PathMD™: Board Review Letter

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1. Which forms of the elements Arsenic (As) and Mercury (Hg) are considered to be the most toxic?

Answer is E) Inorganic arsenic species such as those found in groundwater are considered to be toxic while organic arsenic compounds as found in some foods are generally nontoxic. Elemental mercury is relatively nontoxic, although it can be biotransformed into more toxic organic compounds within the body. Organic mercury compounds such as methyl mercury accumulate in the food chain and result in high mercury concentrations in some animals such as predatory fish.

2. Which of the following are often associated with Wilson's disease?
   I. Elevated ceruloplasm levels.
   II. The Presence of Kayser-Fleisher rings
   III. The Presence of Mees' Lines
   IV. Increased Free Serum Copper
   V. Low Urine Serum copper

Answer is C) Wilson's disease is characterized by accumulation of excess copper. As copper is deposited in body stores total serum copper is of limited utility. Free serum copper is typically elevated, but observed ceruloplasm concentrations are typically normal to slightly lowered. Excess urine copper is indicative of excess body copper burden and is a good screen for Wilson Disease. Other manifestations of Wilson disease are the appearance of Kayser-Fleischer rings in the eyes and elevated copper in liver biopsy. Mees lines are typically associated with excess lead levels.

3. Which of the following elements are found predominately in erythrocytes while in circulation?

Answer is E): Circulating lead and cadmium are both found predominantly in erythrocytes. The majority of circulating copper is found in the serum as it is predominantly bound to the serum protein ceruloplasmin. Aluminum also readily binds serum proteins. The majority (>70%) of both cadmium and lead segregates in the erythrocytes.

4. Which set of elements are all considered to be essential trace elements?

Answer is C): The essential elements of which small amounts are needed to sustain normal function include: Iron, Manganese, Molybdenum, Nickel, Selenium, and Zinc. Non-essential toxic elements include: Arsenic, Cadmium, Cobalt, Lead, and Mercury. Iron is not considered as a trace element by some as it is present in relatively much higher concentrations than the other elements listed here.

5. What is the most appropriate sample type for diagnosing suspected acute arsenic exposure in the previous 3 days.

Answer D): The half life of arsenic in serum and whole blood is extremely brief with a half life of less than 6 hours as it readily incorporates into the rest of the body. However, arsenic in urine can be observed for up to three weeks following exposure. As Arsenic avidly binds sulfhydryl groups which is abundant in keratin hair and nails can also be used to investigate exposure. In some cases early exposure can be substantiated by hair samples taken from the nape of the neck. However, hair samples can often be contaminated by external sources.

The reference for answers 1-5 are The Tietz Textbook of Clinical Chemistry 4th Edition, Chapters 30 and 35; and the Textxtbook of Clincal Occupational and Enviromental Medicine 2nd Edition, Chapter 39.

6. Suppose a hypothetical serum marker "factor X" was discovered to be elevated in cases hepatocellular carcinoma (HCC). Two different plate-based ELISA tests for factor X were developed, test A and test B. Examine the ROC curve of the factor X concentration cutoffs (factor X concentration above which a sample is called positive), and determine the most effective test for the detection of HCC and the best "factor X" cutoff concentration. (See Image #1 on the website for this question set)

Answer is C). 85 mg/L using test B. Test B has higher sensitivity and specificity for most Factor X cutoffs. 85 mg/L gives a ~95% sensitivity with ~90% sensitivity, while 100 mg/dL yields ~98% sensitivity but only has 20% specificity.

7. Suppose a study was performed using a third assay for factor X on a group of 1500 individuals with elevated liver enzymes. The prevalence of HCC was 10% in this population. Of the patients with confirmed HCC, 120 were identified as positive by this assay. Unfortunately 150 patients who did not have HCC were also classified as positive by factor X testing. What is the sensitivity (%) of this test?

Answer C). Of the 1500 individuals 150 have HCC. Of these 120 are True Positive and 30 are False Negative. Of the 1350 people without HCC 150 were False Positive and 1200 were True Negative. Since Sensitivity is TP/(TP+FN) the sensitivity = 0.8 or 80%.

8. What is the specificity (%) of the test described in question 7.

Answer D): Of the 1500 individuals 150 have HCC. Of these 120 are True Positive and 30 are False Negative. Of the 1350 people without HCC 150 were False Positive and 1200 were True Negative. Since Specificity is TN/(TN+FP) the sensitivity = 0.888 or 89%.

9. What is the positive predictive value (%) of the test described in question 7.

Answer A): Of the 1500 individuals 150 have HCC. Of these 120 are True Positive and 30 are False Negative. Of the 1350 people without HCC, 150 were False Positive and 1200 were True Negative. Since Positive Predictive Value is TP/(TP+FP) the sensitivity = 0.444 or 44%.

10. If the same test were performed on an apparently healthy population with a HCC prevalence of 1.0% which of the following values would you expect to change.

Answer C): Prevalence affects the positive and negative predictive value but not the sensitivity or specificity of an assay. This can be proven by repeating the calculations in question 7-9 using the new prevalence.

For Questions 6-10 refer to The Tietz Textbook of Clinical Chemistry 4th Edition, Chapter 15.

