Slide 1

Doses Target Concentration Intervention

Slide 2

Problem 1 Questions 1-2

Susan is a 28 year old woman who has had epilepsy since she was 5 years old. She has been on, and off, anticonvulsant medication since that time. She has been brought to hospital by a work colleague following a generalized seizure. She is drowsy.

Her mother tells you over the phone that she has been taking sodium valproate since she was 17 years old, but takes no other medicines. Sodium valproate has controlled her seizures well.

When Susan wakes up she tells you that she has been very well, but has had several seizures this month. She stopped taking valproate because she thinks it makes her put on weight. . She now weighs 100 kg and is 160cm tall. BMI = 100 kg/(1.6 m x 1.6 m) = 39 kg/m2.

1. What are the reasons for measuring a serum valproate concentration ?

2. When should the sample be taken?

Slide 3

Problem 1 Questions 3-5

3. Her sodium valproate concentration is 0 mg/L. What are the possible explanation(s) for this?

4. Would she benefit from anticonvulsant medication?

5. What treatment options are readily available?

Slide 4	
# Problem 1 Question 6-7 Susan refuses to take carbamazepine because when she used it as a teenager it caused nausea. She developed a rash when she tried lamotrigine. You both agree to initiate phenytoin. 6. Should you give her a loading dose? Why/why not? 7. What route and dose would you give to Susan? Phenytoin is available in 30mg and 100mg capsules and also as an intravenous injection solution.	
Slide 5	
# Problem 1 Questions 8-10 8. How can the effectiveness of this treatment be measured? 9. What would be the value of measuring phenytoin concentration? When?	
Slide 6	
# Problem 1 Questions 10-11 10. You measure the serum concentration after 1 month on 360 mg/day in the middle of the dosing interval. The reported concentration is 7.5mg/L Should the dose be increased? 11. A year later Susan sees you because she has had 2 seizures in the last month. Once again the phenytoin concentration is 7.5 mg/L. In order to achieve a plasma concentration of 15mg/L should the dose be increased to 720 mg/day?	

| Slide 7 | # Problem 2

On a dose of 400 mg/day her repeat phenytoin concentration was 12mg/L and Susan remains seizure free for 14 months.

Then she re-presents to hospital with another seizure. She has a fever and when she wakes up she complains of dysuria and flank pain. She is febrile, tachycardic and her blood pressure is 80/60 [previously 110/70]; she has marked tenderness over her right kidney; her urine microscopy shows a large number of white blood cells and bacteria. Her predicted creatinine clearance is 100 mL/min. You decide to treat her with gentamicin. | |
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| Slide 8 | # Problem 2 Question 1 and 2

1.   What loading dose will you give her?
The initial target concentration is 20 mg/L (peak after first dose)
Volume of distribution is 0.25 L/kg in a normal size person.

2.   What initial maintenance dose would you give her?
The steady state target concentration is 3 mg/L (average concentration). Her creatinine clearance is 100 mL/min. | |
| Slide 9 | # Problem 2 Question 3

2. Should you measure a gentamicin concentration? If so, when? | |

Slide 10

Problem 2 Question 3

3b. The concentration ½ h after a ½ h infusion of 400 mg is 18 mg/L. The concentration 8 h after the start of the infusion is 1.1mg/L. What is the volume and clearance?

Slide 11

Problem 2 Question 4

4. Susan remained on a dose of 400 mg/day. She has another seizure and blood tests are repeated. Her albumin has fallen to 20g/L [normal 40g/L] and the phenytoin concentration is 5mg/L.
Why has the phenytoin concentration fallen? What changes should be made to her dose?