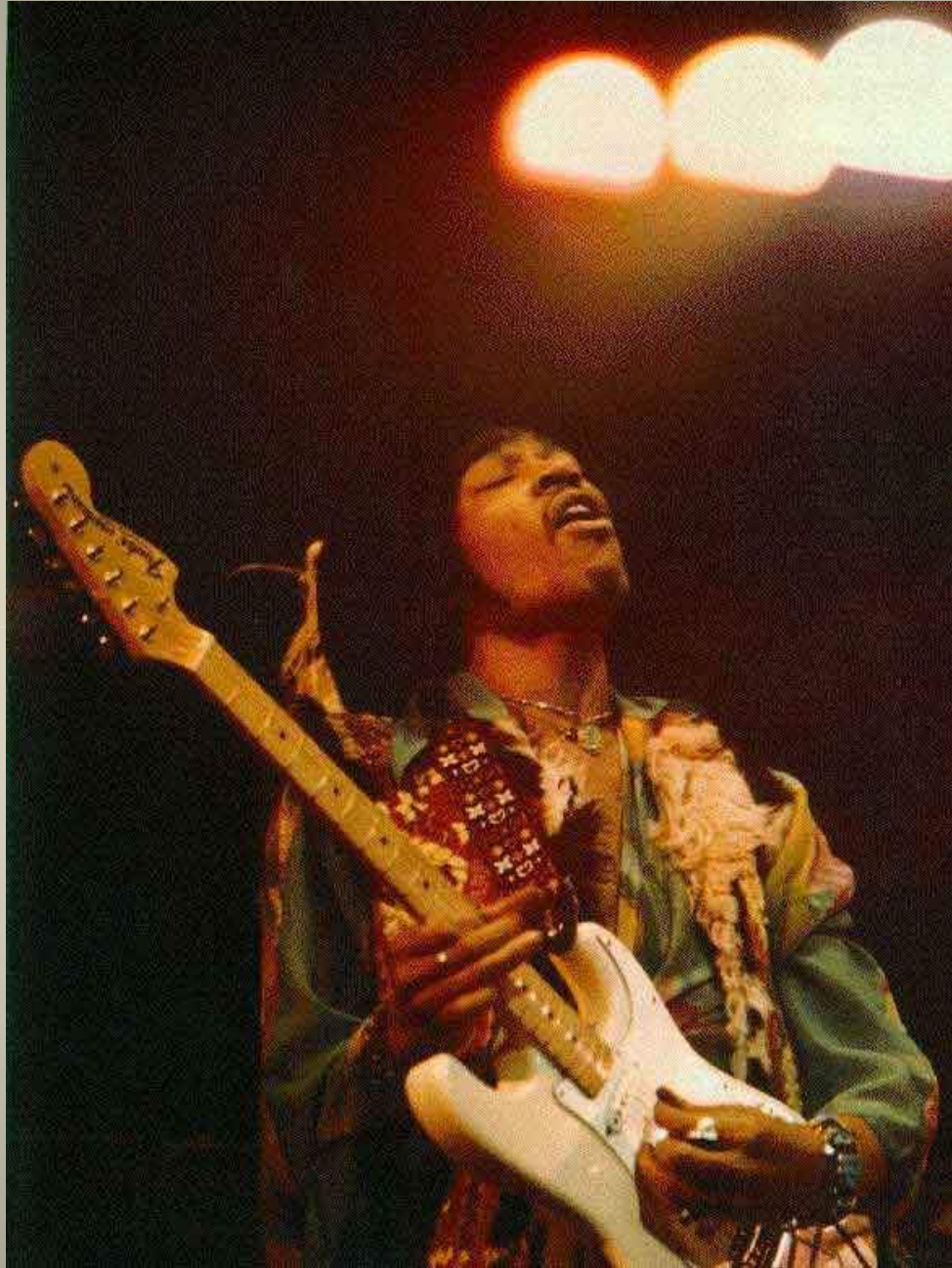
- Gene Clark (founding member) had left the band before Monterey
- Graham Parsons had not yet joined the band







Jimi Hendrix



Jimi Hendrix

- Born: November 27, 1942
- Guitar genius: played right-handed guitar upside-down left-handed
- Hits: Hey Joe, Purple Haze, Foxy Lady
- Monterey Pop Festival considered his “coming out”
- Elected to Rock and Roll Hall of Fame in 1992



Jimi Hendrix

- Died: September 18, 1970 (Age 27)
- Samarkand Hotel, London
- Cause of Death: inhalation of vomit after barbiturate intoxication
- Autopsy report: ethanol (20 mg/dL above legal drinking; large amount of seconol)

Application Number **3019**.....

The fee for this certificate is 5s. 6d.
When application is made by post, a
handling fee is payable in addition.



CAUTION:—Any person who (1) falsifies any
of the particulars on this certificate, or (2)
uses a falsified certificate as true, knowing it
to be false, is liable to prosecution.

QDX 004124

CERTIFIED COPY

OF AN ENTRY

DEATH		Entry No. 7
Registration District Kensington	Administrative Area Royal Borough of Kensington and Chelsea	
S.A. District St. Mary Abbots		
1. Date and place of death Eighteenth September 1970 St. Mary Abbots Hospital, Kensington	3. Sex Male	4. Maiden surname of woman who has married
2. Name and surname James HENDRIX otherwise James Marshall HENDRIX		
5. Date and place of birth 27th November 1942 United States of America		
6. Occupation and usual address a musician, 507/508 Cumberland Hotel Great Cumberland Place, Marylebone.		
7(a) Name and surname of informant received from G. Thurston	7(b) Description Coroner for Inner West London.	
8. Date of registration 21st September 1970	9. Cause of death Inhalation of vomit Barbiturate intoxication (quinallbarbiton) Insufficient evidence of circumstances open verdict	
10. Date of registration 21st September 1970	11. Signature of registrar E. M. Fisher Registrar	

Form R501AN (5/70) (Rev. 1/69) (1/70) (1/71) (1/72)

CERTIFIED to be a true copy of an entry in the certified copy of a register of Deaths in the District above mentioned. Given at the GENERAL REGISTER OFFICE, SOMERSET HOUSE, LONDON, under the Seal of the said Office on **8th September 1970**.

This certificate is issued in pursuance of the Births and Deaths Registration Act 1953. Section 14 provides that any certified copy of an entry purporting to be sealed or stamped with the seal of the General Register Office shall be received as evidence of the birth or death to which it relates without any further or other proof of the entry, and the certified copy purporting to have been given to the said Office shall be of any force or effect which it is sealed or stamped as aforesaid.



Application Number **3919**.....

The fee for this certificate is 8s. 6d.
When application is made by post, a
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to be false, is liable to prosecution.

CERTIFIED COPY

OF AN ENTRY

DEATH

Entry
No.

7

Registration District **Kensington**

Administrative Area

**Royal Borough of Kensington
and Chelsea**

Parish or Church **St. Mary Abbots**

1. Date and place of death

Eighteenth September 1970

2. Name and surname

St. Mary Abbots Hospital, Kensington
Jimi HENDRIX otherwise
James Marshall HENDRIX

3. Sex

Male

4. Maiden surname
of mother who
has survived

5. Date and place of birth

27th November 1942

6. Occupation and usual address

United States of America
a musician,
507/508 Cumberland Hotel
Great Cumberland Place, Marylebone.

7. (a) Name and surname of informant

Certificate received from G. Thurston,

(b) Date and time

**Coroner for Inner West
London. Inquest held 28th September 1970**

(c) Usual address

4. Cause of death

Inhalation of vomit
Barbiturate intoxication (quinallbarbiton)
Insufficient evidence of circumstances
open verdict

5. I certify that the particulars given by me above are true to the best of my knowledge and belief

Signature

of informant

10. Date of registration

twentieth September 1970

11. Signature of registrar

E. M. Fisher Registrar

CERTIFIED to be a true copy of an entry in the certified copy of a register of Deaths in the District above mentioned. Given at the GENERAL REGISTER OFFICE, SOMERSET HOUSE, LONDON, under the Seal of the said Office on *24 September 1970*.

This certificate is issued in pursuance of the Births and Deaths Registration Act 1953, Section 14, which provides that any certified copy of an entry purporting to be sealed or stamped with the seal of the General Register Office shall be received as evidence of the birth or death to which it relates without any further or other proof of the entry, and no certified copy purporting to have been given in the said Office shall be of any force or effect unless it is sealed or stamped as aforesaid.

Barbiturates

- Duration: Short (secobarbital), Intermediate, Long acting
- Sedative-hypnotics (short-intermediate acting)
- Induction of anaesthesia (ultra-short acting)
- Anti-convulsants (Phenobarbital)
- Migraine therapy (Butalbital)
- Reduction of cerebral oedema from head trauma (Pentobarbital)

Metabolism of Barbiturates

- Extensively in liver
- Induce enzymes causes increased metabolism of other drugs
- Elimination half-lives (5 half-lives to clear all drug)
 - Short acting: 1 day
 - Intermediate acting: 2 days
 - Long-acting: 2-5 days

Toxicity of Barbiturates

- Due to progressive CNS depression
 - Potentiated by ethanol
- Respiratory depression greater problem than cardiovascular depression
- Death usually due to respiratory arrest or cardiovascular insufficiency
- Prolonged coma
 - Complication: pneumonia

Management of Barbiturates Overdose

- Symptomatic and supportive therapy
 - Establish airway
 - Support ventilation
 - Assess cardiac output
- Lab used to identify presence of barbs and accompanying drugs

Amfetamines

- Amfetamine & Methamfetamine
 - Methamfetamine metabolized to amfetamine
 - Others: Ecstasy (MDMA), MDA
-
- Detection by immunoassay determined by antibody specificity

Effects of Amfetamines

- Stimulants: Mimic actions of neurotransmitters that stimulate sympathetic nervous system
- Treatment of narcolepsy and depression; alleviate fatigue, elevate mood, produce euphoria, improve performance of simple tasks, increase confidence
- Large doses: cardiac arrhythmias

ETHANOL

Ethanol

- Methods: **enzymatic**
(alcohol dehydrogenase)
gas chromatography
- Units: mg/100mL [percent]

Effects of Ethanol

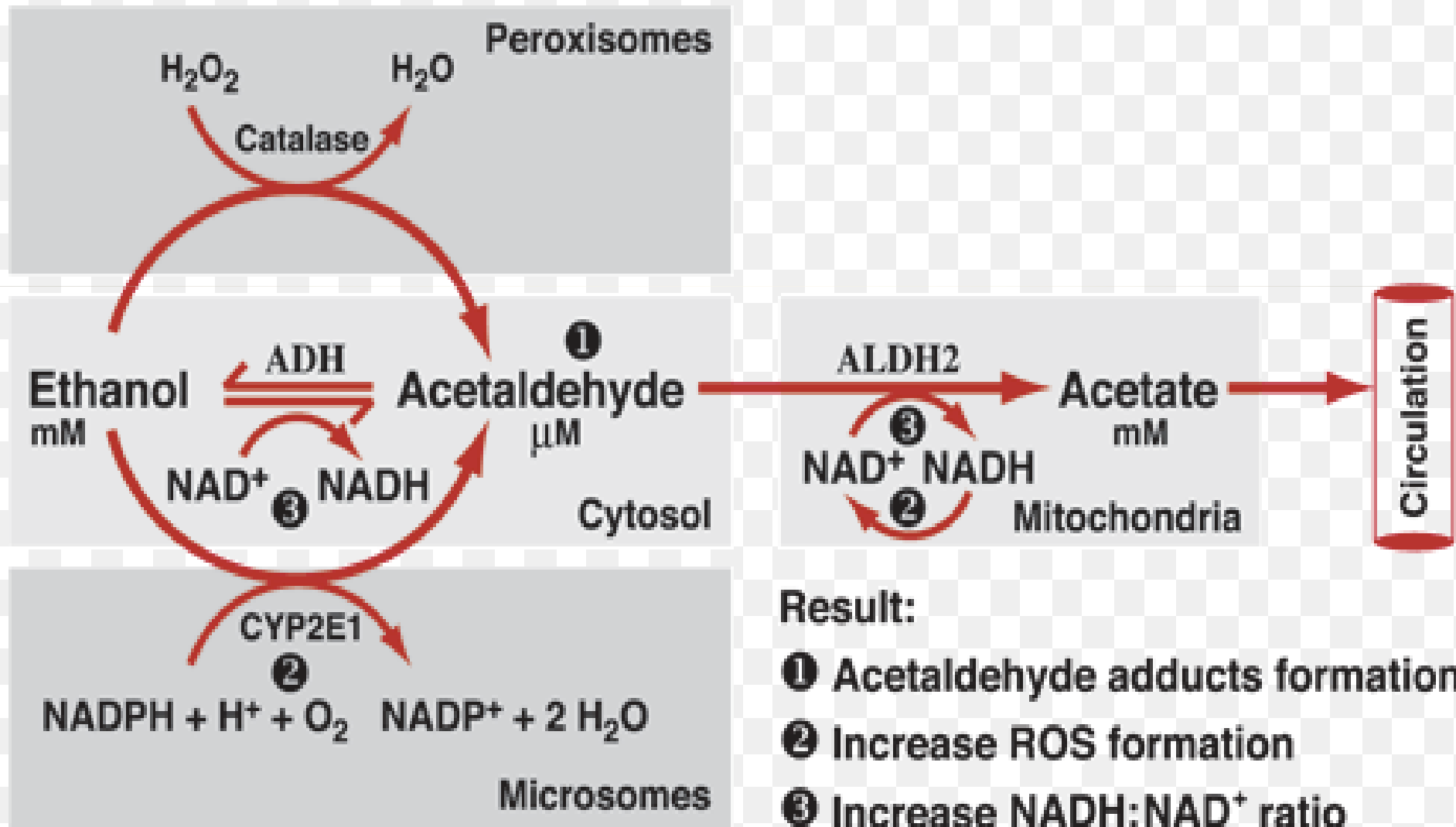
- Cardiovascular: vasodilation and vasoconstriction (not uniform)
- CNS: depression to point of death
- Stomach & GI: chronic - ulcers and inflammation
- Kidney: diuretic
- Liver: chronic - cirrhosis

Effects of Ethanol

mg/100mL

- 50 Moody; Impaired judgment
- 100 Clumsy; Blurred vision
- 200 Loud; Angry; Unusual Behavior
- 300 Disoriented and confused
- 400 Unconscious; CNS depression

Ethanol Metabolism



Ethanol Metabolism

- Intra-individual difference may be due to genetic polymorphisms of ADH & ALDH
- Inactive form of ALDH2 in ~50% Japanese and Chinese: acetaldehyde accumulation, flushing, nausea
- Disulfiram (Antabuse) inhibits ALDH
- Rate of metabolism: 12-23 mg/%/hr

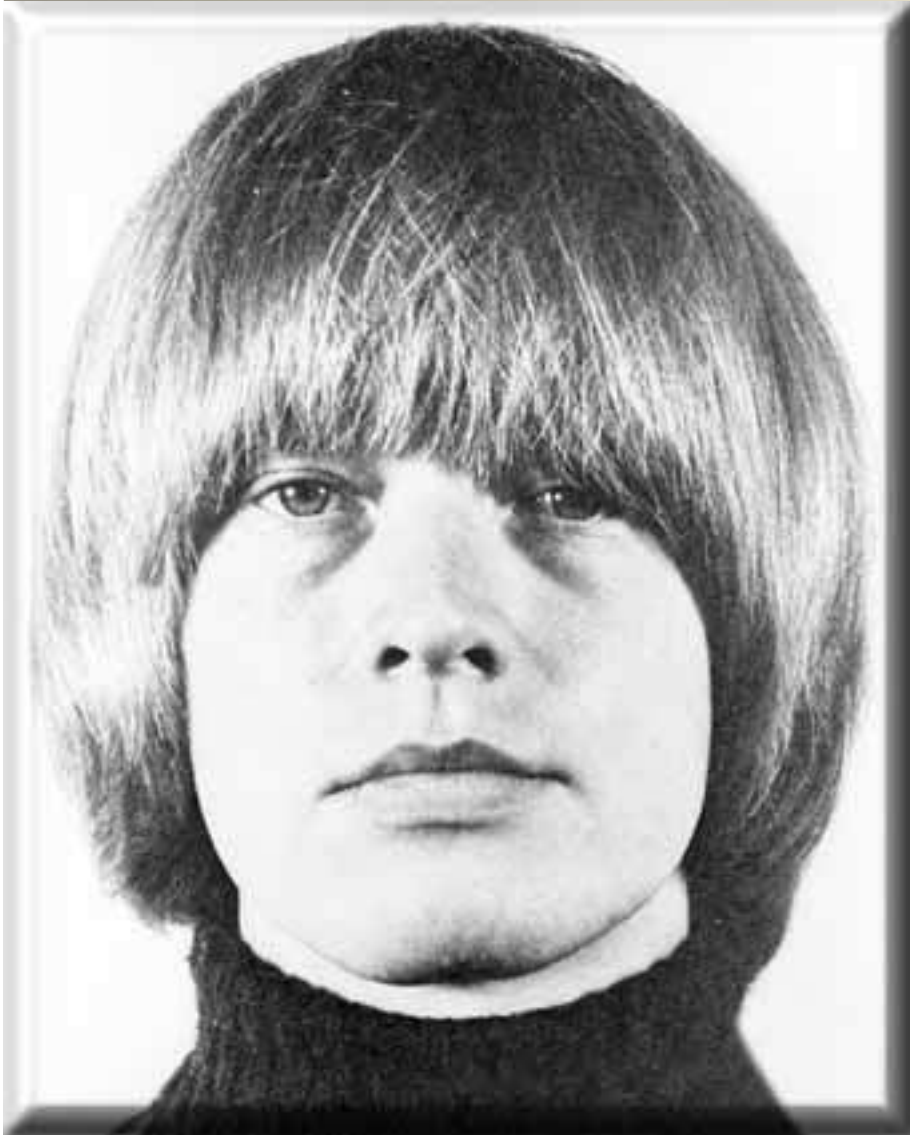
Treatment of Ethanol Intoxication

- Supportive (dependent on ethanol concentration)

Other Alcohol-Related Deaths of Musicians

- *Brian Jones – founder Rolling Stones; drowned in pool, “Misadventure”; ethanol and barbiturates
- *Ron “Pig Pen” McKernan – singer Grateful Dead; stomach hemorrhage & liver failure due to alcoholism; cirrhosis
- *Gene Clark – co-founder Byrds; haematemesis caused by alcoholism

Brian Jones – founder Rolling Stones



*Ron "Pig Pen" – singer Grateful Dead



Gene Clark – co-founder Byrds



Other Alcohol-Related Deaths of Musicians

- Steve Clark – guitarist Def Leppard
- Dennis Wilson – drummer Beach Boys
- John Bonham – drummer Led Zeppelin:
Inhalation of vomit having drunk a bottle of
vodka
- Bon Scott – singer AC/DC



Janis Joplin

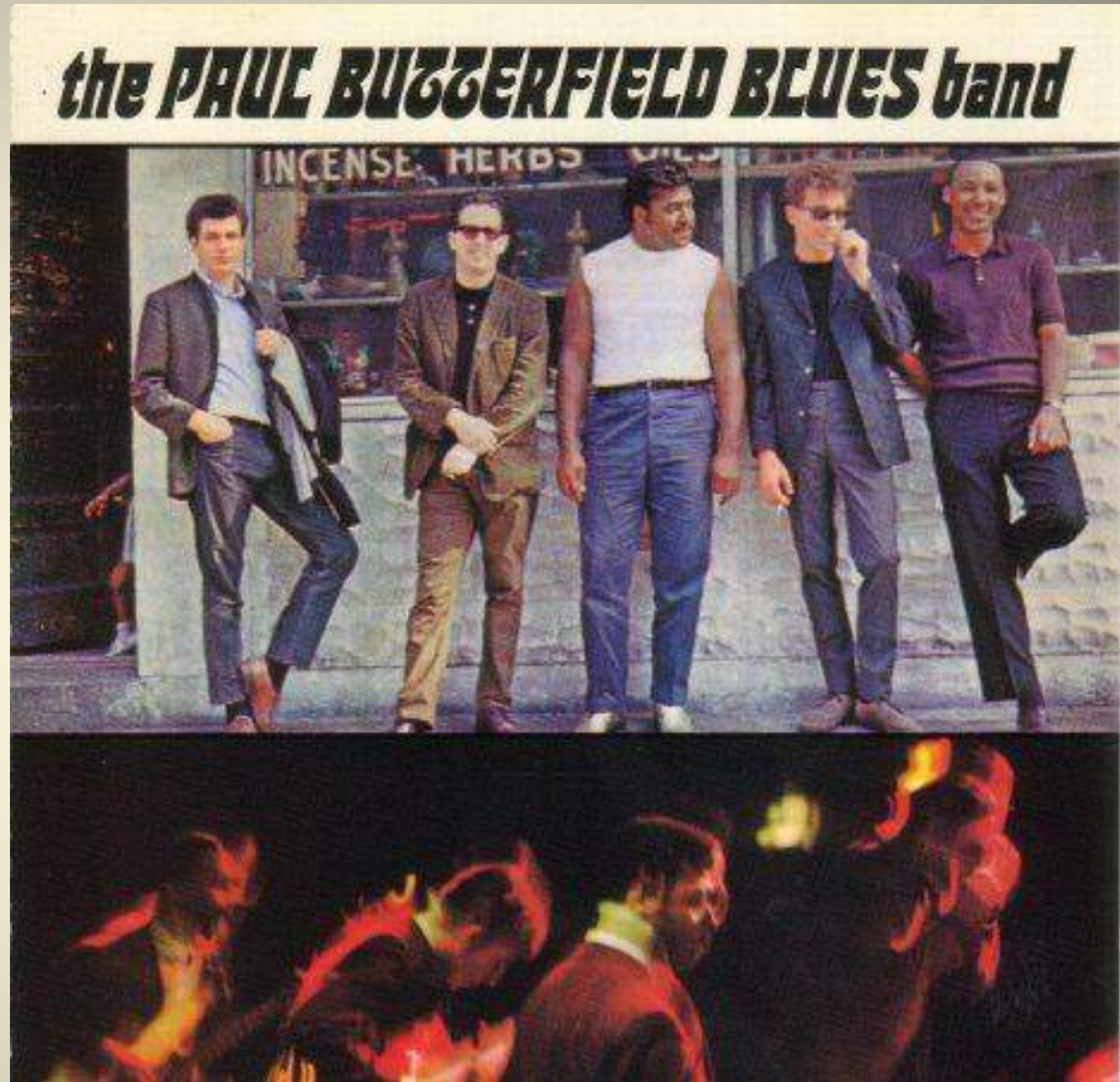
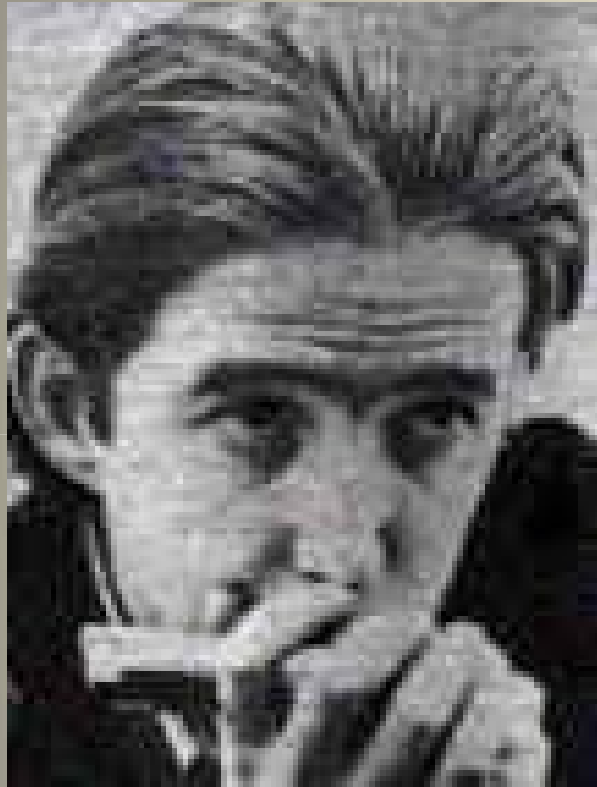
- Born: January 19, 1943
- Band: Big Brother and the Holding Company
- Hits: Piece of My Heart; Me and Bobby McGee (after her death)
- Movie “The Rose” (1979) based on her life

Janis Joplin

- Died: October 4, 1970 (Age 27)
- Landmark Hotel, Hollywood
- Cause of death: accidental heroin overdose
- Found face down; fresh puncture marks
- History: heroin addict; heavy alcohol use (codeine-containing cough syrup in Southern Comfort bottles)

Other Heroin-Related Deaths of Musicians

- Mike Bloomfield (Butterfield Blues Band)
- Paul Butterfield (Butterfield Blues Band)
- Graham Parsons (Byrds)
- Brian Cole (The Association) drug overdose, probably heroin
- Tommy Brolin (Deep Purple)
- Hillel Slovak (The Red Hot Chili Peppers)
- Sid Vicious (Sex Pistols)
- Robbie McIntosh (Average White Band)



Robbie McIntosh

Born: Dundee 1950

Drummer

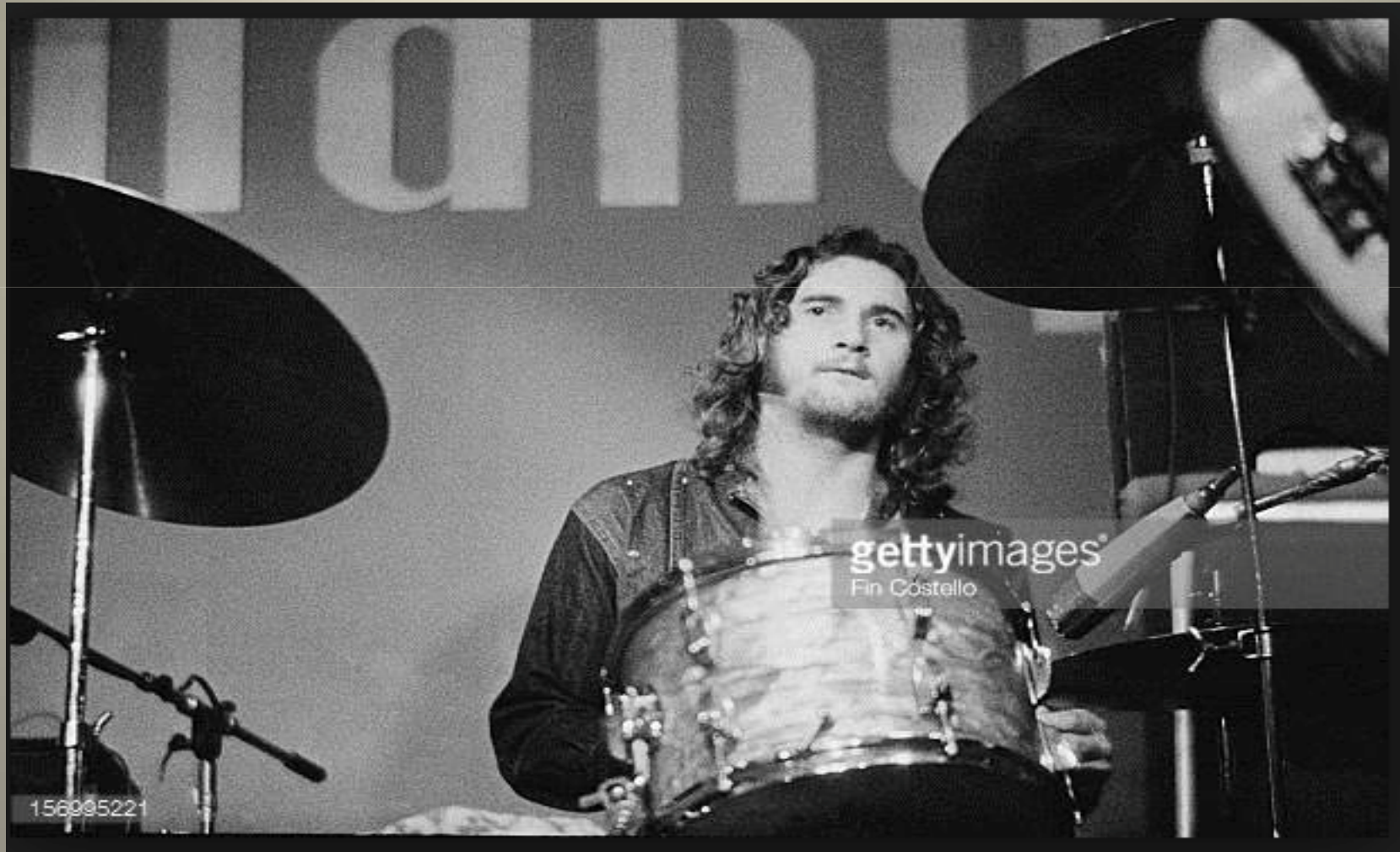
Sat behind me in English at Harris Academy
(and a much better drummer!)

Band: Average White Band

Hits: AWB White Album, 'Pick up the Pieces'

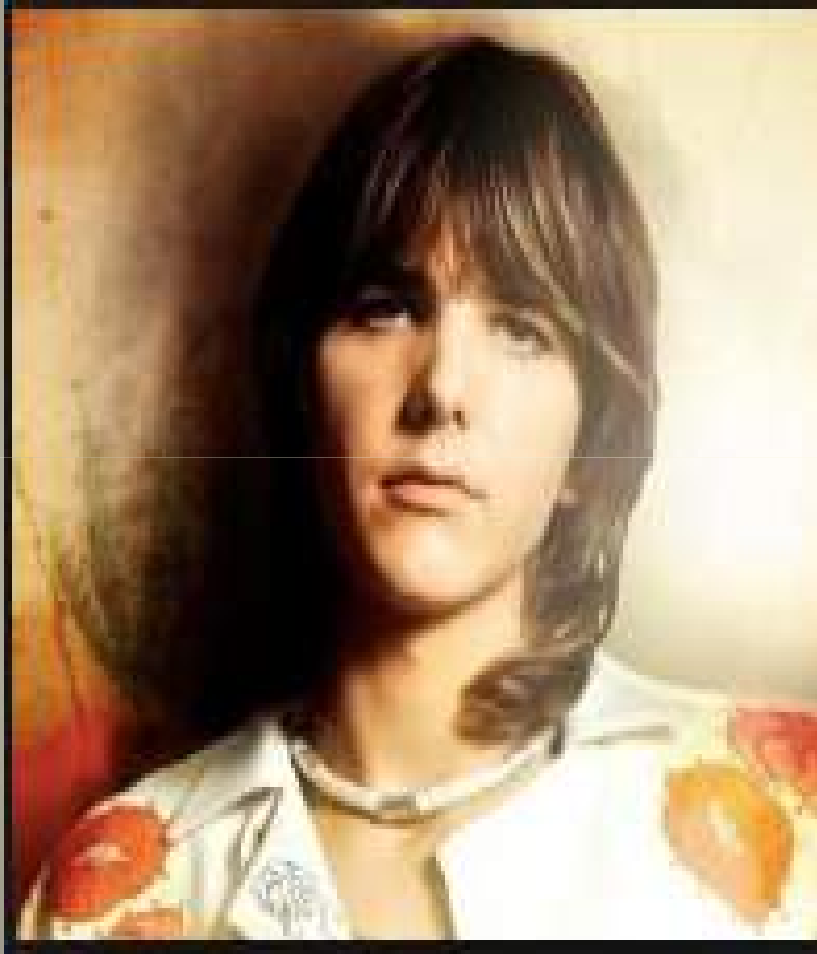
Died Sept 1974 at a party thrown by Greg
Allman of a heroin [laced with strychnine]
overdose

Robbie McIntosh

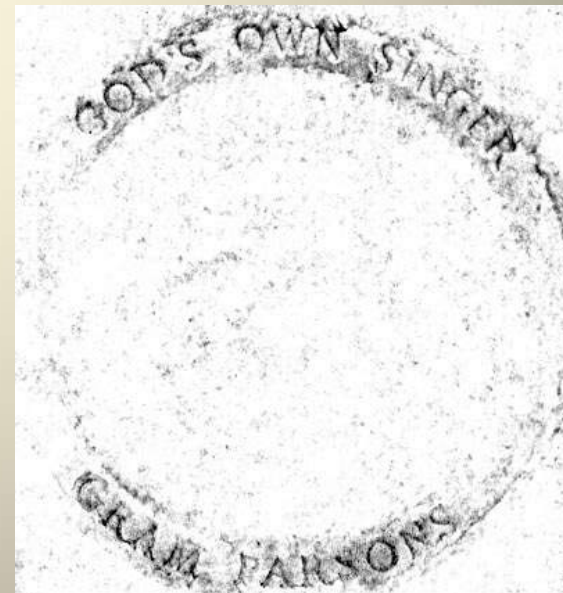


Gram Parsons

- Born: November 5, 1946
- Byrds, Flying Burrito Brothers
- Died: September 19, 1973; Joshua Tree
- Autopsy: BAC 210%, heroin, cocaine, barbiturates
- Cause of Death: “drug toxicity, days, due to multiple drug use, weeks.”



Garden of Memories, New Orleans



Other Heroin-Related Deaths of Musicians

- Allen Woody (Allman Brothers)
- Jonathan Melvoin (Smashing Pumpkins)
- Kristen Pfaff (Hole)
- Bradley Nowell (Sublime)
- Andrew Wood (Mother of Love Bone)
- Billy Murcia & Johnny Thunders (NY Dolls)
- Danny Whitten (the Rockets)
- Tim Hardin (songwriter)
- John Belushi (Blues Brothers); speedball—cocaine and heroin

Heroin

- Semi-synthetic; Di-acetyl morphine (Acetylation of opium extract from poppies)
- Crosses blood-brain barrier easier than morphine; 2.5 times as potent
- Metabolites: 6-acetyl morphine; morphine; codeine
- Heroin acts mostly on MU opioid receptors causing euphoria, analgesia, and respiratory depression.
- Antidote: Narcan (naloxone)

Heroin Overdose: Narcotic/Opiates Toxidrome

- Presentation:
- Miosis (pinpoint pupils)
- Bradycardia
- Hypotension
- Hypoventilation
- Coma

Heroin

- Heroin is rapidly converted to monoacetylmorphine (MAM) and morphine.
- Heroin is more potent and euphoric than morphine.

Heroin

- Heroin is derived from the dried "milk" of the opium poppy which contains morphine and codeine



Poppy Field



Opiates Immunoassay

- Detects primarily codeine and morphine
- Detection of other opiates: depends on antibody specificity

Positive Opiates Screen

- Prescription:
 - Morphine
 - Codeine
- Nonprescription:
 - Poppy seeds (300 ng cutoff)

Confirmation of Heroin Use

- 6-Acetyl morphine and morphine present in urine



Jim Morrison

- Born: December 8, 1943
- Songwriter, Poet
- Band: the Doors (from Aldous Huxley's book on mescaline, the Doors of Perception); played last concert with Morrison in New Orleans

Jim Morrison

- Died: July 3, 1971 (Age 27) in Paris
- Cause of Death: heart failure (possible blood clot from respiratory illness)
- Circumstances: found dead in bath tub; rumors of drug overdose – took heroin thinking it was cocaine; no autopsy
- History: alcohol abuse (fifth/day); drug use
- Buried in Paris
- Wife died of heroin overdose 3 yrs later

Suspicion of Drug Use Prior to Death

- Ethanol
- Heroin
- Cocaine

Cocaine

- Extracted from coca leaves
- Half-life about one hour
- Primary metabolite: benzoylecognine

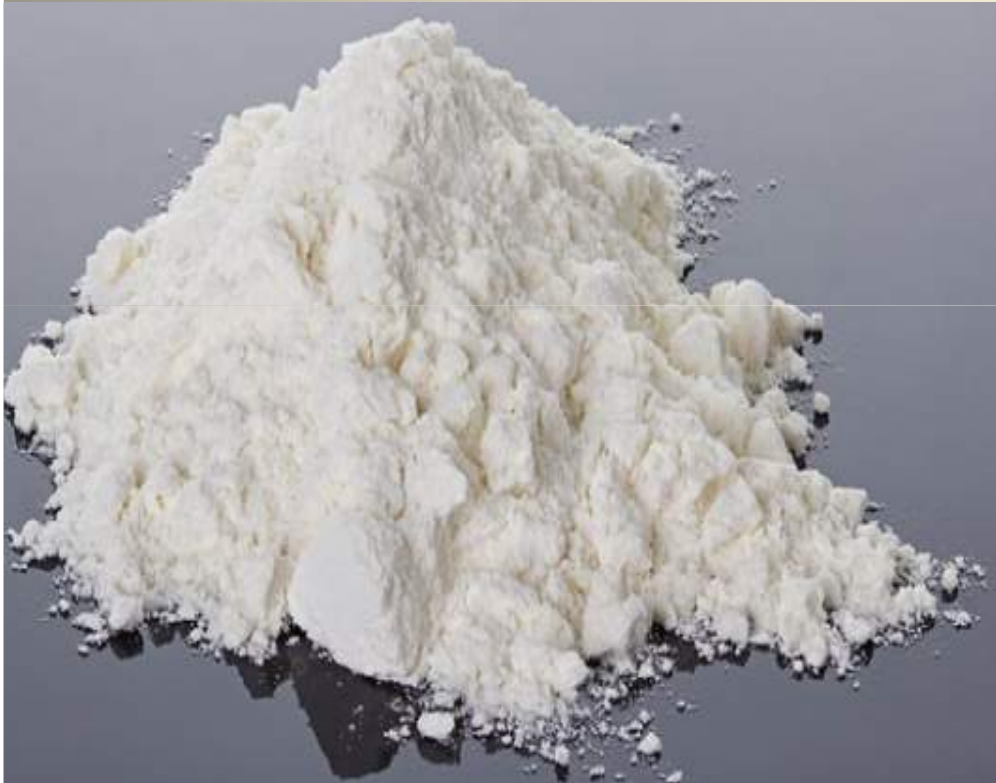
Actions of Cocaine

- Stimulation by blocking reuptake of norepinephrine & dopamine
- Potential cardiac arrhythmias due to blocking fast sodium channels
- Potential for thrombotic event (stroke or heart attack) due to increased thrombogenesis
- Local anesthetic properties

Harvesting Coca Leaves



Cocaine: powder, bricks,...



Cocaine.... Body Stuffers



Forms of Cocaine... crack



Cocaine Overdose

- CNS stimulation, convulsions
- Ventricular arrhythmias
- Respiratory dysfunction with eventual depression
- Increased muscular activity
- Possible hyperthermia

Cocaine-Related Deaths of Musicians

- Shannon Hoon – Blind Melon
- Jim Belushi – Blues Brothers; cocaine and heroin
- Tommy Brolin – James Gang and Deep Purple; cocaine, ethanol, barbiturates
- *Gram Parsons – Byrds; cocaine, ethanol, morphine, barbiturates
- Jeff Porcaro – Toto; heart attack (cocaine)
- Paul Kossoff – Free

REPORT OF THE DEATH OF AN AMERICAN CITIZEN

U.S.

American Embassy, Paris, France, August 11, 1971

(Place and date)

Name in full James Douglas MORRISON

Occupation Singer

Native or naturalized BORN ON December 8, 1943 AT Clearwater,

Last known address

in the United States 8216 Norton Avenue, Los Angeles, California

Date of death July 3 5:00 a.m. 1971

Age 27 years

(Month) (Day) (Hour) (Minute) (Year)

(As nearly as can be ascertained)

Place of death 17, rue Beautreillis, Paris 4, France

(Number and street) or (Hospital or hotel) (City)

(Country)

Cause of death Heart Failure

(Include authority for statement)

As certified by Dr. Max Vassille, 31, rue du Renard, Paris, France

Disposition of the remains Interred in Pere Lachaise Cemetery, 16th Division, Paris, France on July 7, 1971.

Local law as to disinterring remains May be disinterred at any time upon the request of nearest relative or legal representative of the estate. See Decree Law of December 31, 1941, Journal Officiel, January 26-27, 1942, Page 378.

Disposition of the effects In the custody of Pamela Courson, friend.

Person or official responsible for custody of effects and accounting therefor Rear Admiral George S. Morrison, father.

Informed by telegram:

NAME	ADDRESS	RELATIONSHIP	DATE SENT
N/A			

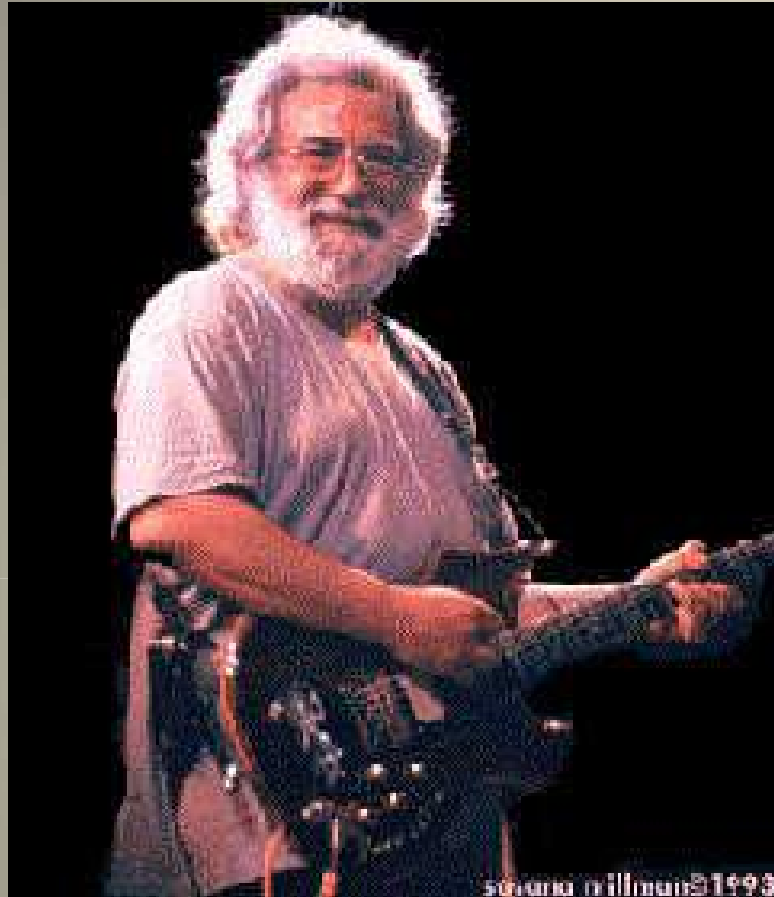
Copy of this report sent to:

NAME	ADDRESS	RELATIONSHIP	DATE SENT
Rear Admiral George S. Morrison	Chief Naval Operations	Father	August 11, 1971
	OPD 3B - Room 4E 552		
	Pentagon, Washington, D.C. 20350		

MORRISON

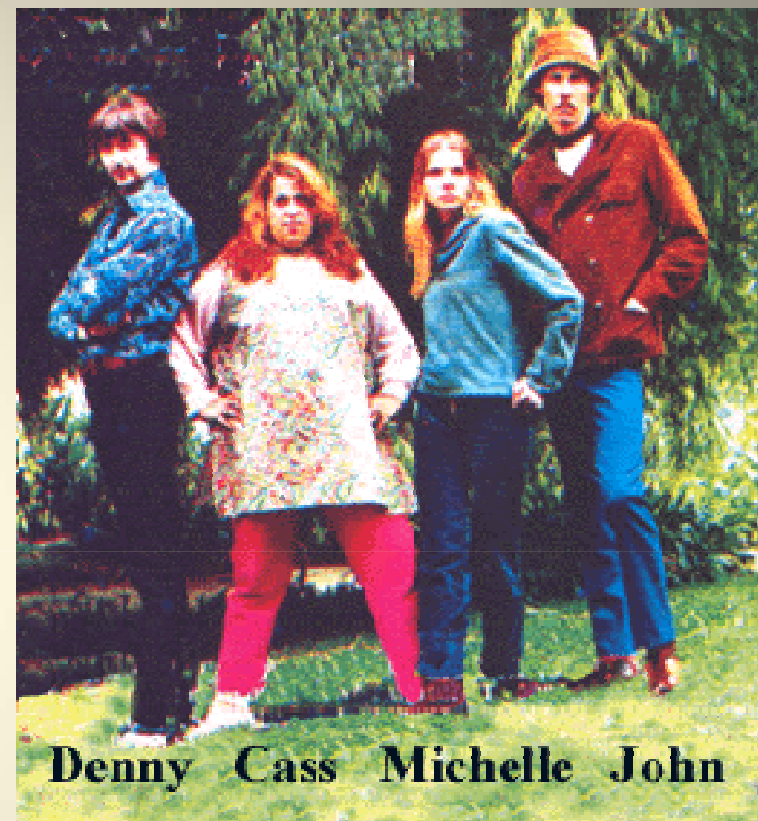
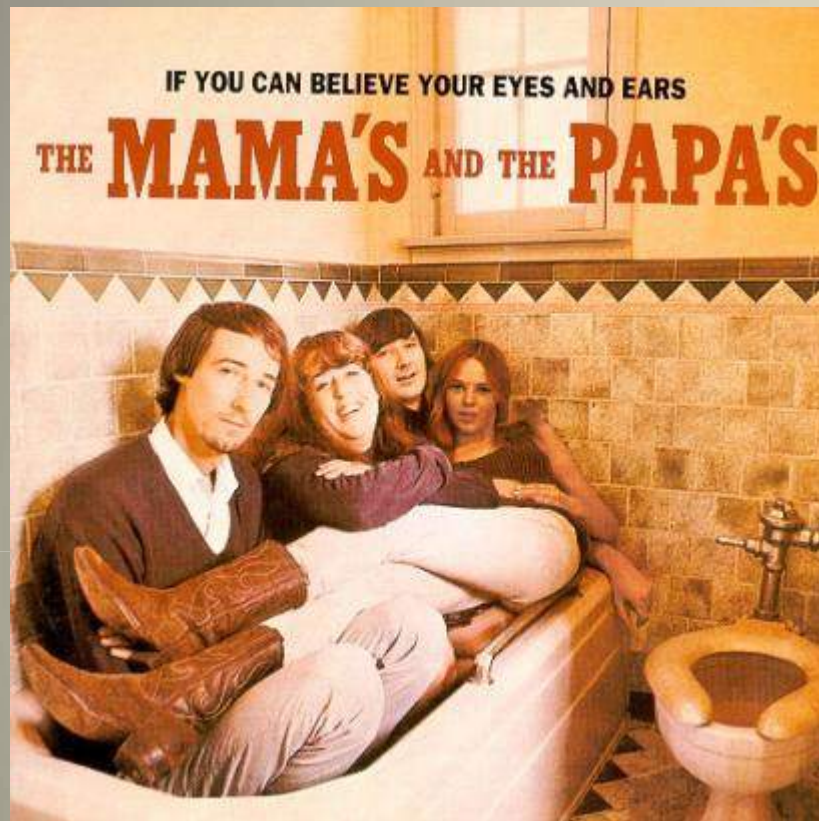
Other Heart-Related Deaths of Musicians

- Illicit Drug-Related:
 - *Jerry Garcia
 - *Mama Cass Elliott
 - *Papa John Phillips
- Prescription Drug Related:
 - Elvis Presley
- Non-Drug Related:
 - Bobby Darin



Jerry Garcia

- History of drug use
- Diabetic: near fatal coma
- Atherosclerosis
- Died at age 53 while in drug rehab for heroin withdrawal



Denny Cass Michelle John



“Mama” Cass Elliot

- Born Ellen Cohen Sept. 19, 1941
- Died July 29, 1974 London
- History of drug use lifestyle
- 225 [~102 kg] pounds at death
- Died of heart failure; poor health apparently accelerated by lifestyle



“Papa” John Phillips

- Born 30/8/1935
- Died 18/3/2001 of heart failure
- Lifetime abuse of heroin, cocaine, amphetamines, alcohol, LSD
- 1981 convicted of narcotics trafficking
- Liver transplant in 1992



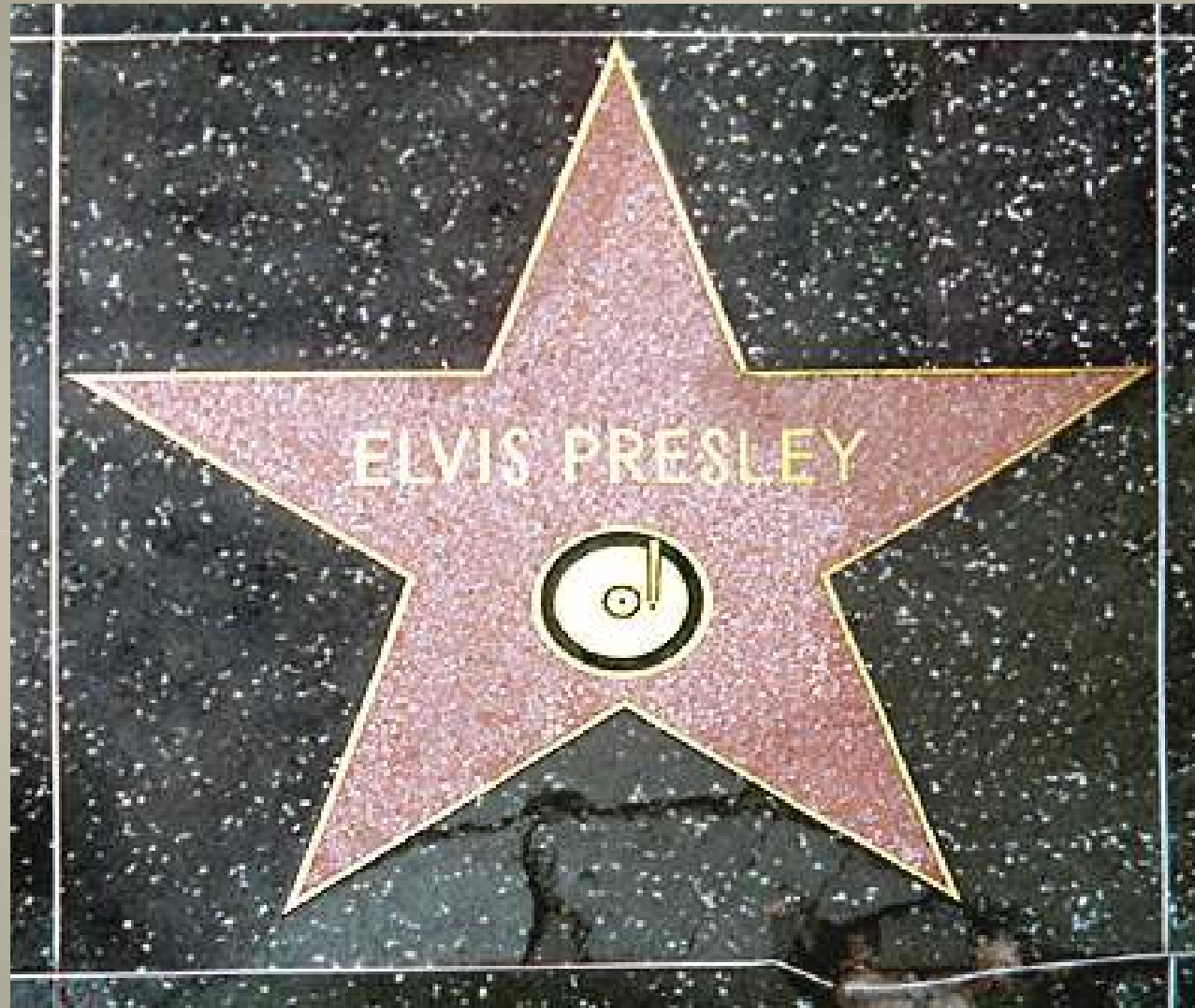
Elvis Presley

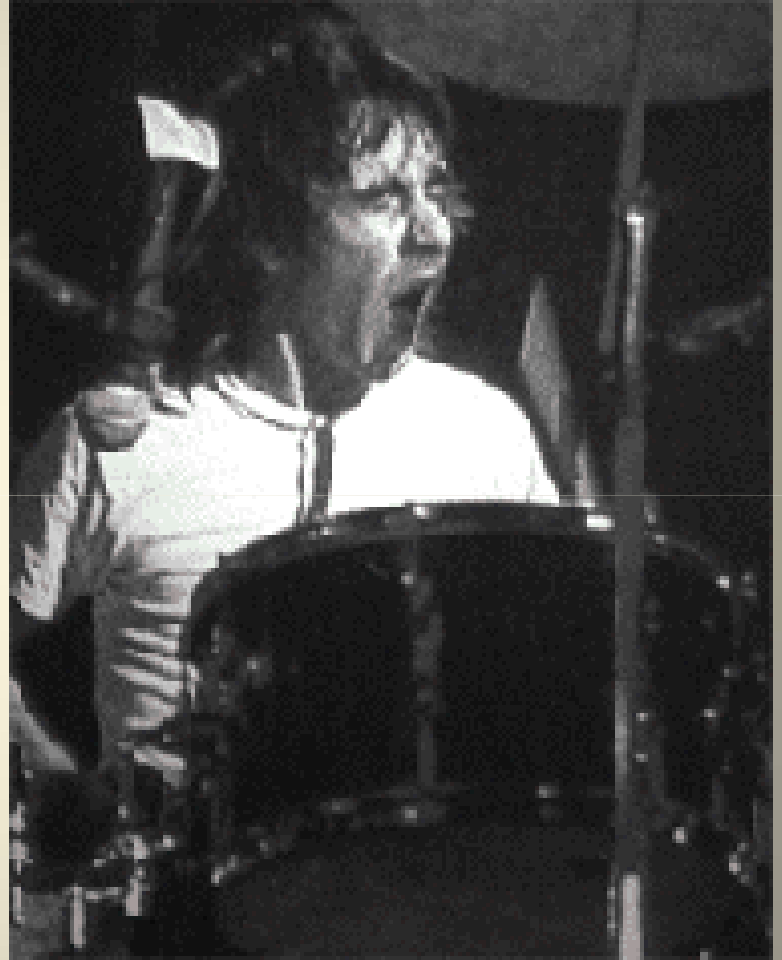
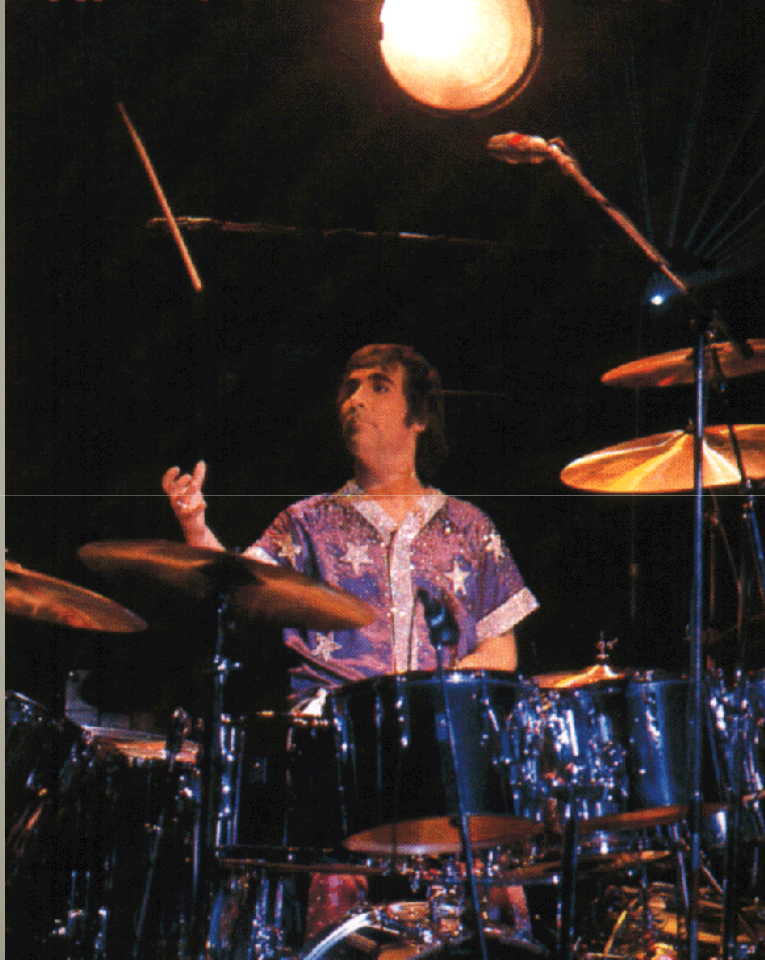
- Born: January 8, 1935
- Died: August 16, 1977
- Cause of Death: Heart Failure (probably due to abuse of prescription medication)
- Toxicology report: 11 drugs detected
- “only drugs prescribed for perfectly normal, rational medical reasons”

Toxicology Report:

11 drugs detected

- 4 in significant quantities:
 - Ethinamate (sedative)
 - Methaqualone (sedative)
 - codeine (opiate)
 - barbiturates (sedative)
- 4 others in insignificant amounts: chlorpheniramine (antihistamine)
 - meperidine (opiate)
 - morphine (metabolite of codeine)
 - Valium (sedative)





Keith Moon

- Born 23/8/46
- Drummer for The Who
- Destructive behavior inspiration for Muppets “Animal”
- Died 7/8/78 same room as Mama Cass
- Overdose of Heminevrin (chlormethizole) used for treatment of alcohol withdrawal



Otis Redding

- Born: September 9, 1941
- Hits: These Arms of Mine; The Dock of the Bay (released 3 days before death)
- 1989: Inducted Rock & Roll Hall of Fame

- Died: December 10, 1967
- Cause of Death: plane crash into Lake Monona, Madison, WI

Musicians Who Died in Airplane Crashes

Bad, Bad Leroy Brown

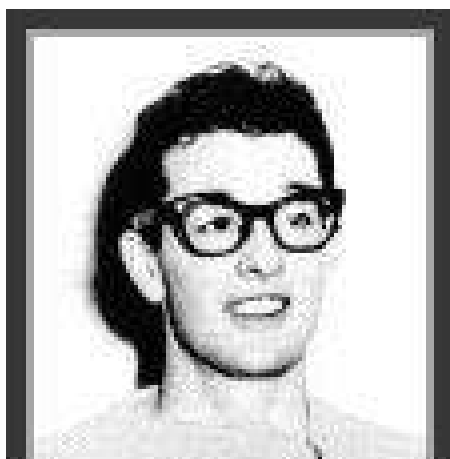
- Born: Jan 10, 1943
- Hits:; Time in a Bottle; I've Got a Name
- Died: Sept 20, 1973
- Jim Croce – Natchitoches, LA after concert at Northwestern





Musicians Who Died in Airplane Crashes

- Buddy Holly, Ritchie Valens, “Big Bopper”
- Feb 3, 1959 Clear Lake, Iowa
- “The Day the Music Died”
- Plane: American Pie



*Buddy
Holly*



*Ritchie
Valens*



*J.P. Richardson
"The Big Bopper"*

WINTER DANCE PARTY



BUDDY HOLLY
and
CRICKETS
"FRONT MAN"



BIG BOPPER
"Cherry Lip"



RITCHIE VALENS
"Donna"
"Come On, Let's Go"

ALL THE
STARBUCKS
START
IN PRISON

DION

and
THE BELMONTS
"RACHAEL WALK"



FRANKIE SARDO

Live
Acoustic

Live
Acoustic

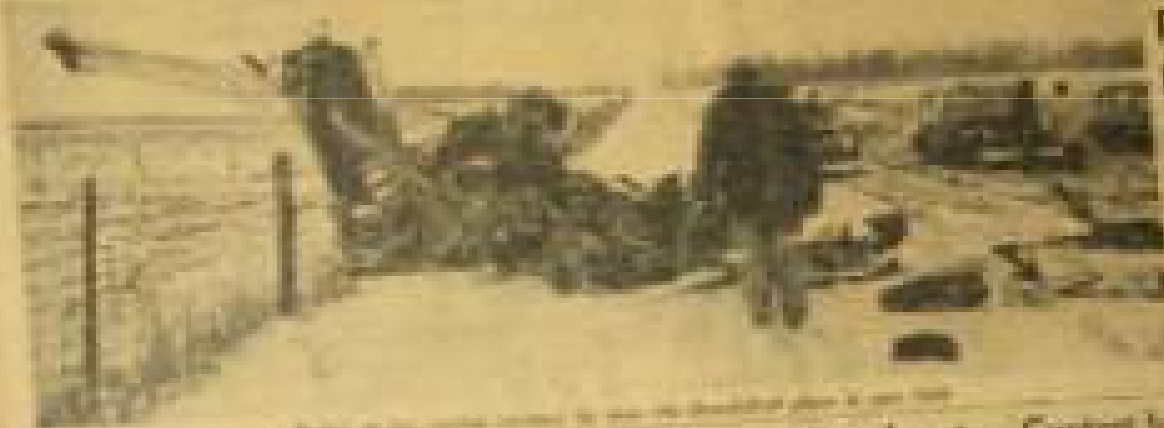
DATED FEBRUARY 3, 1958

MASON CITY GLOBE-GAZETTE

FOUNDED 1877

Four Killed in Clear Lake Plane Crash

Nationally-Known
Rock 'n' Rollers,
Lake Man Victims



Russ Hold
U.S. Army
Convoy

Iowa House in Fiery Debate Over Right-to-Work Law

Control by
House
Disputed

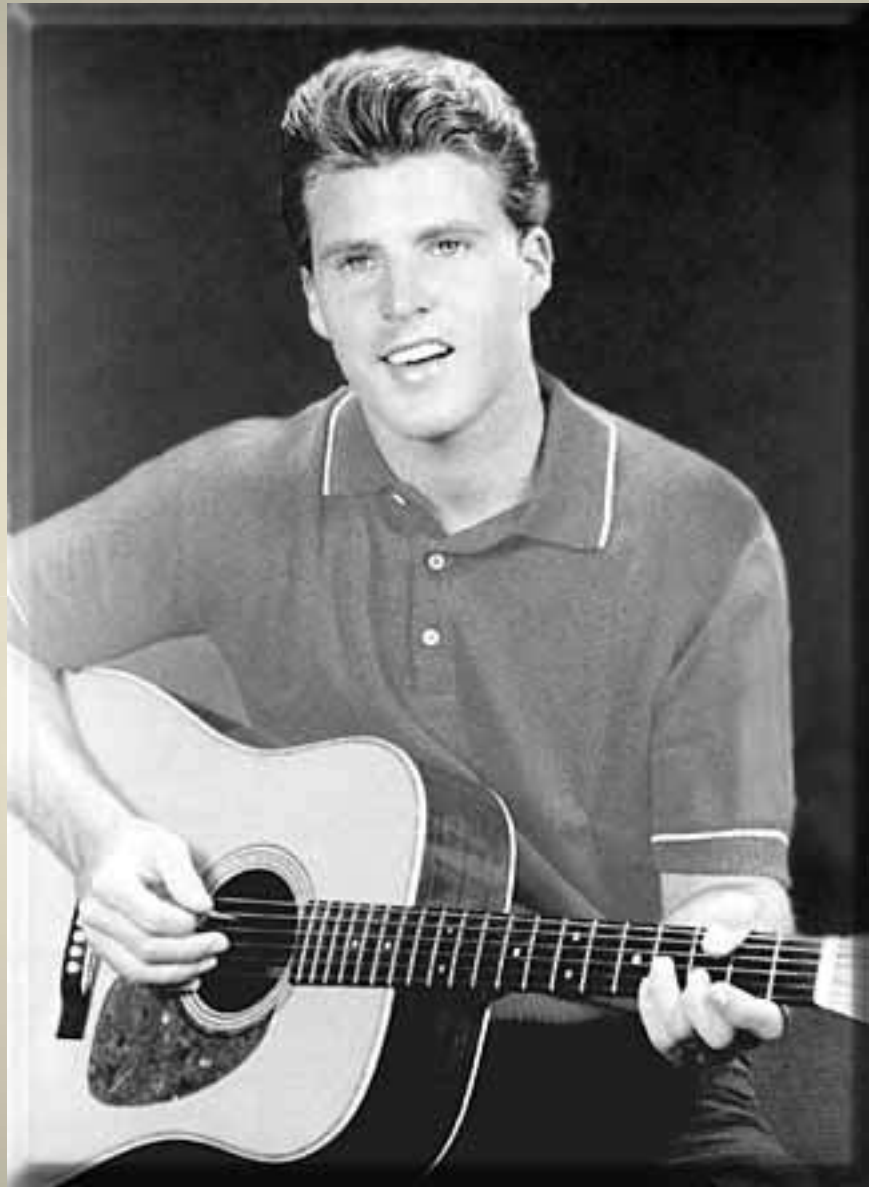


3 Pages
Web Top
Recordings

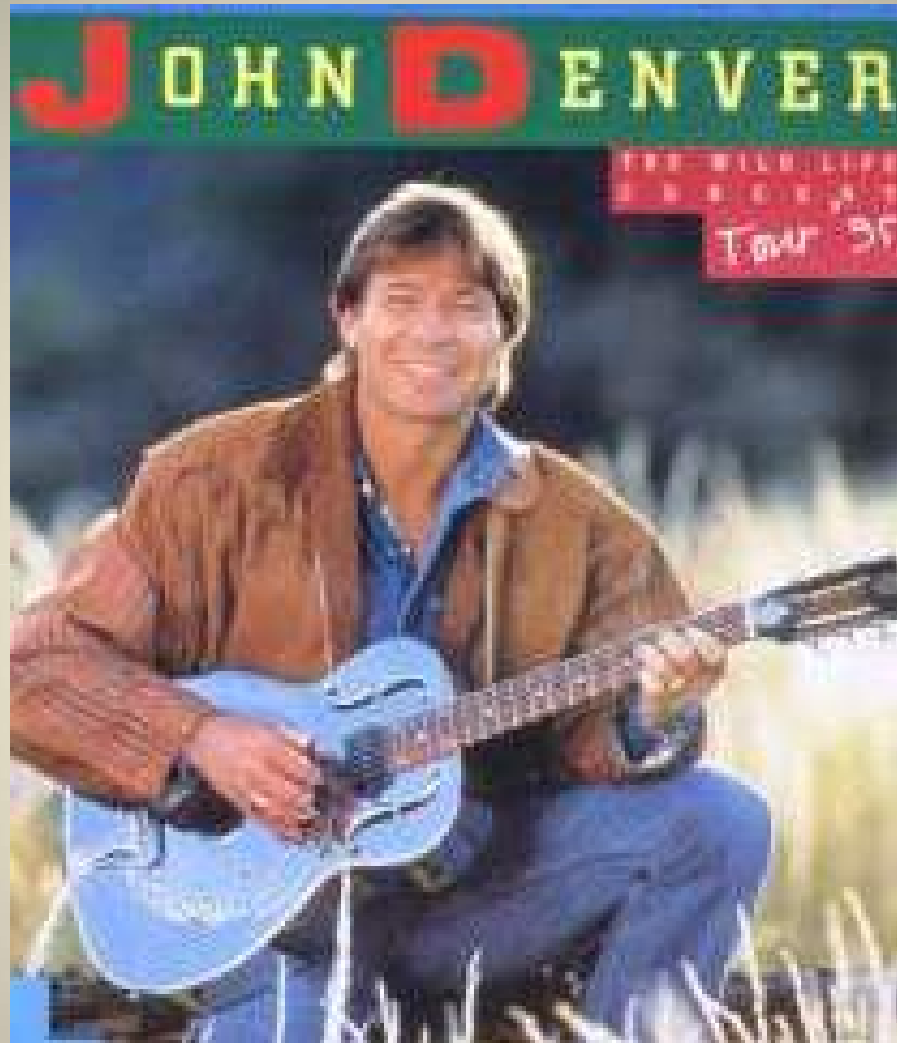


Musicians Who Died in Airplane Crashes

- December 31, 1985: Ricky Nelson
- August 27, 1990: Stevie Ray Vaughn
- October 13, 1997: John Denver










ROCKIN' ROLL
HEAVEN

Performed by: Righteous Brothers



Collectables

BACK TO BACK HIT SERIES

COL 6024-A

SEND FOR
FREE
CATALOG

Cema
SPECIAL
MARKETS

5710-57305-A

Rock 'n' Roll Heaven
RIGHTEOUS BROTHERS

© 1974 Haven Records

© 1990 CEMA Special Markets

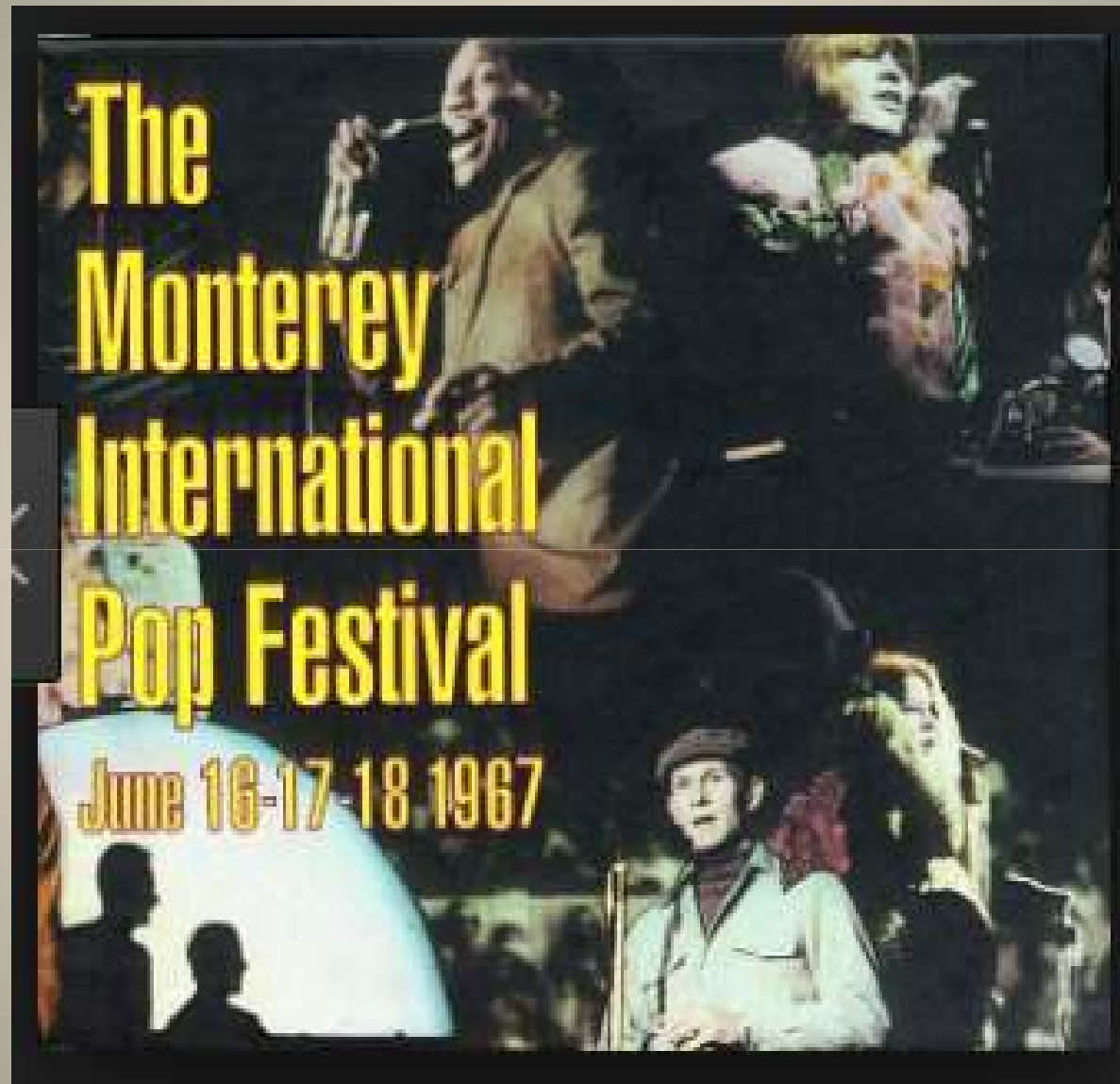
COLLECTABLE RECORD CORP BOX 35 HARRISBURG, PA 17072

STELLAR HEAVEN









WINTER DANCE PARTY



BUDDY HOLLY
and
CRICKETS
"FRONT MAN"



BIG BOPPER
"Cherry Lip"



RITCHIE VALENS
"Donna"
"Come On, Let's Go"

ALL THE
STARS
IN PRISON

DION

and
THE BELMONTS
"RACHAEL WALK"



FRANKIE SARDO

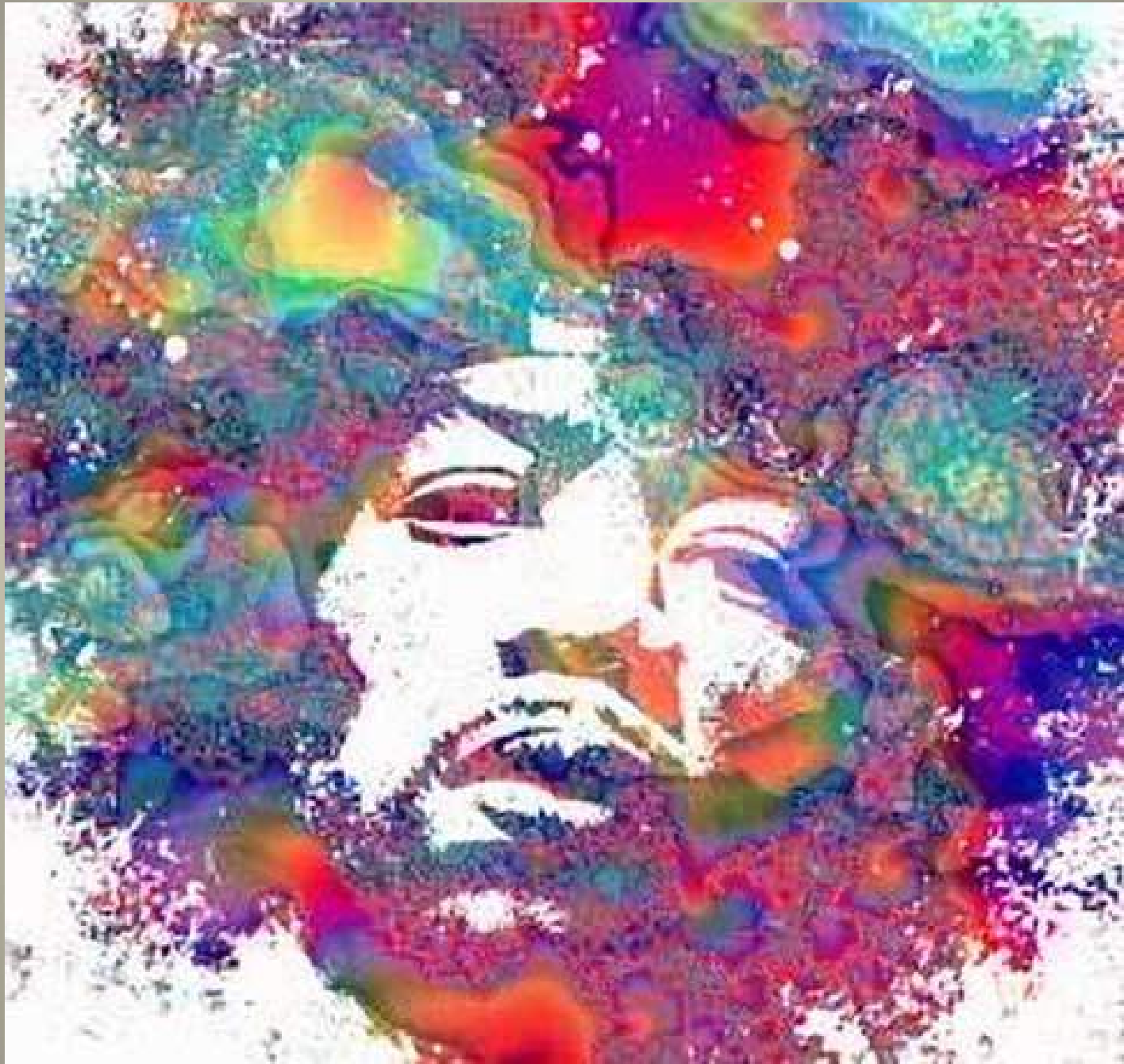
Live
Music

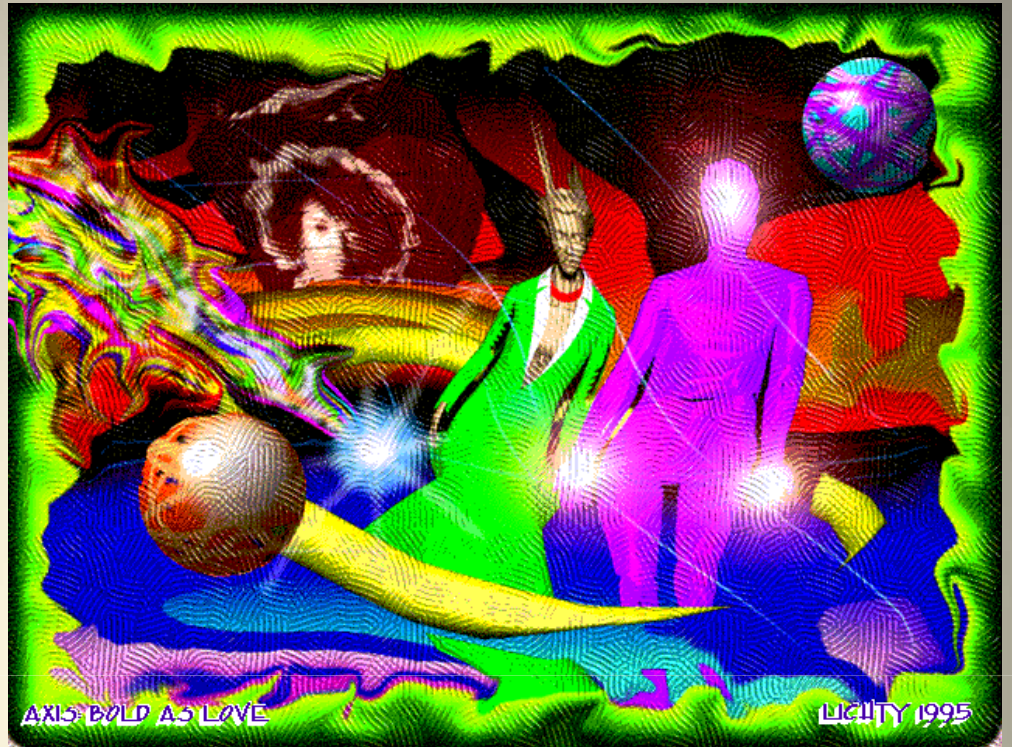
Live
Music



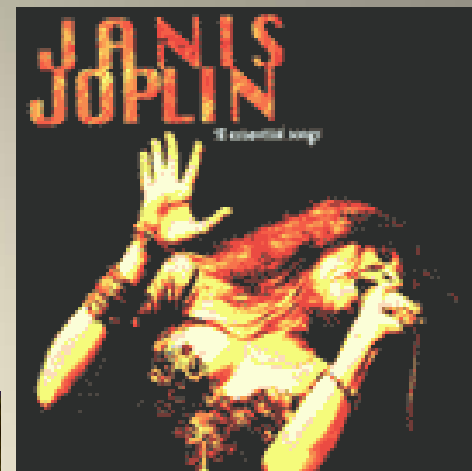












Lillian Hellman: Plain Speaking with Mrs. Carter

ROLLING STONE

JANIS

By Ellen Willis
A Special Preview of
The Rolling Stone
Illustrated History of
Rock & Roll

THE WAYWARD BUTZ

What He
Really Said and What
They Said He Said

By Greil Marcus

Battle of the Bands
THE
WHO/DEAL
SPREAD
By Annie Leibovitz

The Dreams and Dearts of Filmmaker
WERNER HERZOG
By Jonathan Cull



OTIS!
1941-1967

**OTIS REEDING
THE DOCK OF THE BAY**





LIGHT MY FIRE





ROCK N' ROLL HEAVEN









BIG BROTHER & THE HOLDING COMPANY
FEATURING

JANIS JOPLIN

WITH ALBERT KING + ALSO TIM BUCKLEY

MARCH 8 - 1968



FILLMORE EAST (Formerly The Village Theatre)
SECOND AVE. & SIXTH ST., N. Y. C. - TICKETS \$3.00 - \$4.00 - \$5.00

ON ANYONE CHOSEN BY STARS

OTIS REDDING

CARLA THOMAS

PERCY SLEDGE

WILKINS CONLEY

Manhattans

BELIVE SWAIN

of STAR STEPS

JAMES CARR

BETTY HARRIS

N.Y. APOLLO

Theatre

SATURDAY, FEB. 11 1966

del-har production

N.Y. APOLLO

del-har production

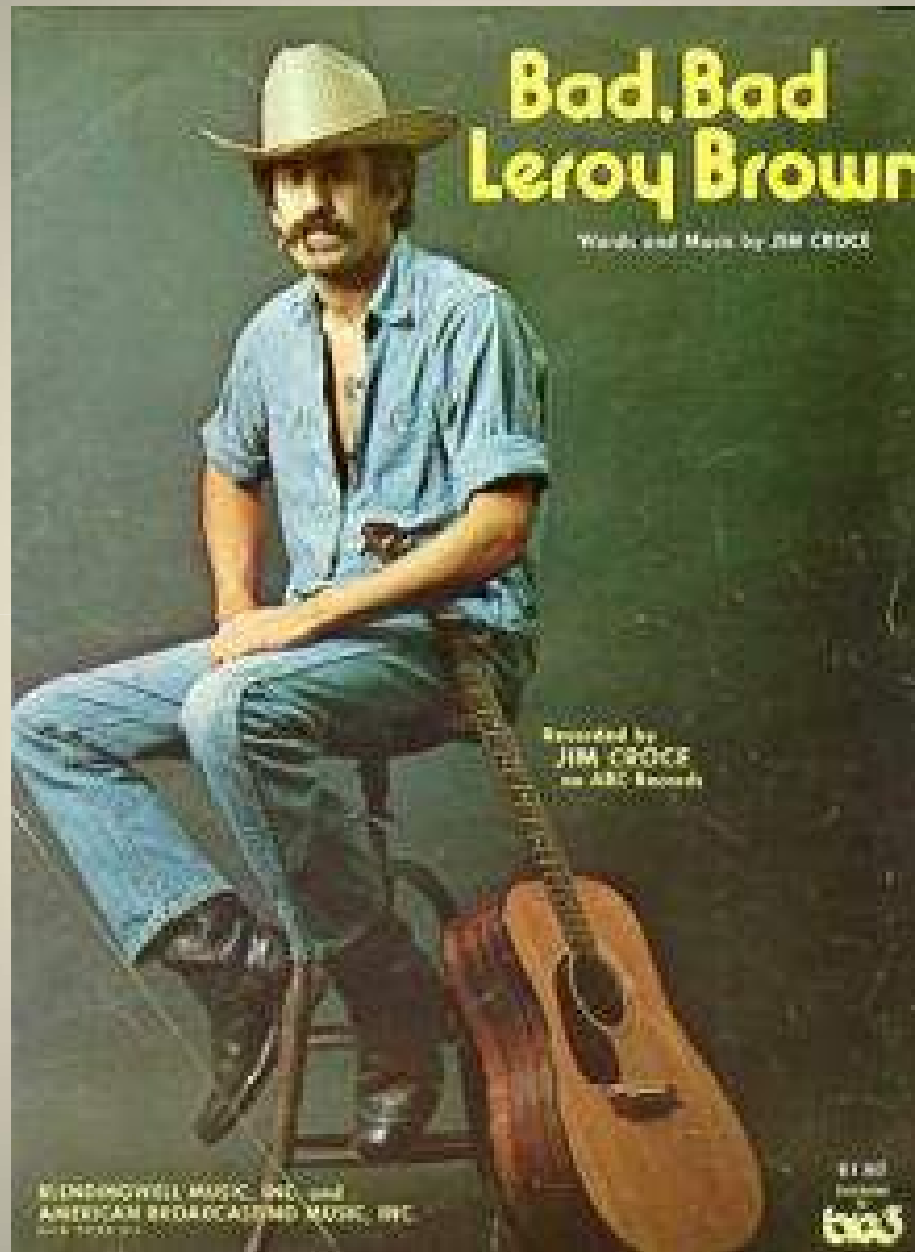
TICKETS

SHERMAN-CLAY, 318 Broadway, Oakland 44-8446; MUSIC BOX OFFICE; Student Union, University of Calif., Ext. 8126; DISCOUNT RECORDS, 2801 Telegraph, Berkeley 840-1102; SAN FRANCISCO STATE Box Office; MUSIC TOWN, Broadway Shopping Center, Walnut Creek 94-1280

SUNDAY, OCTOBER 15 • TWO SHOWS • 3 PM-7:30 PM







Bad, Bad Leroy Brown

Words and Music by JIM CROCE

Recorded by
JIM CROCE
on ABC Records

BLINDHOLE MUSIC, INC. and
AMERICAN BROADCASTING MUSIC, INC.
1974

11 50
ABC
RECORDS





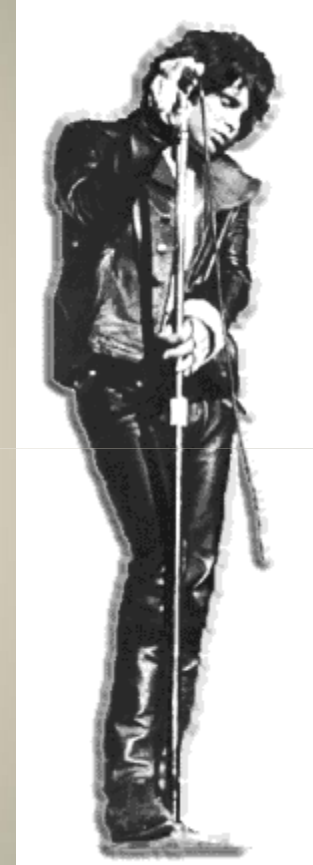


STORY BY JIMMY GORDON

Mack the Knife

Smooth.
Sharp.
Deadly.



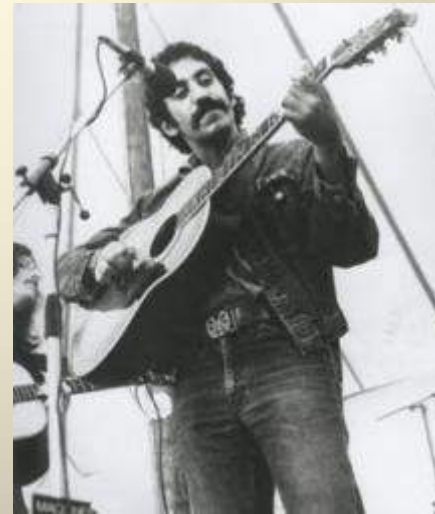


STELLAR HEAVEN







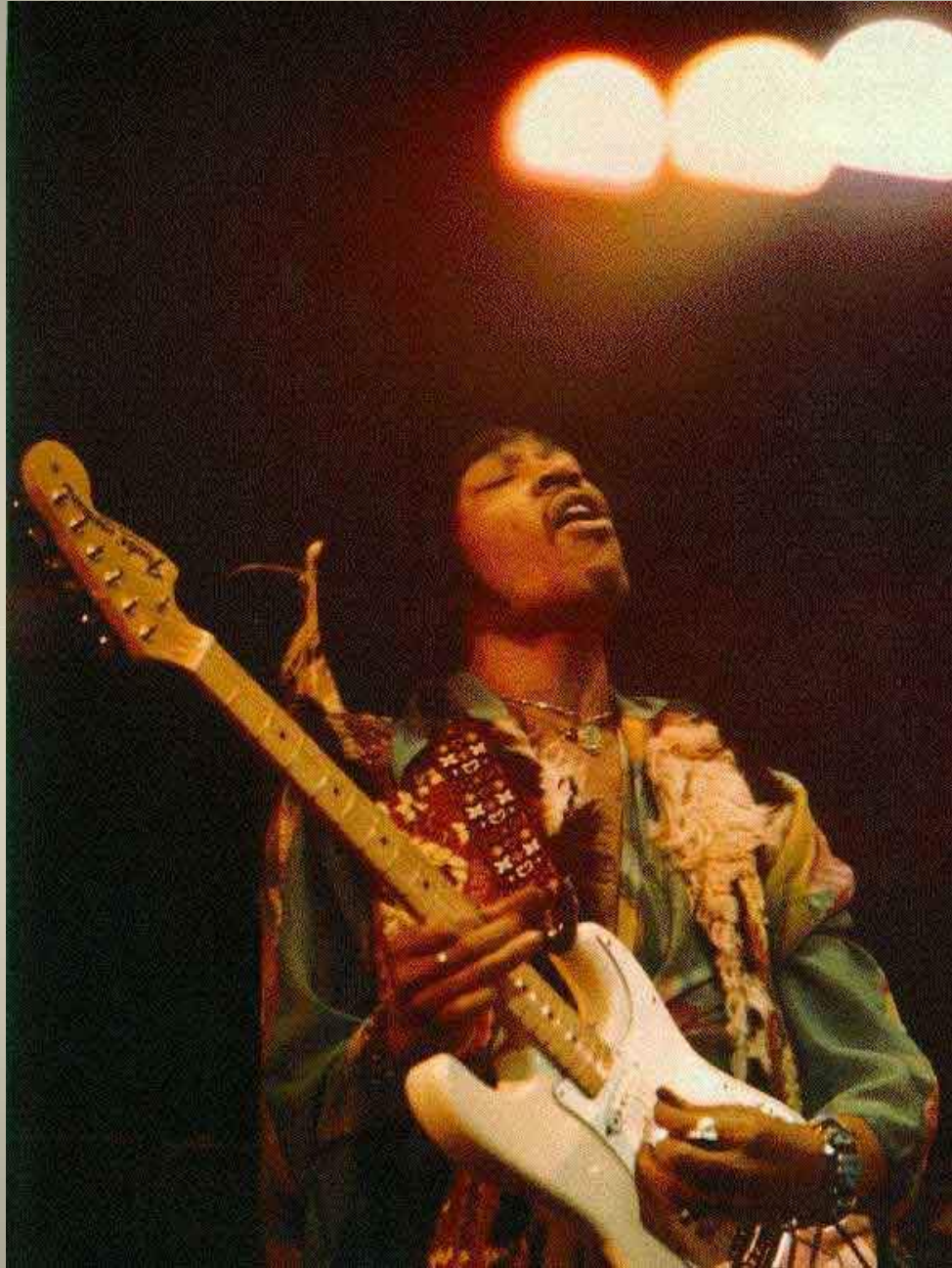
















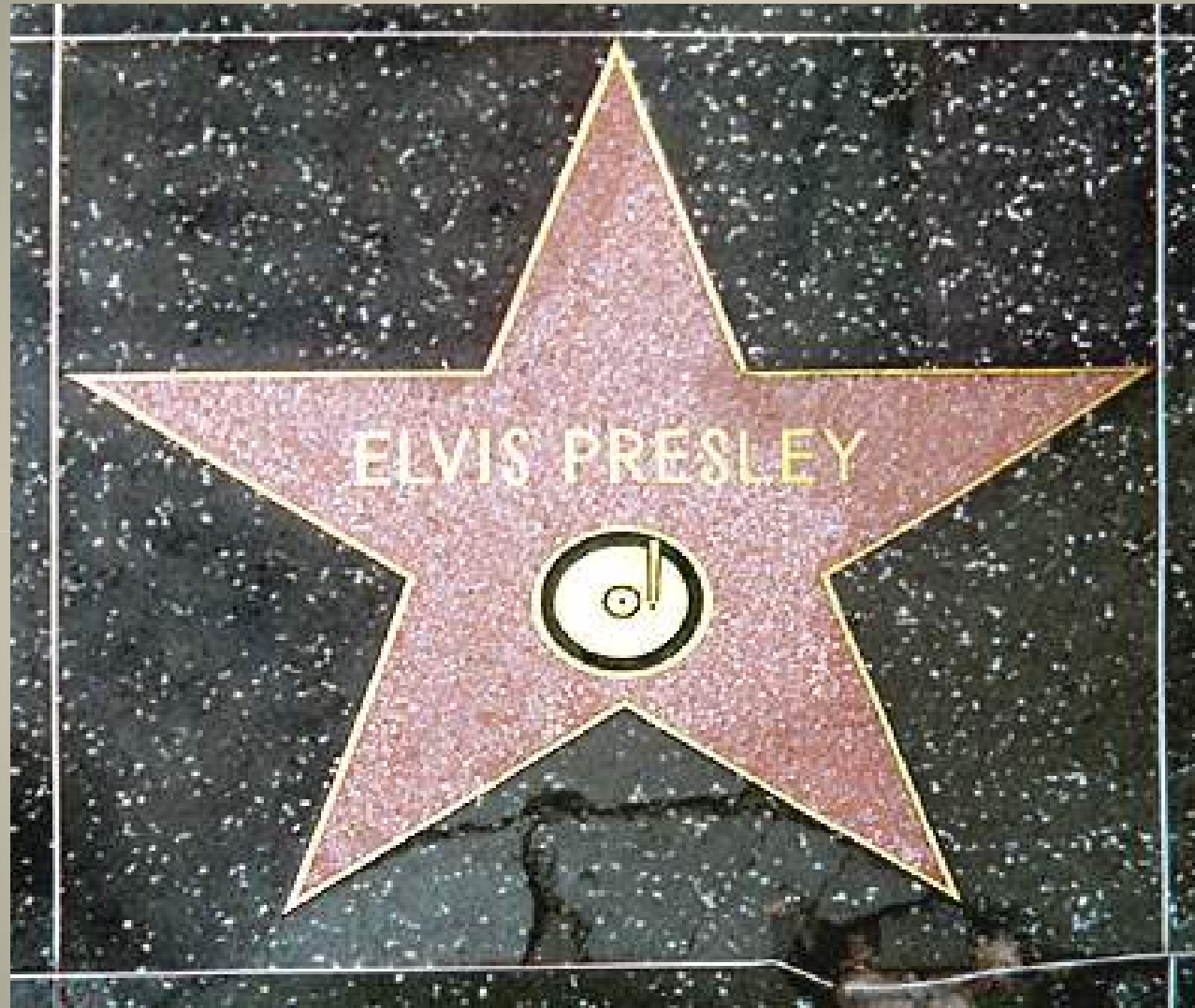




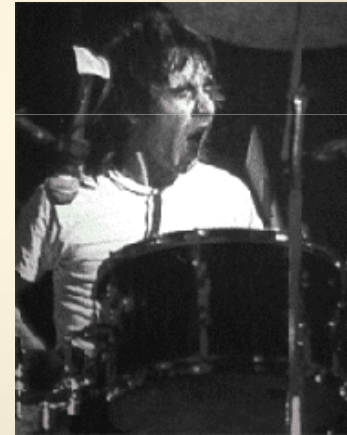
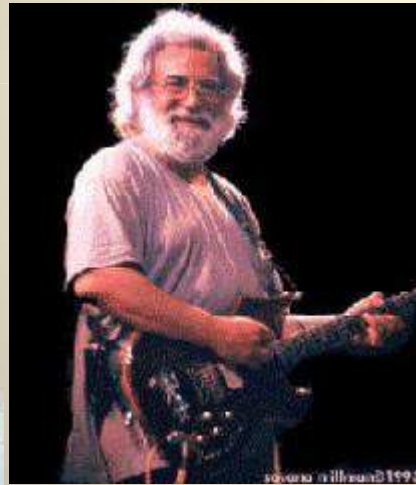
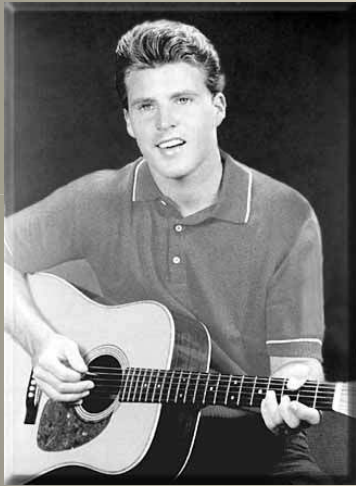






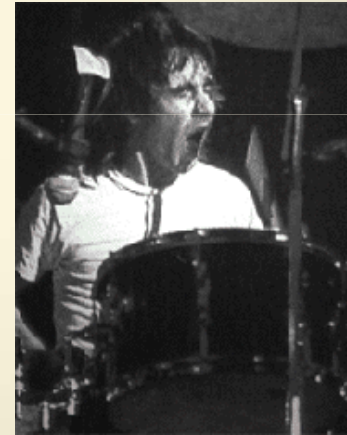
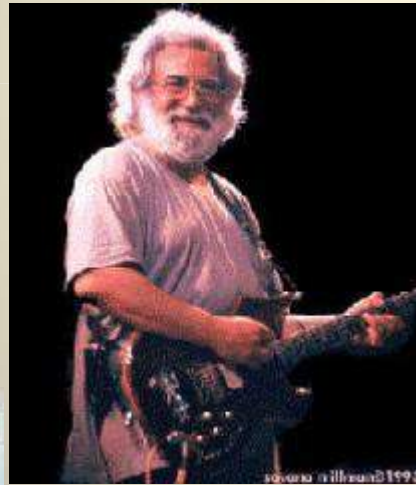
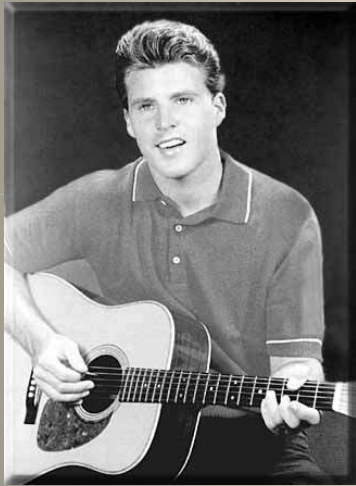


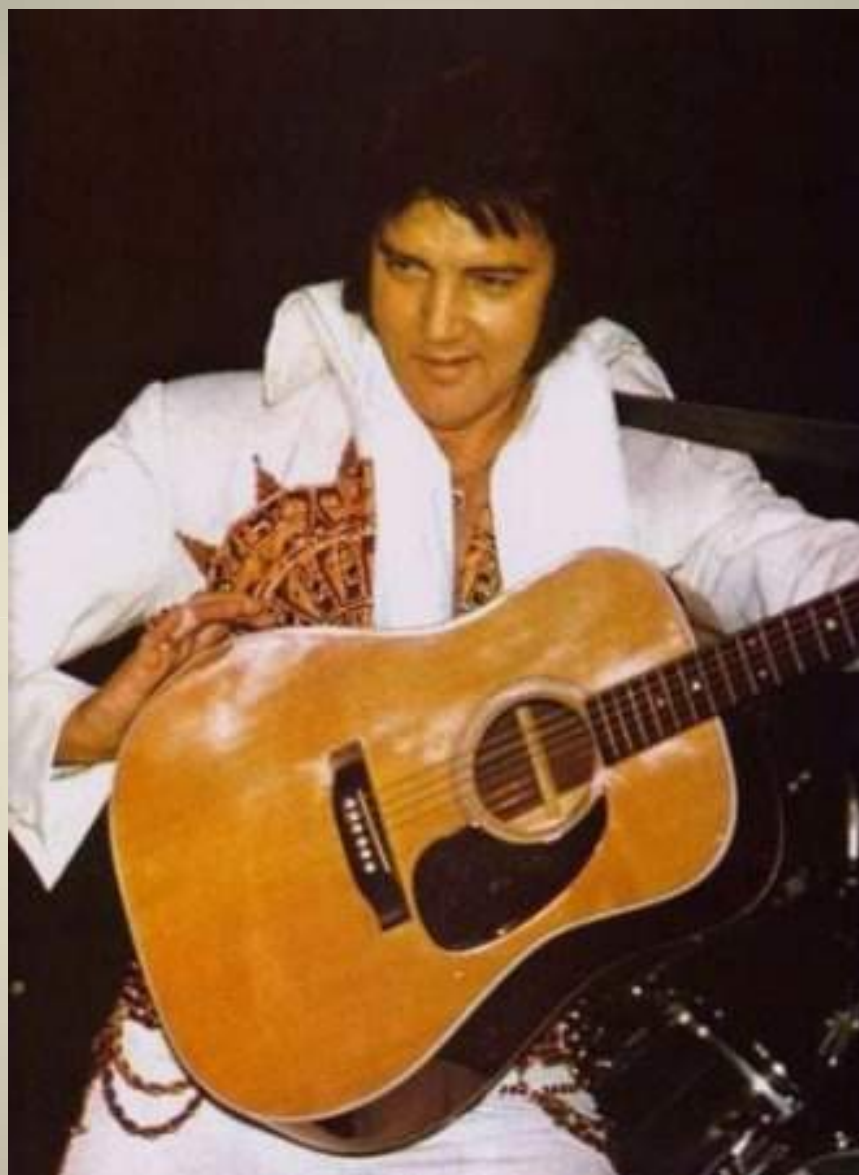
















Thank You For Your Attention