

Question 1: Inborn errors of creatin metabolism & transport
(13 points)

The cerebral creatine deficiency syndromes, inborn errors of creatine metabolism, include the two creatine biosynthesis disorders and the creatine transporter deficiency.

A) Which two enzymes are needed to synthesize creatine in the body? (2 points)

B) Is it possible to restore the creatine levels in the brain of a patient with a creatine transporter defect? Motivate your answer and include in your answer: type of treatment, experience in patients, rational based on the metabolic pathway. (4 points)

C) Is it possible to restore the creatine levels in the brain of patients with a creatine biosynthesis defect? Motivate your answer and include in your answer: type of treatment, experience in patients, rational based on the metabolic pathway. (4 points)

D) Which of these 3 types of creatine disorders is the best candidate to be included in the newborn heelprick screening? Please explain in not more than 5 lines why you came to this conclusion and include all tree disorders in your answer. (3points)

Question 2: What a doctor should know about clinical chemistry (7x 1 point)

What are important pre-analytic issues one needs to take into account when drawing blood for clinical analysis? Name 7.

**Question 3: Development of the mammalian immune system
(6 points/phase, total of 12 points)**

Lymph node development occurs in several phases.
Describe the first two phases of lymph node development. Include the different cells, chemokines and molecules that are involved in these processes.

Question 4: Effects of human milk on the immune system
(2x 5 points)

Beneficial effects of breastfeeding are well-recognized and include both immediate neonatal protection against pathogens and long-term protection against allergies and autoimmune diseases. Fucosylated glycans in human milk, such as those expressed in oligosaccharides or on glycoproteins, play an important role in protecting the infant against infectious agents. Nevertheless, the degree of protection from infectious disease in breastfed infants significantly varies between mothers. (2x 5 points)

A) Why does this level of protection vary between mothers (and their milk)?

B) Why is human milk far superior in its protection against infection compared to cow's milk or formula milk?

Question 5: Feeding and IGF-1
(3x 4 points)

Poor postnatal growth after preterm birth does not match with the normal rapid growth in utero and is associated with preterm morbidities. Insulin-like growth factor 1 (IGF-1) axis is the major hormonal mediator of growth in utero. IGF-1 action mainly occurs during the period of rapid rise in utero i.e. during the postmenstrual age of 22-40 weeks. After preterm birth levels of IGF-1 fall and remain often very low for weeks to months. This may result in a delay of growth and development during this extra uterine period corresponding in time with the third trimester of pregnancy. There have been many reports of correlations between low IGF-1 in preterm infants in the first weeks to months and complications of prematurity leading to serious morbidities.

Describe 3 morbidities of prematurity resembling developmental abnormalities in growth. (3x 4 points)

Question 6: Adrenocortical function in early life
(10 points)

A 9-day old male newborn has a positive heelprick screening for adrogenital syndrome. You are informed about this and decide to see the child the same day at the outpatient department for pediatrics.

A) What are the most important parameters you look at during the physical examination? Name 2 parameters. (2x 2 points)

B) Which are, according to the guidelines, the designated laboratory tests to order first? Name 3 (3x 2 points)

Question 7 was removed from the final exam

Question 8: Prematurity: cardiometabolic risk factors as child and adult
(4 points)

In children born after the hunger winter various long-term health effects have been described. As adults, some have mainly dyslipidemia and increased cardiovascular disease risk, whereas others have mainly glucose intolerance and type 2 diabetes.

Which factor explains the difference between the two groups?

Question 9: The severely ill child
(5 points)

The respiratory quotient is calculated as the ratio of VCO_2/VO_2 . Its value normally is found between 0.7 and 1.0. RQ is influenced by substrate use, eg carbohydrates and fats, but also by over- or underfeeding.

Would you expect RQ to be lowered or increased by underfeeding, e.g. there is insufficient substrate to be oxidized)? Explain your answer.