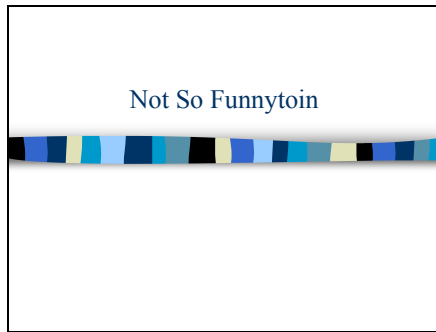


Slide 1



Slide 2

Phenytoin Pharmacokinetics

- Michaelis-Menten pharmacokinetics
 - Non-linear kinetics
 - $t_{1/2}$ = 22 hours (range 7-42 hours)
 - 5-10 days to reach steady state
 - Protein binding >90%

A slide with a white background and a black border. On the left side, there is a vertical decorative bar with a pattern of blue, teal, and black segments. The title "Phenytoin Pharmacokinetics" is in a blue serif font. Below the title is a bulleted list with a blue square bullet point for the main category and black dashes for sub-points.

Slide 3

Phenytoin Toxic Effects

- CNS: Mental status changes, Drowsiness, Dizziness, HA, Insomnia.
- Cardiovascular: Hypotension, bradycardia, cardiac arrhythmias.
- Ocular: Diplopia, nystagmus, blurred vision.

Lacey CF, Armstrong LL, Goldman MP, Lance LL. [Drug Information Handbook](#). Hudson, Ohio: Lexi-Comp; 2003.

A slide with a white background and a black border. On the left side, there is a vertical decorative bar with a pattern of blue, teal, and black segments. The title "Phenytoin Toxic Effects" is in a blue serif font. Below the title is a bulleted list with blue square bullet points. At the bottom left, there is a small line of text in a very small font.

Slide 4

Hypoalbuminemia

- Patients At Risk
 - Elderly
 - Critically Ill
 - Renal or Hepatic Disease
- Patients with hypoalbuminemia will have a higher free fraction of Phenytoin

Slide 5

Phenytoin Levels in Hypoalbuminemia

- Purpose of Adjustment
 - Avoid inappropriate dose changes.
 - Identify potential Phenytoin toxicity that is not obvious by the observed level.

Slide 6

Winter-Tozer Method

- Equation
$$C_{\text{calcn}} = C_{\text{obs}} / (0.2\text{ALB} + 0.1)$$
- This equation normalizes the total Phenytoin level to reflect a level with normal albumin.

Anderson GD, Pak C, Doane KW, et al. Revised Winter-Tozer Equation for Normalized Phenytoin Concentrations in Trauma and Elderly Patients with Hypoalbuminemia. Ann Pharmacotherapy 1997;31:279-84

Slide 7

Revised Winter-Tozer Equation

- $C_{\text{calcn}} = C_{\text{obs}} / (.25\text{ALB} + 0.1)$
- Revised original equation to better predict total phenytoin concentration for.
 - Elderly Nursing home patients
 - Head trauma patients

Anderson GD, Pak C, Doane KW, et al. Revised Winter-Tozer Equation for Normalized Phenytoin Concentrations in Trauma and Elderly Patients with Hypoalbuminemia. Ann Pharmacotherapy 1997;31:279-84

Slide 8

Case Example

- L.P. is a 60 y/o male with a serum albumin level of 2.2g/dL

Phenytoin $C_{\text{obs}} = 7.3\text{ug/ml}$
 $C_{\text{calcn}} = 7.3 / (0.2(2.2) + 0.1)$
Phenytoin $C_{\text{calcn}} = 13.5\text{ug/ml}$

Therapeutic Range 10-20ug/ml


Slide 9

Phenytoin Adjustment

Using the Revised Winter-Tozer Equation

Observed Phenytoin Level (ug/ml)	Albumin (g/dL)			
	3.5	3.0	2.5	2.0
5	5	6	7	8
7	7	8	10	12
9	9	11	12	15
11	11	13	15	18

Slide 10



Conclusions

- Phenytoin dosing should be based on individual patient responses.
- Free phenytoin levels are the most reliable laboratory test.
- The Winston-Tozer method can be useful when free phenytoin levels are not available and questions arise concerning high risk patients on phenytoin.