國立成功大學 107 學年度碩士班招生考試試題

系　　所：醫學檢驗生物技術學系

考試科目：檢驗醫學　　考試日期：0206，節次：1

※ 考生請注意：本試題不可使用計算機。　請於答案卷(卡)作答，於本試題紙上作答者，不予計分。

一、簡答題 (共 50 分)

1. A 60-year-old woman had Roux-en-Y gastric bypass (RYGB)2 surgery 10 years previously for losing weight. She had a history of hypothyroidism, osteoarthritis, and esophageal ulcers. Eight months ago, she sustained bilateral pubic rami fractures. A few months later, she complained of worsening pelvic pain. At that time, a magnetic resonance image revealed sacral insufficiency fractures. Her laboratory data is shown in Table. After then, she was prescribed with 1200 mg of calcium citrate per day, but 50000 IUs of vitamin D (cholecalciferol) once weekly.

Test (reference interval)	Result
Serum calcium (8.6–10.4 mg/dL)	8.1
Parathyroid hormone (10–65 pg/mL)	175
25-OH vitamin D (30–100 ng/mL)	25
Alkaline phosphatase (33–130 IU/L)	182
24-h urine calcium (25–300 mg/day)	108

(A) What is the most likely diagnosis in this patient and please explain why? (5 points)

(B) What mechanisms explain the effects of bariatric surgery on skeletal health? (5 points)

(C) Her blood count data revealed a microcytic anemia, what other biochemistry testes should be subsequently followed? (3 points)

2. A 50-year-old man with a medical history significant for hypertension, depression, and primary biliary cirrhosis was admitted to the hospital. He complained of blurry vision, nausea, and significant pruritus. He declared no family history of hypercholesterolemia or premature heart disease. He was taking multiple medications and his physical exam was remarkable for scleral icterus and mild jaundice; no xanthomas were noted. Laboratory studies were performed.

Test	Value
Sodium, mmol/L (135-148)	121
Potassium, mmol/L (3.5-5.0)	3.0
Chloride, mmol/L (98-107)	87
Blood urea nitrogen, mg/dL (7-21)	16
Creatinine, mg/dL (0.51-0.95)	0.98
Glucose, mg/dL (60-100)	82
Aspartate aminotransferase, U/L (10-50)	150
Alanine aminotransferase, U/L (10-50)	122
Alkaline phosphatase, U/L (30-110)	525
Bilirubin (total), mg/dL (0.2-1.4)	10
Bile acids, μmol/L (<10)	>180
Albumin, g/dL (3.5-5.0)	2.6
Total protein, g/dL (6.4-8.3)	6.7
TC, mg/dL (< 200)	2156
LDL cholesterol, calculated, mg/dL (< 100)	—
HDL cholesterol, mg/dL (> 40)	37
Triglycerides, mg/dL (< 150)	226

The patient was found to have hyponatremia, along with hypokalemia and hypochloremia by using indirect ISE method. Her creatinine was slightly above normal limits but stable compared with past values. A liver profile test panel showed increased transaminases and alkaline phosphatase activity, hypoalbuminemia, significant hyperbilirubinemia, and evidence of cholestasis with increased bile acids in the blood.

(A) The sample was lack of lipemic appearance, thus the medical technologist diluted the sample and retested the lipid profile again. Similar results were obtained. Is this case reasonable? (4 points)

(B) Which experiment could the medical technologist use to further determine the possible cause of hypercholesterolemia? (4 points)

(C) What is the possible cause of the abnormal electrolyte panel? Does this patient should have intravenous fluids (0.9% sodium chloride) infusion? (4 points)

3. Please read this abstract and answer the following questions:

"Clear cell renal cell carcinomas (ccRCCs) frequently exhibit inactivation of the von Hippel–Lindau tumor-suppressor gene, *VHL*, and often harbor multiple copy-number alterations in genes that regulate cell cycle progression. We show here that modeling these genetic alterations by combined deletion of *Vhl*, *Trp53* and *Rb1* specifically in renal epithelial cells in mice caused ccRCC. These tumors arose from proximal tubule epithelial cells and shared molecular markers and mRNA expression profiles with human ccRCC. Exome sequencing revealed that mouse and human ccRCCs exhibit recurrent mutations in genes associated with the primary cilium, uncovering a mutational convergence on this organelle and implicating a subset of ccRCCs as genetic ciliopathies. Different mouse tumors responded differently to standard therapies for advanced human ccRCC, mimicking the range of clinical behaviors in the human disease. Inhibition of hypoxia-inducible factor (HIF)-α transcription factors with acriflavine as third-line therapy had therapeutic effects in some tumors, providing preclinical evidence for further investigation of HIF-α inhibition as a ccRCC treatment. This autochthonous mouse ccRCC model represents a tool to investigate the biology of ccRCC and to identify new treatment strategies."

(*Nature Medicine* **23**:869, 2017)

(A) Explain how tumor suppressor gene mutations contribute to human cancers. (3 points)

(B) Describe the experiments that the authors might have performed to complete this work. (6 points)

(C) Describe the impact of this study on the current knowledge. (2 points)

(D) Describe the diagnostic use of detecting tumor suppressor genes *Vhl*, *Trp53* and *Rb1* in ccRCC. Please include the principles and methods of the analysis. (8 points)

(E) According to this abstract, please describe the potential applications in therapeutic treatment of patients with ccRCCs. (4 points)

(F) Give a title to this abstract (in English). (2 points)

二、選擇題 (請選擇一個正確答案) (共 50 分)

For 1 and 2. Looking at the antigram below, answer the following questions:

	Rh-hr								Kell						Duffy	
Cell#	D	C	E	c	e	f*	C^w	V	K	k	Kp^a	Kp^b	Ls^a	Ls^b	Fy^a	Fy^b
1	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+
2	+	0	+	+	0	0	0	0	+	0	0	+	0	+	+	+

Kidd		Sex Linked	Lewis		MNS				P	Lutheran	
Jk^a	Jk^b	Xg	Le^a	Le^b	S	s	M	N	P_1	Lu^a	Lu^b
+	+	+	0	+	+	0	+	+	+S	0	+
0	+	0	+	0	+	+	+	0	+	0	+

1. The cell (s) that represents homozygous for k is: (3 分)
   A. cell 1
   B. cell 2
   C. cell 1 and cell 2
   D. None of above

2. An anti-s will react more strongly with: (3 分)
   A. cell 1
   B. cell 2
   C. cell 1 and cell 2
   D. None of above

3. Glycophorin A is associated with the antigen: (3 分)
   A. I
   B. N
   C. P
   D. S

4. A 16-year-old female was recently diagnosed with *Mycoplasma pneumonia*. She is now having a type and antibody screen for an upcoming surgery. The immediate spin antibody screen was positive in both cells. The antibody that one would expect to identify is: (3 分)
   A. anti-Le^a
   B. anti-Lu^a

C. anti-k
D. anti-l

5. 有關大交叉測試敘述下列何者是正確的? (3 分)
A. 2 滴受血者血清 +1 滴供血者血球
B. 2 滴供血者血清 +1 滴受血者血球
C. 1 滴受血者血清 +2 滴供血者血球
D. 1 滴供血者血清 +2 滴受血者血球

6. 目前台灣輸血作業中，最常見的不規則抗體是? (3 分)
A. Anti-D
B. Anti-Mi^a
C. Anti-M
D. Anti-K

7. O 型 Rh(-)、Kell(-)但是有 anti-D 的捐血者，若與 O 型 Rh(-)但是有 anti-Kell 的病人合血，其交叉試驗結果會是? (3 分)
A. 大、小交叉都不合
B. 大交叉不合、小交叉合
C. 大交叉合、小交叉不合
D. 大、小交叉都合

8. 下列對於新鮮冷凍血漿(FFP)和冷凍血漿(SFP)的敘述何者為真? (3 分)
A. SFP 所含之第八因子較少
B. FFP 可以用來補充蛋白質，但是 SFP 不可以
C. 冷凍保存時 SFP 存於-80 度 C，而 FFP 保存於-18 度 C
D. FFP 適合 anti-thrombin III 缺乏的病人，SFP 則不行

9. A 60 year-old man from Florida with a history of leukemia refractory to chemotherapy presented to his oncologist for pre-stem cell transplant evaluation. His clinical presentation was notable for fatigue, weakness and low grade fever. Upon evaluation, significant hemolytic anemia was noted which precluded moving forward with a bone marrow transplantation. His CBC was notable for low red blood cells, hemoglobin, hematocrit and platelets and a manual differential showed a normal absolute neutrophil count but lymphocytopenia. Work-up for non-infectious causes of his persistent anemia including the underlying cancer, drug toxicities or the presence of autoantibodies were all negative.

Which of the following pathogen is most likely responsible for this patient presentation? (5 分)
A. Babesia microti
B. Bocavirus

C. Parvovirus B19

D. Epstein-Barr virus

E. Cytomegalovirus

10. A 60 year-old man with a history of recurrent chronic lymphocytic leukemia (CLL) presented to the hospital in February for pre, hematopoietic stem cell transplant (HSCT) evaluation including hepatitis B virus serologies and PCR (see table). Due to recurrent, multiple respiratory tract infections, additional work-up was done prior to the transplant. Patient was diagnosed with hypogammaglobulinemia and started on monthly intravenous immunoglobulin (IVIG) treatment and the HSCT transplant rescheduled for March. Repeat serologies are shown below. You get a call from the transplant physician who is considering delaying the transplant again and starting Entacavir but she would like to confirm her interpretation of the recent serologies.

Marker	February	March
HBV surface Antigen	Non reactive	Non reactive
HBV surface Antibody	Non reactive	Reactive
HBV core Antibody (Total)	Non reactive	Reactive
HBV core Antibody IgM	Non reactive	Non reactive
HBV DNA	Not detected	Not detected

What is the most likely interpretation? (5 分)

A. Resolved or past HBV infection

B. Occult HBV infection

C. Immunity through vaccination

D. Passive immunization

E. False positive results; neutralization assay required to confirm

11. A 33-year-old male from New York City, previously diagnosed with diffuse large cell lymphoma (DLBCL) and in early August completed 3 cycles of rituximab, a B-cell inhibitor, for treatment of his lymphoma.He presented at the end of August to his dermatologist with a diffuse, non-pruritic rash. In early September, he developed a 39.2°C fever and severe right eye pain. He was admitted to the hospital for treatment of fever and neutropenia with broad-spectrum antibiotic therapy.Additional history revealed that he travels to Long Island on the weekends where he spends a lot of time outdoors.Over the next week, he developed lethargy and involuntary jerking movements of the extremities and was treated with acyclovir for the treatment of presumptive encephalitis and meningitis. The patient subsequently had progressive neurologic deficits including slurred speech, hallucinations, and nystagmus eventually requiring intubation and transfer to the intensive care unit.The infectious disease team strongly suspects the patient has West Nile Virus (WNV).

What is the best test for the diagnosis of this patient? (5分)

A. WNV IgM from serum followed by confirmatory plaque-reduction neutralization test
B. WNV IgM from CSF followed by confirmatory plaque-reduction neutralization test from serum sample
C. WNV RT-PCR from serum and/or CSF
D. Viral culture from CSF
E. WNV immunohistochemistry on brain biopsy

12. A 25 year old woman in her first trimester of pregnancy presents for a checkup with her obstetrician. Three weeks ago she returned from a vacation to Puerto Rico. A few days before leaving Puerto Rico she developed an acute febrile illness, accompanied with muscle aches, rash and joint pain. Her doctor suspects possible Zika virus infection and orders a Zika IgM Antibody Capture Enzyme-Linked Immunosorbent Assay (Zika MAC-ELISA) test on the patient's serum. The test results come back two days later as being equivocal for the presence of Zika virus antibodies. Further testing is performed by rRT-PCR (real-time reverse transcription-polymerase chain reaction) for the presence of Zika virus RNA on serum and urine samples. The result is negative.

Which of the following scenarios appear to be most plausible and what might be the next step? (5 分)

A. The patient may still have Zika virus infection; plaque reduction neutralization test (PRNT) should be performed to confirm the presence of anti-Zika antibodies.
B. The negative rRT–PCR rules out Zika virus infection in this patient; no further testing is indicated
C. Amniocentesis should be done and rRT-PCR for Zika virus should be performed on the amniotic fluid specimen urgently.
D. Testing for Dengue virus and Chikungunya virus might be indicated.
E. A and C
F. A and D

13. A 21-year-old male college student from west-central Indiana presented to the emergency department of his local hospital with a 2-day history of severe headaches, fever, neck pain, nausea, and vomiting. The patient disclosed that the pain in his neck was so intense that he has been unable to sleep since his symptoms appeared. The patient denied having delirium, hallucinations, and seizures, but mentioned that he was mildly sensitive to light. A physical examination was largely unrevealing and a review of his past medical history was unremarkable. In addition, he denied recent travel outside of the local community, animal exposures, and illicit substance abuse, but he mentioned that he had 1-2 alcoholic drinks per week

since his 21st birthday several months ago.

Fearing that the patient had meningitis, the clinician performed a lumbar puncture and routine hematological and biochemical blood tests. The patient was simultaneously started on a regimen of ceftriaxone and acyclovir. Blood tests revealed a mild lymphocytopenia, but all other parameters were within normal limits. The cerebrospinal fluid (CSF) sample was clear and colorless, but it contained 816 total nucleated cells/ml; 65% of the cells were lymphocytes, and the remaining 35% were monocytes/macrophages. The CSF glucose and protein were 63 mg/dl (normal, 40 – 70 mg/dl) and 71 mg/dl (normal, 15 – 45 mg/dl), respectively. A number of viruses, including enteroviruses, herpes simplex viruses, and varicella-zoster virus, were not detected by nucleic acid amplification tests. Because he had diagnosed numerous cases of mumps in the college community by clinical evaluation and laboratory testing within the recent months, the physician was curious if the patient was suffering from mumps meningitis, so he ordered a viral culture of the CSF in an attempt to detect this pathogen.

Which of the following statements is true regarding detection of mumps virus in CSF specimens? (6分)

A. Mumps virus antigen detection using a commercially-available lateral-flow assay should be performed on an aliquot of the CSF specimen.
B. Viral culture is not recommended, as mumps virus is classified as a risk group-3 pathogen that requires biosafety level-3 work practices and containment measures.
C. Direct fluorescent antibody testing for demonstration of mumps virus antigens in the CSF specimen using an FDA-approved test is the most widely available method.
D. Viral culture can be performed using standard biosafety level-2 practices, but mumps virus may take from 4 – 8 days to be detected.
E. Mumps virus does not cause meningitis, so any attempts to detect it in this patient's CSF should be.