The Science & Epidemiology of Adolescent Poisonings

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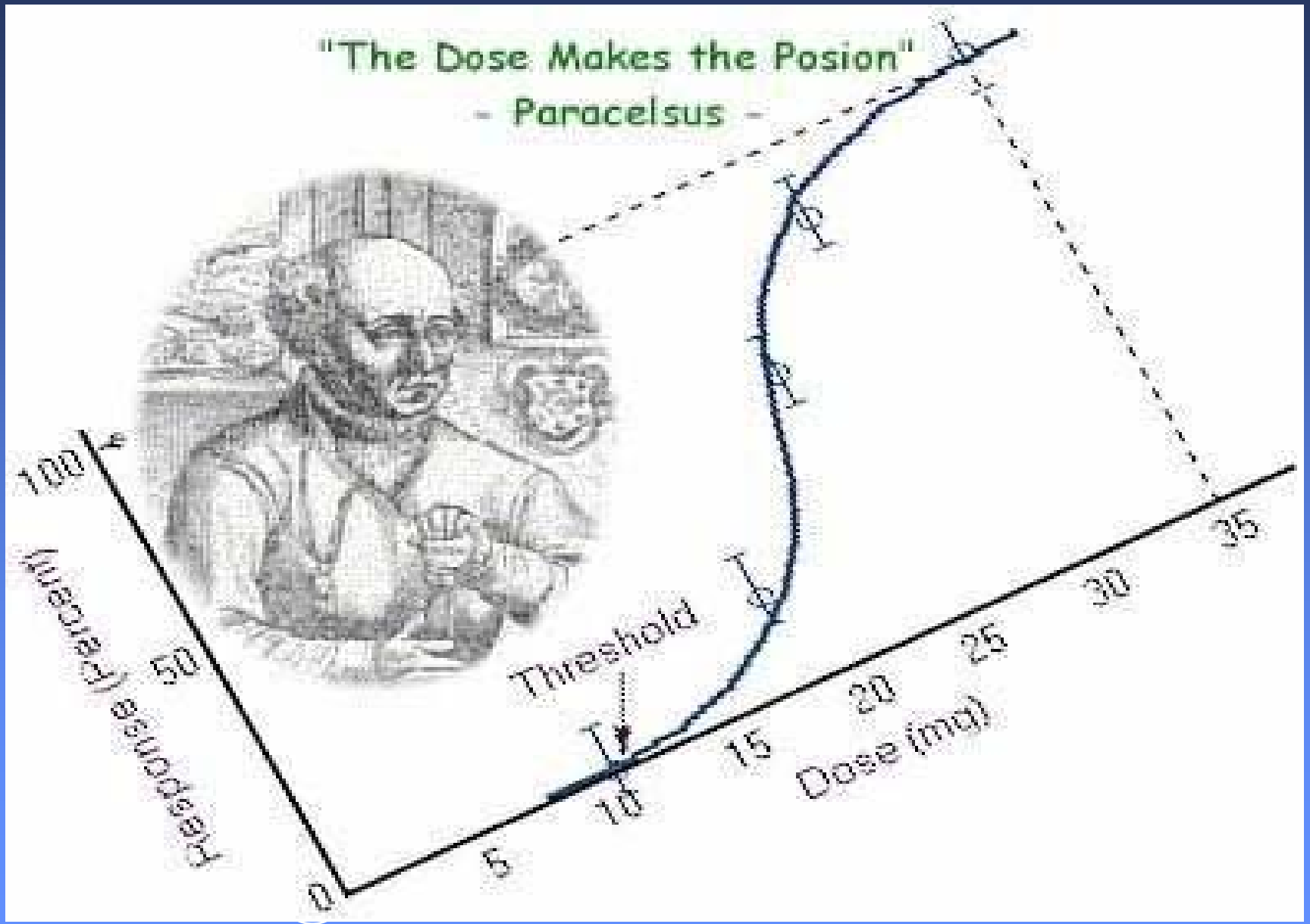
What Makes a Poison?



How does one become poisoned?

- A - How's it get in?
- D - Where does it go?
- M - What happens to it?
- E - How do you get rid of it?

Absorption

- Depends on route of exposure!
  - IV ~ instantaneous
  - INH/Sublingual/SQ ~ slightly slower
  - IM/Oral/Rectal ~ 15 min to 1 hour
  - Dermal ~ slowest & least efficient

$$Cp = \left(\frac{Dose^{*}F}{Vd}\right)^{*}\left(e^{-Ke^{*}t} - e^{-Ka^{*}t}\right)$$

$$Ke = \left(\ln Cp_1 - \ln Cp_2\right) \Big/ \Delta t$$

- $t_{1/2}$ = 0.693/Ke
  - Ke = 0.693 / $t_{1/2}$
- CL= Elim rate/Cp or Ke * Vd
- Δt = ln C_1 - ln C_2 / Ke

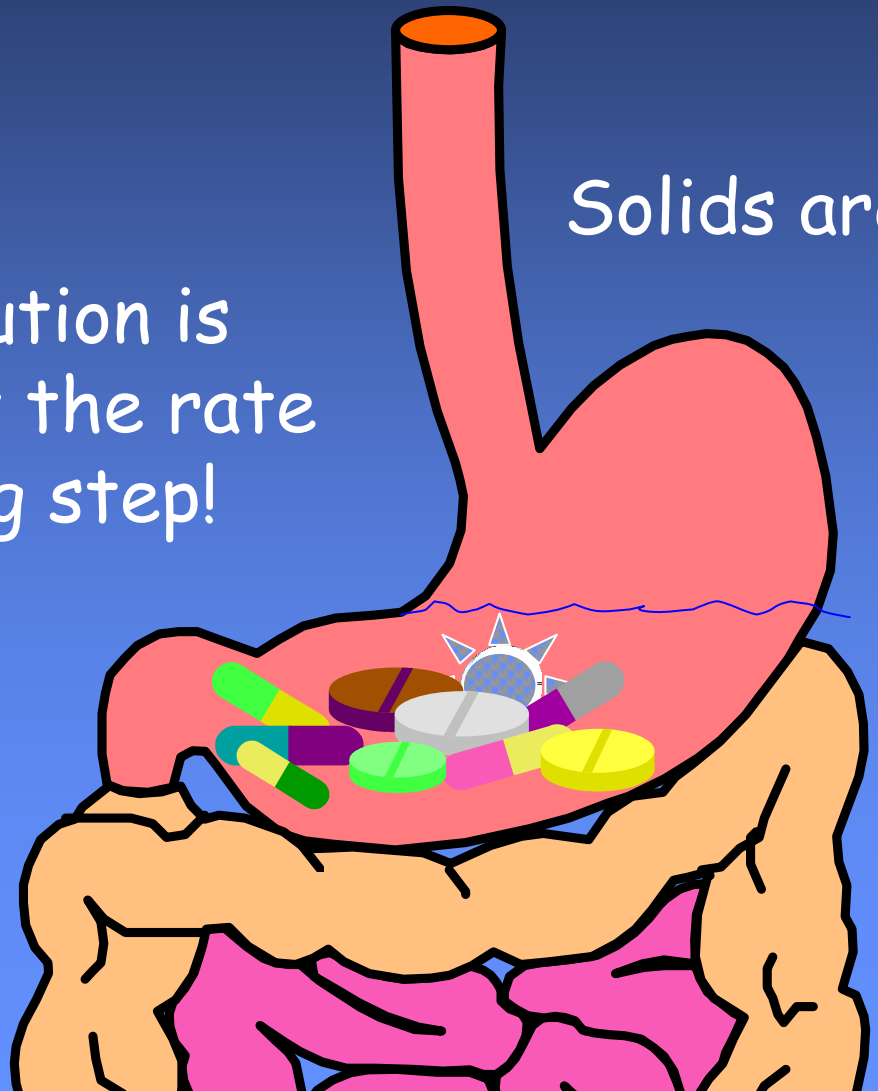
Absorption: Nature of Substance

- Dosage Form
  - Immediate vs Sustained Release
  - Depot Preparations
- Pharmacologic issues
  - Ex Anticholinergeic
  - fight vs flight
- Chemical properties
  - Ionic
  - Weak acid/Weak base

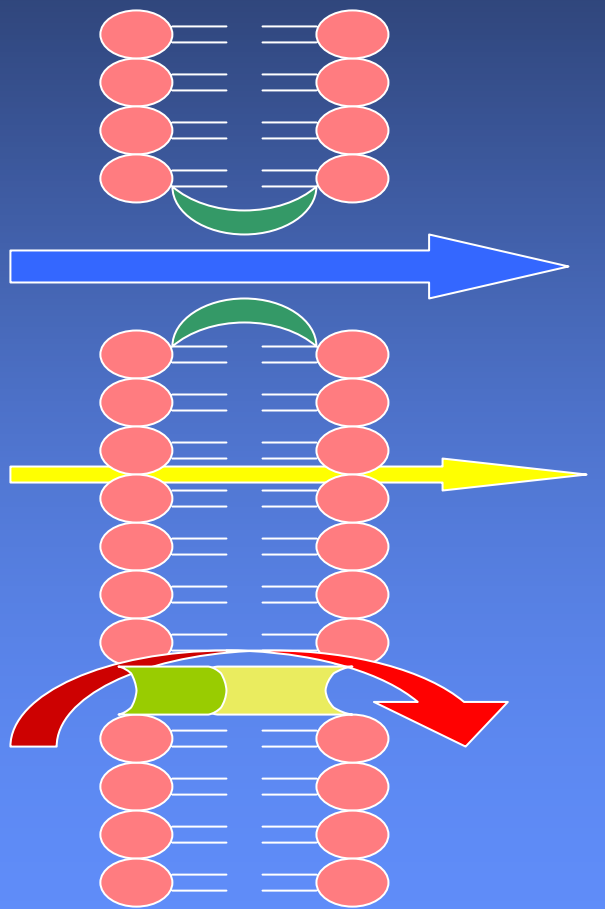
Absorption

Solids are not absorbed!

Dissolution is usually the rate limiting step!



Absorption

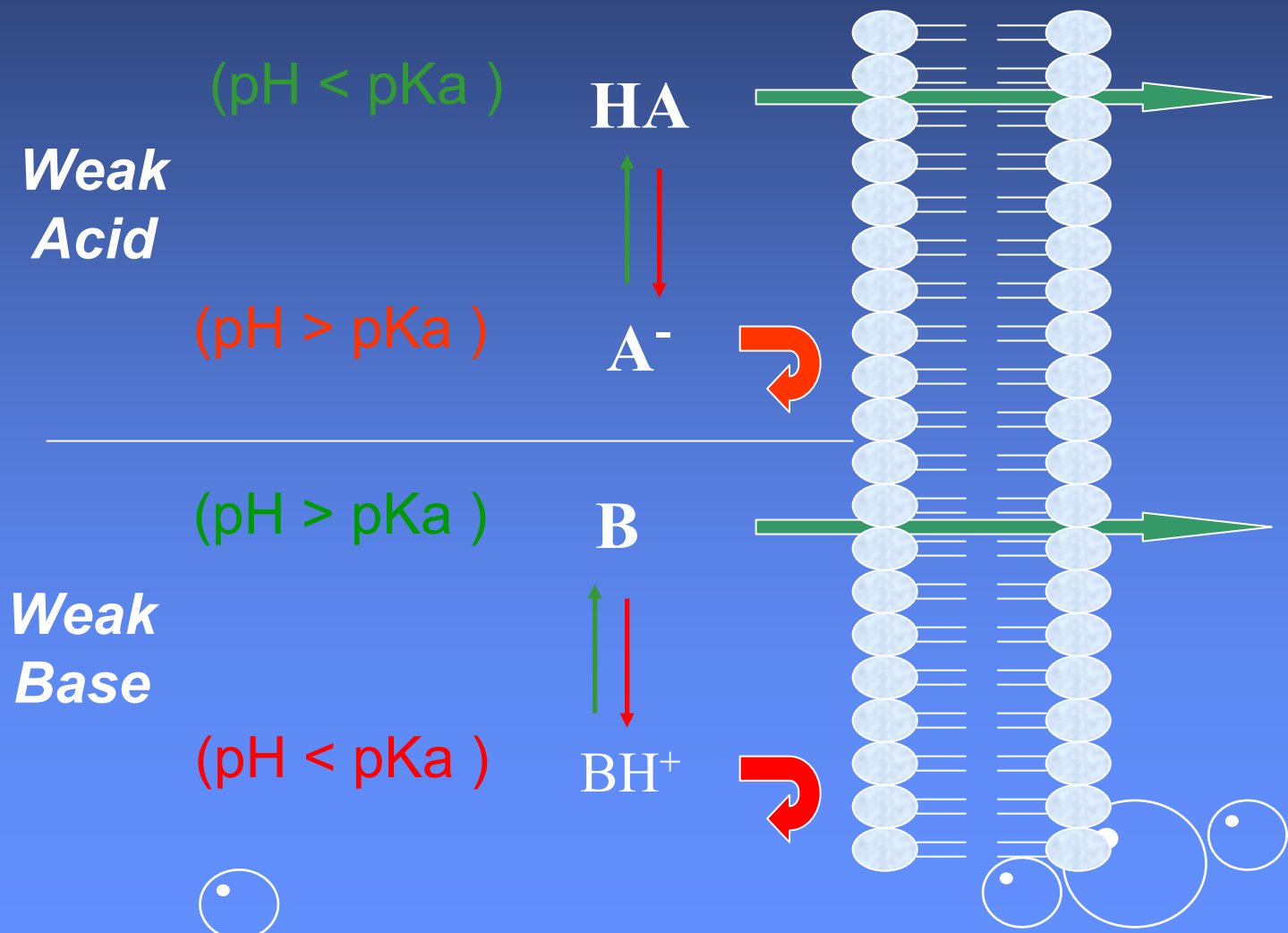


Passive Diffusion Through Pore

Diffusion Across Membrane

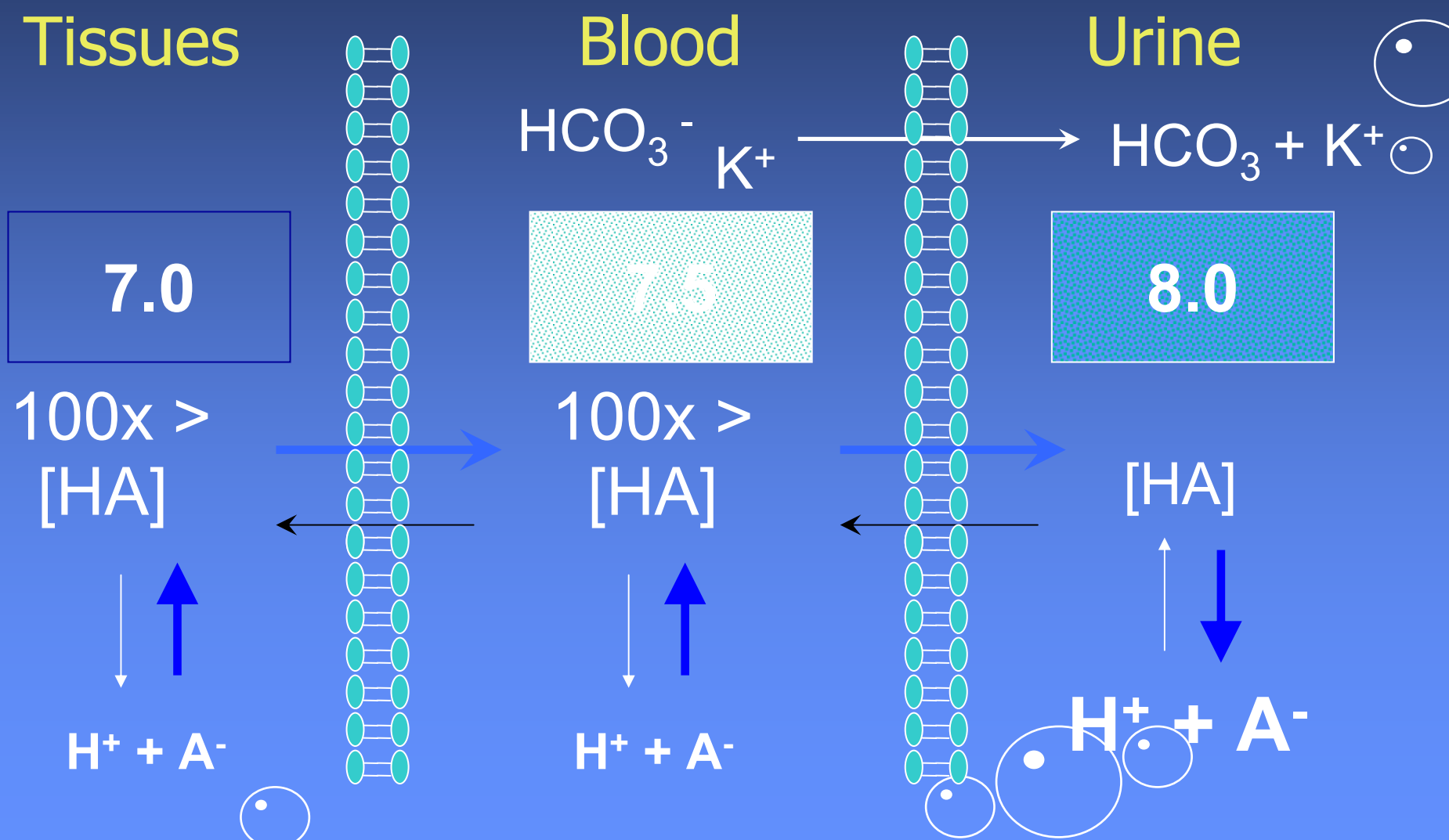
Carrier-Mediated Transport

Diffusion Across Membrane



Alteration of Urine pH

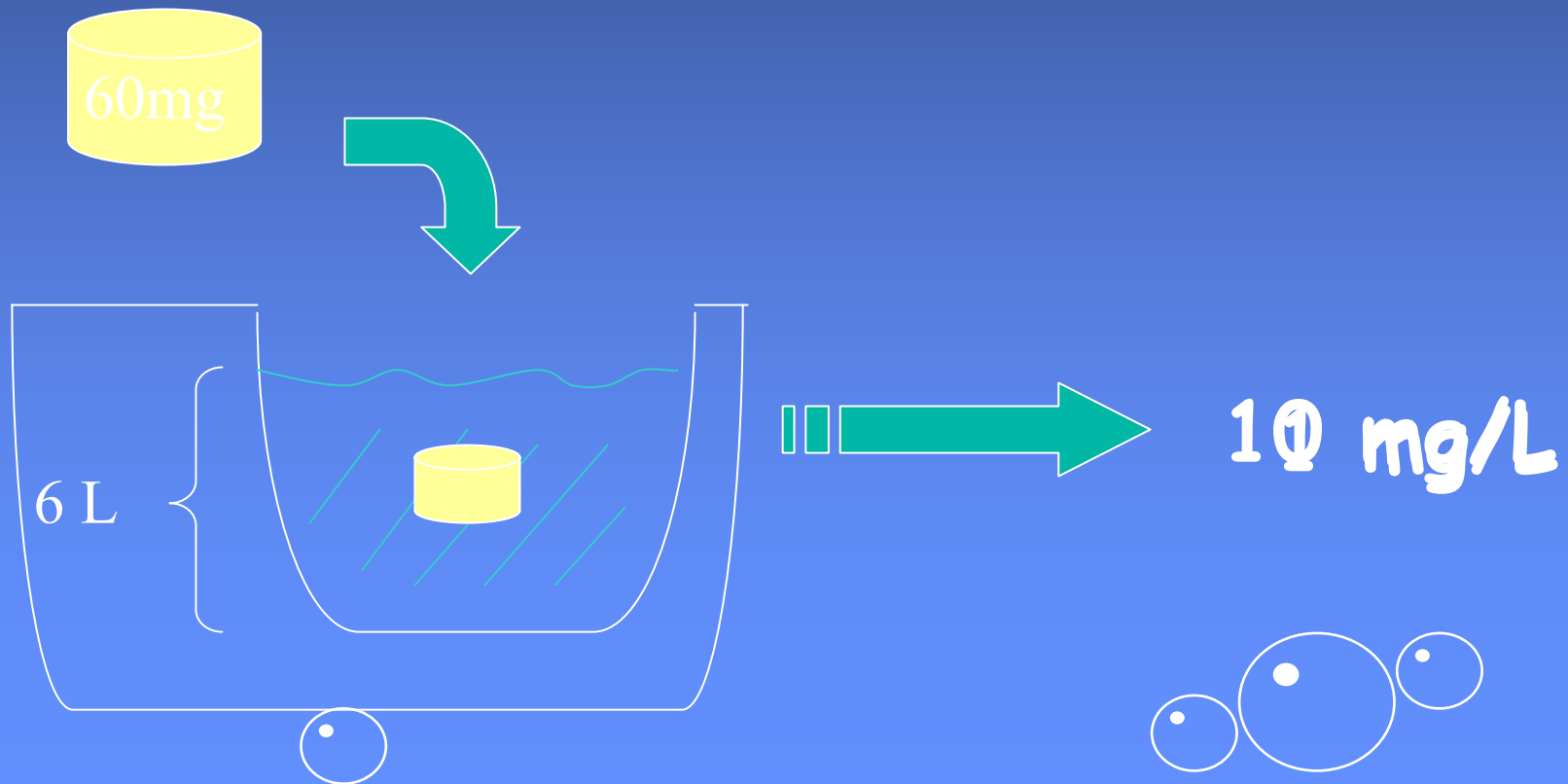
"Ion Trapping"



Distribution

Cp=D*S*F/Vd

Concentration = Amount (dose) / Volume

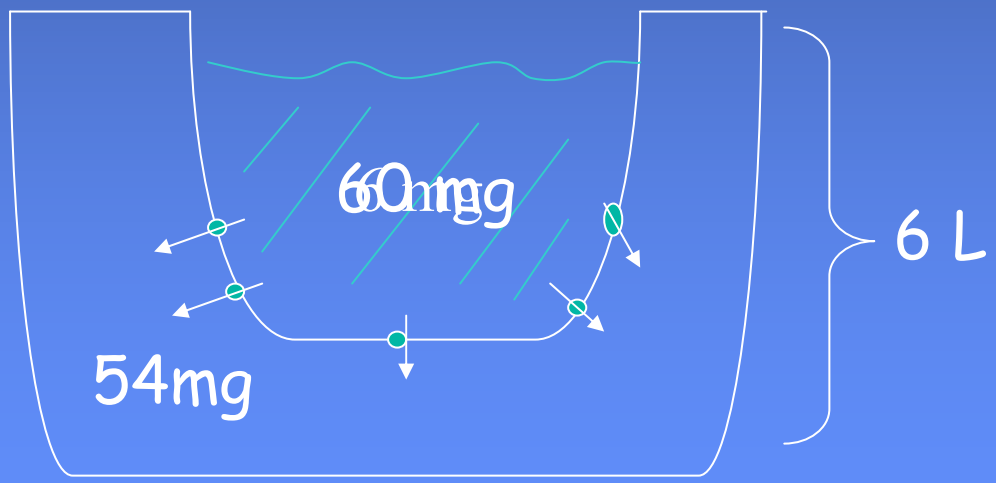


Distribution

Volume = Amount (dose) / Concentration

Gave 60mg
Concentration = 1 mg/L

V = 60mg/1 mg/L
V = 60 L

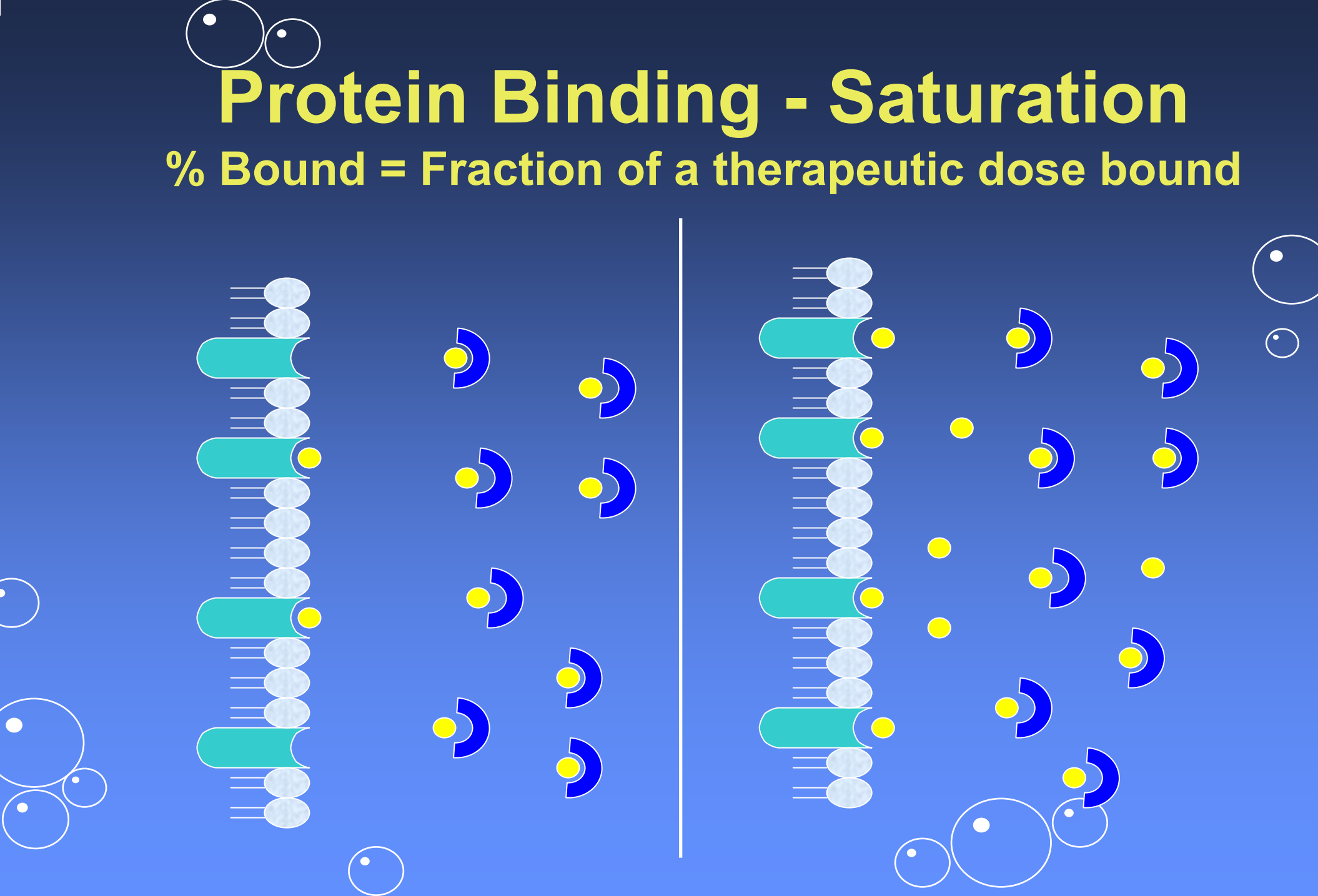


Looks like your 60mg was dissolved into 60L instead of 6L due to unequal partitioning.

This is Apparent Vd!!

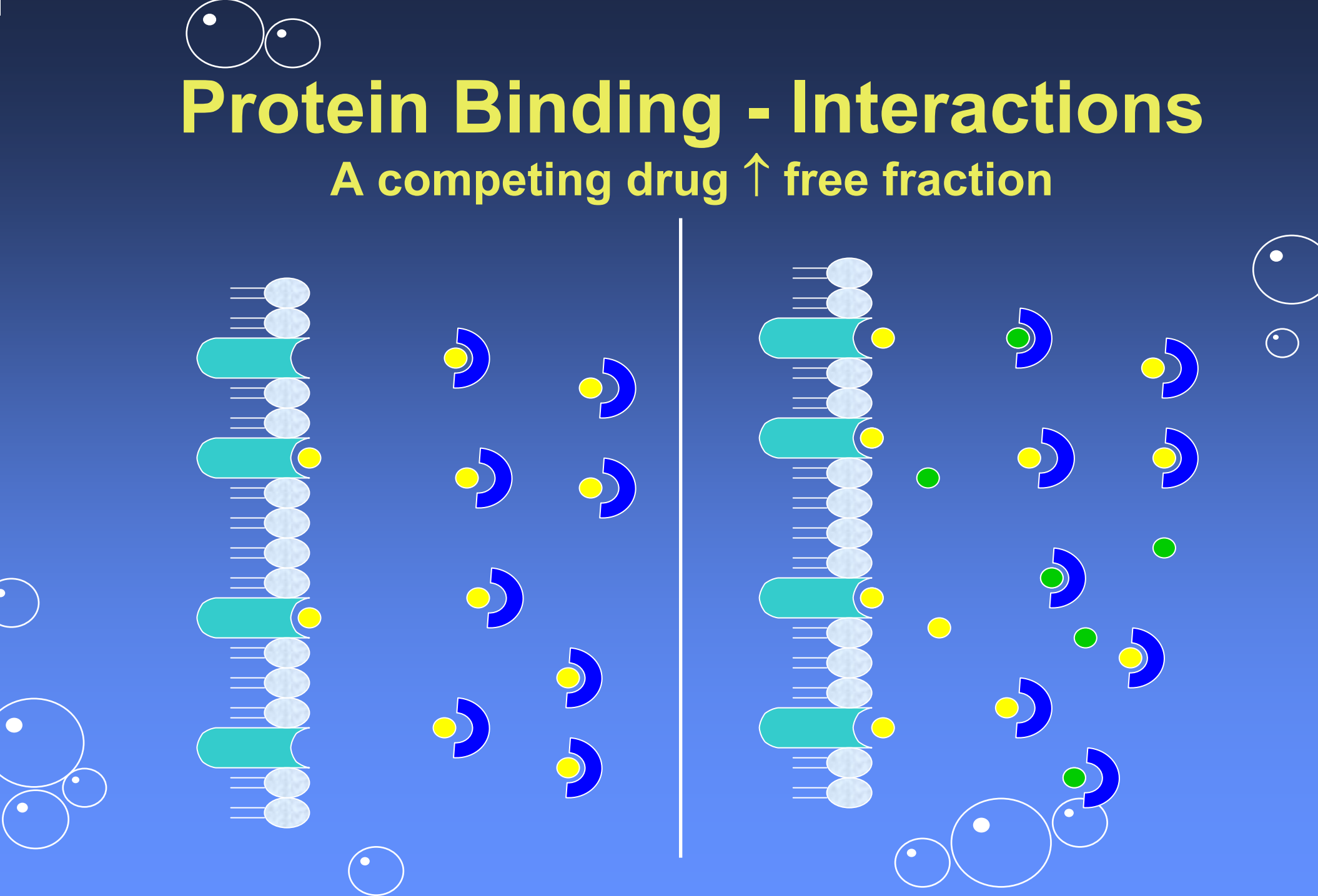
Protein Binding - Saturation

% Bound = Fraction of a therapeutic dose bound



Protein Binding - Interactions

A competing drug ↑ free fraction



Metabolism

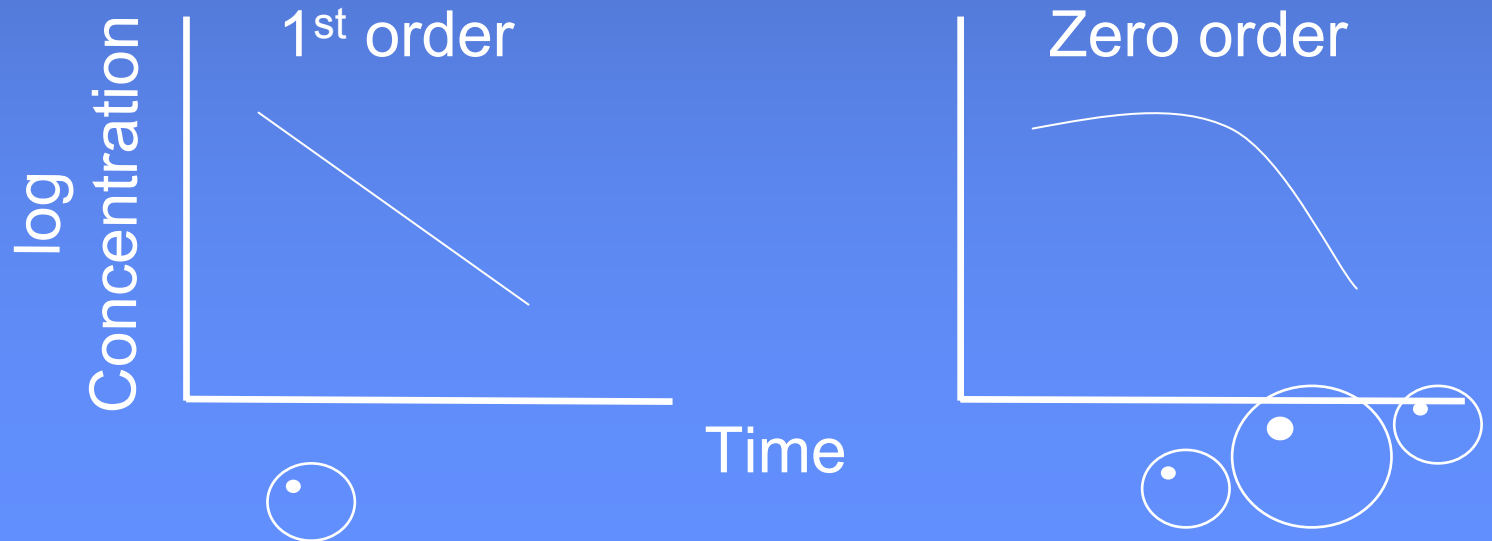
- Where does it occur?
  - 1° Hepatic, 2° Renal
  - All Tissues have some metabolic capability
- What is the purpose of metabolism?
  - To increase water solubility of xenobiotics
  - Utilization of nutrients

Metabolic Reactions

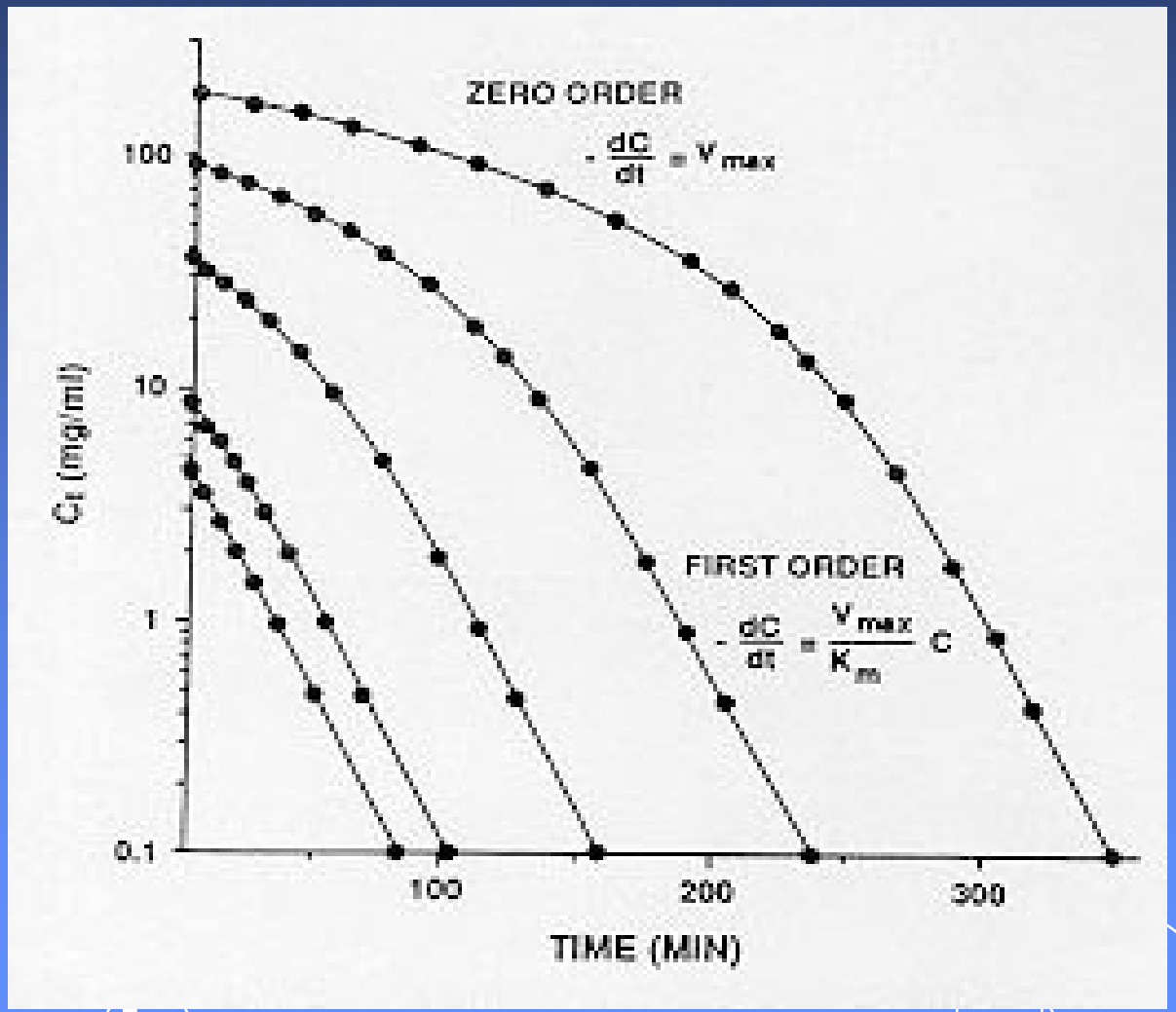
- Phase I: Asynthetic
  - Oxidation: P-450
  - Hydroxylation
  - Reduction
- Phase II: Synthethic
  - Glucuronidation
  - Sulfation
  - Acetylation
  - Glycine
  - Glutathione

Metabolism - Saturation

Metabolic Pathway



Michaelis-Menten Kinetics



Metabolism P-450 Enzymes

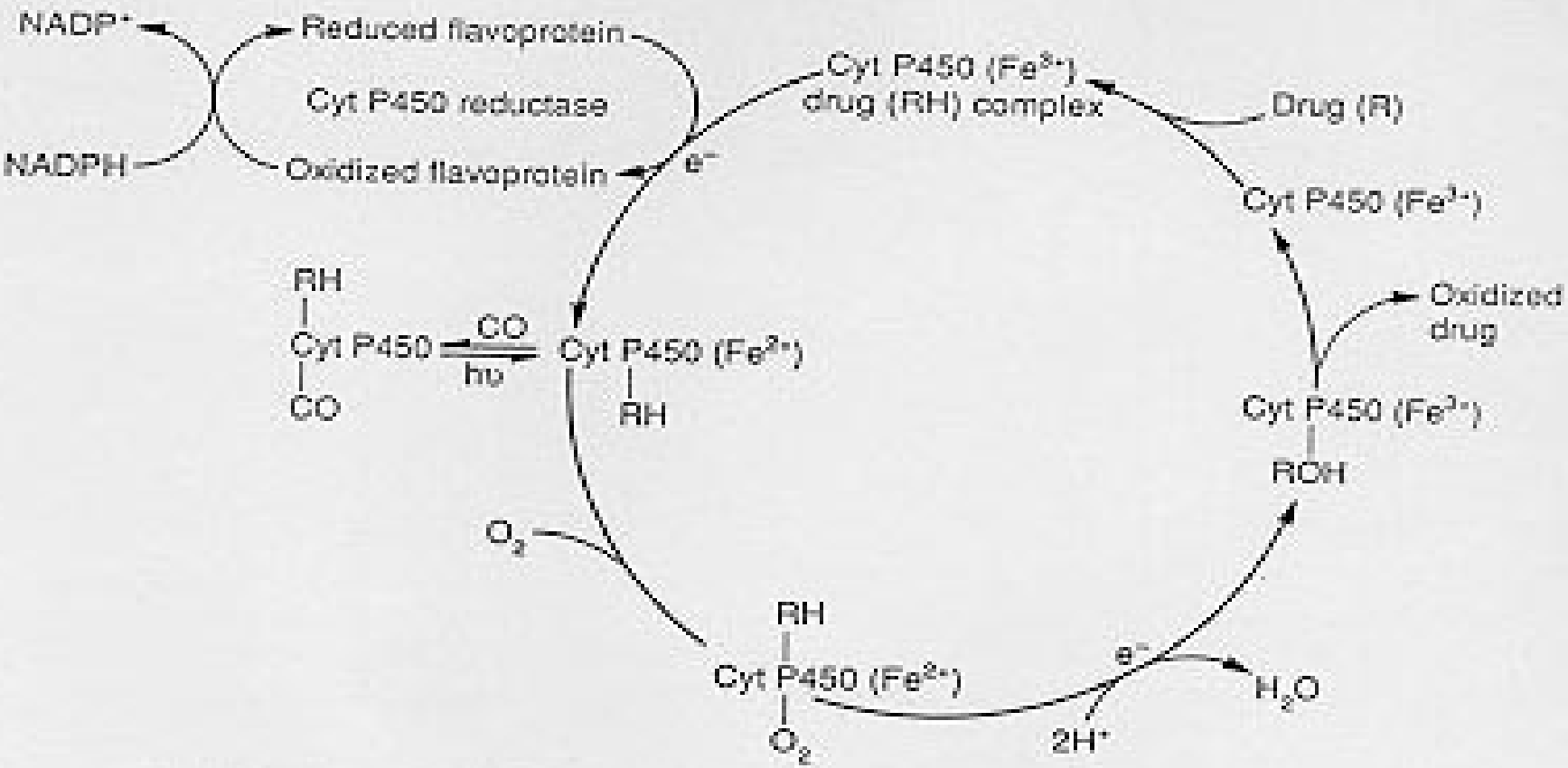


Figure 13–12. Electron flow pathway in the microsomal drug-oxidizing system. *(From Alvares & Pratt 1990, with permission.)*

Metabolism - Inhibition

- Competative
  - 2 substances compete for the same site on the enzyme
- Noncompetative
  - Inhibitor binds to a different site than where drug is metabilized.
- Uncompetative
  - inhibition not related to enzyme (ie. Altered distribution)

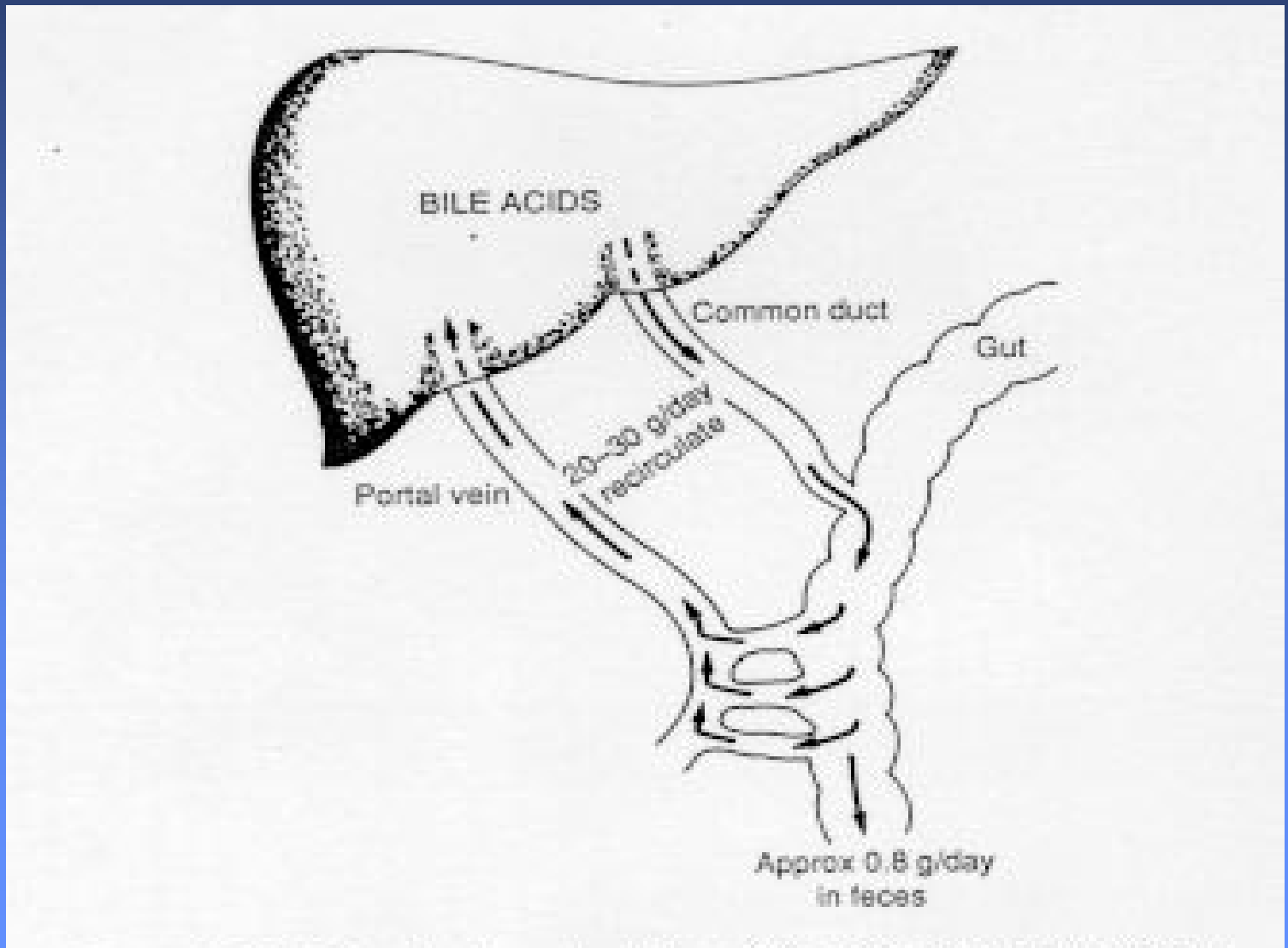
Metabolism:
P-450 Enzymes & Substrates

- Clinically significant subtypes
  - CYP 1A2
  - CYP 2D6
  - CYP 2E1
  - CYP 3A4

Elimination

- Major routes are
  - 1º Renal
  - 2º Hepatic/Billiary
- Depends on:
  - Blood flow to end organ
  - Water/Lipid Solublity
  - Volume of Distribution
  - Size: Smaller than protein
  - Not bound to protein

Hepatic/Billiary Elimination



Who gets poisoned & why?
AAPCC Statistics for 2001

* 2,168,248 Human Exposures
* 70% no or minimal effects
* 86% Unintentional
* 22% managed in HCF
  - 56% were T&R
  - 20% have serious clinical effects
* 52.7% involved children under 6 years of age
* 14.4% involved children 6 to 19 years of age

COMMON SUBSTANCES OF EXPOSURE - AAPCC

< 6 years	6 to 19 years	> 19 years
cosmetics	bite/stings	bite/stings
cleaning products	cleaning products	cleaning products
plants	foreign bodies	food poisoning
foreign bodies	cosmetics	cosmetics
pesticides	plants	pesticides
analgesics	analgesics	analgesics
cold & cough	cold & cough	sedative-hypnotics
topicals	street drugs	antidepressants
antibiotics	antidepressants	cold & cough
GI preparations	antibiotics	antibiotics
vitamins	antihistamines	antihistamines

Reasons for Adolescent Poisoning

Reason	6-12Y	13-19Y	6-19Y
Unintentional	138,756	81,101	219,857
Intentional	8,148	72,731	80,879
Other	1,555	2,019	3,574
Adverse reaction	2,332	3,493	5,825
Unknown	430	1,161	1,591
Total	151,221	160,505	311,726

Known Outcomes for Adolescent Poisoning

Outcome	6-12Y	13-19Y	6-19Y
No Effect	24,668	27,472	52,140
Minor	26,816	40,256	67,072
Moderate	3,947	16,383	20,330
Major	246	1,589	1,835
Death	6	66	72
Unrelated	4,107	4,531	8,638
Total	59,790	90,297	150,087

BACKGROUND ON POISONING IN ADOLESCENTS

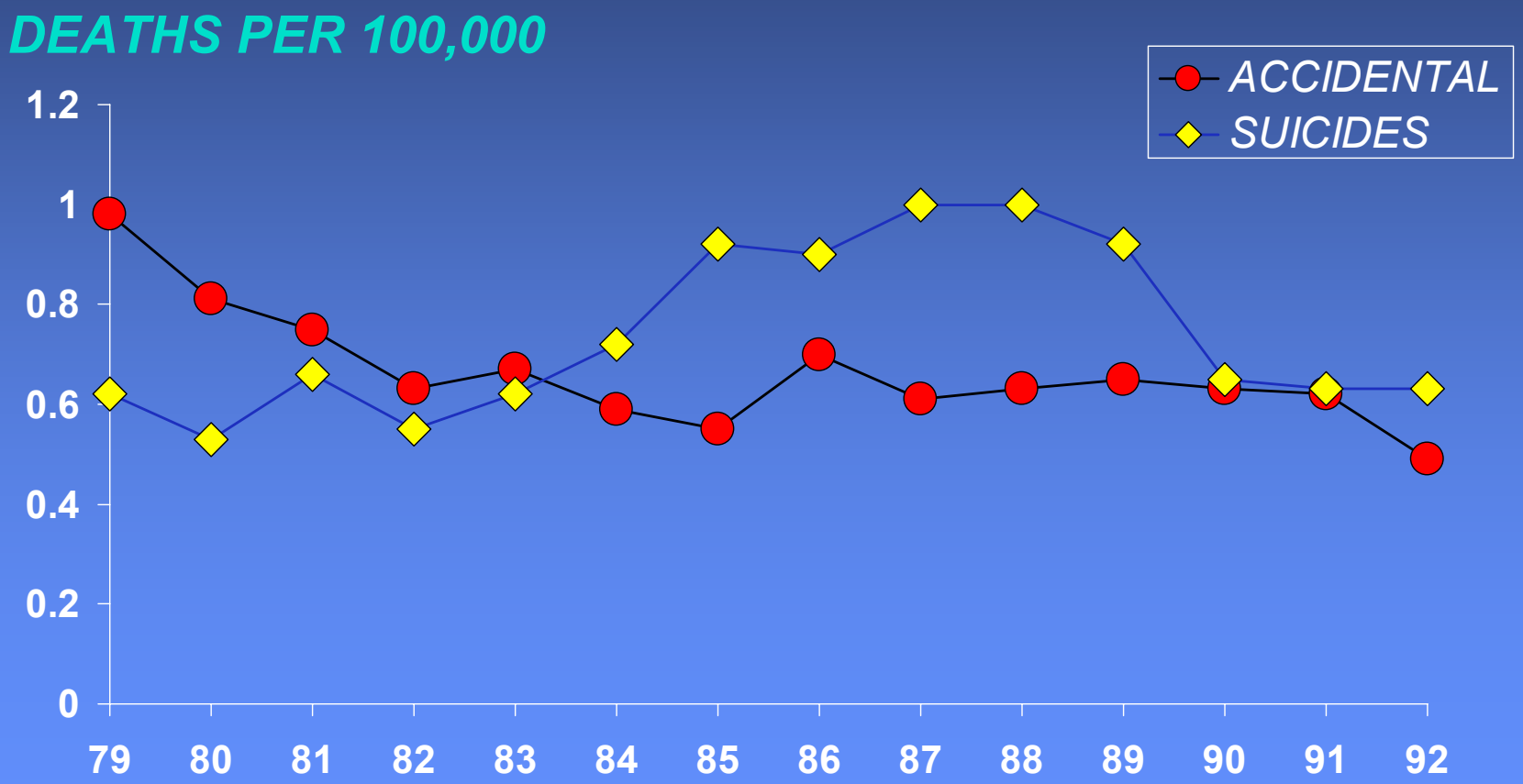
- **National Mortality Statistics**
  - **Accidental injuries are the leading cause of death in 10-19 year olds.**
  - **Suicides are the fourth and third leading cause of death in 10-14 year olds and 15-19 year olds, respectively.**
- **Available on the WEB (http://wonder.cdc.gov/)**
- **Reported by medical examiners & hospitals**
- **Identifies race, gender, ICD-9 codes for cause of death**
- **Reports raw numbers and rates per 100K population**

Adolescent Poisoning Deaths

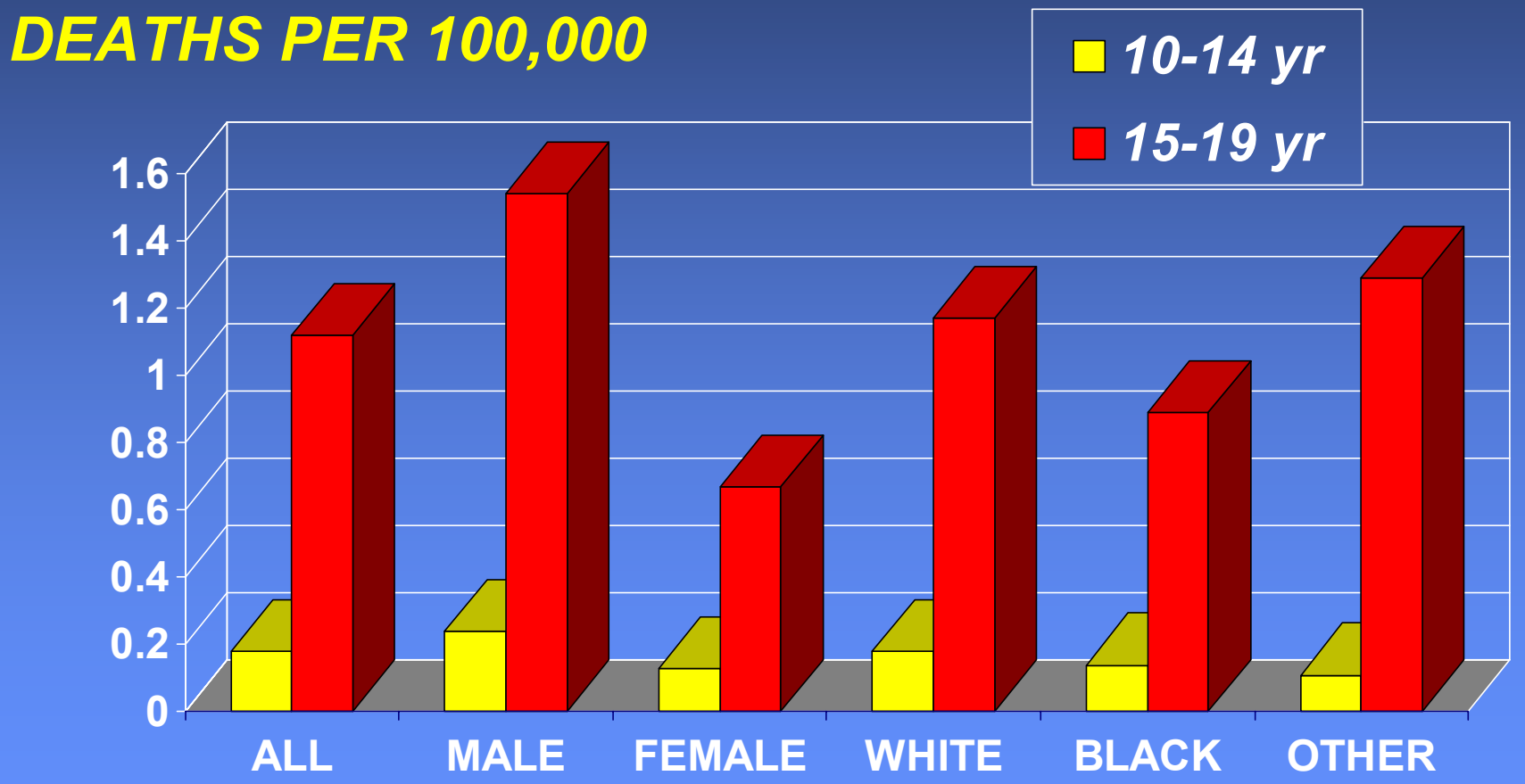
- Between 1979 and 1992
- 7,226 POISONING DEATHS
  - 3,777 Suicides
  - 3,449 Accidental
- Male : Female Ratio 1.8 : 1
- Age Group Number Rate (per 100K population)

Age Group	Number	Rate
10-14 years:	694	0.28
15-19 years:	6,532	2.45

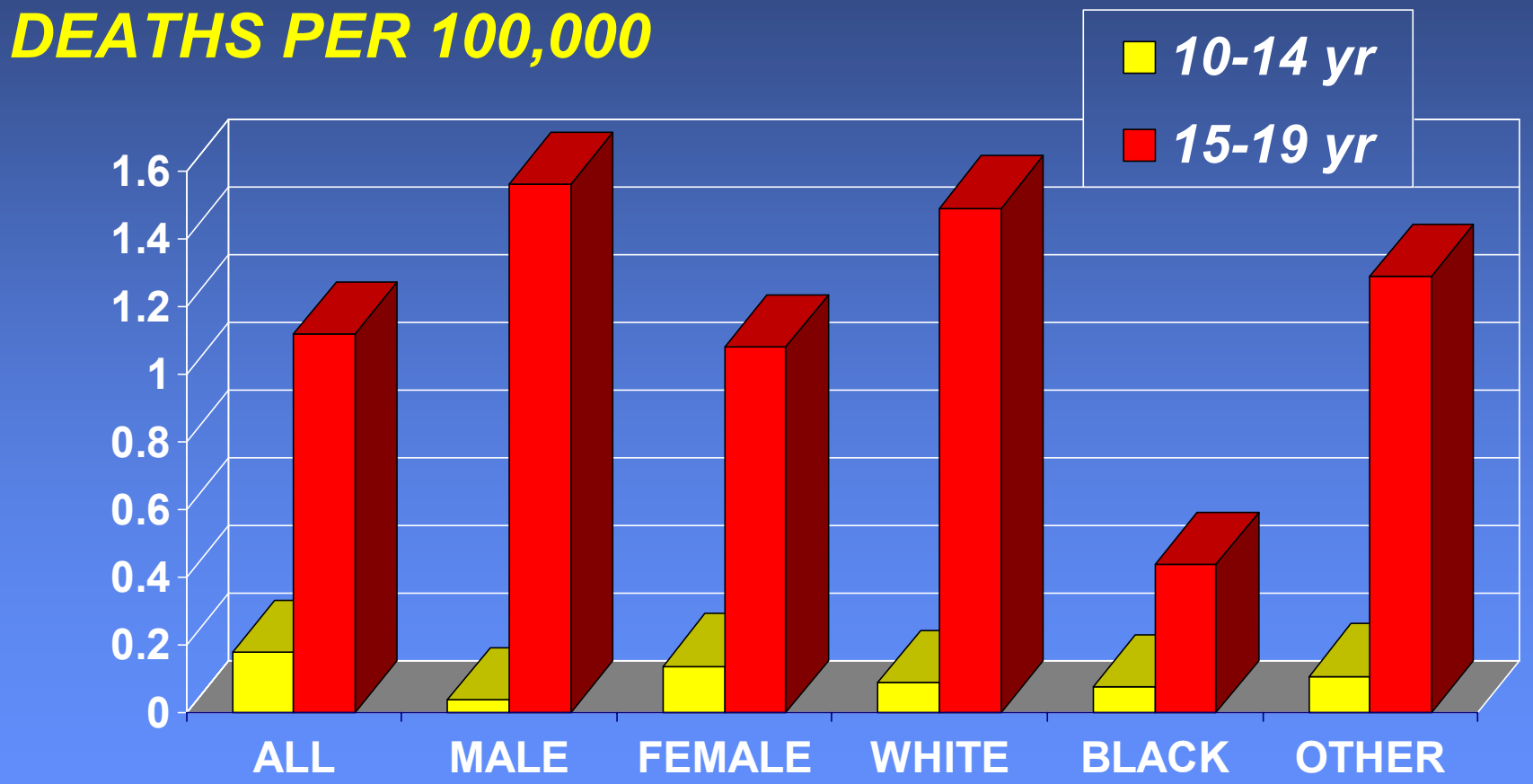
MORTALITY RATES FOR ADOLESCENT POISONINGS BY YEAR



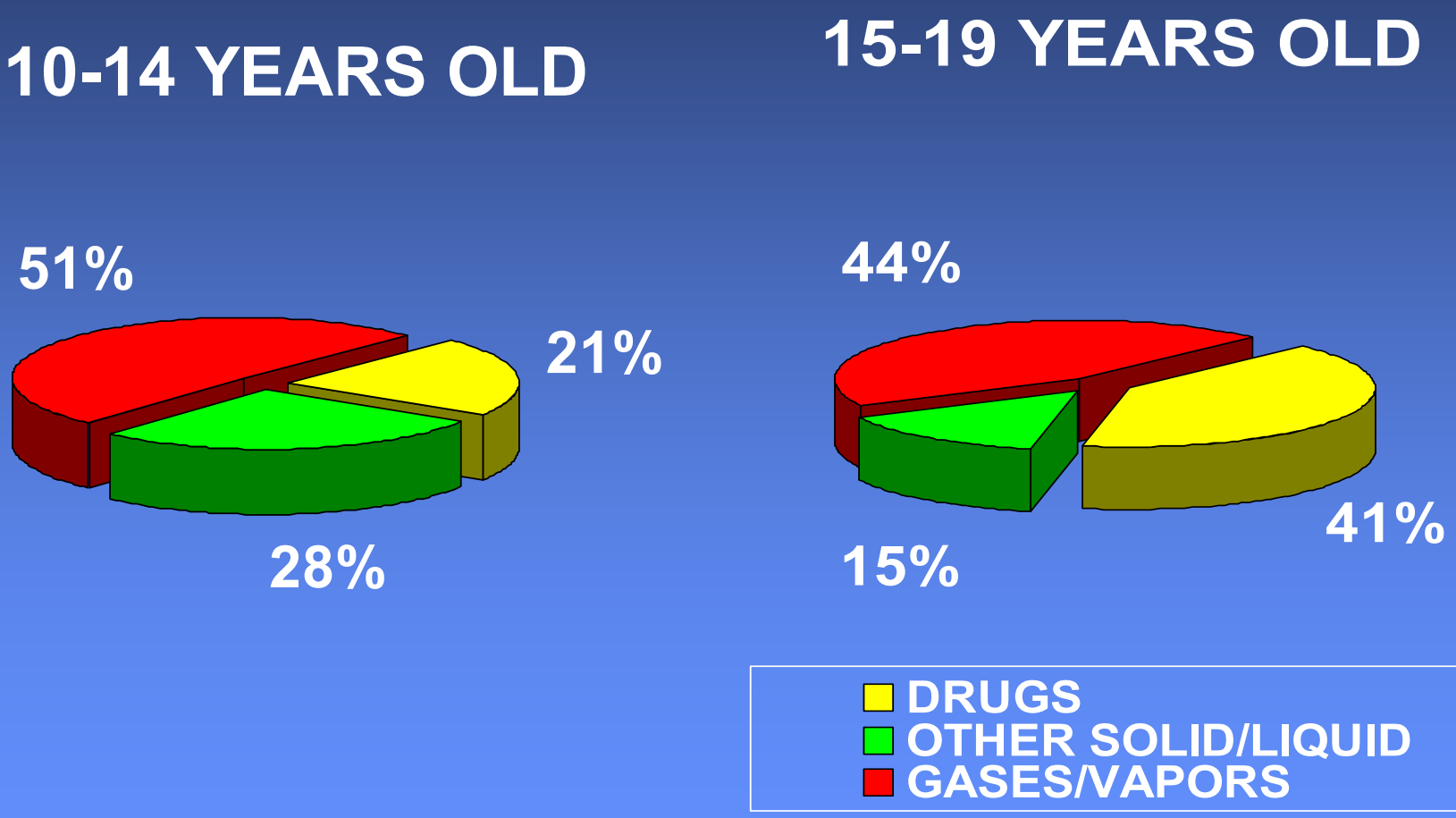
UNINTENTIONAL POISONING DEATHS 1979-1992



SUICIDAL POISONING DEATHS 1979-1992

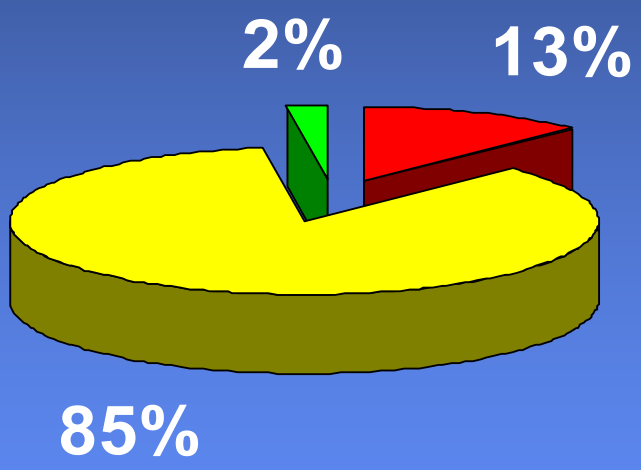


Substances Responsible For Accidental Deaths By Age Group

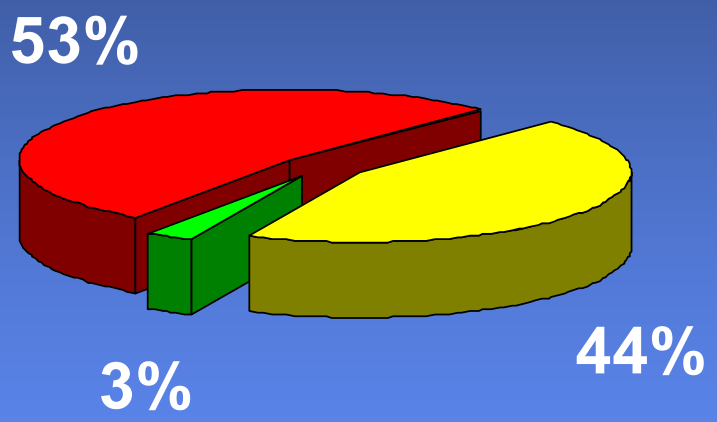


Substances Responsible For Suicides By Age Group

10-14 YEARS OLD



15-19 YEARS OLD



DRUGS
OTHER SOLID/LIQUID
GASES/VAPORS

Observations

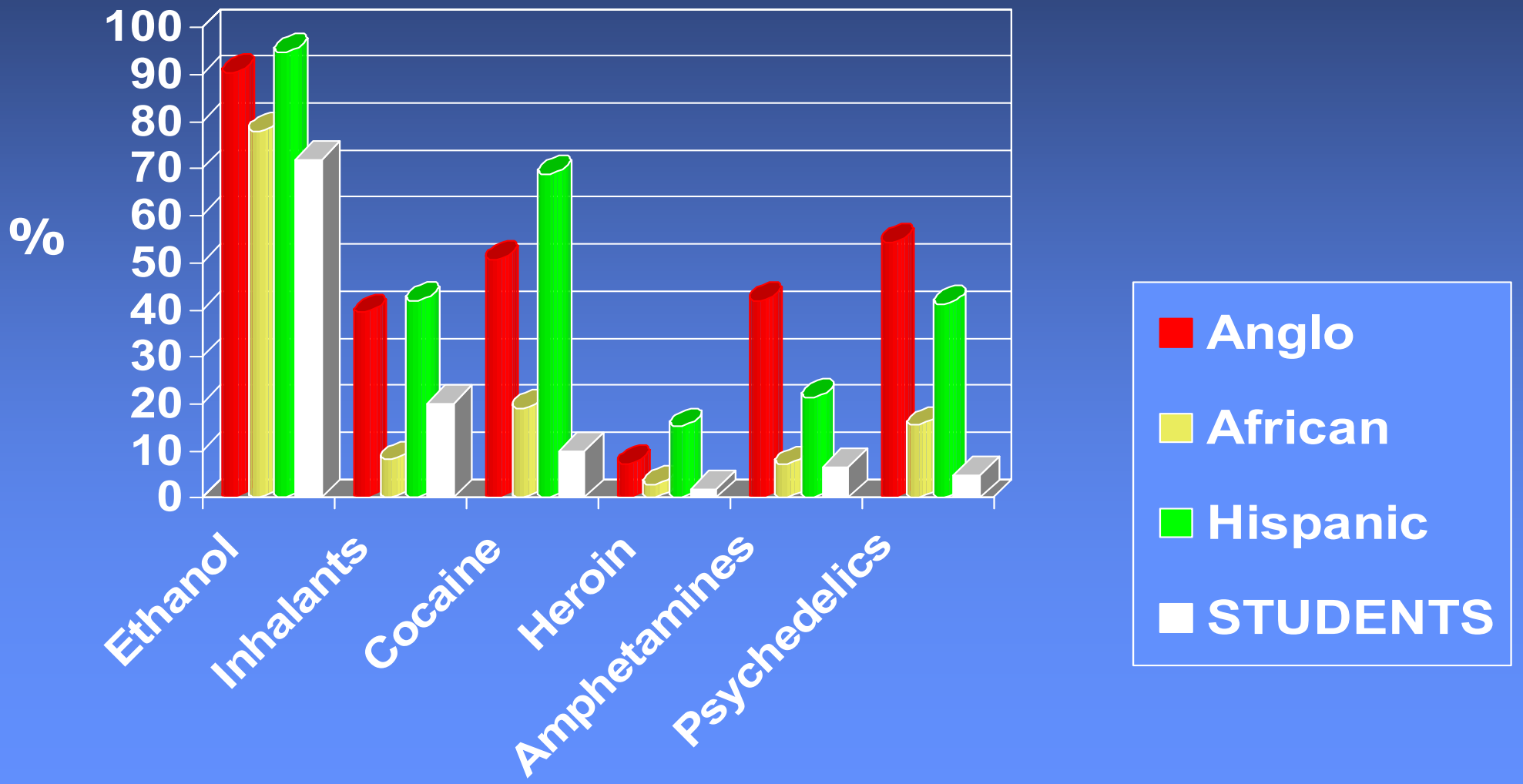
- Poisoning death rates were higher in males than females.
- In 10-14 year olds majority of suicides involve drugs while accidental deaths more likely to involve non-drugs and gases.
- In 15-19 year olds gases are most frequent substance followed closely by drugs for both suicides and accidental poisoning
- Poisoning is a more common means of suicide in adolescent females than males.
- In 15-19 year old blacks the suicide rate was ~2/3 lower than all other races.

Accidental Poisoning Deaths from Alcohols and Freon

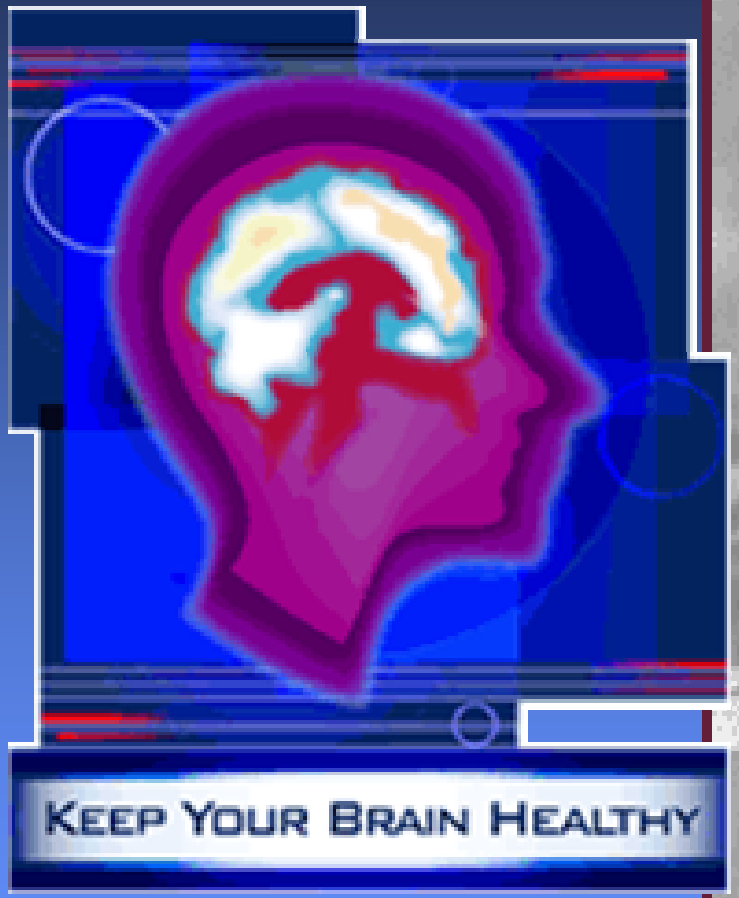
	Number of Accidental Deaths (% of age group)			
	10-14		15-19	
Alcohols	9	(1.9 %)	140	(4.7 %)
Freon	17	(3.7 %)	123	(4.1 %)

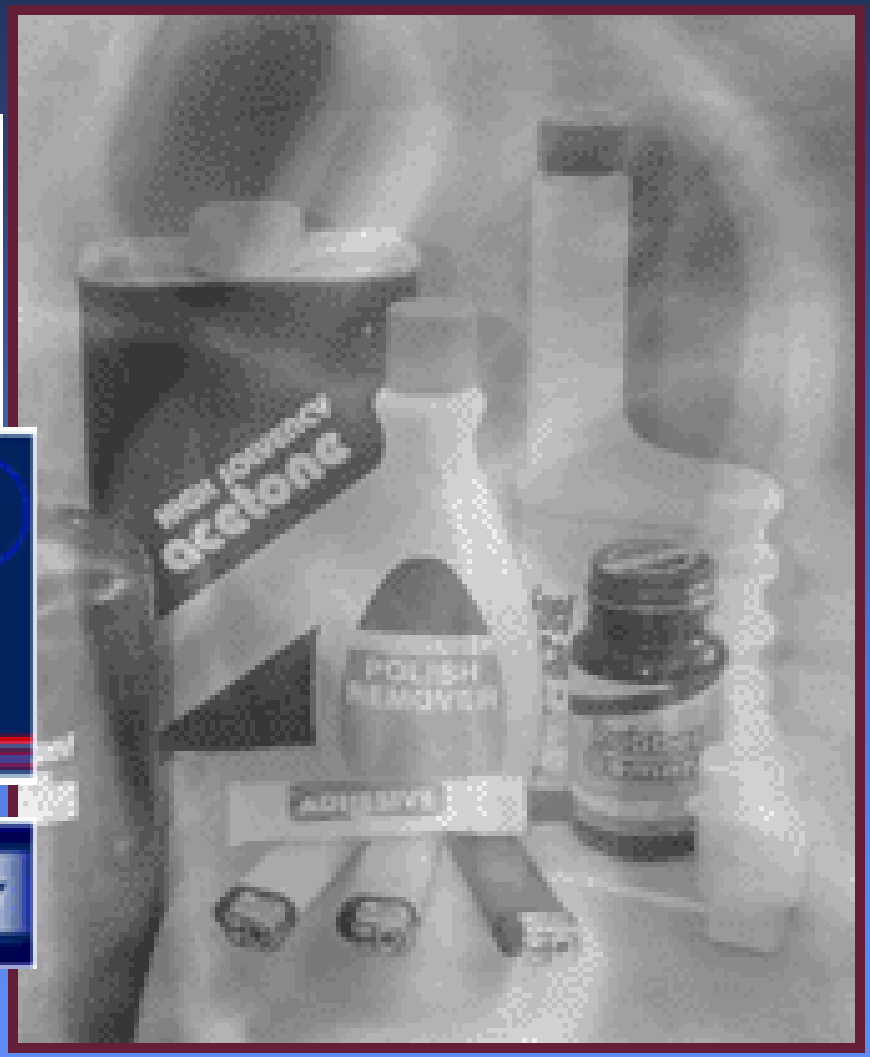
Substance Abuse Issues

Prevalence of substance use by 11-18 year olds in children entering TYC facilities in 2000-2001



Inhalants





Sniffing …Huffing …Bagging

Monitoring the Future Study

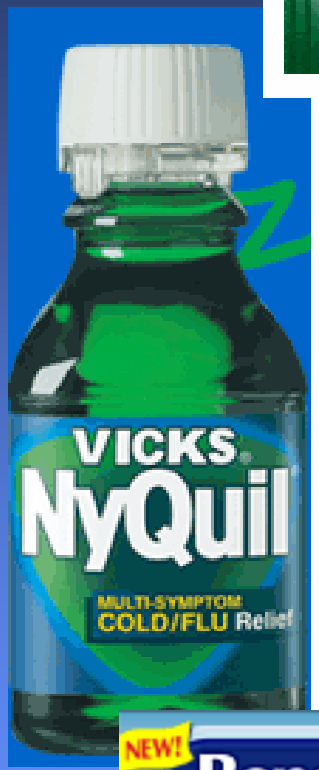
- **Inhalant Use by Students, 2000: Monitoring the Future Study**

	8th	10th	12th
Ever Used	17.9%	16.6%	14.2%
Used in Past Year	9.4%	7.3%	5.9%
Used in Past Month	4.5%	2.6%	2.2%

Recommended by

Physicians, Pharmacists and ...

Dr. Feelgood??



What are they after?

- Dextromethorphan
  - Setrotonergic activity can produce visual & auditory hallucinations
- Antihistamines
  - Antimuscarinic properties produce visual and tactile hallucinations
- Decongestants
  - Stimulant effects

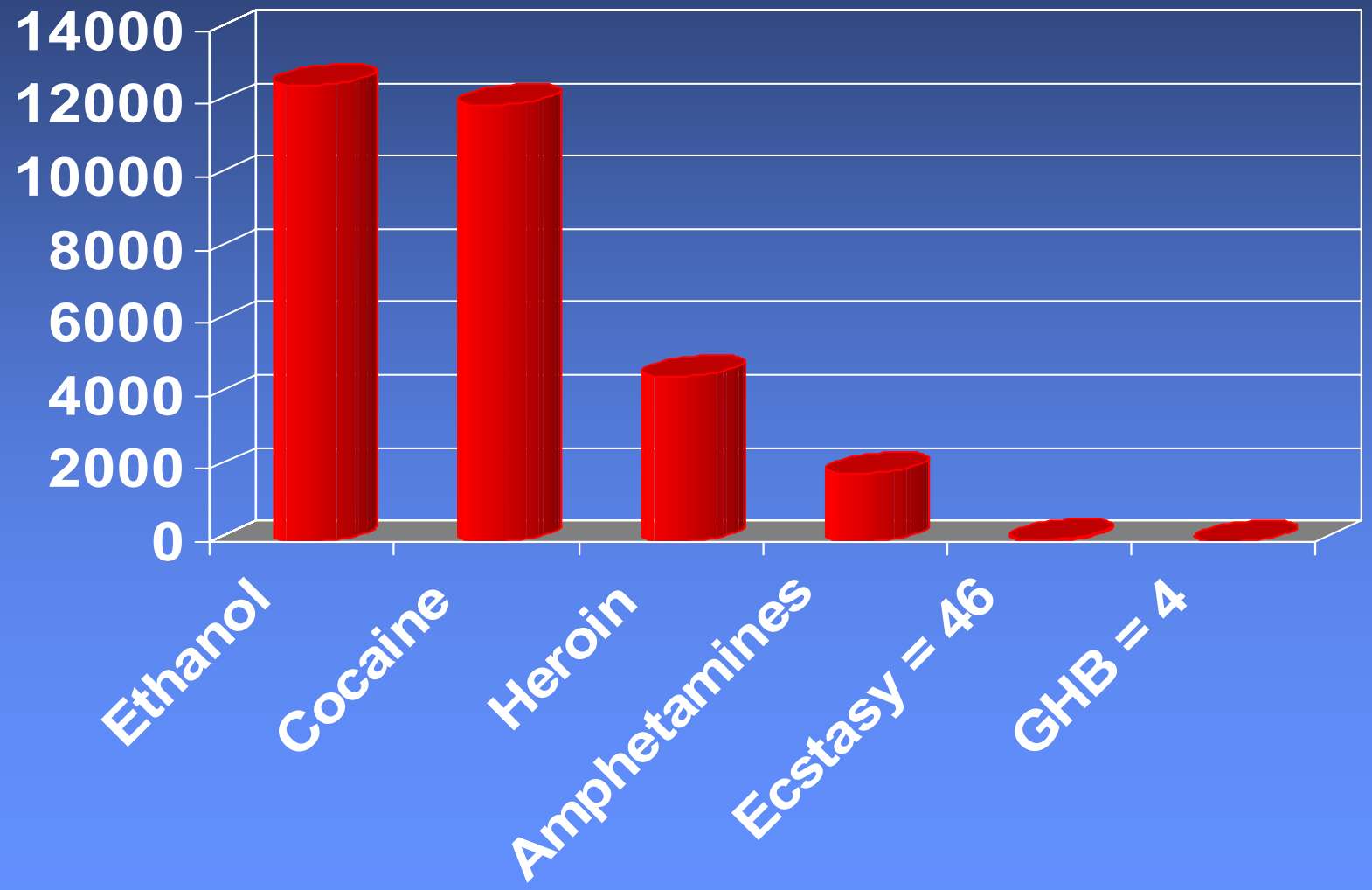
Patterns of use

- Cheap
- Readily available
- Not illegal

- Poor mans ecstasy

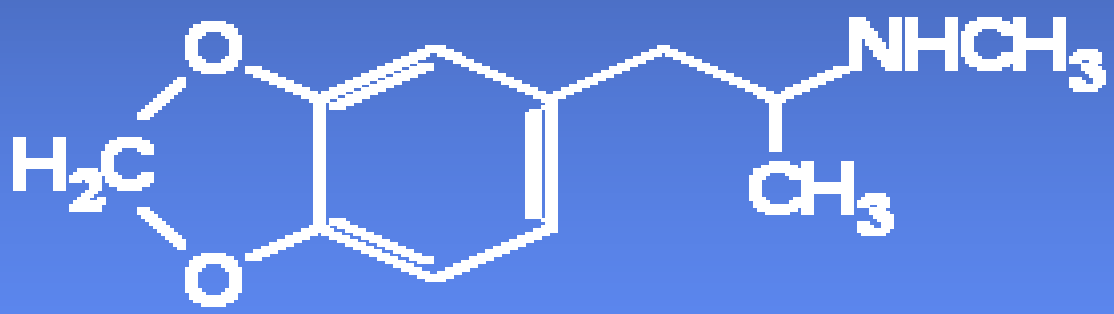
- Not much fun
- “Gateway drug”
- Most tend to use only a few times
- Poison center reports seem to indicate sporadic nature

Patients in TCADA Treatment Programs During 2000

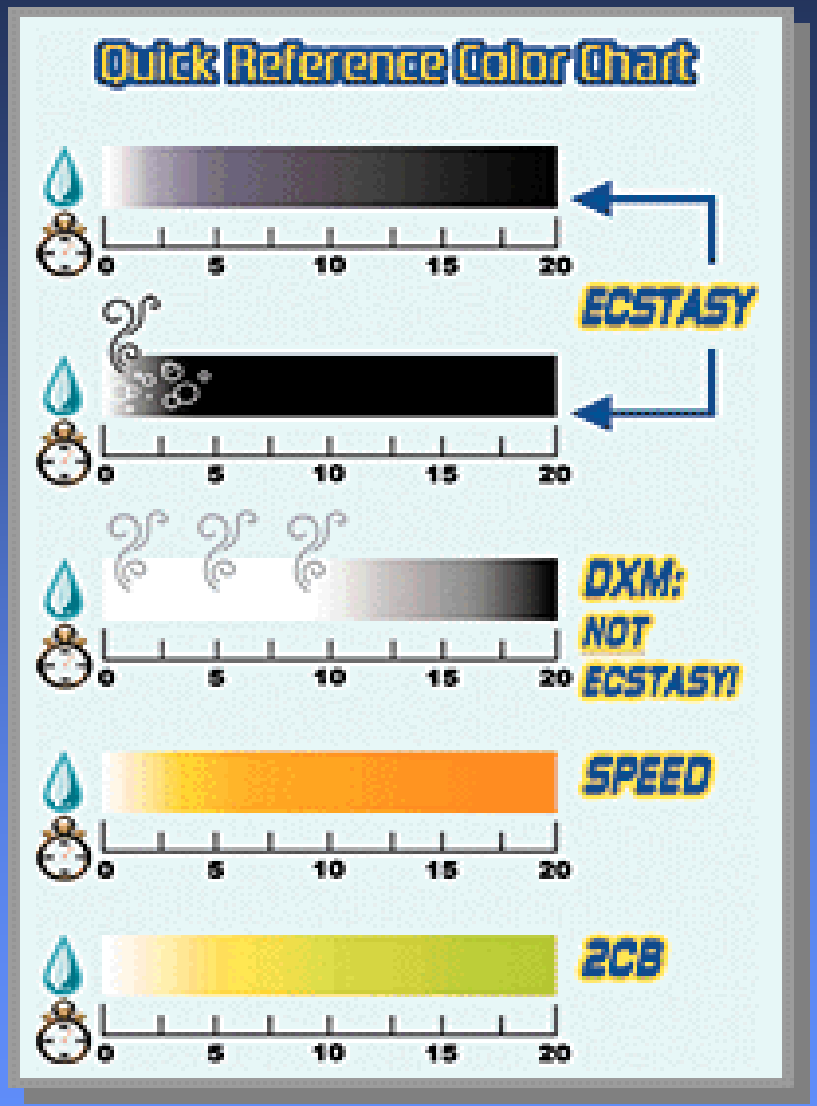


Hallucinogenic Amphetamines

- Phenylalkylamine structure
- Ring modifications to cause serotonergic effects
- MDMA - Ecstasy
  - MDEA
  - MDA
  - MBDB



MDMA



http://www.erowid.org/

Summary

Adolescent poisoning is a significant cause of morbidity and mortality.

As children age poisoning exposures become less frequent but more serious in nature.

Poison prevention in adolescents requires different educational strategies than for younger children due to more complex underlying causes.

Suggested References

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