
بسم الله الرحمن الرحيم

INTERPRETING DRUG TEST RESULTS

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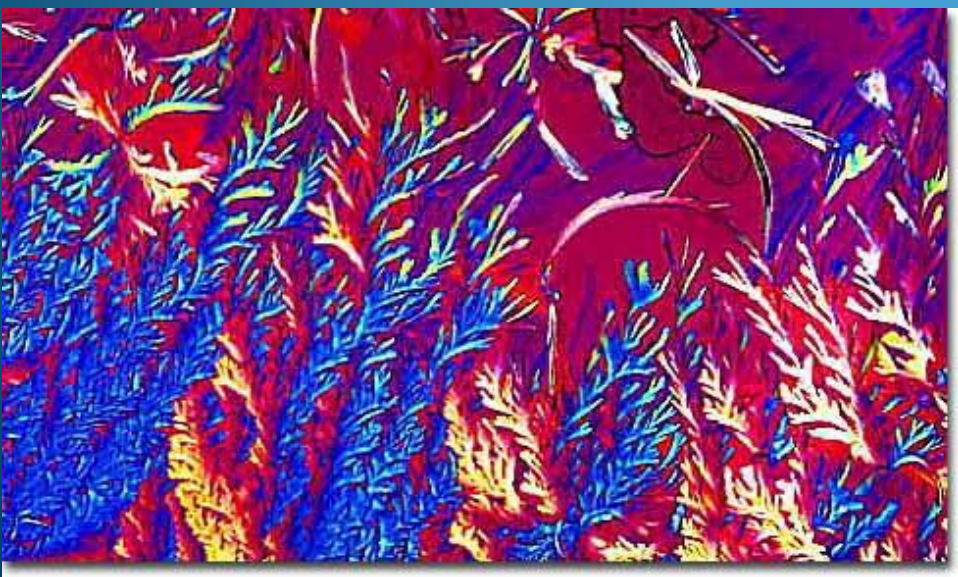
Cocaine

Ephedrine

Stimulants

Methamphetamine



Methylphenidate

Objectives

- Learn the principles of urinary, blood, saliva and hair drug testing
- Understand clinical interpretation of the tests
- Grow insight into period of detection of various substances
- Build awareness of samples alteration to combat deception

Regulated Urine Drug Testing

* Most established use of UDTs "Federal Five"
* marijuana (THC)
* cocaine
* opiates
* phencyclidine (PCP)
* amphetamine/methamphetamine

* Mandated cutoff concentrations too high to be of value in clinical practice
* Requirements of federally regulated testing not always applicable to clinical practice

*Shults TF. Medical Review Officer Handbook. 8th ed. 2002. Gourlay DL, et al. Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies [monograph]. 2004

Regulated Urine Drug Testing

تغییر الگوی مصرف مواد مخدر ایرانیان

از سوی دیگر در طول سال های 84 و 85 بیش از 98 درصد مواد مخدر صنعتی وارداتی بوده اما اکنون اکثر مواد مخدر صنعتی در کشور تولیدی است و توسط قاچاقچیان صادر می شود. همچنین در سال 86 تریاک، کراک، هروئین، شیره تریاک، شیشه، حشیش و کوکائین مهمترین مواد مصرفی معتادان بوده در حالی که در سال گذشته مصرف مواد به ترتیب به تریاک، شیشه، کراک، هروئین، حشیش و کوکائین تغییر یافته است.

کردونی در مورد مصرف مواد مخدر در بین کودکان خیابانی نیز گفت: تحقیقات نشان می دهد کودکان خیابانی در مقایسه با افراد دیگر مصرف الکل بالاتری دارند و مواد مصرفی در آنها نیز احتمالا بالاتر از جمعیت زیر 18 سال است به طوری که در گزارش به دست آمده 17.3 درصد کودکان خیابانی حداقل یک بار در عمر مصرف الکل داشته و 7 درصد کودکان خیابانی حداقل یک بار مصرف یکی از مواد مخدر را تجربه کرده اند.

Scope of abuse

- Unexpected toxicology results demonstrated in about 50% of patients in treatment with controlled substances*
- Recent study of 200,000 urine specimens showed that 60% of results were inconsistent with prescribed regiments**
  - Different drugs found 15%
  - Additional drugs found 20%
  - No drugs found 25%
  - Illicit drugs found 11-24%

* Clarke JJ1, Lawlor TE, Madraymootoo W, et al. Summary of in vitro genetic toxicology assay results: expected and unexpected effects of recent study design modifications. Environ Mol Mutagen. 2012 Oct;53(8):631-5.

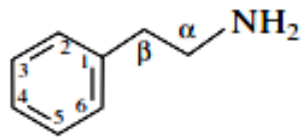
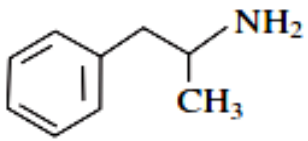
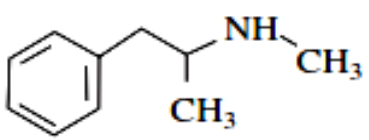
*Michna E, Jamison RN,Pham LD et al. Urine toxicology screening among chronic pain patients on opioid therapy: frequency and predictability of abnormal findings. Clin J Pain.2007;23(2):173-9

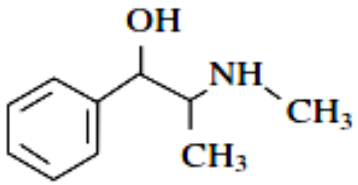
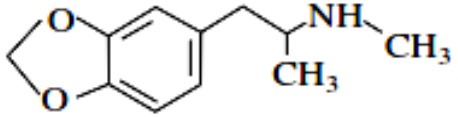
*Quest Diagnostics Health Trends: Prescription Drug Monitoring Report 2013 www.questdiagnostics.com/dms/Documents/health-trends/2013_health_trends_prescription_drug_misuse.pdf

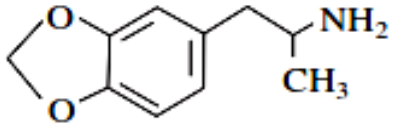
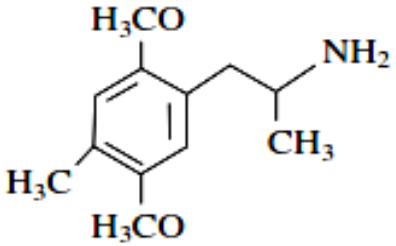
BOX 44-2 AMPHETAMINES AND RELATED COMPOUNDS

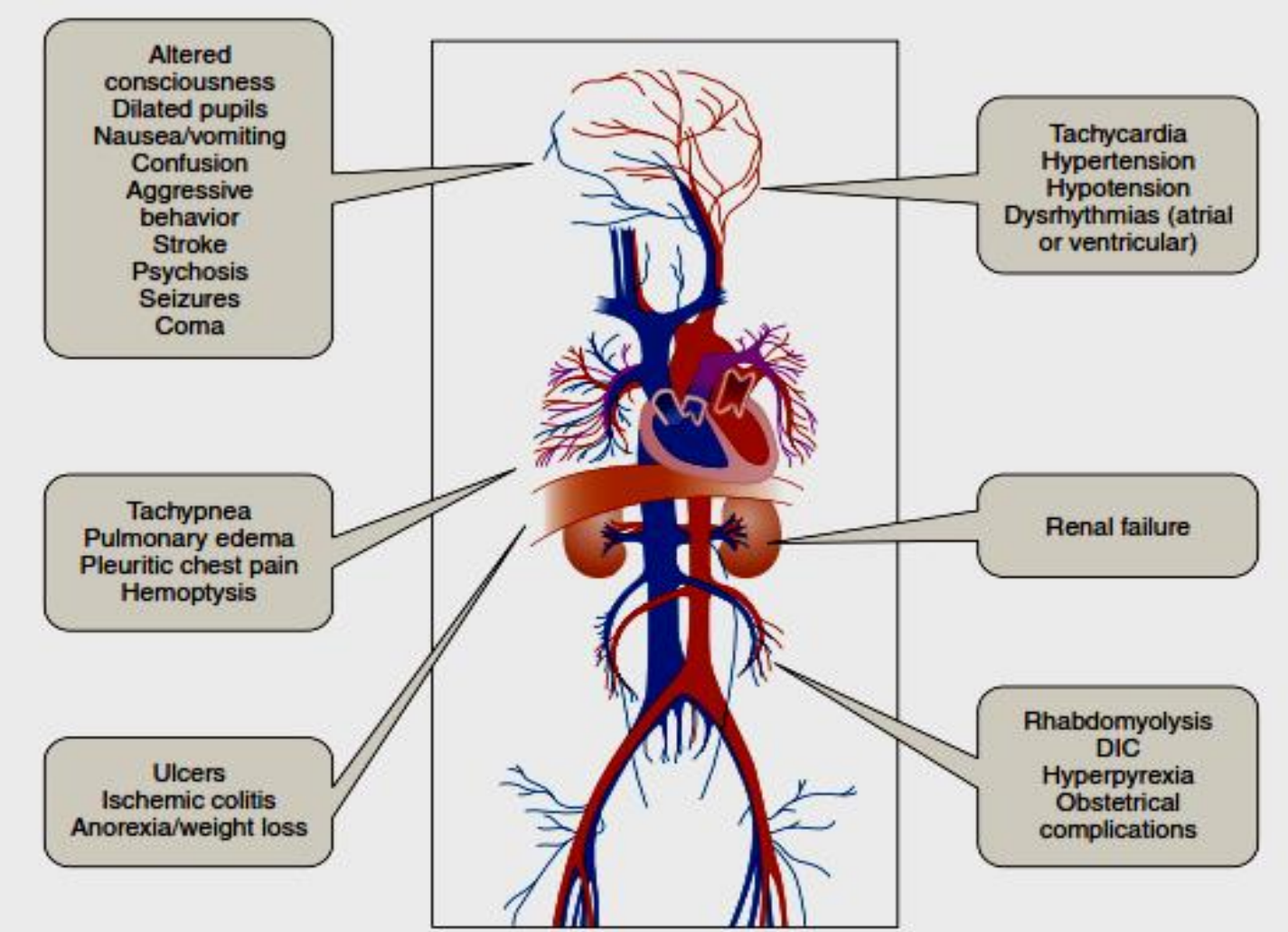
Aminorex fumarate
Amphetamine
Benzphetamine
4-Bromo-2,5-methoxyphenylethylamine (2-CB/MFT)
Cathinone (khat)
Cinnamedrine
Desoxyphedrine
Dextroamphetamine
Diethylpropion
4-Bromo-2,5-dimethoxyamphetamine (DOB)
4-Methyl-2,5-dimethoxyamphetamine (DOM/STP)
Fenfluramine
Mescaline (3,4,5-trimethoxyphenylethylamine)
3,4-Methylenedioxyamphetamine (MDA)
3,4-Methylenedioxyethamphetamine (MDEA)
3,4-Methylenedioxymethamphetamine (MDMA)
Methamphetamine
Methcathinone
Methylphenidate
Methoxyamphetamine (PMA)
Pemoline
Phendimetrazine
Phenmetrazine
Phentermine
Phenylephrine
Phenylethylamine
Phenylpropanolamine
Propylhexadrine
Pseudoephedrine

Methamphetamine and Related Compound

Phenylethylamine	Amphetamine	Methamphetamine
		

Ephedrine	3,4-Methylenedioxymethamphetamine (MDMA)
	

3,4-Methylenedioxy-amphetamine (MDA)	4-Methyl-2,5-Dimethoxyphenylethylamine (DOM/STP)
	



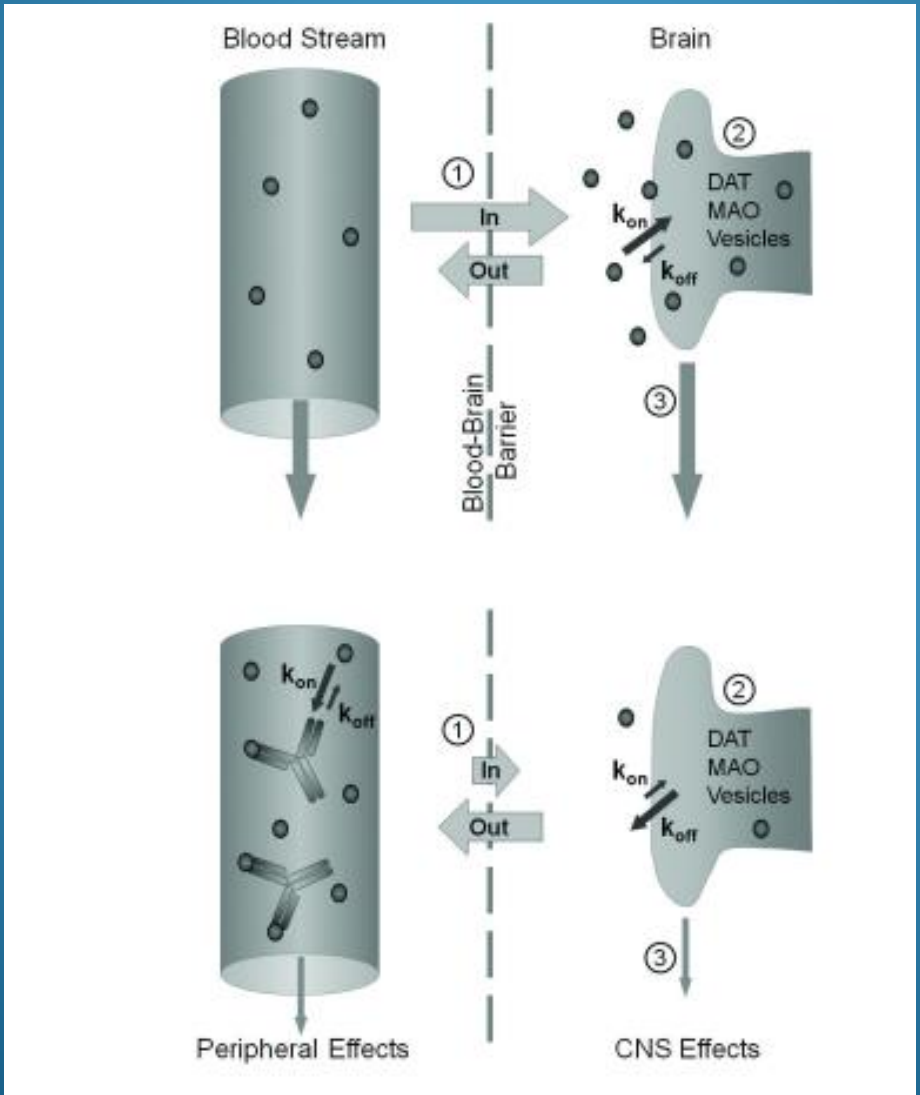
Major signs and symptoms associated with acute amphetamine toxicity.

Summary: Interpretation of UDS Results

Requires that you know

- How specimen is collected
- What is prescribed
- Retention times
- Alternative medical explanations
- Metabolism of drugs
- Scams
- Laws, regulations & guidelines

Development of Active and Passive Human Vaccines to Treat Methamphetamine Addiction

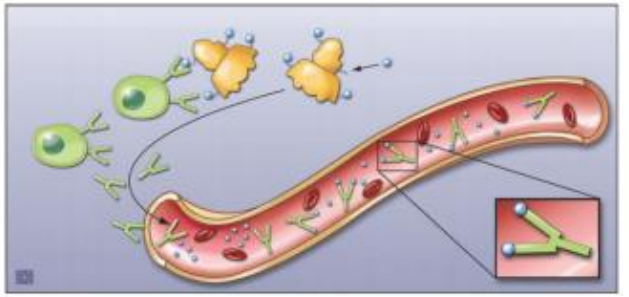


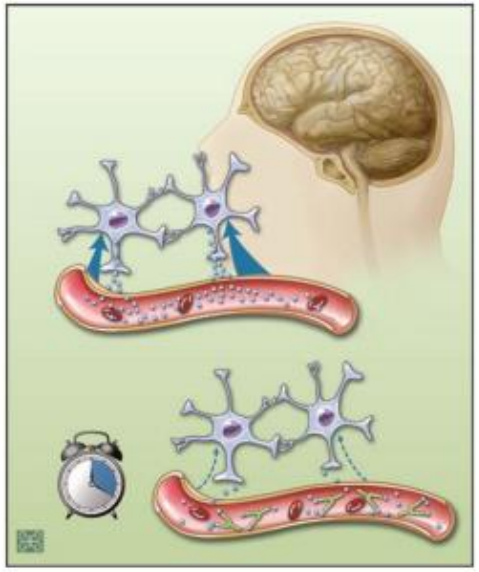
BJCP British Journal of Clinical Pharmacology

Vaccines against stimulants: cocaine and MA

Thomas Kosten,[1,2] Coreen Domingo,[1,2] Frank Orson[2,3] & Berma Kinsey[2,3]

[1]Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, [2]Michael E. DeBakey V.A. Medical Center, Houston, TX and [3]Immunology, Allergy & Rheumatology, Department of Medicine, Baylor College of Medicine, Houston, TX, USA





MENU nature

Letter | Published: 16 August 2017

Vaccine-driven pharmacodynamic dissection and mitigation of fenethylline psychoactivity

Cody J. Wenthur, Bin Zhou & Kim D. Janda

Nature **548**, 476–479(2017) | Cite this article

ORIGINAL ARTICLE

Investigation of Serum Levels and Activity of Matrix Metalloproteinases 2 and 9 (MMP2, 9) in Opioid and Methamphetamine-Dependent Patients

Khadijeh Najafi[1], Daniel Elieh Ali Komi[2,3], Habibolah Khazaie[4,5], Ali Moini[6], Asad Vaisi-Raygani[8], Hamid Reza Ahmadi[5], Mohammad Rasoul Ghadami[4], Amir Kiani[9,7]

Study of Serum Malondialdehyde Level in Opioid and Methamphetamine Dependent Patients

Khadije Najafi[1], Sajad Ahmadi[1], Mahdi Rahpeyma[1], Habibolah Khazaie[2], Asad Vaisi-Raygani[3], Ali Moini[4], and Amir Kiani[5]

Neurobiol Sleep Circadian Rhythms. 2019 Nov; 7: 100046.
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PMCID: PMC6710474
PMID: 31463419

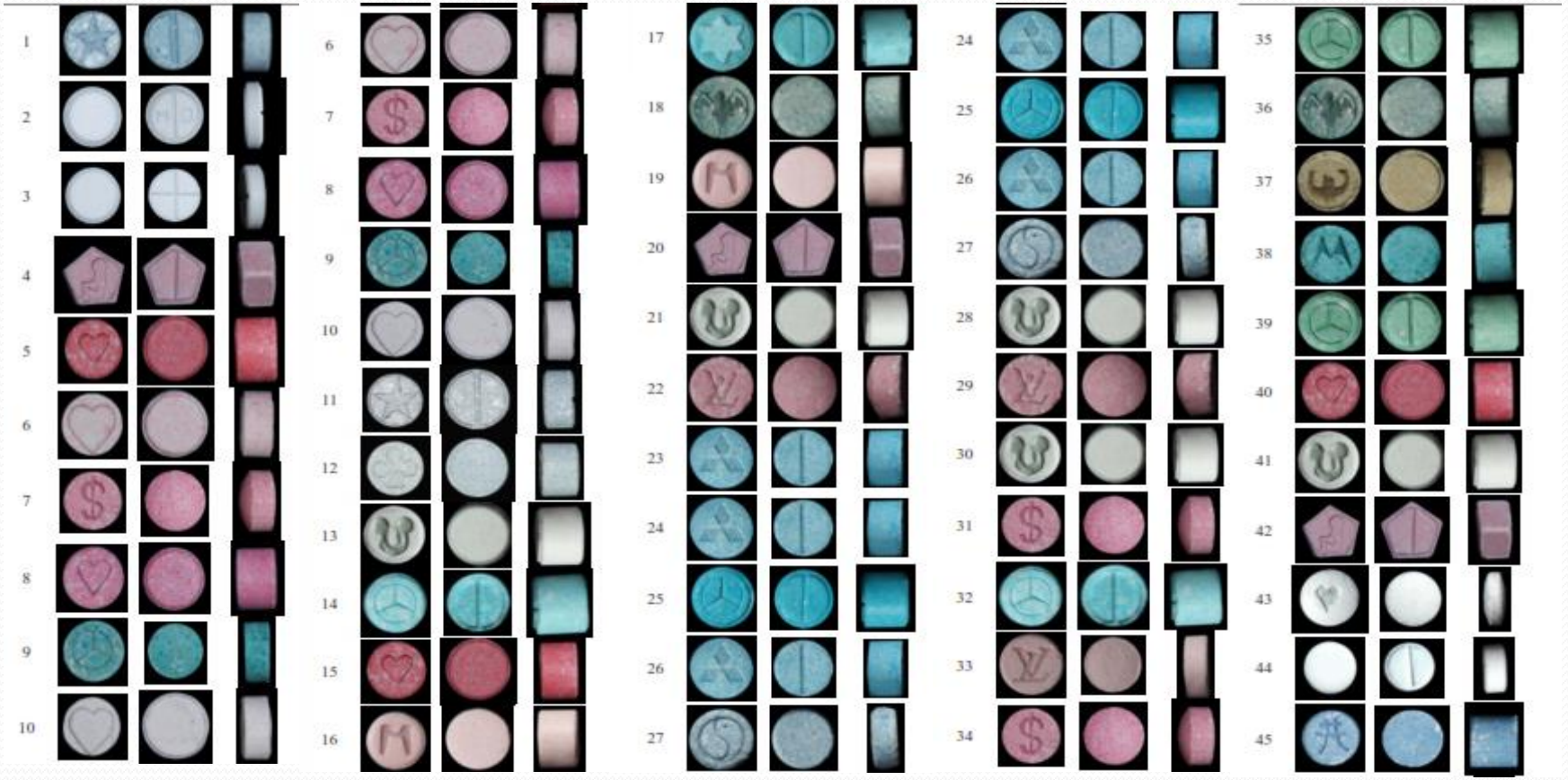
Circadian melatonin profile in opium and amphetamine dependent patients: A preliminary study

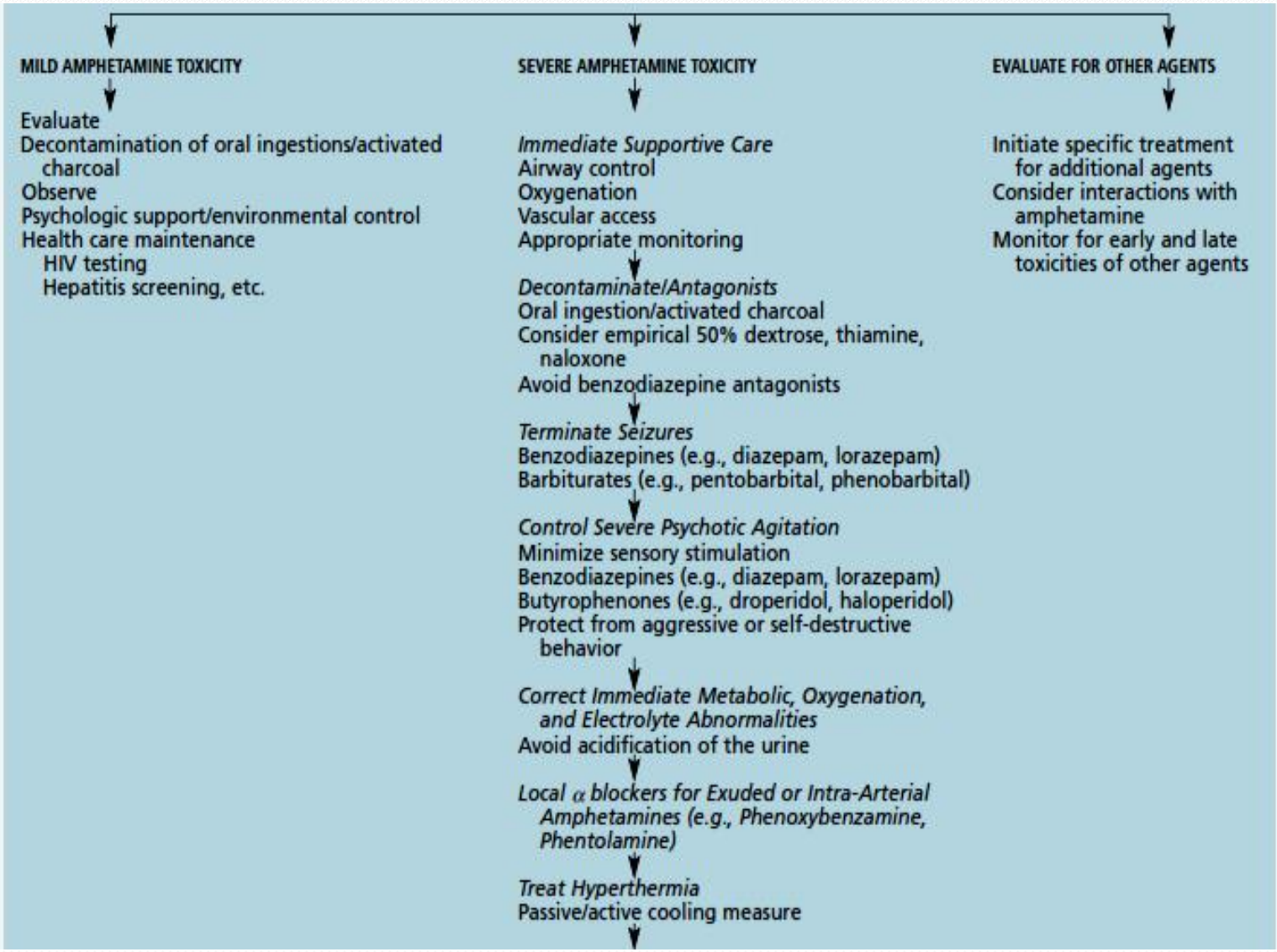
Habibolah Khazaie, MD,[a] Hamid Reza Ahmadi, MD,[a] Amir Kiani, PhD,[b] and Mohammad Rasoul Ghadami, MD[a,*]

تشخیص مسمومیت

تست غربالگری ادرار در درجه اول با استفاده از تکنیک های سنجش ایمنولوژیك ترکیبات آمفتامیني انجام میشود که جزیي از برنامه غربالگري سو مصرف مواد مخدر است. اطلاعات نمونه ادرار و خون توسط کروماتوگرافی گازی همراه با طیف سنجی جرمی (GCMS) تجزیه و تحلیل میشوند .ادرار می تواند برای بیشتر از 48ساعت پس از قرار گرفتن فرد در معرض مواد مخدر مثبت باشد البته این زمان به مسیر مصرف، سرعت جذب، pHادرار و وضعیت هیدراتاسیون بدن فرد وابسته است.

طیف سنجی مادون قرمز برای تشخیص مت آمفتامین استفاده شده است .یك راه تشخیصي سریع ، روش کاپیلاری الکتروفورز غیرآبي با طیف سنجی فلورسانس برای MDMA میباشد. استفاده از مو برای ردیابي ترکیبات آمفتامیني نیز کاربرد دارد، اما استفاده چندانی از نظر بالینی به دلیل تفاوت هاي بین آزمایشگاهي ندارد.




MILD AMPHETAMINE TOXICITY
Evaluate
Decontamination of oral ingestions/activated charcoal
Observe
Psychologic support/environmental control
Health care maintenance
HIV testing
Hepatitis screening, etc.
SEVERE AMPHETAMINE TOXICITY
Immediate Supportive Care
Airway control
Oxygenation
Vascular access
Appropriate monitoring
Decontaminate/Antagonists
Oral ingestion/activated charcoal
Consider empirical 50% dextrose, thiamine, naloxone
Avoid benzodiazepine antagonists
Terminate Seizures
Benzodiazepines (e.g., diazepam, lorazepam)
Barbiturates (e.g., pentobarbital, phenobarbital)
Control Severe Psychotic Agitation
Minimize sensory stimulation
Benzodiazepines (e.g., diazepam, lorazepam)
Butyrophenones (e.g., droperidol, haloperidol)
Protect from aggressive or self-destructive behavior
Correct Immediate Metabolic, Oxygenation, and Electrolyte Abnormalities
Avoid acidification of the urine
Local α blockers for Exuded or Intra-Arterial Amphetamines (e.g., Phenoxybenzamine, Phentolamine)
Treat Hyperthermia
Passive/active cooling measure
EVALUATE FOR OTHER AGENTS
Initiate specific treatment for additional agents
Consider interactions with amphetamine
Monitor for early and late toxicities of other agents

Treat Arrhythmias
Antiarrhythmic (e.g., lidocaine)
Supraventricular arrhythmias (e.g., esmolol)
Electrolyte correction
Acid–base/oxygenation correction

Second-Level Evaluations to Check for Persistent Abnormalities

Persistent Hypotension

Intravascular volume resuscitation
Acute cardiopulmonary support
Central hemodynamic monitoring

Pulmonary Edema/Respiratory Failure
Ventilator
Oxygen
Positive end-expiratory pressure

Rhabdomyolysis
Alkalize urine (e.g., intravenous bicarbonate)
Calcium replacement (e.g., calcium gluconate)
Intravascular volume

Renal Failure/Rhabdomyolysis/Renal Ischemia
Hemodialysis
Intravascular volume

Supportive Care

Observation/monitoring
Psychologic and pharmacologic support for amphetamine abstinence and long-term recovery
Health maintenance/education (e.g., HIV and hepatitis testing)

Coronary Artery Ischemia
Calcium channel blockers (e.g., nifedipine, diltiazem)
β blockers (e.g., esmolol, metoprolol)
Nitrates (e.g., nitroglycerin)

Hypertension
Sedation (e.g., diazepam, haloperidol)
Calcium channel blockers (e.g., nifedipine, nicardipine)
β blockers (e.g., esmolol)
Nitroprusside

Electrolyte Abnormalities
Correct hypokalemia (e.g., potassium chloride)
Correct hypocalcemia (e.g., calcium gluconate)
Correct hypoglycemia (e.g., dextrose as D_{50})

Central Nervous System Abnormality
Seizures
Strokes
Bleeds
Vasculitis
Agitation

Specific interventions for non-cardiovascular related amphetamine toxicity

Table 9. Specific interventions for non-cardiovascular related amphetamine toxicity

- Agitation (treat aggressively)
  - First line – benzodiazepines
    - Diazepam – 2.5–5 mg i.v. boluses
    - Midazolam – 5–10 mg i.m. initially if i.v. access unavailable
    - Clonazepam – 0.5–1 mg i.v. boluses
  - Agitation associated with paranoia/hallucinations
    - Benzodiazepines
    - Droperidol – 2–5 mg i.v. (beware seizures, hypotension)
- Seizures (remember hyponatraemia)
  - First line
    - Diazepam – 2.5–5 mg i.v. boluses
    - Clonazepam – 0.5–1 mg i.v. boluses
  - Second line
    - Phenobarbitone – 20 mg/kg i.v.
    - Sedation with airway control using thiopentone/propofol
  - Computed tomography brain scan in cases of incomplete neurological recovery
- Decreased conscious level (remember hyponatraemia)
  - Exclude hypoglycaemia and hyponatraemia
  - Protect airway and support respiration
  - Computed tomography brain scan
- Hyponatraemia (beware central pontine myelinolysis)
  - Avoid hypotonic fluid administration
  - Fluid restrict in non-dehydrated patients
  - Cautious administration of 3% saline in severe symptomatic cases (sodium concentration <115 mmol/L) – seek advice
- Hyperthermia (treat aggressively)
  - Benzodiazepines – diazepam or clonazepam boluses
  - Active cooling measures – ice packs or baths
  - Neuromuscular blockade
  - 5HT2 antagonist – cyproheptadine 12 mg orally or via a nasogastric tube
- Rhabdomyolysis
  - Maintain urine output
  - Urinary alkalinization (beware increased amphetamine half-life)

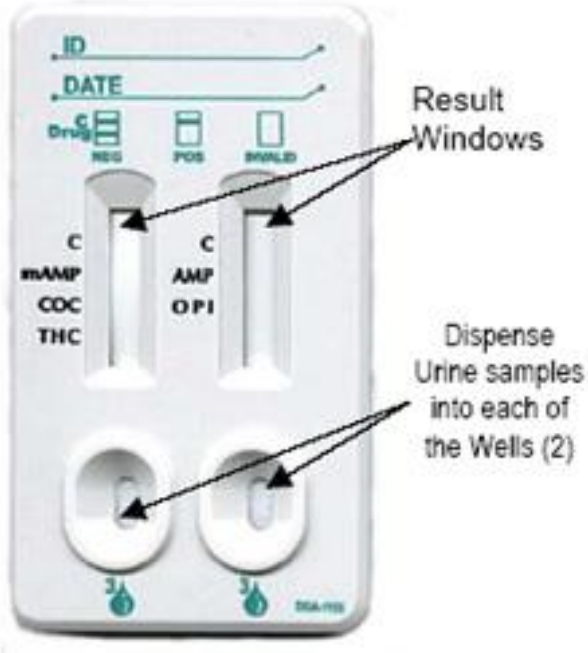
اندازه گیری و تشخیص داروها

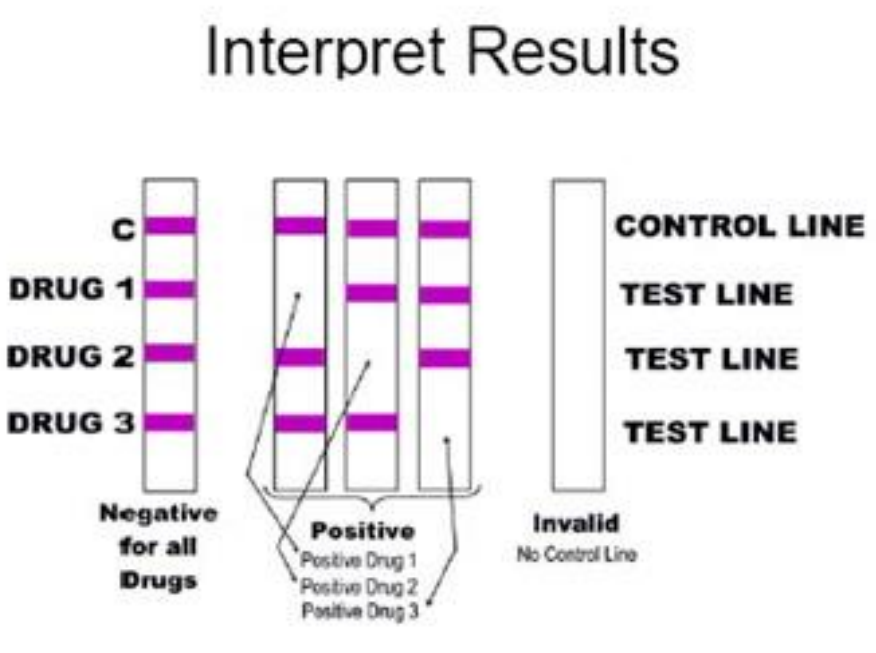
- تست غربالگری با نوار
- الایزا
- روش کرماتوگرافی لایه نازک (TLC)
- روش کرماتوگرافی با کارایی بالا (HPLC)
- گاز کروماتوگرافی جرمی(GC-MS)

تست غربالگری با نوار

- بررسی ادرار
- بررسی بزاق
- بررسی عرق
- بررسی خون
- بررسی مو و ناخن

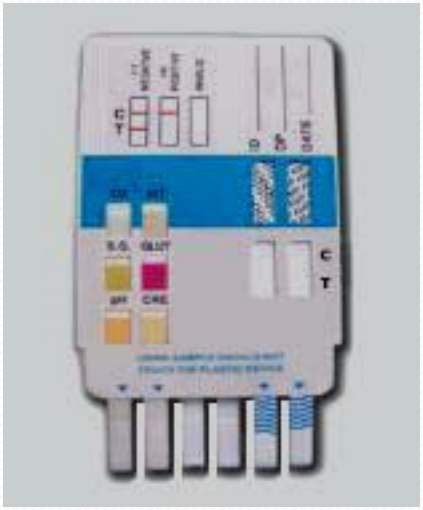
بررسی ادرار


ID
DATE
Drug
NEG
POS
INVALID
C
mAMP
COC
THC
C
AMP
OPI
Result Windows
Dispense Urine samples into each of the Wells (2)


Interpret Results
C
DRUG 1
DRUG 2
DRUG 3
CONTROL LINE
TEST LINE
TEST LINE
TEST LINE
Negative for all Drugs
Positive
Positive Drug 1
Positive Drug 2
Positive Drug 3
Invalid
No Control Line

انواع نوار ها

۶ Panel Drug

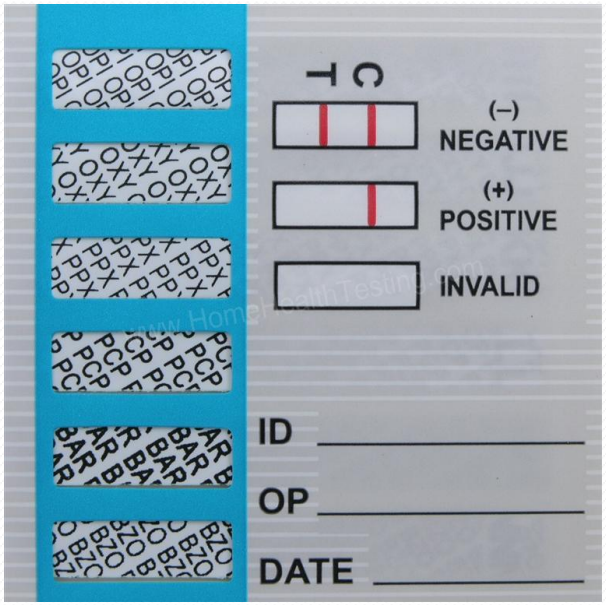


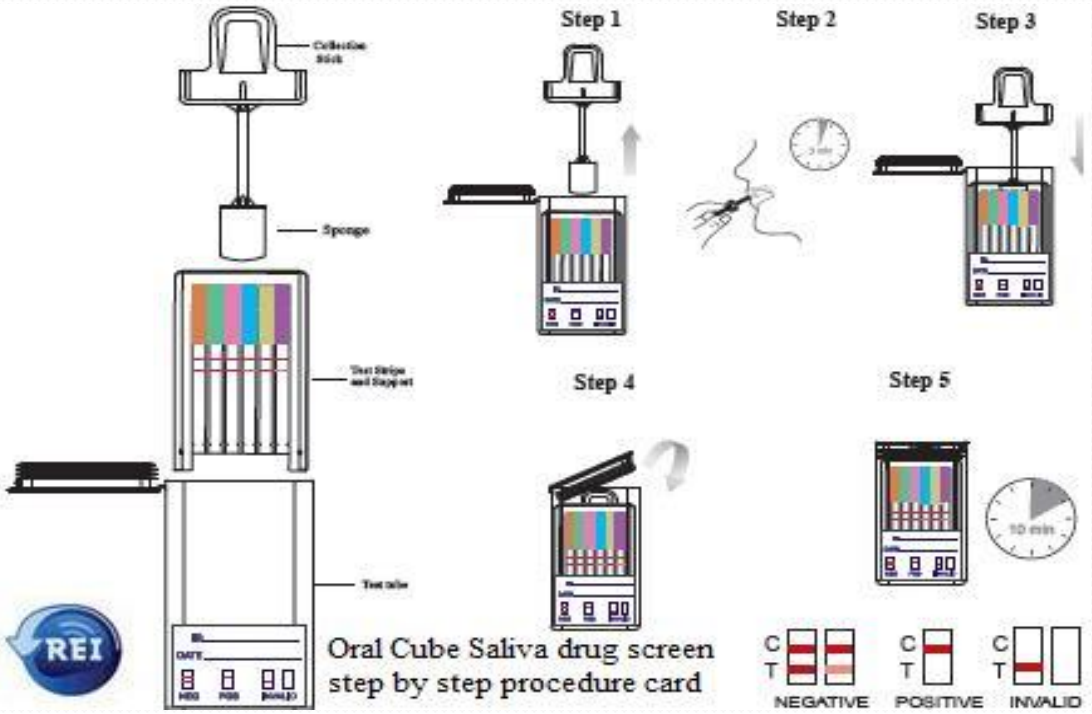
8 Panel Drug

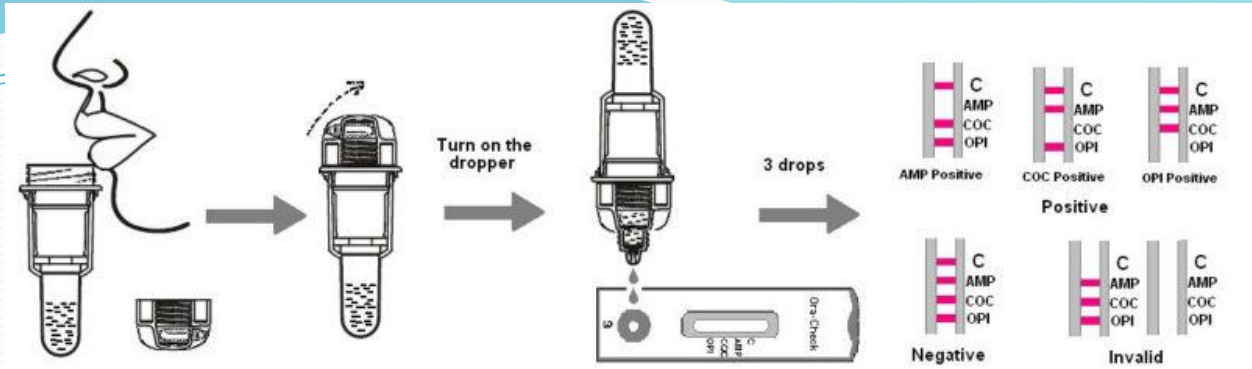
12 Panel Drug

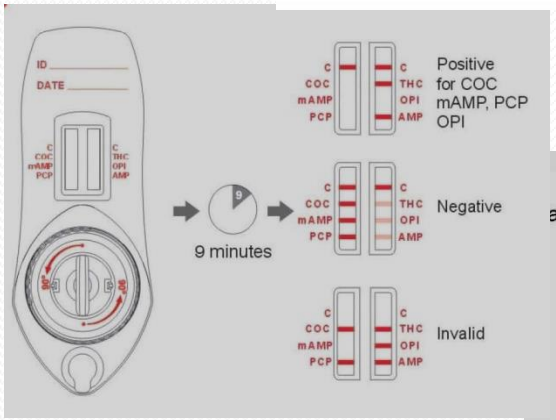
#DIP-1201 - Cocaine, Amphetamine, Methamphetamine, Marijuana, Methadone, Opiates, Oxycodone, Propoxyphene, Phencyclidine, Barbiturates, Ecstasy (MDMA) & Benzodiazepines

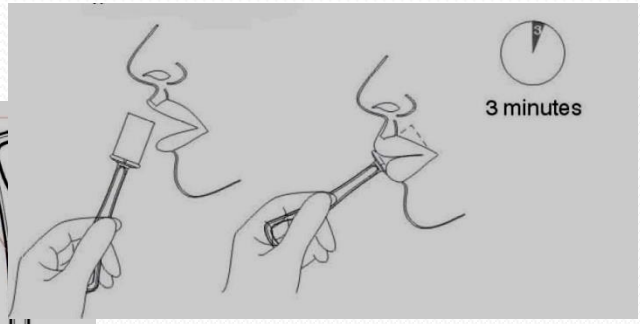
بررسی بزاق

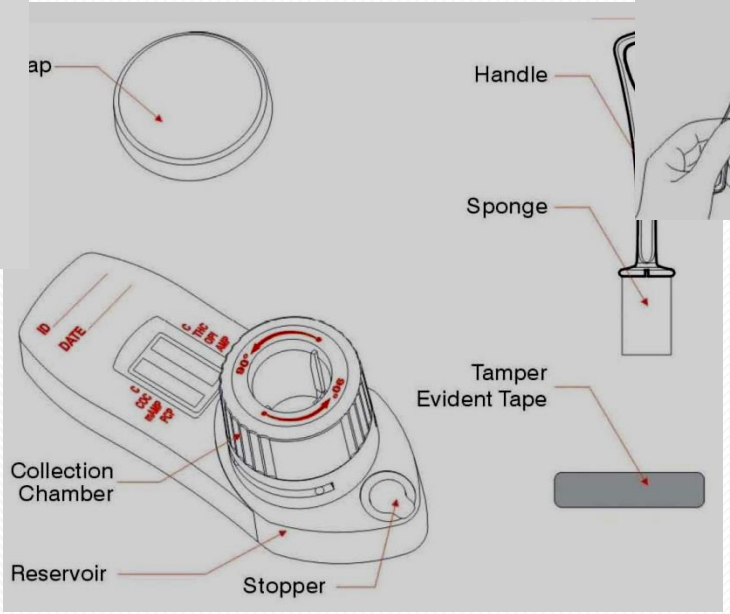

T C
(–)
NEGATIVE
(+)
POSITIVE
INVALID
ID
OP
DATE


Step 1
Step 2
Step 3
Step 4
Step 5
Sponge
REI
Oral Cube Saliva drug screen
step by step procedure card
NEGATIVE
POSITIVE
INVALID

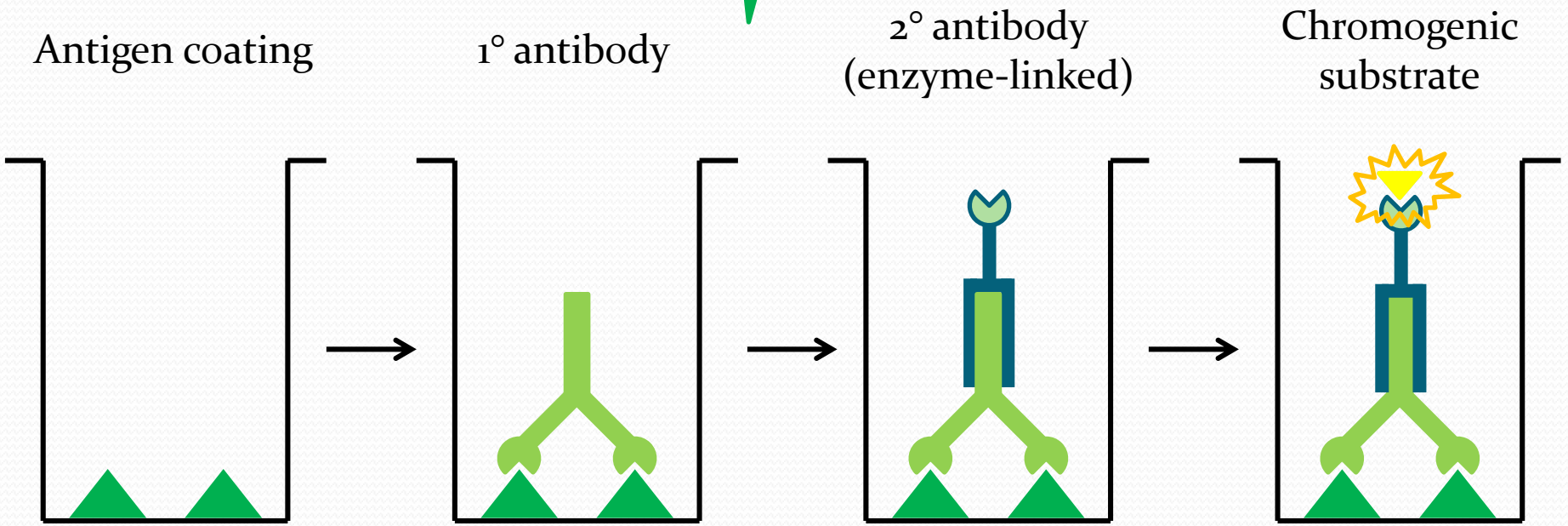

Turn on the dropper
3 drops
C
AMP
COC
OPI
AMP Positive
COC Positive
OPI Positive
Positive
Negative
Invalid


ID
DATE
C
COC
mAMP
PCP
THC
OPI
AMP
9 minutes
Positive for COC mAMP, PCP OPI
Negative
Invalid


3 minutes

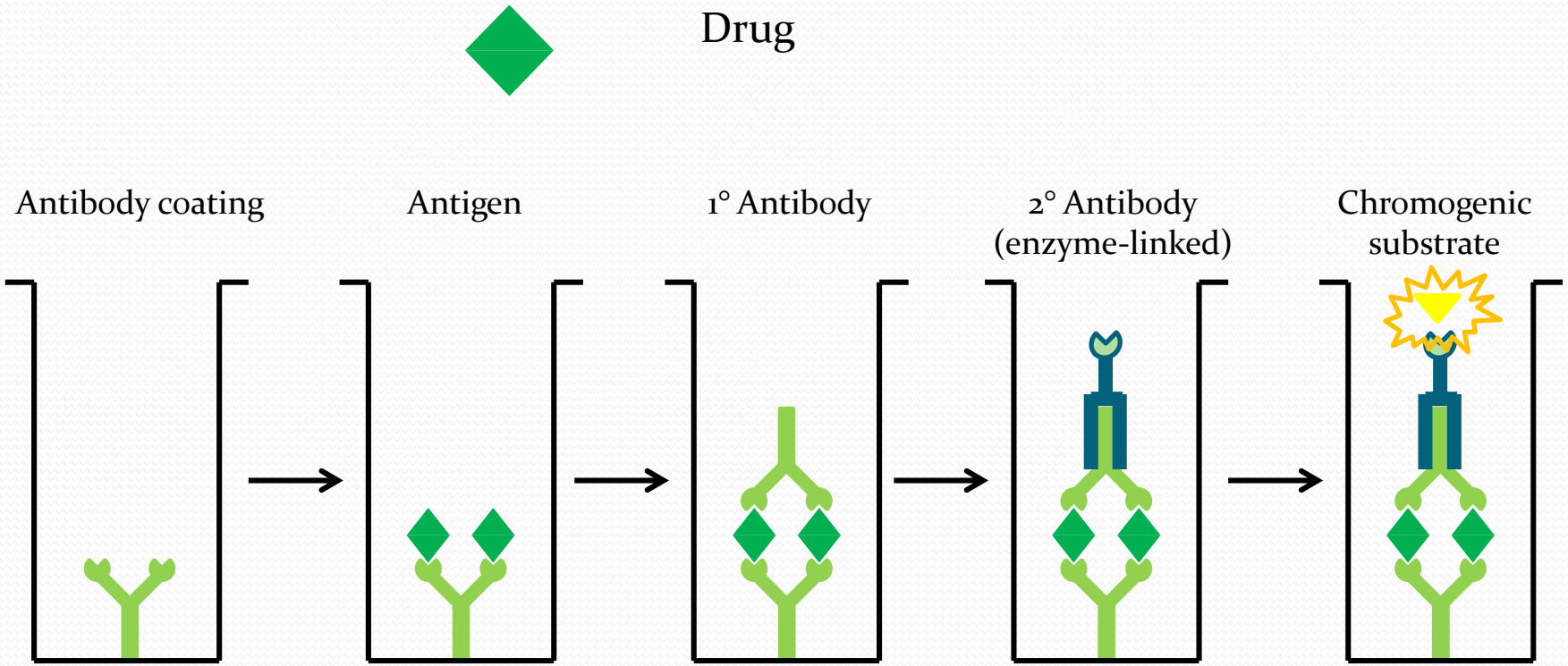

Handle
Sponge
Tamper Evident Tape
Collection Chamber
Reservoir
Stopper

ELISA Immunohistochemistry



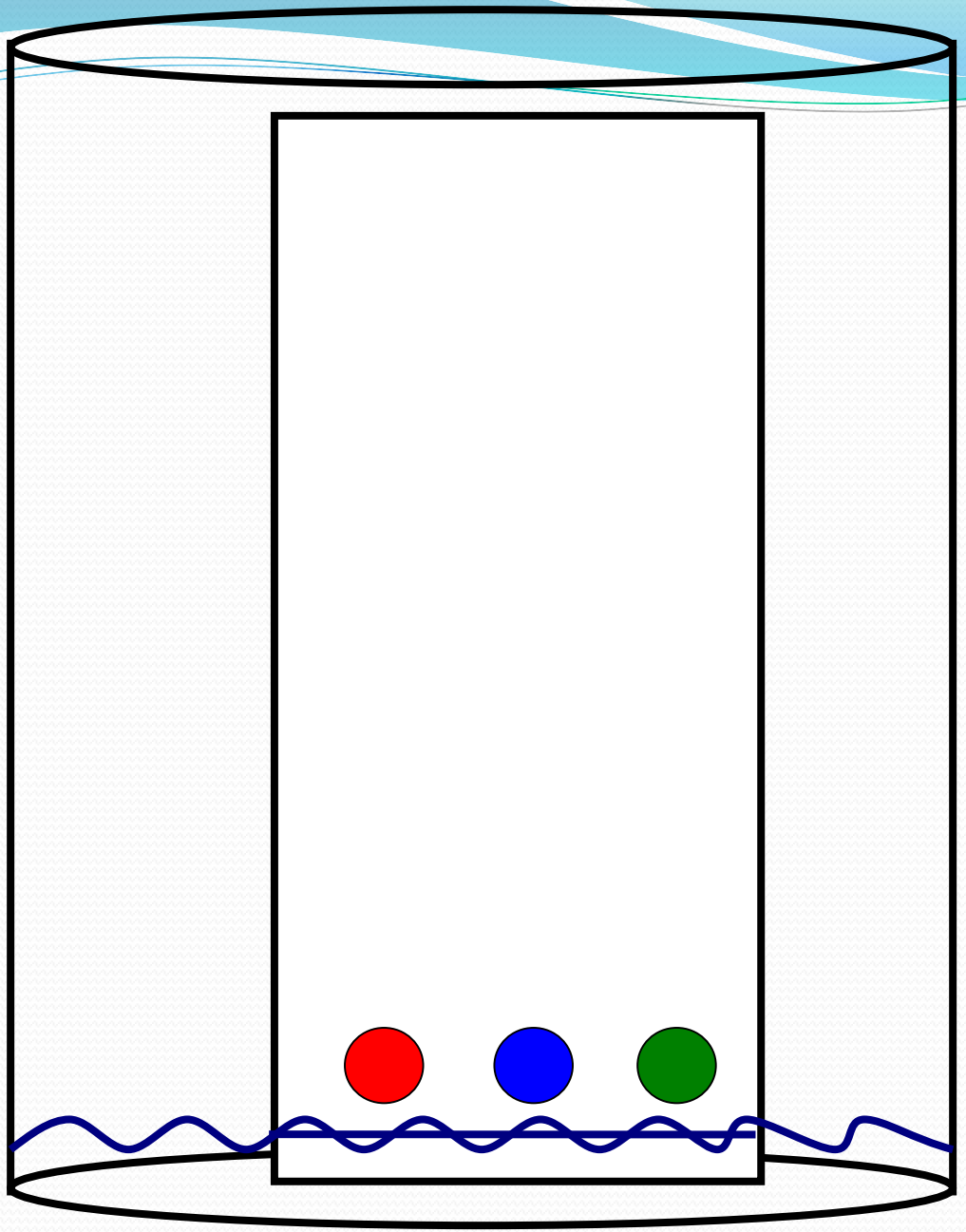
Indirect ELISA

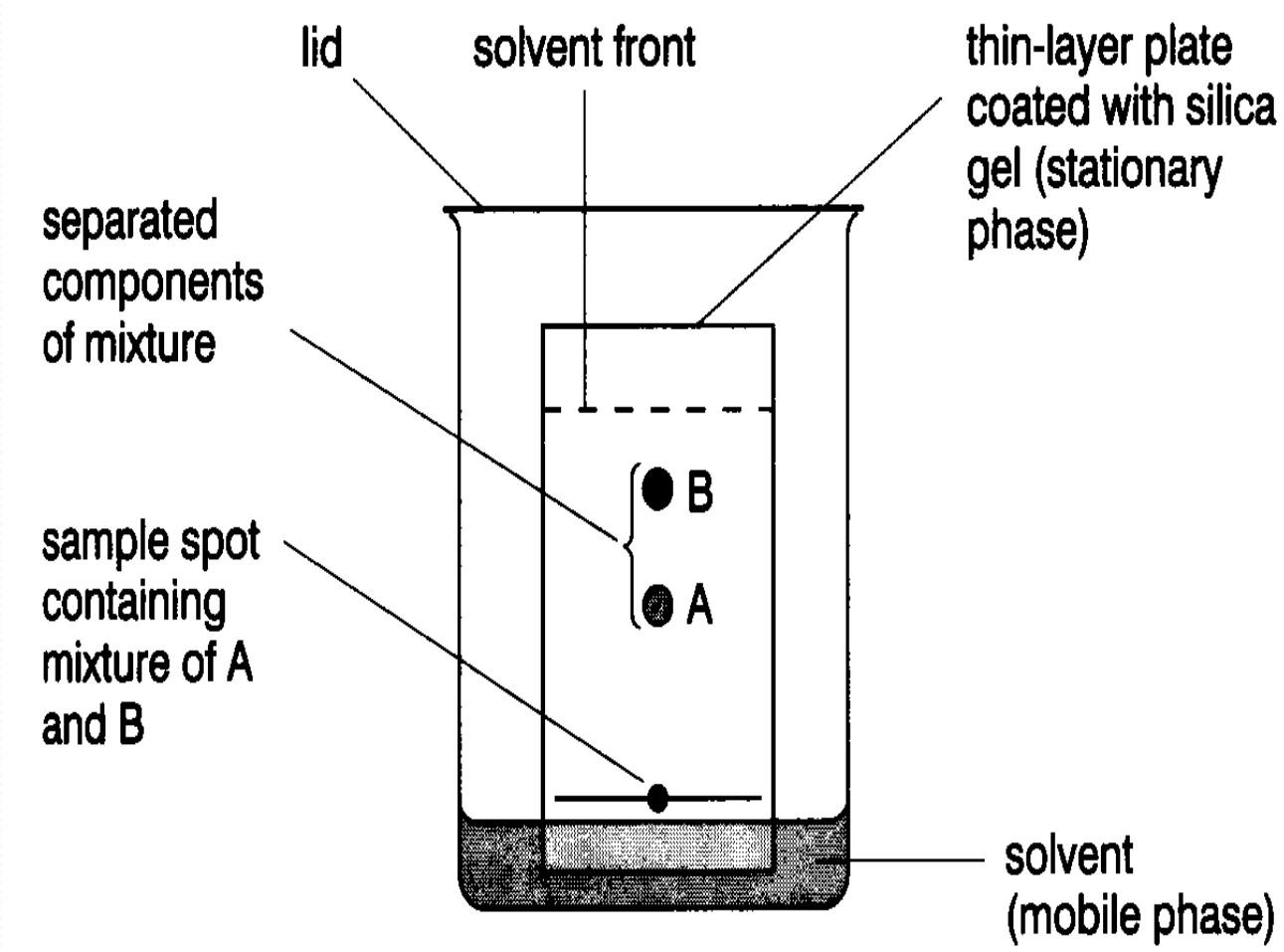
ELISA Immunohistochemistry



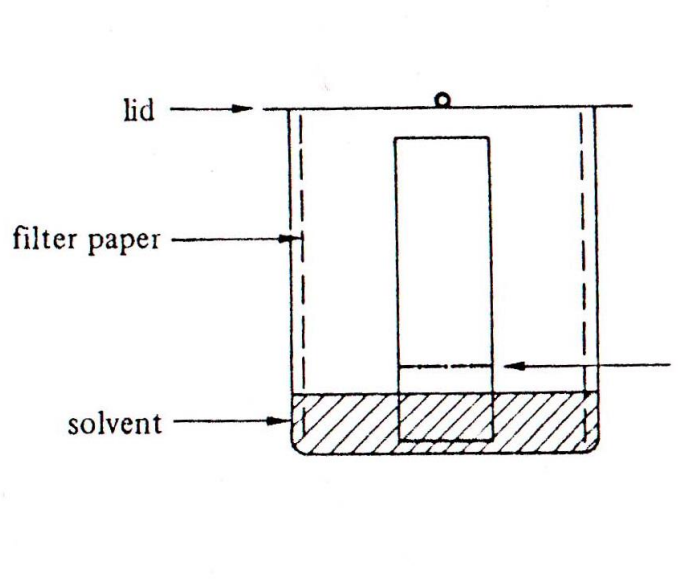
Sandwich ELISA

کروماتوگرافی لایه نازک

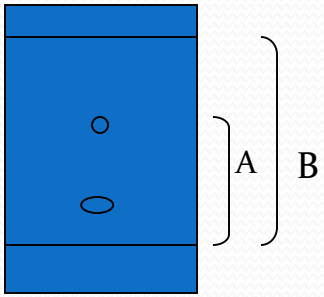


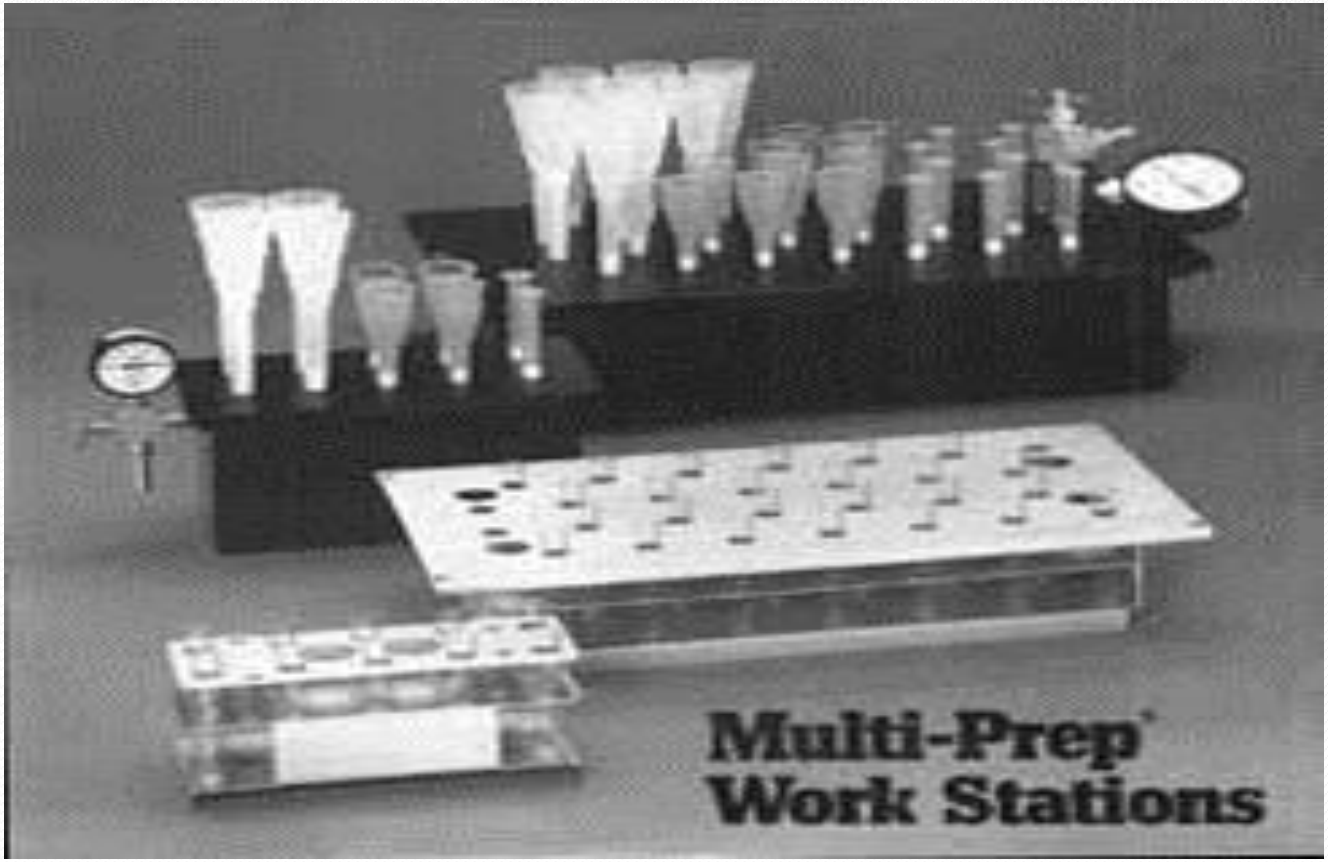

lid
solvent front
thin-layer plate coated with silica gel (stationary phase)
separated components of mixture
B
A
sample spot containing mixture of A and B
solvent (mobile phase)

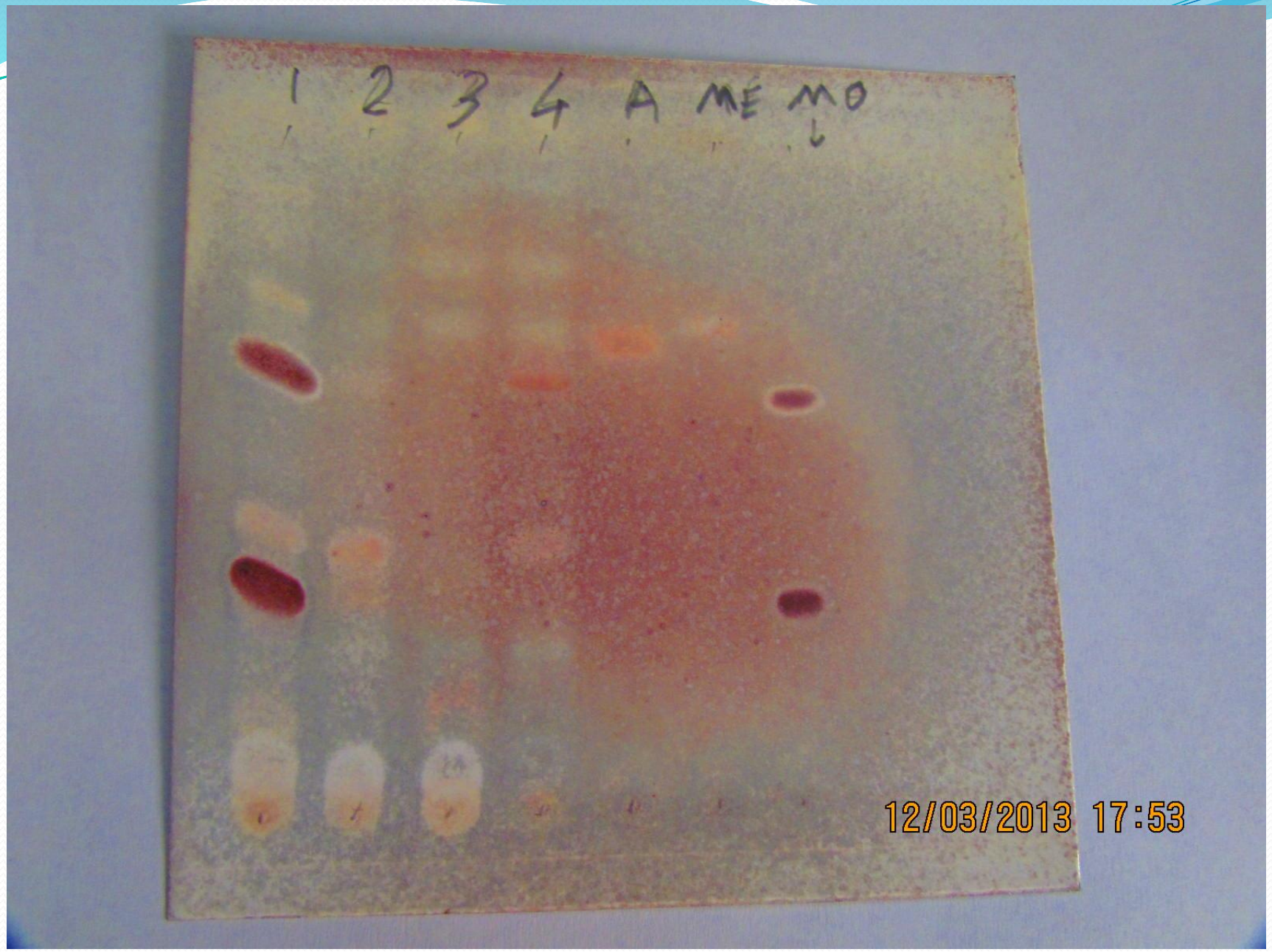
کروماتوگرافی بر روی غشاء نازک (TLC)

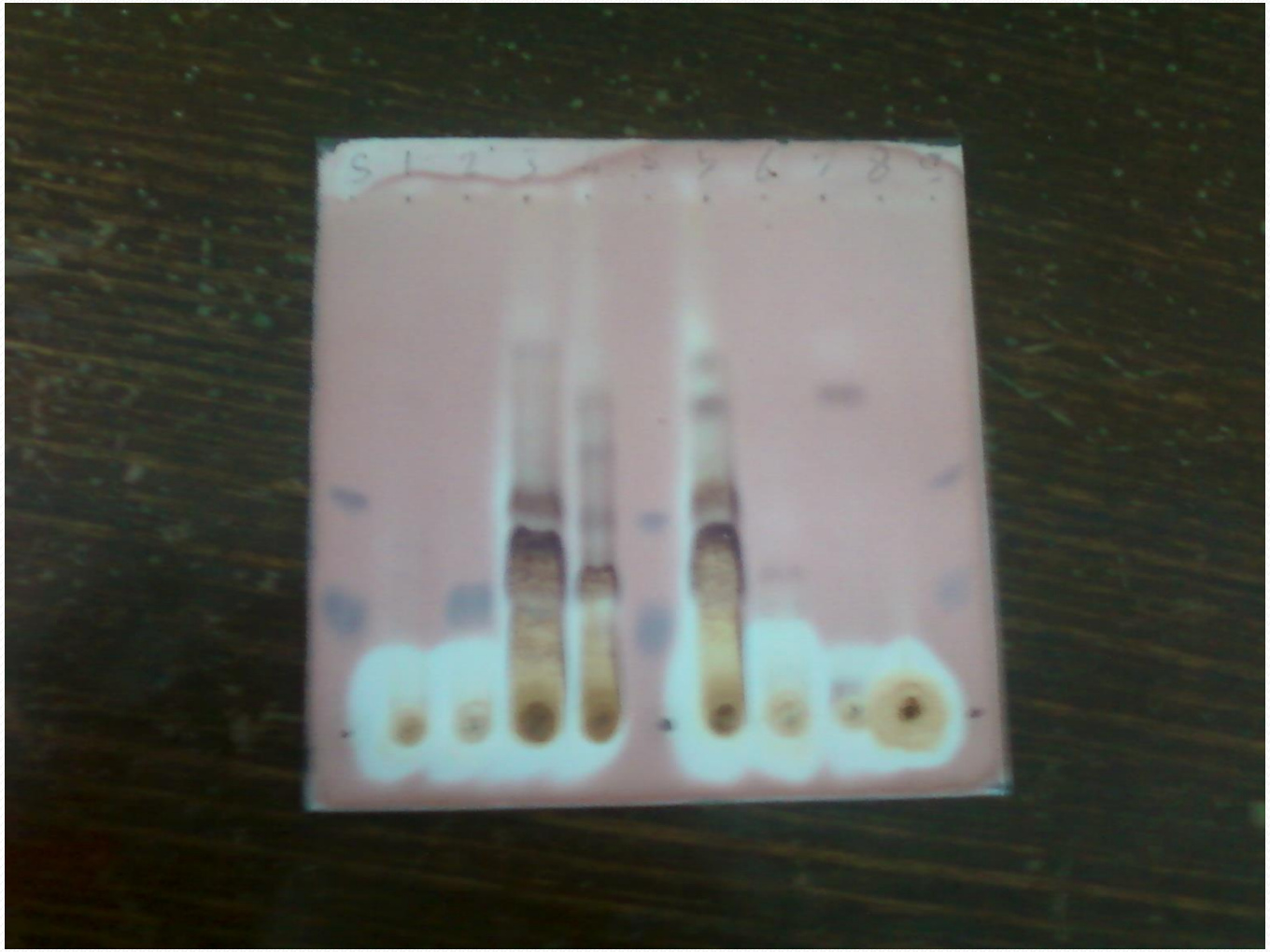


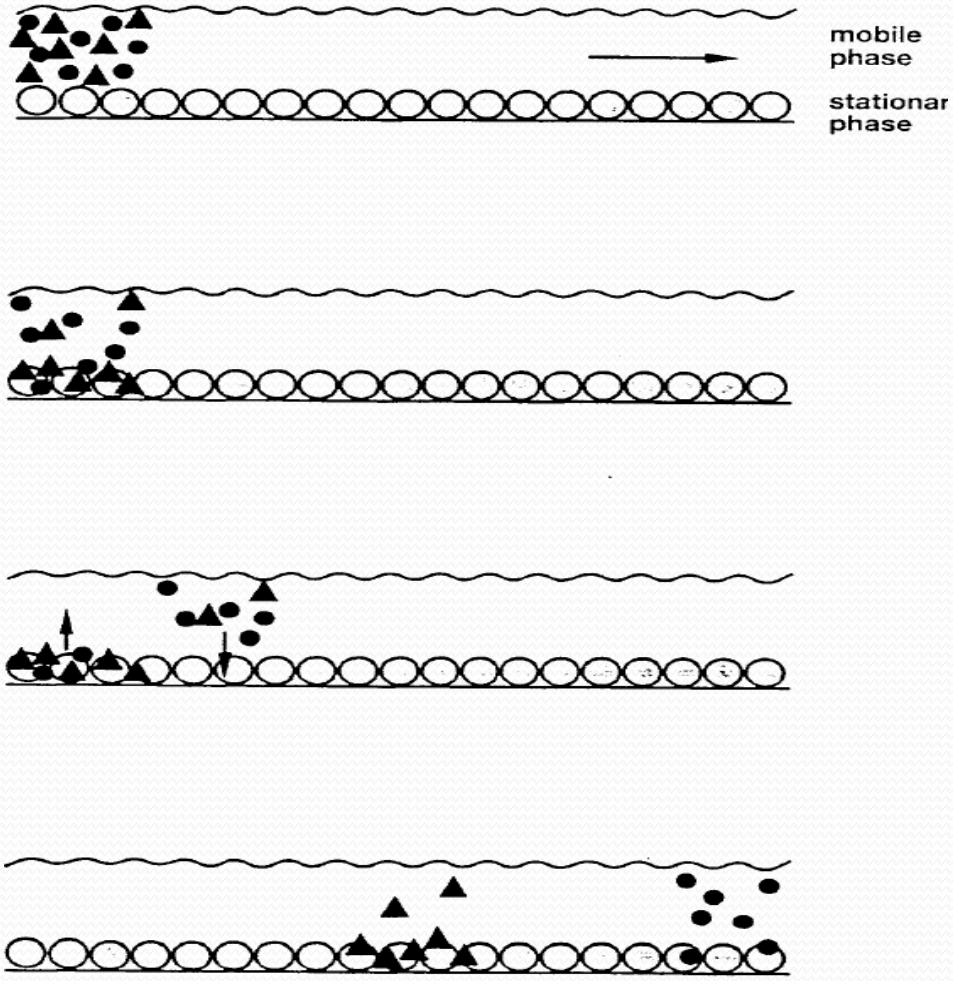
$R_f = A/B$

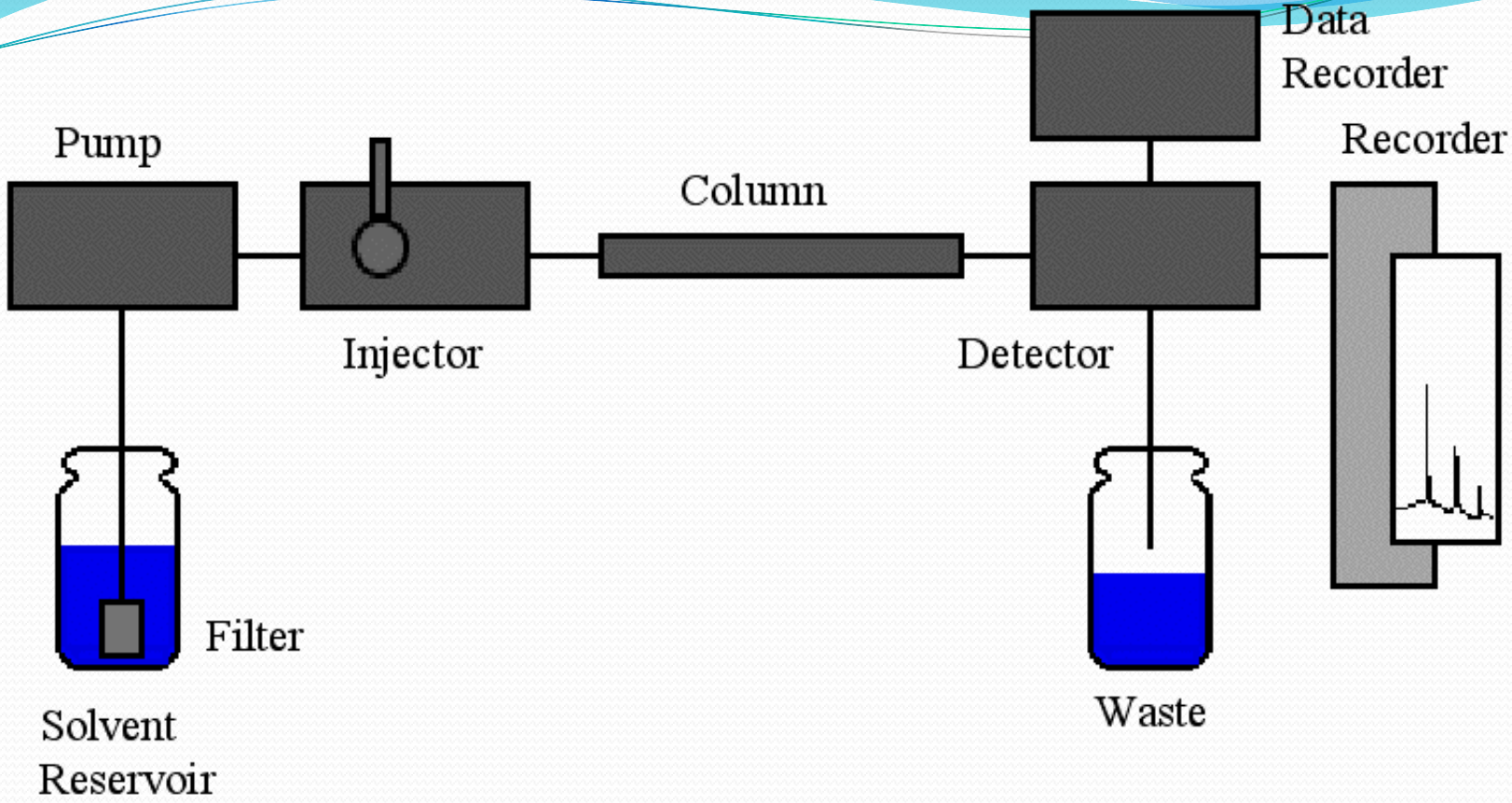



Multi-Prep
Work Stations


1 2 3 4 A MÉ MO
12/03/2013 17:53

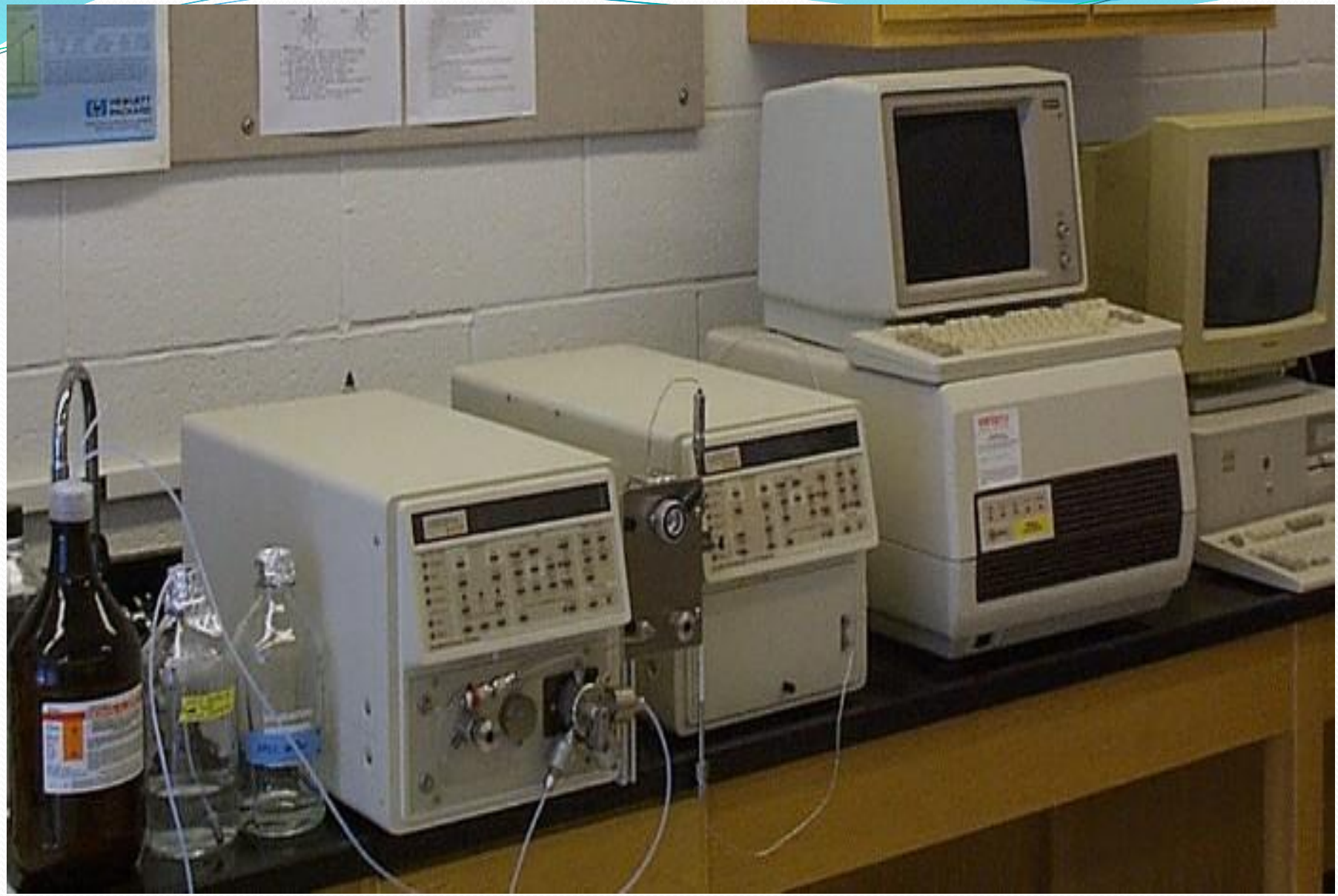


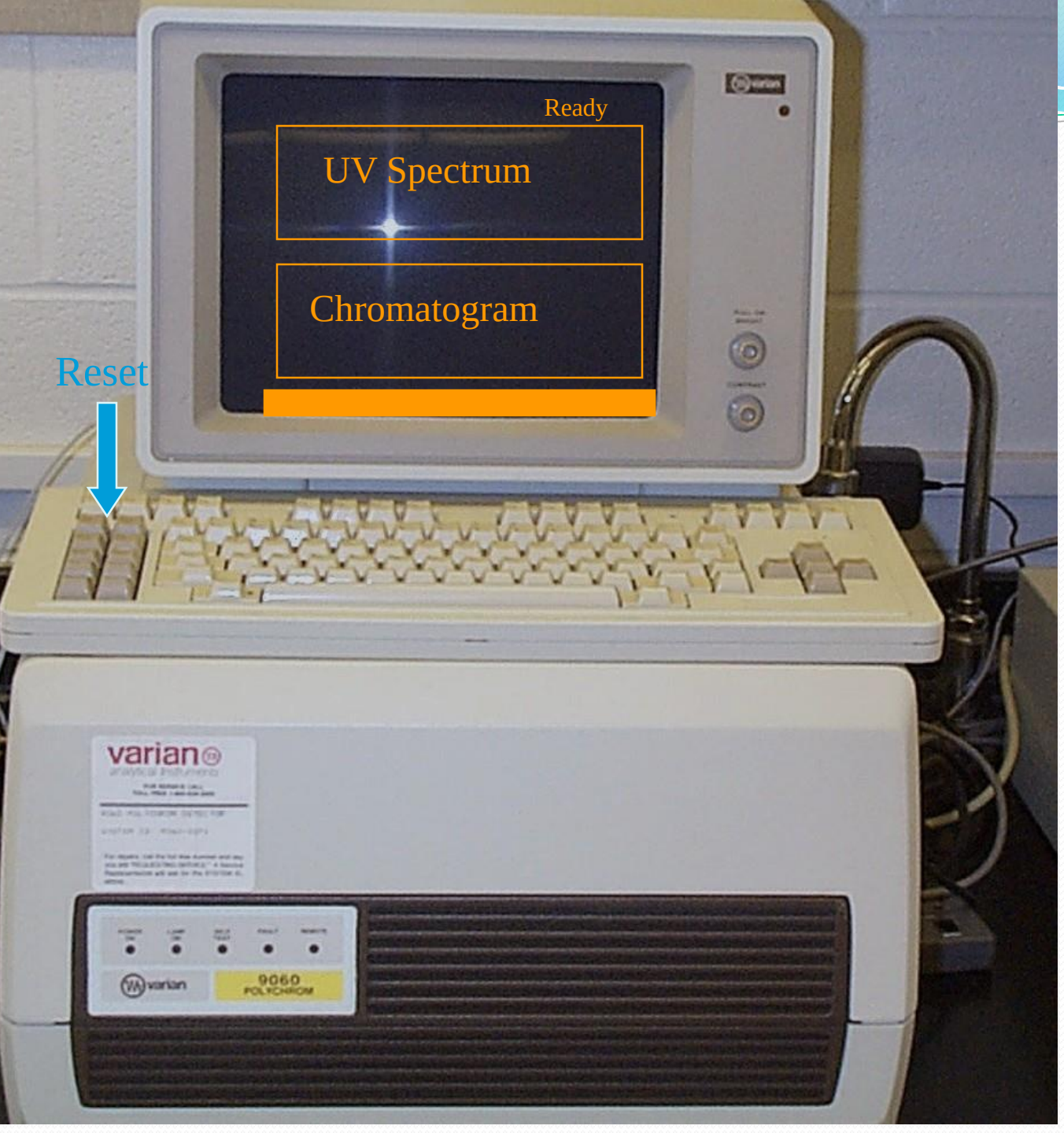

mobile
phase
stationar
phase



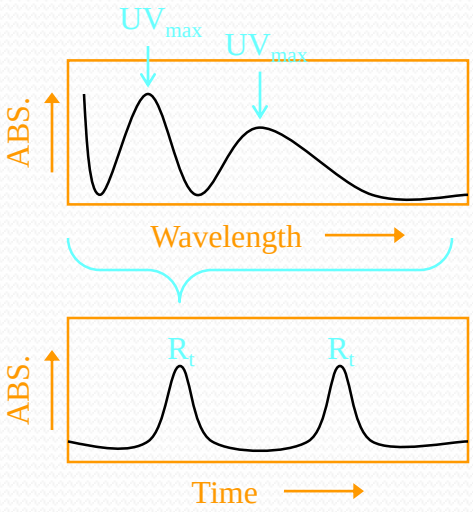
HPLC is characterized by the use of high pressure to push a *mobile phase* solution through a column of *stationary phase*

allowing separation of complex mixtures with high resolution.



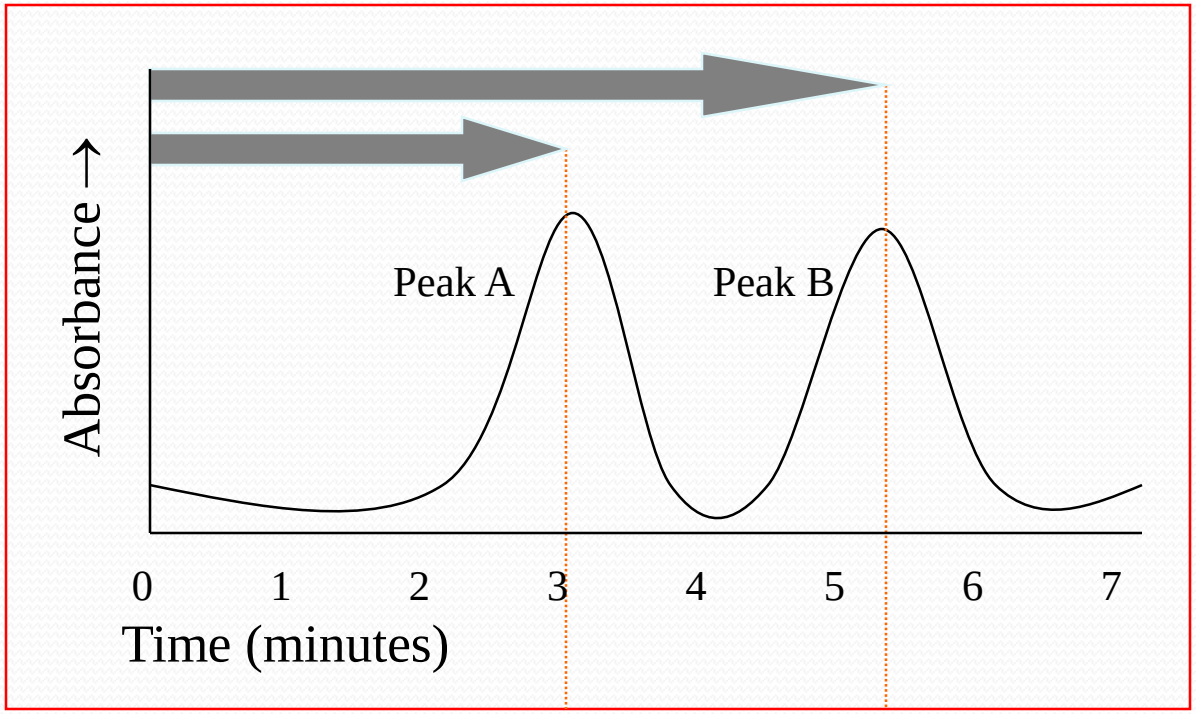


UV Spectrum
{shows full UV abs.}



Chromatogram
{shows peaks, R_t}

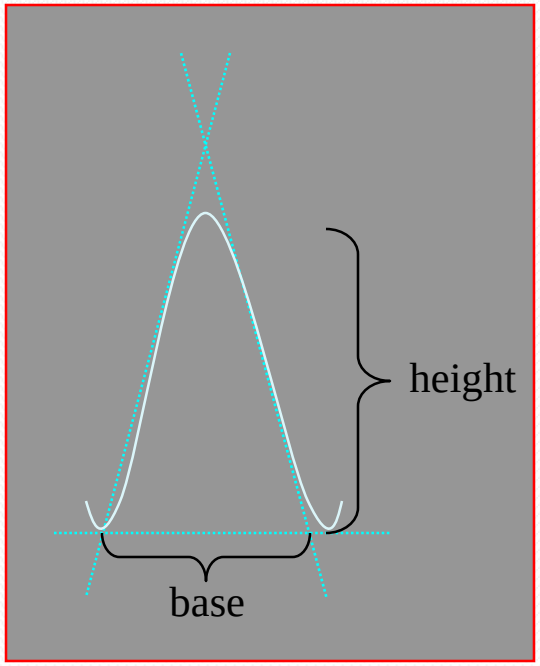
HPLC Chromatograms



R_t = 3.0 min.
faster moving
less retained

R_t = 5.2 min.
slower moving
more retained

Approximation of peak area by triangulation



$$\text{Area} = \frac{\text{base x height}}{2}$$

Specimen Collection in Clinical Practice

- Random collection preferred
  - Adulterants, substituted specimens
- Unobserved usually acceptable
- Collection facility
  - No basin
  - Pigmented toilet water
- If tampering suspected, check
  - Temperature 90°F-100°F – pH 4.5-8.0
  - Creatinine >20 mg/dL – Color

* Cook JD, et al. *J Anal Toxicol*. 2000;24:579-88.
** Galloway JH, et al. *J Clin Pathol*. 1999;52:713-8.
***Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.

Specimen Validity

Analyte	Normal range
Creatinine	>2 mg/dl
Specific gravity	>1. 020
pH	3.5-9.0
Nitrites	<200 mcg/ml
Chromates	<50 mcg/ml

Creatinine Interpretation

Concentration	Specimen	Possible reasons
100 mg/dl	Average	
<20 mg/dl	Dilute	Adulteration; increase water intake
<2 mg/dl	Substituted	Not urine

Specific Gravity Interpretation

Value	Specimen	Possible reasons
>1.04	Concentrated	Disease state; adulteration with salt or other compound
1.0200	Average urine	
<1.0020	Dilute	Adulteration; increased water intake
<1.0010	Substituted	Not urine

Urine Drug Screening Process

1. **Immunoassay** screening
   - Laboratory-based or at point of care
   - Classify substances as present or absent
   - Presumptive positives
2. **Confirmatory** & quantitative
   - Laboratory-based specific drug identification
   - GC/MS standard
   - **No** correlation between urine drug concentration & dose

Use a reputable laboratory (DHHS or CAP certified)

GC/MS=gas chromatography/mass spectrometry; DHHS=Department of Health & Human Services; CAP=College of American Pathologists

*Pesce A,,West C, Egan K, et al, Interpretation of Urine Drug Testing in Pain PatientsPain Medicine, Volume 13, Issue 7, 1 July 2012, Pages 868–885.
*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.
*Braithwaite RA, et al. *Ann Clin Biochem*. 1995;32:123-53.

Immunoassay

- Based on competitive binding to antibody to a target substance
- If a drug has a similar structure to a target analyte, it may trigger false positive result
- Sometimes a drug without structural similarity may bind to antibody (false positive)
- Lack of cross reactivity across a class may result in false negatives
- Qualitative result only (or semi-qualitative)
- Rapid result

*Jagerdeo E, Schaff JE. UPLC-Orbitrap® Screening for over 35 Drugs of Abuse and Metabolites in Biological Fluids in Under 10 min. Methods Mol Biol. 2018;1810:75-87

*DePriest AZ1, Black DL2, Robert TA. Immunoassay in healthcare testing applications. J Opioid Manag. 2015 Jan-Feb;11(1):13-25

**Gourlay DL, Heit HA, Caplan YH. Urine drug testing in clinical practice: the art and science of patient care. 5th ed. Baltimore, MD; The Johns Hopkins University School of Medicine; 2012:1-20

*Hetsley R, Zichterman A, Black DL, et al. Urine drug testing of chronic pain patients. II. Prevalence patterns of prescription opiates and metabolites. 2010;34(1):32-8

*DePriest A, Heltsley R, BlackDL, et al. Urine drug testing of chronic pain patients. III. No rmetabolites as biomarkers of synthetic opioid use. J Anal Toxicol. 2010;34:444-9

False Positives on Immunoassay

Immunoassay	Manchicanti et al. (2011) %	Passik at al. (2013) %
Amphetamines	52.9	21.4
Barbiturates	------	21.5
Benzodiazepines	-------	11.4
Cocaine	0.0	12.3
Marijuana	38.7	21.3
Methadone	18.3	45.3
Opiates	3.6	22.4
Oxycodone	38.8	41.3
MDMA/Meth	85.7	99.5
PCP	------	100
TCA	------	76.2

Dmitry M. Arbuck, M.D.
President, Indiana Polyclinic

False Positives on Immunoassay

Table 1
Drugs that gave false positive with the amphetamine immunoassay.

Results	2005/2006	2011/2012
No Drug found / unconfirmed	13*	5*
Bupropion	26	19
Pseudoephedrine/Ephedrine	46	22
Trazodone	2	4
Oxycodone	15	7
Benzylpiperazine		4
Methadone + EDDP		7
Ranitidine	25	6

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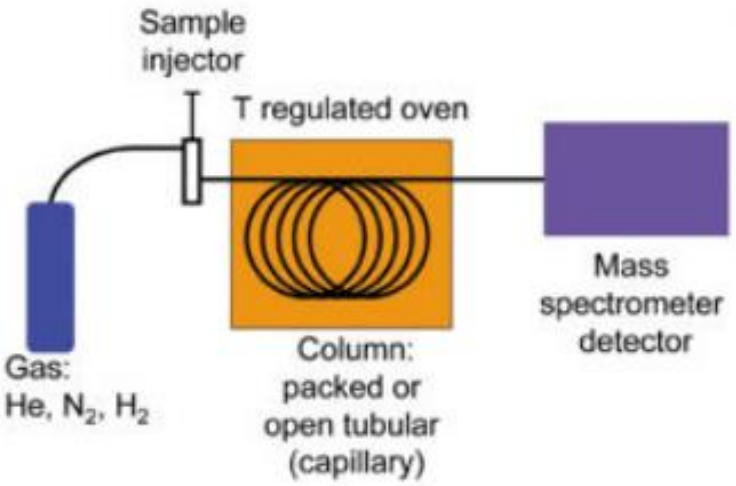
Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

False positive drugs of abuse immunoassays

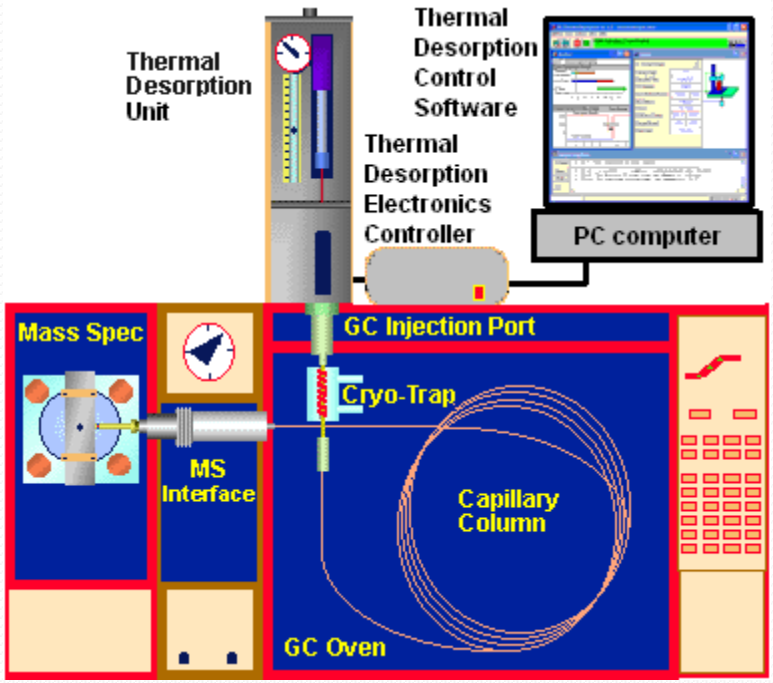
Gas Chromatography/Mass Spectrometry (GC/MS)



- Specialized personnel.
- Quantitative
- Drug is identified based on the molecular mass and ion ratios

Abe H, Takei C, Sakakura M, et al. Comprehensive Drug Screening by Thermal Desorption and Pyrolysis Combined with Direct Analysis in Real Time-Mass Spectrometry (TDP/DART-MS). Methods Mol Biol. 2018;1810:115-124

Gas Chromatography/Mass Spectrometry (GC/MS)



False Positives on Gas Chromatography/Mass Spectrometry (GC/MS)

- Technical errors
- Clerical errors
- Poor laboratory methods
- Contaminants

Emerging Technologies for Drug Testing

Saliva

Advantages

- Collection ease
- Minimal invasiveness
- Close supervision
- Limited preanalytical manipulation

Disadvantages

- Shorter retention, lower levels than typically in urine

Hair

Advantage

- Long-term measure related to hair length

Disadvantages

- Dark hair greater capacity to bind drug
- Irregular growth
- Accessibility
- Labor-intensive sample preparation

*Wong JKY, Choi TLS, Kwok KY, et al. Doping control analysis of 121 prohibited substances in equine hair by liquid chromatography-tandem mass spectrometry. J Pharm Biomed Anal. 2018 Sep 5
*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002. Wolff K, et al. *Addiction*. 1999;94:1279-98. Braithwaite RA, et al. *Ann Clin Biochem*. 1995;32:123-53. Kintz P, et al. *Ther Drug Monit*. 2002;24:239-46. Caplan YH, et al. *J Anal Toxicol*. 2001;25:396-9.

Emerging Technologies for Drug Testing

Sweat

Advantage

- Noninvasive, cumulative measure over days to weeks

Disadvantages

- Varying sweat production
- Risk of accidentally removing/contaminating collection device

Blood

Advantage

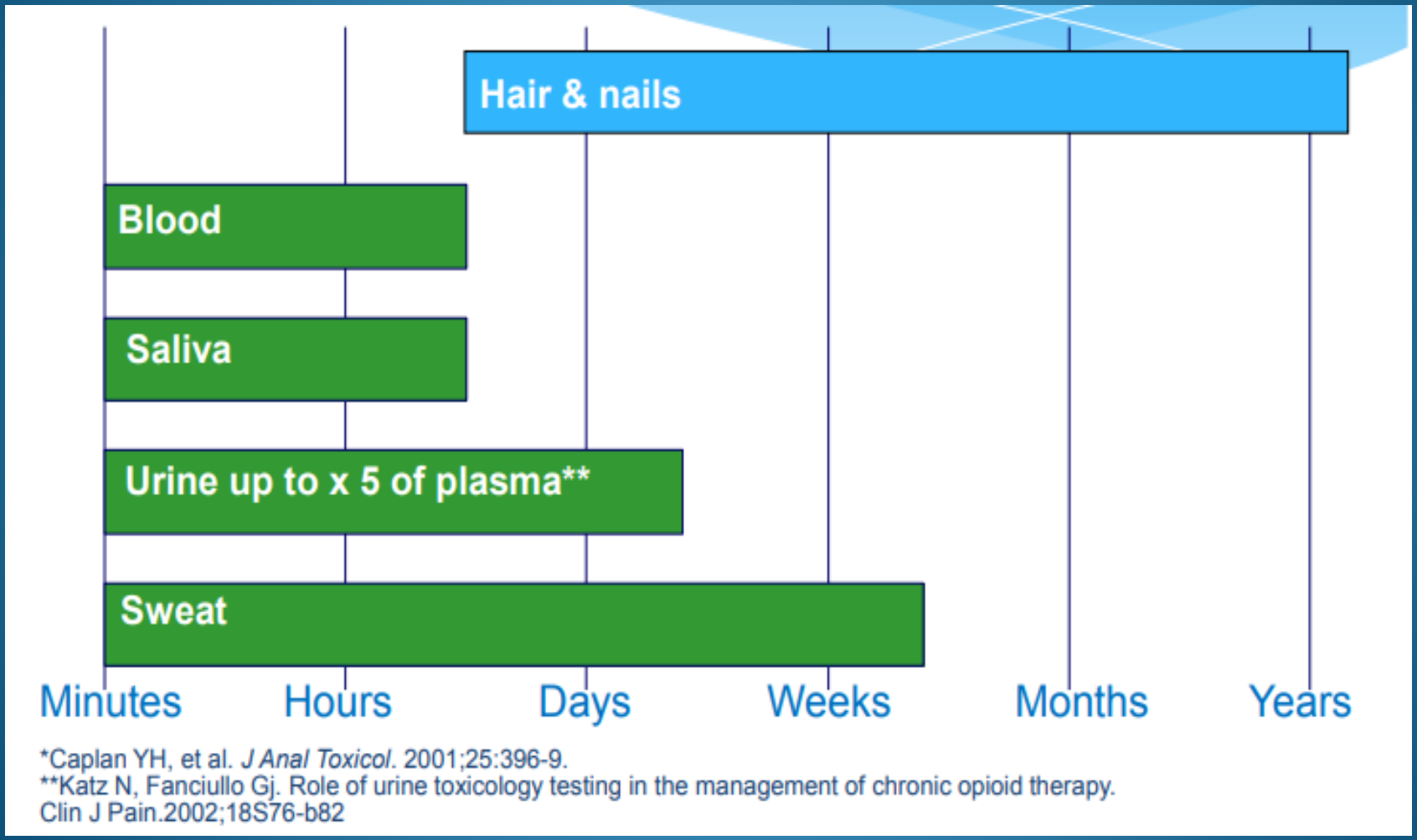
- Reduced chance of patients influencing test results

Disadvantages

- Not amenable to rapid screening
- Low concentration
- Invasive collection

*Wagner E, Raabe F, Martin G et al. Concomitant drug abuse of opioid dependent patients in maintenance treatment detected with a multi-target screening of oral fluid. Am J Addict. 2018 May 24
*Braithwaite RA, et al. *Ann Clin Biochem*. 1995;32:123-53.
*Wolff K, et al. *Addiction*. 1999;94:1279-98. Caplan YH, et al. *J Anal Toxicol*. 2001;25:396-9.

Relative Drug Detection Times in Biologic Specimens*



*Caplan YH, et al. *J Anal Toxicol*. 2001;25:396-9.
**Katz N, Fanciullo Gj. Role of urine toxicology testing in the management of chronic opioid therapy. Clin J Pain.2002;18S76-b82

Drug-Class–Specific Windows of Detection in Urine

Drug	Federal immunoassay cutoff (ng/mL)	Days
• Amphetamine (misuse)	1000	≤5
• Cannabinoids, 1 cigarette – Chronic smoker	50	2-4 ≤30
• Benzoylecgonine after street doses of cocaine	300	≤7
• Opiates (morphine, codeine)	2000	1-2
• Phencyclidine – Chronic user	25	8 ≤30

*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.
*Vandevenne M, et al. *Acta Clinica Belgica*. 2000;55:323-33.
*Wolff K, et al. *Addiction*. 1999;94:1279-98.

Thresholds used

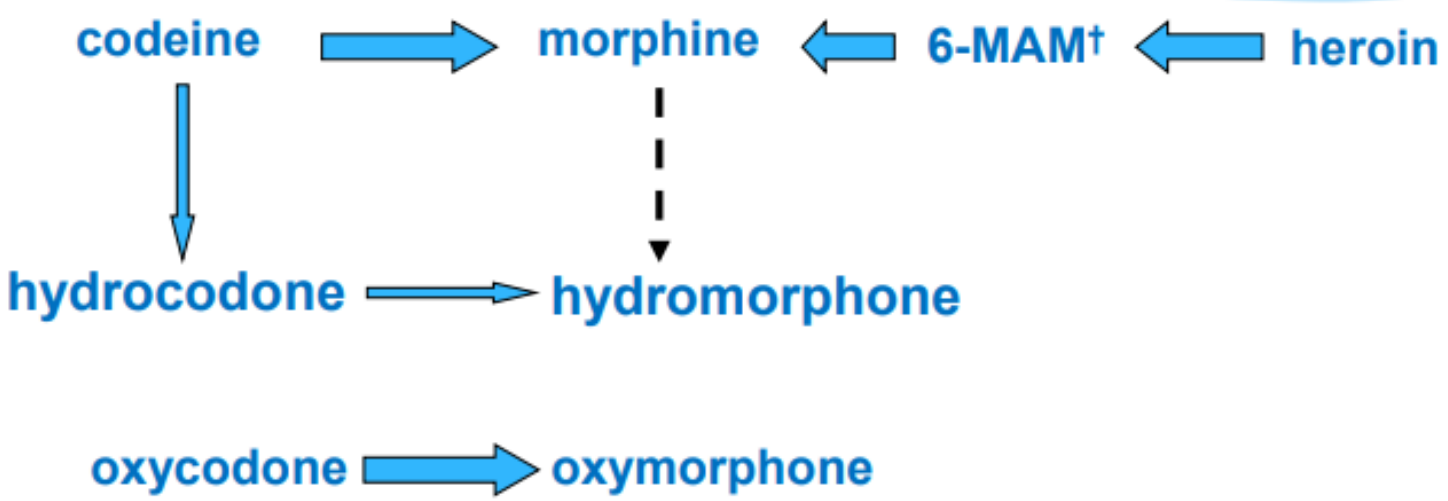
Drug Class	Workplace screening (ng/ml)	Pain management (ng/ml)
Amphetamines	500-1000	100-250
Barbiturates	300	100-200
Benzodiazepines	300	50
Cocaine	150-300	50
Marijuana	50	5
Opiates	300-2000	50-100

Interpretation of UDT Results

	Patient has taken drug	Patient has not taken drug
Positive result	True positive	False positive
Negative result	False negative	True negative

Wolff K, et al. *Addiction*. 1999;94:1279-1298.

Metabolism of Opioids



Not comprehensive pathways, but may explain the presence of apparently unprescribed drugs

†6-MAM=6-monoacetylmorphine, an intermediate metabolite

Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.

False-Positive Results

- Technician or clerical error
- Cross-reaction with other compounds in urine
  - May be structurally unrelated; e.g., quinolone antibiotics can cause positive opiate results
  - GC/MS not influenced by cross-reacting compounds

GC/MS=gas chromatography/mass spectrometry

*Brahm NC, Yeager LL, Fox MD. Commonly prescribed medications and potential false-positive urine drug screens. Am J Health Syst Pharm. 2010 Aug 15;67(16):1344-50
*Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.
*Baden LR, et al. *JAMA*. 2001;286:3115-9.
*Zacher JL, et al. *Ann Pharmacother*. 2004;38:1525-8.

False-Positive Results

- In OxyContin - 1% of hydrocodone is allowed
- Hydromorphone – hydrocodone and morphine allowed
- Contaminated herbal supplements – about 25% contain diuretics, benzodiazepines, steroids and amphetamines
- In pharmacies pill counters are rarely cleaned other than after dispensing sulfa or penicillin drugs

* Haddox JD, Kupper RJ, Cone EJ Clinical considerations for interpretation of unexpected results from UDS. Pain Med. 2010

**FDA Consumer Update: Beware of fraudulent weight-loss dietary supplements. March 15, 2011 www.fda.gov/ForConsumers/ConsumerUpdates/ucm246742.htm

UDS Results Reported as "None Detected"

- May mean any of following
  - Patient
    - Does not use drug
    - Has not recently used drug
    - Excretes drug/metabolite faster than normal
  - UDS used not sufficiently sensitive to detect drug at concentration present
    - Ask for "no threshold" testing
  - Clerical error
- In adherence testing, may raise concerns about misuse/diversion

*Wolff K, et al. *Addiction*. 1999;94:1279-98.
*Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.

False-Negative Results

- Technical or clerical error
- Tampering with urine sample
  - Dilution
  - Substitution
  - Adulteration

1. Feldhammer M, Saitman A, Nguyen L, Milstid B. Dilution of Urine Followed by Adulteration in an Attempt to Deceive the Laboratory. J Anal Toxicol. 2018 Sep 6

2. Shults TF. *Medical Review Officer Handbook*. 8th ed. 2002.
Wolff K, et al. *Addiction*. 1999;94:1279-98.

Dilution

- Most common method – many "cleansing" teas and products available on line, including Vit B to restore color to avoid diluted appearance
- 40oz of water intake under 3h
- 8oz of water under 30min
- Measure Cr
- Measure specific gravity

Moeller KE, Lee KC, Kissack JC.
Urine drug screening: practical guide for clinicians.
Mayo Clin Proc. 2008 Jan;83(1):66-76

Substitution

- Another person's urine
- Synthetic urine
- Animal urine

Whizzinator

AVAILABLE IN :

WHITE

TAN

LATINO

BROWN

BLACK

Adulteration

- Adding chemicals to a urine sample after voiding to mask the presence of illicit or prescription drugs
- Household products: bleach, vinegar, lemon juice, dish soap, drain cleaners, ammonia, hydrogen peroxide, Visine, table salt, pectin
- Commercial products: glutaraldehyde, sodium and potassium nitrate, peroxide and peroxidase, pyridinium chlorochromate (PCC)
- Marijuana is the most masked ingredient

*Murnion BP, Granot R, Day RO. Utility of urine drug screening: a clinical audit. Emerg Med A 2007 Jun;19(3):246-52.

*Moeller KE, Lee KC, Kissack JC. Urine drug screening: practical guide for clinicians. Mayo Cli 2008 Jan;83(1):66-76

Adulteration Products Are Many

- Klear, Whizzies, Urine Luck – not detected by traditional specimen integrity tests
- Mary Jane SuperClean 13, Instant Clean ADD-IT-ive
- UrinAid, Amber 13, THC-Free, Randy's Clear
- LL418, Sweet Pee's Spoiler, Stealth

PassYourTest.com
Industry leading drug test solutions.

UDS Results Reported as "None Detected"

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  - Patient
    - Does not use drug
    - Has not recently used drug
    - Excretes drug/metabolite faster than normal
  - UDS used not sufficiently sensitive to detect drug at concentration present
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  - Clerical error
- In adherence testing, may raise concerns about misuse/diversion

*Wolff K, et al. *Addiction*. 1999;94:1279-98.
*Gourlay DL, et al. *Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies* [monograph]. 2004.

False-Positive Results on Screening

- **Marijuana** - PPIs (especially pantoprazole -Protonix), ASA, baby wash/soaps, ibuprofen, naproxen
- **Opioids** - quinolone antibiotics (levofloxacin, ofloxacin), verapamil, procaine, rifampin and tonic water (quinine), dextromethorphan, diphenhydramine
- **Tramadol** - venlafaxine (Effexor)
- **PCP** – lamotrigine, tramadol, venlafaxine

- Craven C, Fileger M, Woster P. Demystifying benzodiazepine urine drug screen results, Pract Pain Manage. 2014;14(1):38-41
- Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoessays: a review. J Alal Toxicol.2014;38(7):387-396

False-Positive Results on Screening

- **Methadone** – clomipramine, chlorpromazine, diphenhydramine, olanzapine, quetiapine, tapentadol, verapamil, thioridazine
- **Phencyclidine (PCP)** – dextromethorphan, diphenhydramine, ibuprofen, imipramine, ketamine, lamotrigine, meperidine, thioridazine, tramadol, venlafaxine
- **Tricyclic Antidepressants** – carbamazepine, cyclobenzaprine, cyproheptadine, diphenhydramine, hydroxyzine, promethazine, quetiapine

False-Positive Results on Screening

- **Amphetamines** – amantadine, bupropion, desipramine, ephedrine, Vicks inhailer, metronidazole, selegiline, ranitidine, promethazine, trazodone
- **Benzodiazepines** – chlorpromazine, fenoprofen, flurbiprofen, indomethacin, sertraline, efavirenz
- **Barbiturates** – ibuprofen, naproxen, phenytoin
- **Fentanyl** – trazodone

- Craven C, Fileger M, Woster P. Demystifying benzodiazepine urine drug screen results, Pract Pain Manage. 2014;14(1):38-41
- Saitman A, Park HD, Fitzgerald RL. False-positive interferences of common urine drug screen immunoessays: a review. J Alal Toxicol.2014;38(7):387-396

False-Positive Results on Screening References

- Snozek CLH, Kaleta EJ, Jannetto PJ, et al. False-positive amphetamine results on several drug screening platforms due to mexiletine. Clin Biochem. 2018 Aug;58:125-127
- Gourlay DL, Heit HA, Caplan YH. Urine drug testing in clinical practice: the art and science of patient care. 5th ed. Baltimore, MD; The Johns Hopkins University School of Medicine; 2012:1-20
- Allen KR. Interference by venlafaxine ingestion in the detection of tramadol by liquid chromatography linked to tandem mass spectrometry for the screening of illicit drugs in human urine Clin Toxicol (Phila) 2006;44(2)
- Moeller KE, Lee KC, Kissack JC Urine drug screening: practical guide for clinicians. Mayo Clin Proc 2008;83(1)66-76
- Reisfield GM, Goldenberg BA, Bertholf RL 'False-positive'and 'false-negative' test results in clinical urine drug testing. Bioanalysis 2009;1(5):937-52
- Brahm NC, Yeager LL, Fox MD, et al. Commonly prescribed medications and potential false-positive urine drug screens. Am J Health-Sys Pharm. 2010;67:1344-50
- Christo PJ, Manchikanti L, Ruan Xet al. Urine drug testing in chronic pain. Pain Physician 2011;14:175-87

Interpretation of Dose Compliance

- Studies repeatedly demonstrated that urine drug concentrations MAY NOT be interpreted to determine the amount of drug taken, when the last dose was administered or the source of the drug

- UDS cannot reliably determine whether a pt. is abusing the prescribed medication, has reached a toxic level, has hoarded or binged, taken more than prescribed, or diverted the prescription while taking a few doses before the test

*Katz N, Fanciullo Gj. Role of urine toxicology testing in the management of chronic opioid therapy. Clin J Pain.2002;18S76-b82

**Gourlay DL, et al. Urine Drug Testing in Clinical Practice: Dispelling the Myths & Designing Strategies [monograph]. 2004

*** Cone EJ, Caplan YH. Urine toxicology testing in chronic pain management Postgrad Med . 2009;121(4):91-102

Therapeutic blood levels are not established for BZs and opiates

- Pharmacokinetics (what the body does to the drug) and pharmacodynamics (what the drug does to the body) are too complex
- Blood level does not correlate with therapeutic response
- Serum blood levels do not correlate with CNS levels
- Genetic variations in receptor subtypes and P-450 system
- P- Glycoprotein transporter activity
- Drug tolerance

*Lotsch J Pharmacokinetic-pharmacodynamic modeling of opioids J Pain Symptom Manag 2005;29(5S):S90-103

*Levy S, Harris SK, Sherritt L, et al. Drug testing of adolescents in ambulatory medicine: physician practices and knowledge. Arch Pediatr Adolesc Med. 2006 Feb;160(2):146-50

Testing for Alcohol

- Majority of ethanol testing is done in blood
- Ethanol in urine 7-8h
- Maybe positive due to post collection fermentation (diabetes, Candida) – up to 1/3 of positives caused
- UDS is not admissible as legal evidence of intoxication due to lack of correlation between amount ingested and urine concentration
- Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) are metabolites – in urine in 1h and up to 1-5 days

- Foley KF. A Positive Urine Alcohol with Negative Urine Ethyl-Glucuronide. Lab Med. 2018 Jul 5;49(3):276-279
- Crews B, West R, Gutierrez R, et al. An improved method of determining ethanol use in chronic pain population. J Opioid Manage. 2011;7(1):27-34
- Kissak JC, Bishop J, Leatherwood Roper A., Ethylglucuronide as a biomarker for ethanol detection. Pharmacother. 2008;28(6):769-81

Testing for Alcohol

- Hand sanitizer does not contribute to EtS levels above 100ng/ml
- Ingestion of an active baker's yeast combined with sugar may result in high EtS and EtG concentration
- 2l apple juice, 1,320g sauerkraut, 690g bananas – produce levels below 500ng/ml of EtS and EtG
- Mouthwash – produce level below 500ng/ml of EtS and EtG
- Grape juice contains EtS and ethanol
- Nonalcoholic beverages contain alcohol (up to 0.5 vol %)

* Reisfield GM, Goldberger BA, Crews BO, et al, Ethyl glucuronide, ethyl sulfate, and ethanol in urine after sustained exposure to an ethanol based hand sanitizer. J Anal Toxicol 2011;35:85-91

* Thierauf A, Wolhlfarth A, Auwarter V, et al. Urine tested positive for ethyl glucoronide and ethyl sulfate after the consumption of yeast and sugar. Forensic Sci Int 2010;202:e45-47

* Mussfoff F, Albermann E, Madea B. Ethyl glucoronide and ethyl sulfate in urine after consumption of various beverages and food-misleading results? Int J Legal Med 2010;124:623-30

Testing for Marijuana

- Before passive exposure could result in positive urine tests, the atmosphere has to become so saturated with marijuana smoke that subjects have to wear goggles to protect their eyes; the smoke is also strongly irritating the nose and throat.
- Ventilation of any sort prevents positive tests for passive subjects.
- Such an exposure is not "passive" as individuals must actively force themselves to remain in the smoke saturated atmosphere to test positive.
- The same works for oral fluid

*Lee D1, Huestis MA. Current knowledge on cannabinoids in oral fluid. Drug Test Anal. 2014 Jan-Feb;6(1-2):88-111

*MuleSL, Lomax P, Gross SJ. Active and realistic passive marijuana exposure tested by three immunoassays and GC/MS in urine J Anal Toxicol. 1988;12(3):113-6

*Cone EJ. Marijuana effects and urinalysis after passive inhalation and oral injestion. NIDA Res Monogr. 1990;99:88-96

Testing for Synthetic Cathinones

- A myriad of synthetic compounds which are active at cannabinoid receptors
- Introduced in 2004, first reported in the US in 2008, not scheduled before 2011, smoked or ingested, frequently contaminated
- Structurally unrelated to marijuana
- High number of compounds and ever-changing nature of these substances results in detection of some, but not all spice products

- Bonaccorso S, Metastasio A, Ricciardi A, et al. Synthetic Cannabinoid use in a Case Series of Patients with Psychosis Presenting to Acute Psychiatric Settings: Clinical Presentation and Management Issues. Brain Sci. 2018 Jul 14;8(7).
- Drugs of Abuse 2017 edition . A DEA Resource Guide. https://www.dea.gov/pr/multimedia-library/publications/drug_of_abuse.pdf

Testing for Synthetic Cannabinoids

Gundersen POM, Spigset O, Josefsson M. Screening, quantification, and confirmation of synthetic cannabinoid metabolites in urine by UHPLC-QTOF-MS.
Drug Test Anal. 2018 Jul 11

Testing for Synthetic Cathinones (Bath Salts)

- Inhalation, oral ingestion, or injections
- Sold under the guise of plant food, jewelry cleaner, etc.
- Derivatives of khat, East African plant
- Abused in Europe since 2009 and the US since 2010
- Stimulants similar to cocaine, methamphetamine and ecstasy
- False positive for meth on immunoassays
- Period of detection in urine 5 days

* DrugFacts: Synthetic Cathinones ("Bath Salts"). NIH National Institute of Drug Abuse. www.drugabuse.gov/publications/drugfacts/synthetic-cathinones-bath-salts

*German CL, Fleckenstein AE Hanson GR. Bath salts and synthetic cathinones: an emerging designer drug phenomenon. Life Sci 2013