Questions for this month's clinical challenge are based on articles in this issue. The style and scope of questions is in keeping with the MCQ of the College Fellowship exam. The quiz is endorsed by the RACGP Quality Assurance and Continuing Professional Development Program and has been allocated 4 CPD points per issue. Answers to this clinical challenge will be published next month, and are available immediately following successful completion online at www.racgp.org.au/clinicalchallenge. Check clinical challenge online for this month's completion date. **Kath O'Connor**

SINGLE COMPLETION ITEMS

DIRECTIONS Each of the questions or incomplete statements below is followed by five suggested answers or completions. Select the most appropriate statement as your answer.

Case 1 – Xiu Xiu and Li Leen

Xiu Xiu and Li Leen are a recently married Malay Chinese couple from Kuala Lumpur. They present to you for a pre-pregnancy visit. They are concerned that a 'blood disorder' runs in the family on both sides.

Question 1

Which of the following is true regarding family history:

A. a family history is not necessary if it has been taken before
B. Xiu Xiu and Li Leen should be referred to a genetics clinic in the first instance
C. cause of death is not important
D. a family history cannot be taken because of privacy legislation
E. information from three generations on both sides of the family should be documented for both Xiu Xiu and Li Leen.

Question 2

You take a full family history and complete a pedigree. You find that 'low blood count', anaemia and pre-term delivery were common in Xiu Xiu's paternal family and Li Leen's maternal family. As Xiu Xiu and Li Leen come from Southeast Asia, you are concerned that this may indicate a family history of:

A. HbA
B. sickle cell anaemia
C. α-thalassaemia
D. ß-thalassaemia
E. protein C deficiency.

Question 3

Initial testing of both Xiu Xiu and Li Leen for the carrier state includes:

A. FBE, clotting studies and Hb electrophoresis
B. FBE, ferritin and Hb electrophoresis
C. FBE, factor V Leiden and prothrombin gene variant
D. MCH, MCV and ferritin
E. DNA testing for sickle cell trait.

Question 4

Both Xiu Xiu and Li Leen have a low MCV and MCH, a normal ferritin and a normal Hb electrophoresis. Which of the following is true:

A. the α-thalassaemia carrier state is excluded
B. Xiu Xiu and Li Leen require DNA testing and referral to specialist service
C. both Xiu Xiu and Li Leen are Fe deficient
D. both Xiu Xiu and Li Leen are at risk of haemachromatosis
E. Xiu Xiu and Li Leen require DNA testing for factor V Leiden and prothrombin gene variant and referral to specialist service.

Case 2 – Mark Donaldson

Mark Donaldson, 70 years of age, is a retired scientist with a recent history of depression. He has not responded well to two different antidepressants. He comes in with an internet web page print out which describes testing for variations in liver enzymes to inform antidepressant prescribing. He is interested in how these tests might apply to him now or in the future.

Question 5

Which of the following is true regarding single nucleotide polymorphisms (SNPs) in hepatic enzyme metabolism:

A. if Mark has not responded well to a low dose of antidepressant he is probably a slow metaboliser
B. ultra rapid metabolisers require lower doses
C. ultra rapid metabolisers are more likely to experience side effects at lower doses
D. testing may inform initial antidepressant drug dosing in the future
E. the cytochrome MDR1 system is implicated.

Question 6

You discuss with Mark the recent advances in pharmacogenomics regarding liver metabolism. He asks if it is possible to test for genetic differences in the brain. You explain that:

A. a genetic test for polymorphisms in blood brain barrier (BBB) transport mechanisms is already available
B. you can refer him for testing for serotonin transport gene polymorphisms
C. research has revealed polymorphisms in BBB transport and serotonin and noradrenaline regulation may be used in the future to target antidepressant dosing
D. the brain is the same in everyone and there is no explanation for differences in response to antidepressants
E. genetic differences in the brain are reflected in skull size.

Question 7

Mark is also on warfarin as he is in atrial fibrillation. When he first started the drug it took a long time to get him to therapeutic levels. He asks whether pharmacogenomics might explain this. Regarding warfarin metabolism:

A. polymorphisms of the platelet endoplasmic reticulum enzyme vitamin K reductase complex 1 (VKRC1) genotype modify dose requirements to obtain therapeutic anticoagulation
B. polymorphisms of liver enzyme genotypes including cytochrome p450 CYP2C9 and endoplasmic reticulum enzyme vitamin K reductase complex 1 (VKRC1) modify dose requirements to obtain therapeutic anticoagulation
C. polymorphisms of the BBB endoplasmic reticulum enzyme vitamin K reductase complex 1 (VKRC1) modify risk of intracerebral bleeding
D. polymorphisms of kidney enzyme genotypes including cytochrome p450 CYP2C9 and endoplasmic reticulum enzyme vitamin K reductase complex 1 (VKRC1) modify dose requirements to obtain therapeutic anticoagulation

E. pharmacogenomics cannot explain individual differences.

Question 8

Mark asks whether genotype testing will mean he will not need INR testing in the future. You explain that when genotype testing becomes available it is likely that:

A. he will still need INR testing because non-genomic factors (BMI, dietary vitamin K, comorbid disease and drug interactions) also influence warfarin dosing
B. he will no longer require INR testing
C. it will be preferred to INR testing as it will be more cost effective
D. he will still need INR testing because genomic factors influencing warfarin dosing may change over time
E. INR testing will become obsolete.

Case 3 – Anke Liebgen

Anke Liebgen, 35 years of age, presents with 6 weeks of amenorrhoea. Urine BHCG is positive. This is her first pregnancy. You arrange a long appointment for early pregnancy counselling.

Question 9

You discuss folate supplementation with Anke. She has no personal past history or family history of neural tube defects, is not diabetic and is not on any medication. Which of the following is true:

A. she does not need to take folate tablets
B. she should take 5 mg/day of folate
C. folate 400 µg/day is recommended
D. a diary rich diet will provide her with enough folate
E. she only needs to take folate if her MCV is high.

Question 10

You order early pregnancy tests. Which of the following can be considered a genetic screening test:

A. rubella immune status
B. MSU
C. dating scan
D. ferritin
E. FBE.

Question 11

You counsel Anke regarding screening for fetal chromosomal abnormalities. Which of the following is true:

A. second trimester screening will give a risk value for neural tube defects in addition to trisomy 18 and 21
B. first trimester screening involves a blood test for levels of α-fetoprotein, unconjugated oestradiol, free BHCG and inhibin A
C. nuchal translucency (NT) alone will pick up the same percentage of babies with trisomy 18 and 21 as combined testing with NT and blood level of pregnancy associated plasma protein (PAPP-A) and human chorionic gonadatropohin (free BHCG)
D. screening tests will identify all patients with Down syndrome
E. screening should only be offered if Anke would consider termination of the pregnancy.

Question 12

Anke decides to go ahead with first trimester screening. The results show a risk of trisomy 21 of one in 224 which is more than Anke's maternal age risk (one in 338). You discuss diagnostic testing. Which of the following is true:

A. amniocentesis has a higher risk of miscarriage than chorionic villus sampling (CVS)
B. amniocentesis can be performed at an earlier gestation than CVS
C. an 18 week ultrasound is the best diagnostic test for Down syndrome
D. amniocentesis is slightly more accurate than CVS
E. 18 week ultrasound scanning carries with it the same risk of miscarriage as CVS.

Case 4 – Sophie Liebgen

Anke Liebgen from Case 3 had a negative CVS and went on to have a normal vaginal delivery at 38 weeks gestation. She had a healthy baby girl named Sophie. Sophie is 48 hours old.

Question 13

You are working in the postnatal ward and a midwife asks you to counsel Anke regarding the newborn screening test. Anke asks what conditions are tested for. You tell her that the test will screen Sophie for:

A. Down syndrome, cystic fibrosis and primary congenital hypothyroidism
B. cystic fibrosis, hepatitis B, HIV, inborn errors of metabolism and primary congenital hypothyroidism
C. cystic fibrosis, inborn errors of metabolism and primary congenital hypothyroidism
D. Guthrie disease, inborn errors of metabolism and primary congenital hypothyroidism
E. fragile X syndrome, cystic fibrosis and inborn errors of metabolism.

Question 14

The newborn screening test meets the criteria for screening for a disorder because all diseases tested:

A. have a possible cure
B. may be treated at the onset of symptoms
C. may be treated before they are symptomatic with significant reduction in morbidity
D. are common
E. cause intellectual disability.

Question 15

Anke asks when she will get the results. You explain that:

A. negative results will not be sent to the GP
B. only negative results will be sent to the GP
C. she will be contacted only if there is a problem with the initial sample
D. she will be contacted only if she requires screening for other genetic disorders (eg. haemachromatosis and fragile X syndrome)
E. the sample will only be tested if Sophie has symptoms.

Question 16

Anke says that she has a condition called familial hypercholesterolaemia (FH). She asks whether Sophie should be screened for this condition. You explain that:

A. FH results from a new mutation so genetic testing is not required unless she is found to have high cholesterol
B. Sophie should be tested for an FH causing gene mutation
C. as FH is an autosomal recessive condition, Sophie only needs testing if her FH exists in her father's family
D. Sophie should have her cholesterol level tested urgently
E. treatment does not reduce morbidity or mortality so screening is not required.

ANSWERS TO SEPTEMBER CLINICAL CHALLENGE

Case 1 – Jane Hunt

1. Answer D
This is an example of delayed phase chemotherapy induced nausea and vomiting (CINV). CINV may be classified into acute phase (5–6 hours after treatment), delayed phase (up to 5 days after treatment) and anticipatory (any time after the first cycle). The oncologist is likely to have placed Jane on an antiemetic regimen to CINV but breakthrough symptoms may still occur.

2. Answer A
Chemotherapeutic drugs vary in their emetogenicity. Cyclophosphamide has a high emetogenetic potential particularly when combined with doxorubin or epirubicin. It commonly causes delayed phase nausea and vomiting.

3. Answer C
It is important to exclude other causes of vomiting with a history and examination before instituting rescue treatment for breakthrough CINV.

4. Answer A
Jane is mildly dehydrated so a trial of outpatient care is appropriate. She may need hospitalisation if outpatient treatment fails. It may be worth speaking to her oncologist to discuss management. As she is unable to take oral medication rectal prochlorperazine and sublingual lorazepam or ondansetron is appropriate as first line. This can be followed after 30 minutes with an increased dose of dexamethasone and other oral emetic treatment such as promethazine or metoclopramide.

Case 2 – Moira O'Donnell

5. Answer E
Nausea and vomiting of pregnancy is likely as the peak incidence of this condition is at 9 weeks gestation. Less than 2% of women experience nausea only in the morning. There is a temporal relationship with high HCG levels but causation has not been established.

6. Answer B
An abdominal X-ray is not indicated as she denies bowel symptoms and this would expose her to unnecessary radiation. A TSH is reasonable given her family history and an MSU to exclude infection should be considered given her dipstick findings. Urea and electrolytes will exclude metabolic consequences of nausea and vomiting and an LFT will exclude hepatitis.

7. Answer C
While there are no clinical trials on lifestyle advice for hyperemesis, it has been reported by women as helpful. Nibbling on dry biscuits frequently, especially before rising may help. Other suggestions include: avoiding an empty stomach, eating salty foods and eating and drinking small amounts often.

8. Answer D
First line treatment is pyridoxine plus an antiemetic medication such as metoclopramide and prochlorperazine.

Case 3 – Hiresh Chandra

9. Answer D
Diarrhoea may indicate viral gastroenteritis and as long as it is not profuse, blood stained or has resulted in dehydration may be treated as an outpatient in the absence of 'red flags' including abdominal tenderness and guarding, neck stiffness or photophobia, high fever, tachycardia or hypotension and projectile vomiting in babies (pyloric stenosis usually presents at 2–6 weeks of age).

10. Answer B and E
The following clinical signs may be found in the moderately dehydrated child (4–6%): restlessness, irritability, slow tissue turgor (1–2 seconds), cool peripheries, dry mucous membranes, sunken eyes and normal breathing BP and heart rate.

11. Answer C
Hiresh is moderately dehydrated and refusing fluids. An admission to hospital for rehydration (usually by nasogastric tube) is appropriate.

12. Answer B
If Hiresh weighs 15 kg then a 5% deficit is 750 mL. Over 6 hours this would be 125 mL/hr.

Case 4– Santo Benedetto

13. Answer D
The most common cause of acute nausea and vomiting in adults is viral gastroenteritis or bacterial food poisoning.

14. Answer C
Severe dehydration may prompt you to send Santo to hospital for an assessment and management of dehydration and the metabolic consequences of nausea and vomiting. A surgical opinion is recommended any indication of surgical intraabdominal pathology is found on examination (eg. sucussion splash, abdominal tenderness with guarding and rebound, an incarcerated inguinal hernia or tinkling bowel sounds).

15. Answer E
It is likely that Santo's symptoms are caused by the codeine he is taking in Panadeine Forte. As he is only mildly dehydrated he does not need further investigation at this stage for either diagnosis or assessment of metabolic consequences of nausea and vomiting.

16. Answer D
Finding an alternative to Panadeine Forte for pain management is vital as this addresses the likely cause of his symptoms. Oral rehydration is appropriate in this setting if tolerated. An antiemetic such as maxolon could be prescribed in case he has any residual nausea after ceasing codeine. If his symptoms are self limiting he does not require further investigation or referral.

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