
West Midlands Training Course in Clinical Biochemistry

Course Assessment – Spring 2010

1) Write short notes on **two** of the following:

a. B-type natriuretic peptide

1. B-type natriuretic peptide (BNP) belongs to a family of natriuretic peptides
2. BNP is coded on the short arm of human chromosome 1¹³.
3. Pre-pro BNP (134AA) is cleaved to proBNP of (108AA). Further cleavage on release produces an equimolar proportion of N-terminal pro BNP (NT-ProBNP;72AA) and active BNP (32AA).
4. The primary stimulus of BNP release is cardiac wall stretch.
5. BNP is an antagonist of the renin-angiotensin-aldosterone system and the sympathetic nervous system.
6. The direct natriuretic effects are two staged: a short-term increase in glomerular filtration rate coupled with antagonism of angiotensin II stimulated sodium reabsorption in the proximal tubule, and a longer term inhibition of sodium reabsorption in the collecting duct and within the thick ascending limb.
7. Commercial immunoassays on automated analyzers are now available for measurement of BNP and NT-proBNP. A point-of-care assay for BNP is also available
8. BNP and NT-proBNP increases with age and is higher in women.
9. The clinical utility of BNP and NT-proBNP is in delineating the failing heart.
10. BNP or NT- proBNP are used in the differential diagnosis of acute dyspnoea either in primary care or to triage patients in the emergency environment.
11. Rule out test: Their main clinical utility is that when normal (especially with normal ECG), in drug naive subjects, heart failure is virtually ruled out.
12. An elevated BNP or NT-proBNP cannot be used to diagnose heart failure because of many false positives. False positives include a high sodium diet, exercise prior to sampling, renal failure, myocardial infarction, acute coronary syndrome, pulmonary embolism, tachyarrhythmias.
13. The gold standard for diagnosing heart failure is echocardiography (ECHO).
14. Although a relatively expensive laboratory test, BNP and NT-proBNP are cheaper than ECHO
15. Elevated BNP or NT-proBNP have, therefore, been used a screening test for ECHO.
16. BNP/ NT-proBNP measurements may have a role in the objective monitoring of treatment for heart failure and as a prognostic indicator in acute coronary syndromes.

b. Lead poisoning

1. In the UK lead poisoning is due to occupational exposure in adults and pica in children.
2. Lead poisoning from Asian traditional remedies is rare but should be considered
3. GIT absorption, inhalation, skin absorption
4. Lead poisoning may present as acute medical emergencies in any age group
5. It commonly presents with peripheral muscle weakness, fatigue, confusion (encephalopathy), abdominal colic, constipation, and sometimes with diarrhoea and vomiting. Upper abdominal pain is said to indicate more acute exposure whilst lower abdominal pain a more chronic exposure to lead.
6. Lead interferes with the delivery of iron into the haem synthetic pathway. Two proposed mechanisms for this are, lead inhibition of ferroketolase, the enzyme responsible for incorporation of ferrous iron into protoporphyrin XI, or lead inhibition of ferrereductase, the enzyme responsible for reducing iron to the ferrous state, thus limiting its supply to ferroketolase. Both result in anaemia with an increase in porphyrins including protoporphyrin, which combines with zinc to form ZPP.
7. Laboratory investigations characteristically show increased concentrations of blood lead and ZPP, and anaemia with basophilic stippling.
8. ZPP remains in the erythrocyte for the life of the cell and acts as a sensitive marker for lead exposure at lead concentrations greater than 1.5 μ mol/L in adults.
9. Whole blood lead assayed by graphite furnace atomic absorption analysis and ZPP by haematoflurometer.
10. The presence of anaemia with or without basophil stippling almost invariably provides the clue to the diagnosis of lead toxicity in patients with abdominal pain.
11. The differential diagnosis of increased urine porphyrins and abdominal pain includes acute porphyria, cholestatic liver disease, and lead poisoning.
12. Treatment of lead poisoning is by eliminating exposure to lead, and in more severe poisoning chelation therapy with 2,3-dimercaptosuccinic acid or 2,3-dimercaptopropane sulphonate

c. Role of the laboratory in the assessment of CSF xanthochromia

1. Xanthochromia is the yellowish discolouration of CSF due to the presence of bilirubin
 2. SAH diagnosis is crucial to select patients for angiography and preventative surgery
 3. CT scan is positive in up to 98% of patients with SAH presenting within 12h and thereafter falls to <50% within 1 week
 4. Spectrophotometric detection of bilirubin in CSF is useful in confirming SAH.
 5. Visual inspection for xanthochromia is not acceptable
 6. Analysis is performed on undiluted samples by carrying out an absorption scan in the visible region in which both bilirubin (450-460nm; 476nm) and oxyhaemoglobin (410-418nm) absorb strongly.
 7. The presence of bilirubin (and methaemoglobin; 403-410nm) is more significant than that of oxyHb since bilirubin can only be formed in-vivo whereas oxyhaemoglobin may be the result of a traumatic tap.
 8. CSF from a SAH will typically show bilirubin and oxyHb
 9. LPs should only be performed if CT head scan is negative for SAH
 10. CSF should only be collected >12hours and <2weeks post event to avoid false negatives
 11. Order of draw of CSF: least blood-stained CSF sample taken (usually the last of 4 sequential samples) is sent for bilirubin analysis
 12. CSF Specimens should be protected from a) light (false negative) and b) not exposed to agitation eg pneumatic air tubes (false positives)
 13. Samples should be centrifuged on receipt in laboratory and stored in the dark at 4⁰c until analysis
 14. Blood sample should accompany CSF sample for serum bilirubin measurement
 15. Large quantities of oxyhaemoglobin may reduce the sensitivity of the method because a large oxyHb peak may obscure a small bilirubin peak
 16. False positive raised CSF bilirubin may be due to a) increased CSF protein and b) hyperbilirubinaemia. The latter should be corrected for using appropriate calculations.
 17. Interpretation using Revised national guidelines for analysis of CSF for bilirubin in suspected subarachnoid haemorrhage (2008)
 18. Use of automated computer programmes with interpretative software Vs ruler and pencil
 19. EQA
 20. Laboratory support in clinical decision making
-
-