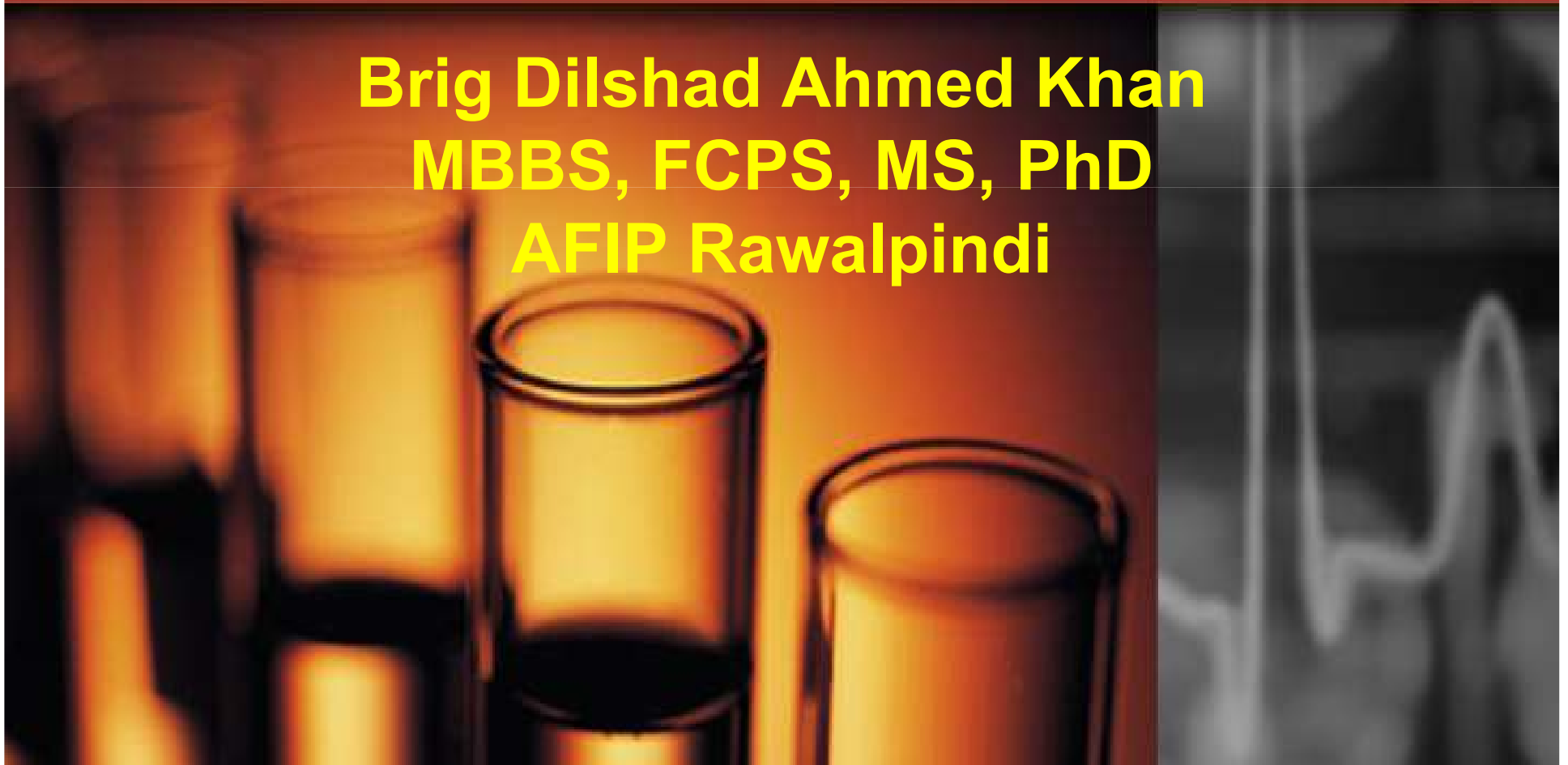


# Laboratory Evaluation of The Poisoned Patient

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**AFIP Rawalpindi**



# Clinical Toxicology

- Toxicology is the study of the adverse effects of chemicals on living organisms.
- Is concerned with diseases and illnesses associated with short term or long term exposure to toxic chemicals /drugs

# **Toxicological Testing for Patient Care**

- **Most of the poisoned patients are misdiagnosed in Pakistan because of lack of toxicological lab facility.**
- **Detection of the specific toxin in blood can affect the treatment of the patient.**
- **A specific antidote for particular drug can be given to save life.**

# Toxicological Testing for Patient Care



# **Toxicological Testing for Patient Care**

- **Quantitation of the toxin may affect the approach to therapy.**
- **Multiple drugs may be identified by toxicology testing.**
- **'Negative' results from toxicology testing may help the clinician to consider other etiologies in patient's**

# Routes of Exposure

©Cinetel Productions

- Dermal

- Inhalation

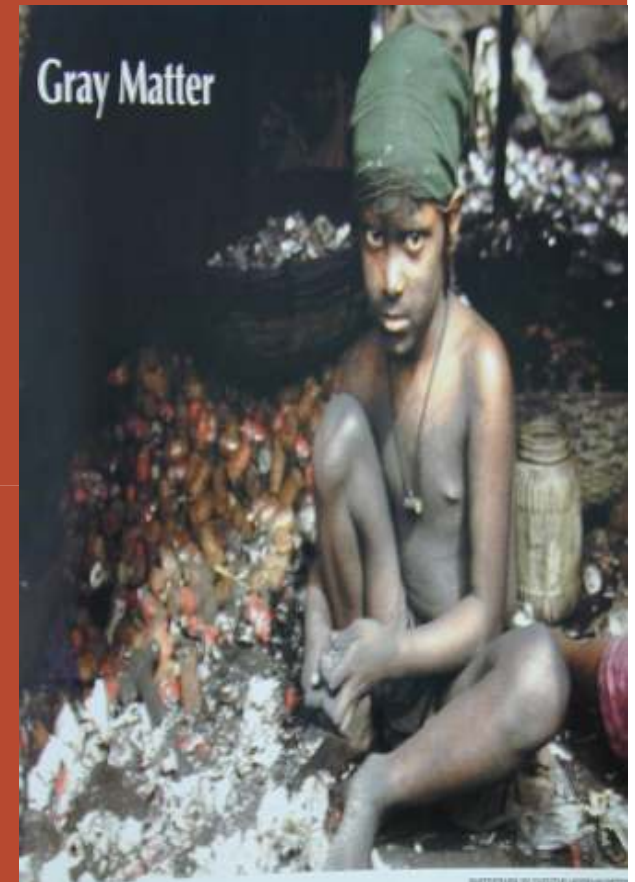
- Ingestion

Injection

intravenous, intramuscular, intraperitoneal

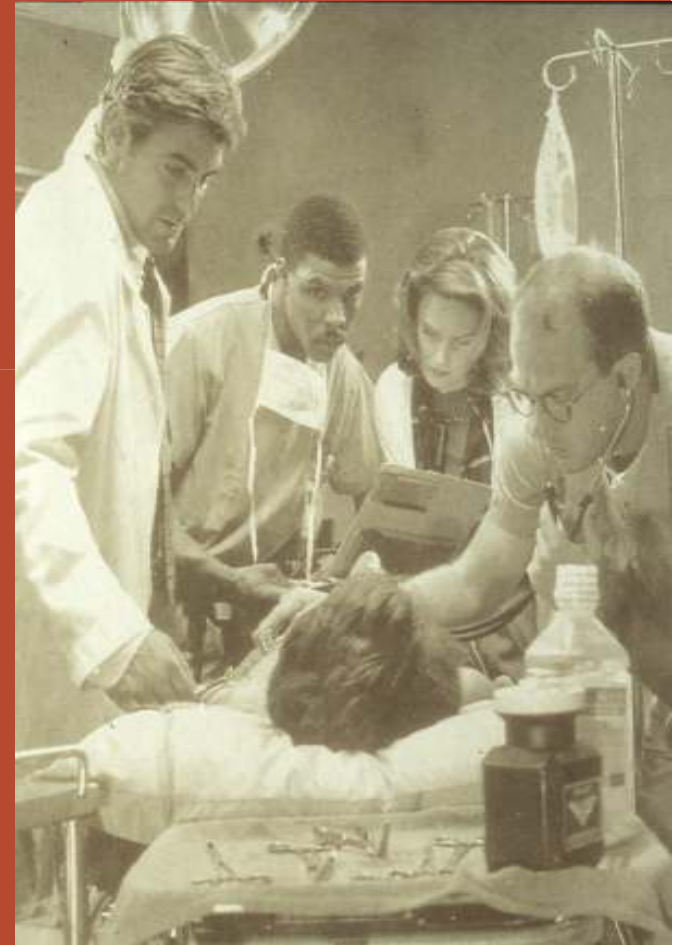
# Routes of Exposure: **Pediatric**

- Unintentional
- Very small quantities  
drugs
- Only one substance  
involved
- Medical care is  
immediate



# Routes of Exposure: **Adult**

- **Intentional/suicide attempts**
- **Multiple substances**
- **Medical care often delayed**
- **May be large quantities**





# Chronic Drug Exposures

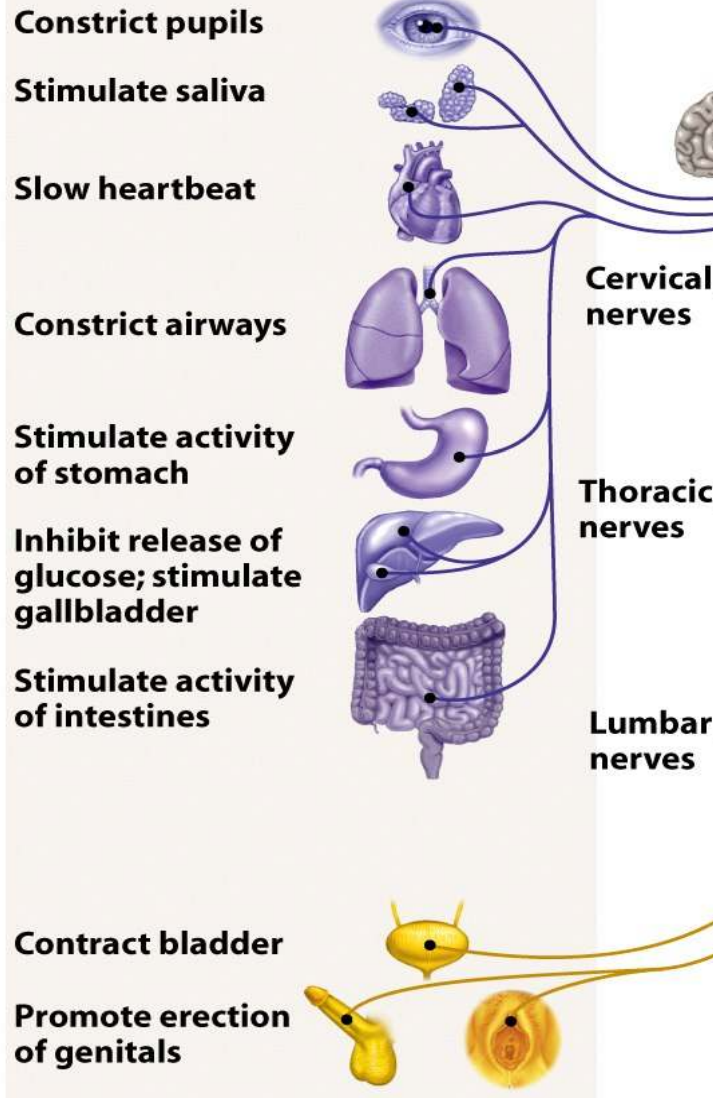
- Iatrogenic
- Adverse drug interactions
- Therapeutic errors



# DIAGNOSIS

## PARASYMPATHETIC NERVES

"Rest and digest"

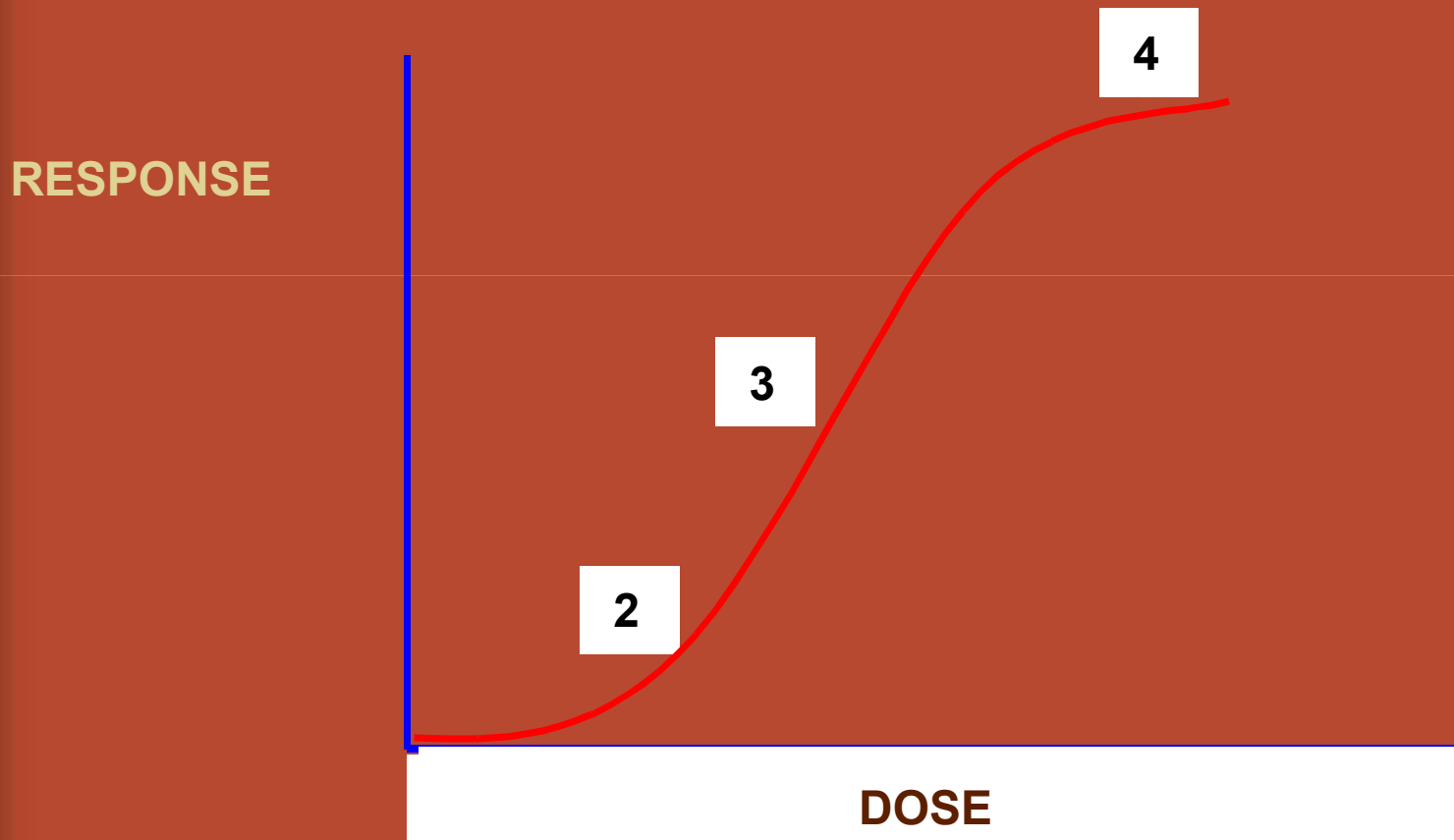


## Characteristic signs / symptoms

- ✓ Headache
- ✓ Pinpointed pupils
- ✓ Rinorrhea
- ✓ Difficulty in breathing and coughing
- ✓ Stomach cramps, nausea or vomiting
- ✓ Bradycardia
- ✓ Localized sweating and muscular twitching
- ✓ General weakness
- ✓ Convulsions
- ✓ Unconsciousness

# Dose-Response Relationship:

As the dose of a toxicant increases, so does the response.



DOSE DETERMINES THE BIOLOGICAL RESPONSE

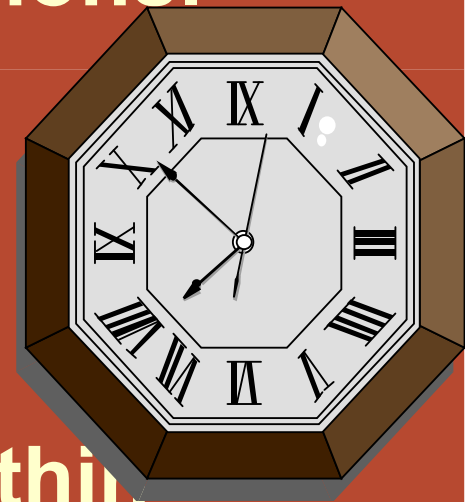
# Toxicology Laboratory

Identifies the toxicant through analysis of body fluids, stomach content or suspected containers



# Essential Drug Screen

- Identify the drugs in urine and serum which have the greatest impact on diagnostic/ management decisions.
- Develop toxicology assays in consultation with clinicians.
- Results should be available within
- 2 hours/ 24 hrs/ 7 days per week



# Biological Specimens

- Urine
- Blood
- Stomach contents
- Nail
- Hair
- Saliva
- Amniotic fluid



# Urine Assays (Qualitative)

Urine sampling & testing



Chain of custody documents



# Drug Detection Window

Blood



1-2 Day

Oral Fluid



1 - 2 Days

Urine



3-5 Days

Nail



4 - 30 Days

Hair



250 Days



# General Laboratory Tests

✓ Blood gases

Renal profile

✓ Electrolytes

Serum Osmolality

✓ Glucose

Blood CP

✓ Hepatic profile

Urinalysis

# Essential Drug Screen

## Urine Assays (Qualitative)

Cannabinoid

Opiates

Amphetamines

Cocaine

Benzodiazepines

Barbiturates

Tricyclic antidepressants

Propoxyphene

# Essential Drug Screen

## Serum Assays (Quantitative)

Acetaminophen

Salicylates

Ethanol

Lithium

Digoxin

Iron

Carbamazepine

Phenytoin

Phenobarbital

Theophylline

Pesticides

# The Screening Step

- A screening test is normally employed to provide the analyst with quick insight into the likelihood that a specimen contains a drug substance.
- Positive results arising from a screening test are considered to be tentative at best and must be verified with a confirmation test.
- The most widely used screening tests are color test, thin layer chromatography and immunoassay

# What Technological Capabilities are Required?

- **Spot tests**
  - Acetaminophen
  - Salicylates
  - Phenothiazines
- **Photometric tests**
  - Ethanol
  - Lithium

# Diagnostic Testing

- **Immunoassays**
  - Drugs of abuse
  - Therapeutic drugs
- **Plasma Cholinesterase (ChE)**
  - Cholinesterase
  - Butyrylcholinesterase,

## **What Technological Capabilities are Required?**

- **Screening results should be identified as presumptive and not confirmed.**
- **Screening results should be verified by another method, especially when positive results have implications beyond the acute episode of care.**



# **Quantitative Analysis Affecting Acute Clinical Management**

## **Initiation of specific antidotes**

- **Acetaminophen (N-acetylcysteine)**
- **Digoxin (digoxin specific antibody fragments)**
- **Iron ? (deferoxamine)**





# **Quantitative Analysis Affecting Acute Clinical Management**

## **Hemodialysis/hemoperfusion**

- **Theophylline**
- **Aspirin**
- **Lithium**
- **Methanol**
- **Ethylene glycol**

# **Advanced Toxicology Testing**

- **Requires additional time beyond 2 h.**
- **Less frequently needed than the Essential Drug Screen.**
- **Most hospital laboratories will not find it cost effective or of sufficient clinical utility to provide.**

# What Technological Capabilities are Required?

## Advanced Toxicology Service

- Identify a Specific Drug in a Class:

Alcohols, amines, opiates, antidepressants, phenothiazines, h<sub>2</sub>-receptor blockers, benzodiazepines, carbamates, analgesics

- Measure a Specific Alcohol(quantitative blood):

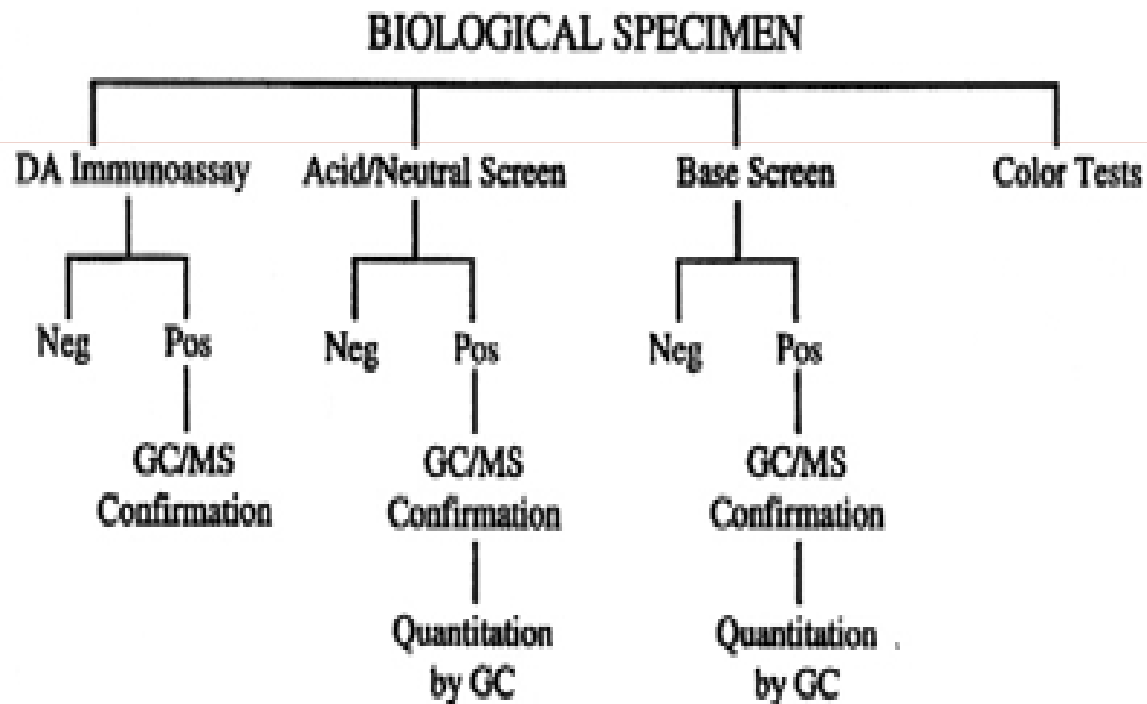
Ethanol, methanol, isopropanol, ethylene glycol

# Advanced Toxicology Lab

- **Immunoassays**
- **Fluorescence chemiluminescence**
- **Thin Layer Chromatography**
- **Ultra-Visible Spectrophotometry**
- **Gas Chromatography**
- **Gas Chromatography-Mass Spectrometry**
- **Liquid Chromatography-Mass Spectrometry**
- **Atomic Absorption Spectrophotometry (AAS)**
- **Inductively Coupled – Mass Spectrometry (ICP-MS)**

# Drugs: Comprehensive Approach

## COMPREHENSIVE DRUG TESTING - ONE APPROACH

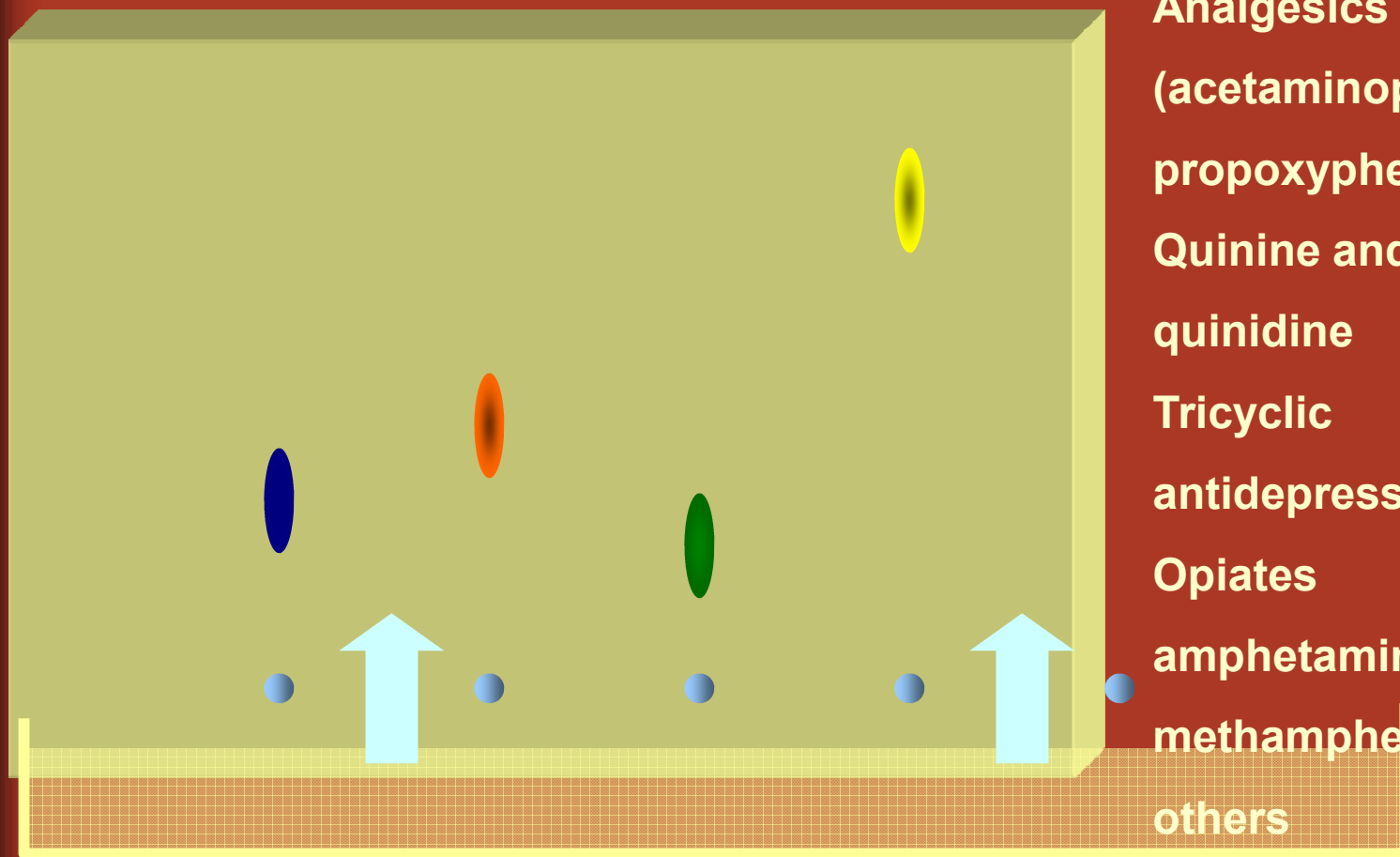


# Presumptive (Color Tests)

- COLOR TESTS many drug tests yield characteristics of color when brought into contact with chemical reagents.
- Color tests are used as screening tests and not conclusive.
- Impurities may affect the test



# Thin Layer Chromatography



**Analgesics**

(acetaminophen,  
propoxyphene,

Quinine and  
quinidine

**Tricyclic**

**antidepressants**

**Opiates**

amphetamine and  
methamphetamine

**others**

# Advanced Toxicology Service

## Liquid Chromatography

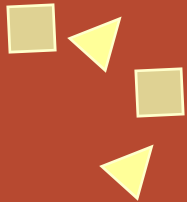
- Amines (identify specific compound)
- Opiates (identify specific compound)
- Tricyclic antidepressants
- Phenothiazines (identify specific compound)
- H<sub>2</sub>-receptor blockers





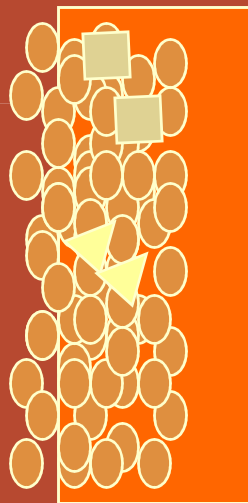
# Chromatography

Gas chromatography offers the toxicologist the most widely used approach for determining drugs levels in blood



– Methanol

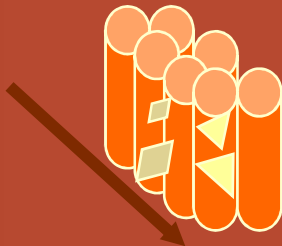
– Isopropanol



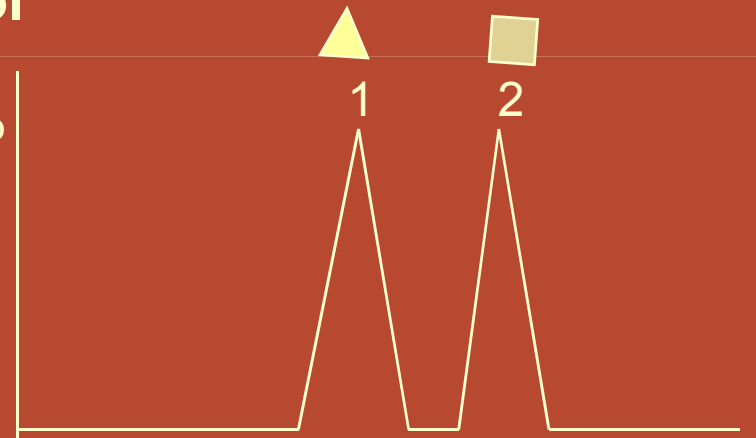
Ethylene glycol

Basic drugs

(sedatives)

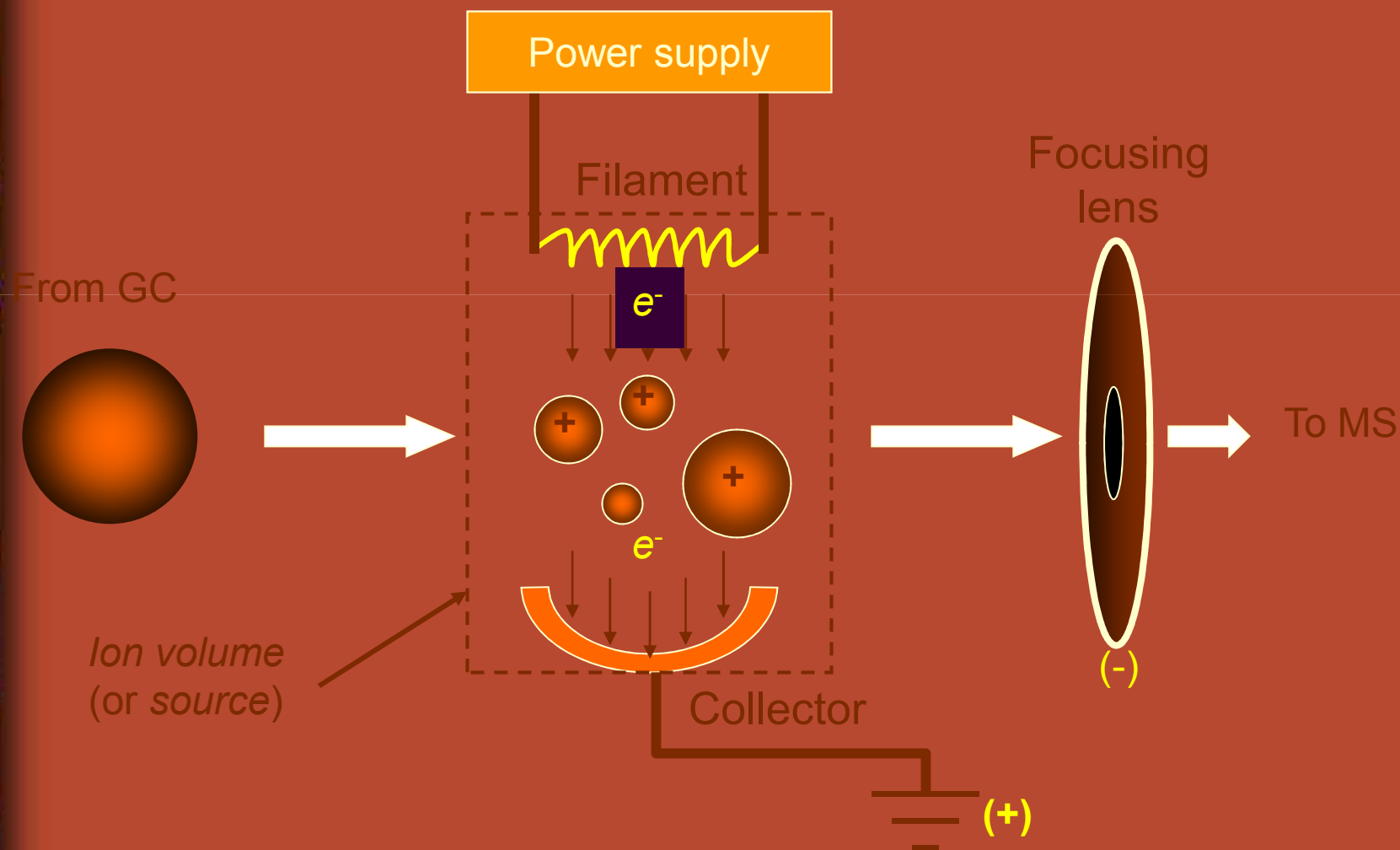


Detector Signal



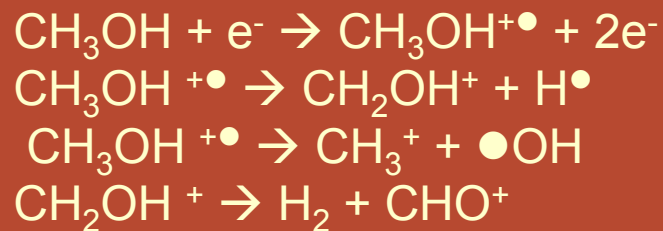
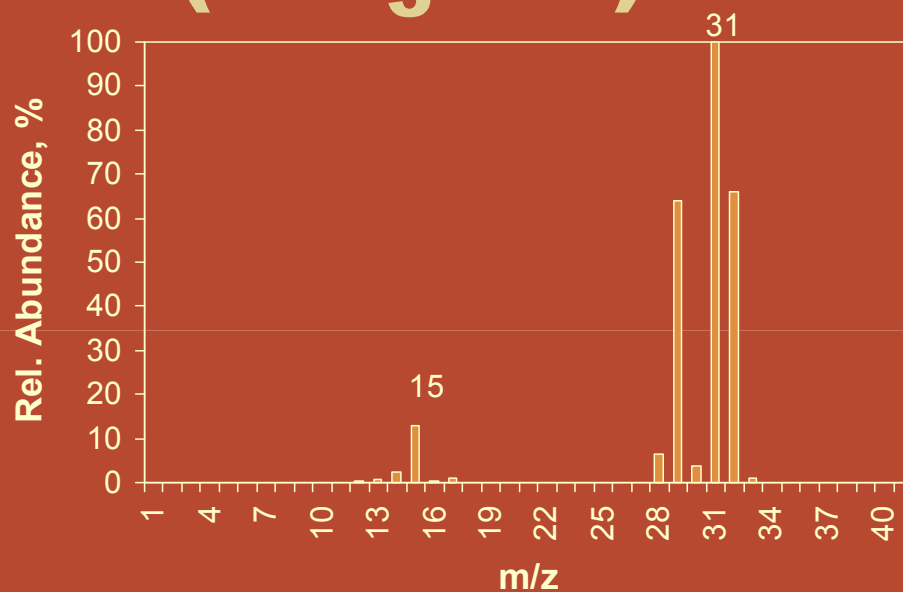
time or volume

# Electron impact ionization



# Example: Mass Spectrum of Methanol (CH<sub>3</sub>OH)

m/z	Rel. Abundance
12	0.33
13	0.72
14	2.4
15	13.
16	0.21
17	1.0
28	6.3
29	64
30	3.8
31	100.
32	66.
33	0.98
34	0.14



# Advanced Toxicology Service

- Mass Spectrometry (example drugs)

Amobarbital

Atropine

Betaxolol

Butabarbital

Carisoprodol

Chlordiazepoxide

Chloroquine

Chlorpheniramine Clonidine

Clozapine

Dextromethorphan Diazepam

Doxylamine

Fentanyl

Fluoxetine

Fluvoxamine

Haloperidol

Hydroxyzine

Ibuprofen

Lorazepam

Meprobamate

Metoprolol Pentobarbital

Phenobarbital

Propoxyphene

Secobarbital

Selegiline

Sertraline Tacrine

# What Technological Capabilities are Required?

## Comparison of Methods

<u>Method</u>	<u>Specificity</u>		<u>Sensitivity</u>	<u>Multidrug Detection</u>	<u>Quantitative Capability</u>
Spot	+		+	No	No
Photo	++	++		No	Yes
IA	++	++		Some	Some
GC	++	++		Yes	Yes
LC	++	++		Yes	Yes
TLC	++	+		Yes	No
GC/MS	+++	+++		Yes	Yes

Osterloh, JD, Laboratory Diagnoses and Drug Screening, in Clinical Management of Poisoning and Drug Overdose, 3rd ed., Haddad, et al., editors, W.B. Saunders, Philadelphia, 1998.

# Summary

- **Toxicology laboratory analysis must be available in tertiary care hospital.**
- **Testing must be evolving to reflect the regional need and exposures**
- **Clinical affiliations with Emergency physicians and timely report will help the patients management.**

# Conclusions

## Considerations for Toxicology Testing

