(*University of Choice*)

MASINDE MULIRO UNIVERSITY OF SCIENCE AND TECHNOLOGY (MMUST)

MAIN CAMPUS

UNIVERSITY EXAMINATIONS
2019/2020 ACADEMIC YEAR

THIRD YEAR SECOND TRIMESTER EXAMINATIONS

FOR THE DEGREE OF BACHELOR OF SCIENCE MEDICAL BIOTECHNOLOGY MAIN EXAM

COURSE CODE: BMB 321

COURSE TITLE: MEDICAL GENETICS

DATE: 7th December 2020 **TIME:** 8.00 -10.00 am

INSTRUCTIONS TO CANDIDATES

This paper is divided into three sections, **A B** and **C,** carrying respectively: Multiple Choice Questions (**MCQs**), Short Answer Questions (**SAQs**) and Long Answer Questions (**LAQs**).

TIME: 2 Hours

MMUST observes ZERO tolerance to examination cheating

This Paper Consists of 5 Printed Pages. Please Turn Over.

SECTION A: MULTIPLE CHOICE QUESTIONS (20 MARKS)

1. A 25-year-old woman has mild expression of haemophilia A. A genetic diagnosis reveals that she is a heterozygous carrier of a mutation in the X-linked factor VIII gene. What is the most likely explanation for mild expression of the disease in this individual?
A. A high proportion of the X chromosomes carrying the mutation are active in this woman
B. Her father is affected, and her mother is a heterozygous carrier
C. Nonsense mutation causing truncated protein
D. One of her X chromosomes carries the SRY gene

2. A large, three-generation family in whom multiple members are affected with a rare, undiagnosed disease is being studied. Affected males never produce affected children but affected females do produce affected children of both sexes when they mate with unaffected males. What is the most likely mode of inheritance?
A. Autosomal dominant, with expression limited to females
B. Y-linked
C. Mitochondrial
D. X-linked dominant

3. The severe form of alpha-1 antitrypsin deficiency is the result of a single nucleotide substitution that produces a single amino acid substitution. This is best described as a
A. Frameshift mutation
B. In-frame mutation
C. Missense mutation
D. Nonsense mutation

4. In assessing a patient with osteogenesis imperfecta, a history of bone fractures, as well as blue sclerae, are noted. These findings are an example of
A. Allelic heterogeneity
B. Locus heterogeneity
C. Multiple mutations
D. Pleiotropy

5. A man and woman are both affected by an autosomal dominant disorder that has 80% penetrance. They are both heterozygotes for the disease-causing mutation. What is the probability that they will produce phenotypically normal offspring?
A. 20%
B. 25%
C. 40%
D. 60%

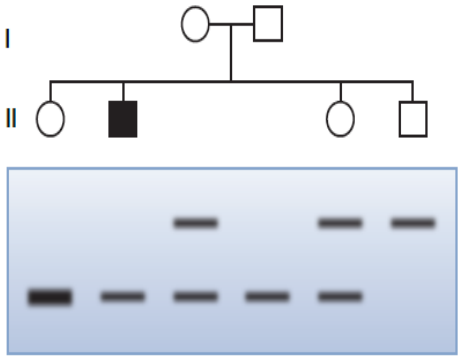
6. A 26-year-old woman has produced two children with Down syndrome, and she has also had two miscarriages. Which of the following would be the best explanation?
A Her first cousin has Down syndrome.
B Her husband is 62 years old.
C She carries a reciprocal translocation involving chromosomes 14 and 18.
D She carries a Robertsonian translocation involving chromosomes 14 and 21.

7. A 6-year-old boy has a family history of mental retardation and has developmental delay and some unusual facial features. He is being evaluated for possible fragile X syndrome. Which of the following would be most useful in helping establish the diagnosis?
A Genetic test for a trinucleotide repeat expansion in the fragile X gene
B IQ test
C Karyotype of the child's chromosomes
D Karyotype of the father's chromosomes

8. 38-year-old woman in her 15th week of pregnancy undergoes ultrasonography that reveals an increased area of nuchal transparency. Amniocentesis is recommended and performed at 16 weeks' gestation. The amniotic karyotype is 46, XYadd (18) (p.11.2), indicating additional chromosomal material on the short arm of one chromosome 18 at band 11.2. All other chromosomes are normal. What is the most likely cause of this foetal karyotype?
A A balanced reciprocal translocation in one of the parents
B A balanced Robertsonian translocation in one of the parents
C An isochromosome 18i(p) in one of the parents
D Nondisjunction during meiosis 1 in one of the parents

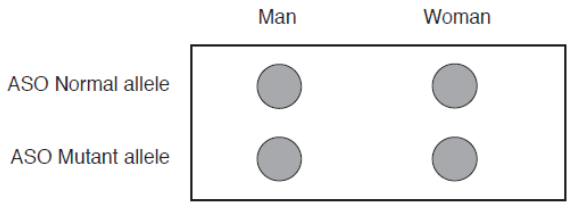
9. A man who has alkaptonuria marries a woman who has hereditary sucrose intolerance. Both are autosomal recessive diseases and both map to 3q with a distance of 10 cM separating the two loci. What is the chance they will have a child with alkaptonuria and sucrose intolerance?
A 0%
B 25%
C 50%
D 100%

10. The pedigree below shows a family in which haemophilia A, an X-linked disorder, is segregating. PCR products for each member of the family are also shown for a short tandem repeat polymorphism located within an intron of the factor VIII gene. What is the best explanation for the phenotype of individual II-1?



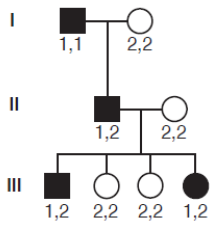
A Heterozygous for the disease-producing allele
B Homozygous for the disease-producing allele
C Homozygous for the normal allele
D Incomplete penetrance

11. Two phenotypically normal second cousins marry and would like to have a child. They are aware that one ancestor (great-grandfather) had PKU and are concerned about having an affected offspring. They request ASO testing and get the following results. What is the probability that their child will be affected?



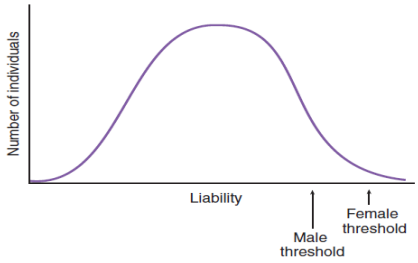
A 1.0
B 0.25
C 0.67
D 0.50

12. A family with an autosomal dominant disorder is typed for a 2-allele marker, which is closely linked to the disease locus. Based on the individuals in Generation III, what is the recombination rate between the disease locus and the marker locus?



A 0
B 0.25
C 0.50
D 1.0

13. Pyloric stenosis is five times more common in males than in females in certain Japanese populations. The liability curve for the development of this condition in that population is shown below: Within this population, which of the following is most at risk for the development of disease?



A. The daughters of affected fathers
B. The daughters of affected mothers
C. The sons of affected fathers
D. The sons of affected mothers

14. In studying a large number of families with a small deletion in a specific chromosome region, it is noted that the disease phenotype is distinctly different when the deletion is inherited from the mother as opposed to the father. What is the most likely explanation?
A. Imprinting
B. Mitochondrial inheritance
C. Sex-dependent penetrance
D. X-linked dominant inheritance

15. Waardenburg syndrome is an autosomal dominant disorder in which patients may exhibit a variety of clinical features, including patches of prematurely grey hair, white eyelashes, a broad nasal root, and moderate to severe hearing impairment. Occasionally, affected individuals display two eyes of different colours and a cleft lip and/or palate. Patients who possess a mutation in the *PAX3* gene on chromosome 2 can present with all of these disparate signs and symptoms. Which of the following characteristics of genetic traits is illustrated by this example?

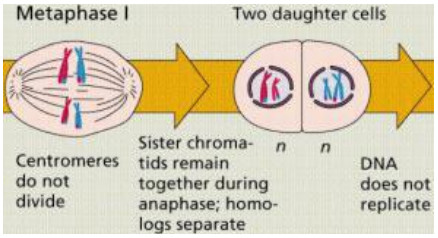
A. Anticipation
B. Pleiotropy
C. Incomplete penetrance
D. Locus heterogeneity

16. Endonuclease activation and chromatin fragmentation are characteristic features of eukaryotic cell death by apoptosis. Which of the following chromosome structures would most likely be degraded first in an apoptotic cell?
A. Barr body
B. 10-nm fiber
C. 30-nm fiber
D. Centromere

17. The cells that have no nucleus are known as:
A. Eukaryotic cells
B. Proliferative cells

C. Prokaryotic cells
D. Animalcules

18. Study the following illustration of a cell division stage where the chromosomes have gathered at the equator and answer the question to follow: In which organ of the human body did this process take place?



A. Liver
B. Spleen
C. Ovarium
D. Bone marrow

Question 19 and 20
A. ATGCAA…→ ATGTAA
B. ATGAAA…→ GTGAAA
C. TATAAG…→ TCTAAG
D. CTTAAG…→ GTTAAG
The options above represent mutations in the DNA with base changes indicated in boldface type. For each mutation described in the questions below, choose the most closely related sequence change in the options above.
19. Nonsense mutation.
20. Mutation decreasing the initiation of transcription.

SECTION B: SHORT ANSWER QUESTIONS (40 MARKS)

1. Describe major types of single-gene mutations. [8 Marks]
2. a) List any four autosomal dominant diseases. [4 Marks]
   b) Briefly describe autosomal recessive inheritance. [4 Marks]
3. a) Describe chromosomal nomenclature. [4 marks]
   b) Briefly describe X-inactivation. [4 Marks]
4. Discuss briefly advances in molecular cytogenetics. [8 Marks]
5. Describe how recurrent risks for multifactorial diseases is assessed. [8 Marks]

SECTION C: LONG ANSWER QUESTIONS (40 MARKS)

1. a) Give a detailed account of recombination frequencies and gene mapping. [10 Marks]
   b) What are the applications of genetic diagnosis? [10 Marks]

2. Compare and contrast X-linked recessive and dominant inheritance giving examples in each case. [20 Marks]

3. Discuss chromosomal structural aberrations and their implication in genetic diseases. [20 Marks]