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West Midlands Training Course in Clinical Biochemistry

Course Assessment – Spring 2009

Short Answer Questions. **<u>Answer all questions</u>.**
Time allowed 1 hour.

1. Define prerenal failure **(2 marks)**
   Which of the following results are more likely to be associated with prerenal failure than acute renal failure? List all that apply.
   (8 marks)

   a) Urine sodium > 40 mmol/L
   b) Urine: Serum Urea >10:1
   c) Urine: Serum osmolality >1.5:1
   d) Urine osmolality >600 mmol/L

   Renal hypoperfusion and decreased GFR resulting from circulatory insufficiency. Tubular function is preserved and decreased GFR is reversible if adequate perfusion is rapidly restored
   Answer b, c & d

2. AFP has a physiological half life of 4.5 days in plasma. What plasma level would you expect 15 days after surgery for stage 1 teratoma, when the result 2 days post –operatively was 11.3 kU/L? **(10 marks)**

   Assuming a first order elimination of AFP then the relationship between the initial concentration(C_0) and the concentration (C) at time t can be described by the following formula: -

   $$\mathbf{C = C_0 \cdot e^{-kt}}$$

   Where k = the elimination constant

   C = the concentration of AFP @ time t

   C_0= the starting concentration

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To solve the problem *k* must be determined.

$$\frac{C}{C_0} = e^{-kt}$$

$t_{½}$ = 4.5 days

After one half life:

$$\frac{C}{C_0} = 0.5$$

So

$0.5 = e^{-(k.4.5)}$

ln 0.5 = -k.4.5

-0.693 = -k.4.5

k = 0.693/4.5

k = 0.154

Now calculate the AFP concentration at 15 days post-operation.

The concentration 2 days post-operatively can, for the purpose of the question, be taken as $\mathbf{C_0}$.

Therefore: -

C_0 = 11.3 kU/L

The sample was taken 15 days post-operatively and therefore: -

t = 15 – 2 = 13

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$C/11.3 \quad = e^{-(0.154 \times 13)}$

therefore:-

ln (C/11.3) = -2.002

C = 0.135 x 11.3 = 1.53 kU/L

Concentration of AFP at 15 days post op	1.53 kU/L

3. A patient was asked to collect urine over a 24 hour period. The volume was found to be 1800 mL and the concentration of creatinine in an aliquot of this urine 12.0 mmol/l. Calculate the 24 hour urinary excretion of creatinine in mmol. **(10 marks)**

Concentration = Amount/Volume

Therefore:

Amount = Concentration x Volume

Creatinine concentration = 12.0 mmol/L

24h urine volume = 1800 mL = 1.8 L

Creatinine Excretion = 12.0 x 1.8 = 21.6 mmol

24 hour urinary excretion of creatinine	21.6 mmol

.

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4. List five cellular consequences of hypoxia **(2 marks each)**

Cytosol

- Mitochondrial ATP synthesis fails
- Anaerobic glycolysis only ATP source
- Increased lactate and phosphate
- Intracellular pH falls
- Na & Ca rush in, K leaks out
- Cell swells

Nucleus

- Clumping and margination of chromatin
- Depressed RNA synthesis
- Reduced RNA polymerase activity

(Many different answers received – some of which have been deemed to be correct)

5. A laboratory using a method with an analytical coefficient of variation of 7% at a concentration of 120 mmol/L for a serum constituent examined samples from a healthy population and found a Gaussian distribution with a 95% reference range of 85-155 mmol/L. If the method coefficient of variation had been 18%, what reference range would the laboratory have found? **(10 marks)**

The total variation contributing to the reference range is composed of both biological variation and analytical imprecision. Their variances (i.e. their SDs squared) or CVs squared are additive.

Total SD

95% reference range = mean +/- 2SD.

155-85 = 4SD

17.5 = Total SD

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<u>Analytical SD</u>

$\%CV = SD_{anal} / mean * 100$

$SD_{anal} = (\%CV * mean)/100$

$SD_{anal} = (7 * 120)/100$

$SD_{anal} = 8.4$

<u>Biological SD</u>

$SD_{biol}^2 = SD_{total}^2 - SD_{anall}^2 = 306.3 – 70.6 = 236$
$SD_{bio} = \sqrt{236} = 15.4$

New analytical CV = 18%

$SD_{anal} = (\%CV * mean)/100$

$SD_{anal} = (18 * 120)/100$

$SD_{anal} = 21.6$

Substituting back in

$SD_{total}^2 = SD_{analnewl}^2 + SD_{biol}^2 = 467 + 236 = 703$

$SD_{newtotal} = \sqrt{703} = 26.6$

So reference range 67-173 mmol/L

67 – 173 mmol/L

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Reference Range

.

6. List five renal tubular disorders that may result in hypokalaemia **(2 marks each)**

Fanconi Syndromes (Wilson's disease, Dent's disease, Lowe's syndrome, Proximal renal tubular acidosis)
Distal Renal Tubular Acidosis
Bartter's syndrome
Gittleman's syndrome
Liddle's syndrome

7. Give the three tumour markers that **MUST** be measured if testicular cancer is suspected. **(3 marks)**

hCG
AFP
LDH

What biochemical test may be used to help distinguish men with prostatic cancer from those with benign prostatic hypertrophy when PSA is in the range 4-10 ug/L and digital rectal examination is negative? **(1 mark)**

% Free PSA

PSA may be raised in urinary tract infections: True or False **(1 mark)**

True

. Which of the following is **NOT** true?

a) CA125 levels in women increase with age
b) CA125 levels should not be measured during menstruation
c) CA125 levels may be mildly elevated in the first two trimesters of pregnancy **(1 mark)**

a)

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Give two conditions where CA125 concentrations > 1000 kU/L may be found in the absence of malignancy **(2 marks)**

Ascites
Heart Failure

There is an International Standard for CA125 measurement. True or False. **(1 mark)**

False

True or false: Smoking decreases CEA concentrations. **(1 mark)**

False

8. Calculate the osmolarity of a 5% mannitol solution in 0.9% saline. Mannitol has a molecular weight of 182 .

Assume for simplicity that sodium chloride is fully ionised.

Concentration of NaCl in 0.9% saline = 0.9g/100 mL = 9 g/L

Molar concentration of NaCl = 9/Mol Wt of NaCl = 9/58.5 = 0.154 M or 154 mmol/L

As NaCl ionises to Na^+ + Cl^-

The concentration of osmotically active species arising from NaCL = 154 x 2 = 308 mmol/L

Mannitol is not ionised.

Concentration = 5 g/100 mL = 50 g/L = 50/182 M = 0.275 M = 275 mmol/L

Osmolarity of 5% w/v mannitol in 0.9% w/v saline = 308 + 275 = 583 mmol/L

Osmolarity | 583 mmol/L

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9. The absorbance of a coloured solution is 1.8 in a 1cm cell at a concentration of 0.002M. For a more accurate measurement an absorbance of 0.50 is required. If the molecular weight of the coloured compound is 560, what weight of the compound should be used to prepare 50mL of the solution.

0.002 M solution has A= 1.8

Therefore by direct proportions
0.002 * 0.5/1.8 = 5.56×10^{-4} M required for an absorbance of 0.5

5.56×10^{-4} * 560 g/L = 0.311 g/L = 311 mg/L

Require 50 mL so 15.6 mg

Weight of compound | 15.6 mg |

10. You need to make up a phosphate buffer with a pH of 7.4 and a total phosphate concentration of 50 mmol/L. Calculate the amounts of sodium dihydrogen phosphate and disodium monohydrogen phosphate that need to be weighed into 1L of water, given that the pKa is 6.82 (atomic weight P = 31)

The relevant dissociation is:

$$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$$

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Henderson-Hasselbalch equation

$$pH = pKa + \log10 \frac{[HPO_4^{2-}]}{[H_2PO_4^-]}$$

$$7.4 = 6.82 + \log10 \frac{[HPO_4^{2-}]}{[H_2PO_4^-]}$$

$$\log10 \frac{[HPO_4^{2-}]}{[H_2PO_4^-]} = 7.4 – 6.82 = 0.58$$

$$\frac{[HPO_4^{2-}]}{[H_2PO_4^-]} = \text{antilog}_{10}\ 0.58 = 3.8$$

Total phosphate concentration = 50 mmol/L (=0.05 mol/L)

Therefore:

$[HPO_4^{2-}] + [H_2PO_4^-] = 0.05$ mol/L

Next express the concentration of one of the phosphate species in terms of the other

$[HPO_4^{2-}] = 0.05 - [H_2PO_4^-]$

$$\frac{0.05 - [H_2PO_4^-]}{[H_2PO_4^-]} = 3.80$$

$0.05 - [H_2PO_4^-] = 3.80.[H_2PO_4^-]$

$3.80.[H_2PO_4^-] + [H_2PO_4^-] = 0.05$

$4.80.[H_2PO_4^-] = 0.05$

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$[H_2PO_4^-]$ = 0.05/4.8 = 0.0104 mol/L

The concentration of the other phosphate species is obtained by subtraction

$[HPO_4^{2-}]$ = 0.05 - $[H_2PO_4^-]$ = 0.05 – 0.0104 = 0.0396 mol/L

The amount of each phosphate to be weighed out to prepare 1L of buffer is obtained by multiplication of each molar concentration by its molecular weight.

Concentration (g/L) = Concentration (mol/L) x Molecular weight

MW NaH_2PO_4 = 23 + (2x1) + 31 + (4x16) = 120

MW Na_2HPO_4 = (2 x23) + 1 +31 + (4x16) = 142

Weight of NaH_2PO_4 = 0.0104 x 120 = 1.248g

Weight of Na_2HPO_4 = 0.0396 x 142 = 5.623g

Weight of NaH_2PO_4	1.248g
Weight of Na_2HPO_4	5.623g

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