**Instruction:**
1. Please use pencil to shade the box for the best and correct answer (only one answer for each question).
2. Send back the answer sheet (see loose leaf page) to the Hong Kong College of Paediatricians. One point will be awarded to each article if ≥3 of the 5 answers are correct. The total score of the 4 articles will be 4 CME points.

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(A) **Clinical Utility of Second-tier Testing in Newborn Screening for Congenital Adrenal Hyperplasia: The Hong Kong Experience**

1. What methodology is adopted for first-tier newborn screening test of measuring 17-hydroxyprogesterone (17-OHP) levels in dried blood spots in Hong Kong?
   a. High performance liquid chromatography
   b. Inductively coupled plasma mass spectrometry
   c. Gas chromatography with flame ionization detector
   d. Next generation sequencing
   e. Immunoassay

2. Which of the following is NOT associated with elevated 17-hydroxyprogesterone (17-OHP) levels in newborn?
   a. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency
   b. Low birth weight
   c. Prematurity
   d. Congenital adrenal hyperplasia due to 11 beta-hydroxylase deficiency
   e. Antenatal use of exogenous corticosteroid to enhance fetal lung maturation

3. First-tier screening test of measuring 17-hydroxyprogesterone (17-OHP) levels in dried blood spots suffers from poor specificity. Which of the following strategies can BEST improve the positive predictive value of congenital adrenal hyperplasia screening?
   a. Second-tier test by steroid profiling using liquid chromatography-tandem mass spectrometry (LC-MS/MS)
   b. Ensure adequate feed before blood taking
   c. Blood taking in the morning
   d. Improvement in analytical specificity of antibodies employed in immunoassay
   e. Lower the screening cutoff values for 17-OHP

4. What analytes are currently being measured in second tier test of congenital adrenal hyperplasia in Hong Kong?
   a. 17-hydroxyprogesterone (17-OHP), 11-deoxycortisol and 21-deoxycortisol
   b. 17-hydroxyprogesterone (17-OHP), cortisol and androstenedione (4-AD)
   c. 17-hydroxyprogesterone (17-OHP), cortisol and dehydroepiandrosterone sulfate (DHEA-S)
   d. 17-hydroxypregnenolone, cortisol and androstenedione (4-AD)
   e. 17-hydroxypregnenolone, dehydroepiandrosterone sulfate (DHEA-S) and androstenedione (4-AD)

5. Which of the following statements is WRONG?
   a. False negative result can occur in both first- and second-tier test, and a negative newborn screening result does not rule out all possibility of CAH, even for severe classical salt wasting type.
   b. Incorporation of second tier test for CAH can reduce false positive rate and reduce unnecessary follow up testing, healthcare expenditures and worry of parents.
   c. For first tier testing for CAH, a universal cutoff of 17-hydroxyprogesterone (17-OHP) is adopted for both term and preterm newborns.
   d. Newborn screening tests for CAH are performed on dried blood spots samples collected from newborns.
   e. In Hong Kong, for neonates less than 34 weeks' gestation or birth weight less than 2,000 grams or requiring neonatal intensive care, a second dried blood spot sample will be collected on day 28 of life or at discharge whenever comes first.
(B) Ethical Issues of Dried Blood Spot Storage and Its Secondary Use After Newborn Screening Programme in Hong Kong

1. What is/are the benefit(s) of establishing a local-wide dried blood spot storage programme?
   a. To evaluate quality assurance and control of the newborn screening programme
   b. To enable early disease diagnosis and prevent child mortality
   c. To foster biomedical research and public health programme development
   d. To facilitate research to develop new technologies and new treatments
   e. All of the above

2. Which of the following is NOT of clinical and ethical concern in the dried blood spot storage and its secondary use?
   a. Data management and handling
   b. Approach to obtain informed consent
   c. Researcher's responsibility to return incidental findings
   d. Privacy
   e. None of the above

3. Which of the following(s) is/are the essence of informed consent procedures?
   a. Informedness
   b. Incentives
   c. Voluntariness
   d. (A) and (C)
   e. (A), (B), and (C)

4. What of the following is/are the best approach(es) to alleviating privacy and confidentiality concerns?
   a. Do not collect personally identifiable information at all
   b. Store personal identifier separately from the residual sample
   c. Apply a unique number to each sample
   d. (A) and (C)
   e. (B) and (C)

5. Which of the following is a true statement?
   a. DBS storage and its secondary use does not entail ethical concerns because it does not involve invasive procedures
   b. Obtaining parental consent is not mandatory as newborn screening is part of the standard of care
   c. Completely removing all personal identifiers from biospecimens is not an ideal approach to avoid privacy and confidentiality concerns in research involving residual DBS
   d. (A) and (C)
   e. (B) and (C)

(C) Evaluation of the 18-month "Pilot Study of Newborn Screening for Inborn Errors of Metabolism" in Hong Kong

1. Which type of specimen was taken from newborn babies for inborn errors of metabolism (IEM) screening?
   a. urine
   b. cord blood
   c. dried blood spots
   d. hair
   e. stool

2. In Phase II of the Pilot Study, which group of newborn babies needed to have more than one specimen tested?
   a. ≥34 weeks of gestation
   b. ≥34 weeks of gestation OR birth weight >2000 g
   c. ≥34 weeks of gestation AND birth weight >2000 g
   d. <34 weeks of gestation OR birth weight <2000 g OR being admitted to Neonatal Intensive Care Unit (NICU)
   e. <34 weeks of gestation AND birth weight <2000 g AND being admitted to Neonatal Intensive Care Unit (NICU)

3. Which of following condition or group of IEM disorders was NOT included in the Pilot Study?
   a. organic acid disorders
   b. lysosomal storage disorders
   c. fatty acid oxidation disorders
   d. congenital adrenal hyperplasia
   e. amino acid disorders
4. In the Pilot Study, what was the commonest IEM disorder picked up?
   a. Carnitine uptake deficiency (CUD)
   b. Phenylketonuria (not classic PKU) (Mild PKU)
   c. Citrullinaemia type II (CIT type II)
   d. Methylmalonic acidaemia (MMA)
   e. Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD)

2. Which of the following is a founder mutation in SLC22A5 (OCTN2) gene causing primary carnitine deficiency in Southern Chinese?
   a. R254X
   b. S467C
   c. F17Q
   d. P478X
   e. R169C

5. Which IEM condition was commented to be easily missed in the Pilot Study?
   a. Carnitine uptake deficiency (CUD)
   b. Phenylketonuria (not classic PKU) (Mild PKU)
   c. Citrullinaemia type II (CIT type II)
   d. Methylmalonic acidaemia (MMA)
   e. Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD)

3. Which of the following mutation is commonly associated with maternal carnitine uptake defect?
   a. R254X
   b. S467C
   c. F17X
   d. P478X
   e. R169C

4. Which of the following is the cellular location of carnitine transporter encoded by SLC22A5 gene?
   a. plasma membrane
   b. cytoplasm
   c. mitochondria
   d. nucleus
   e. peroxisome

5. Which of the following is NOT a feature in fatty acid oxidation defect?
   a. Hypoglycaemia
   b. Low ketone (hypoketotic)
   c. High ketone (ketosis)
   d. Negative for urine reducing substances
   e. High plasma ammonia

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**Answers of October issue 2019**

(A)  1. b; 2. e; 3. d; 4. a; 5. a
(B)  1. c; 2. d; 3. a; 4. e; 5. d
(C)  1. b; 2. a; 3. b; 4. d; 5. a
(D)  1. b; 2. e; 3. a; 4. e; 5. d