Sample Written Exam – Medical Biochemistry

Question 1

    a.   Describe how prostate-specific antigen (PSA) is distributed in plasma?

MODEL ANSWER (2 marks total)

- 89% is bound to a2-macroglobulin and a1-antichymotrypsin. Rest of PSA is in a free form.

    b.   List the cut-off values used clinically for PSA levels.

        List and briefly describe how PSA cut-off values are applied to clinical practice.

MODEL ANSWER (2 marks total)

- Normal < 4 ug/L
  Between 4 and 10 ug/L (or between 2 and 10 ug/L according to centre): to investigate benign prostate hyperplasia (BPH), etc.
  > 10 ug/L is suggestive of cancer.

    c.   How is the free PSA to total PSA ratio used to differentiate between malignant prostate cancer and benign prostathyperplasia?

MODEL ANSWER (2 marks total)

- While most of the PSA is protein-bound in the plasma of a healthy adult male, the protein-bound proportion is higher in the presence of prostate cancer. Therefore, the ratio of free PSA to total PSA (f/t) is decreased in the presence of a malignant prostate tumour and normal in the presence of benign conditions such as prostate hypertrophy (f/t > 25 ug/L in benign conditions).

Question 2

Hypercalcemia is a frequent clinical finding.

    a.   In an apparently healthy, asymptomatic individual, what would be the **MOST** likely cause of hypercalcemia?

MODEL ANSWER: (1 mark total)

- Primary hyperparathyroidism

b. In the following diseases, briefly describe the pathophysiologic mechanism(s) involved in the development of hypercalcemia.

    i. Oat cell tumour of the lung

MODEL ANSWER (2 marks total)

- Secretion of a "PTH-like" factor

    ii. Sarcoidosis

MODEL ANSWER (2 marks total)

- Endogenous extra-renal production of 1,25 dihydroxyvitamin D (1 hydroxylase activity in the granulomatous tissue)

    iii. Multiple myeloma

MODEL ANSWER (2 marks total)

- Local bone destruction, local production of cytokines

Question 3

a. Briefly explain the principle of immunoturbidimetric assay of a protein.

MODEL ANSWER (2 marks total)

- A polyclonal antibody is added with a buffer usually containing polyethylene glycol as precipitant. The antigen forms complexes with the antibody which absorb or scatter the light of the spectrophotometer. The angle of measurement relative to the incident light is 0 degrees.

b. Can a monoclonal antibody be used in immunoturbidimetry? Justify your answer.

MODEL ANSWER (2 marks total)

- In principle, no (unless the protein contains a repeated antigenic epitope), since it will at best form small complexes between one or two antigens and a single antibody molecule. There will be no formation of the large multimolecular complexes that cause the measured signal. In practice, the signal emitted by a monoclonal antibody is too weak to be of any use.

c. Briefly explain the hook effect in immunoturbidimetry.

MODEL ANSWER (2 marks total)

- A large excess of antigen can consume the antibody and limit formation of large immune complexes. Eventually, only free antigens and antigens bound to a single antibody will be found. Past a certain concentration threshold, the increase in antigen causes dissolution of the complexes and a decrease in the observed signal.

Question 4

List **FOUR** biochemical tests whose results could be potentially affected by **EACH** of the

a. Exercise

MODEL ANSWER (0.5 marks each, 2 marks total)

- CK, lactate, LD, AST, pH, urea

b. Recent food ingestion

MODEL ANSWER (0.5 marks each, 2 marks total)

- ALT, ALP, TG, LDL-C, glucose, uric acid

c. Pregnancy

MODEL ANSWER (0.5 marks each, 2 marks total)

- ALP, cholesterol, glucose, CK, albumin, Hb/Ht, creatinine

Question 5

a. Briefly describe the recommended method to determine the reference interval for an analyte.

MODEL ANSWER (4 marks total)

2 marks for preanalytical:

- Define selection criteria for reference population
- Partitioning criteria for sub-group analysis if applicable (age, gender, criteria for
- health/disease, pregnancy, obesity, etc.)
- Select random sample (or non-random representative sample) of individuals
- (minimum 40; recommended 120 for each group)
- Standardize preanalytical conditions (collection time, method, etc.)

2 marks for analytical / post-analytical:

- Standardize analytical conditions, analyze samples
- Statistical analysis: test need for partitioning, inspect distribution, remove outliers
- Non-parametric - select central 95% interval
- Parametric - test for Gaussian distribution, transform data if required, 2 SD limits

b. Give **ONE** example of an analyte for which a personal or subject-based reference interval may be more appropriate than a population-based reference interval. Explain your answer.

MODEL ANSWER (2 marks total)

- Creatinine, serum proteins, enzymes or other analytes not under tight hormonal
- control.
- Comparison to population reference interval lacks sensitivity for changes in
- biochemical status if intraindividual variation is less than 60% of interindividual
- variation. For such analytes, previous values in the individual make the best comparison.