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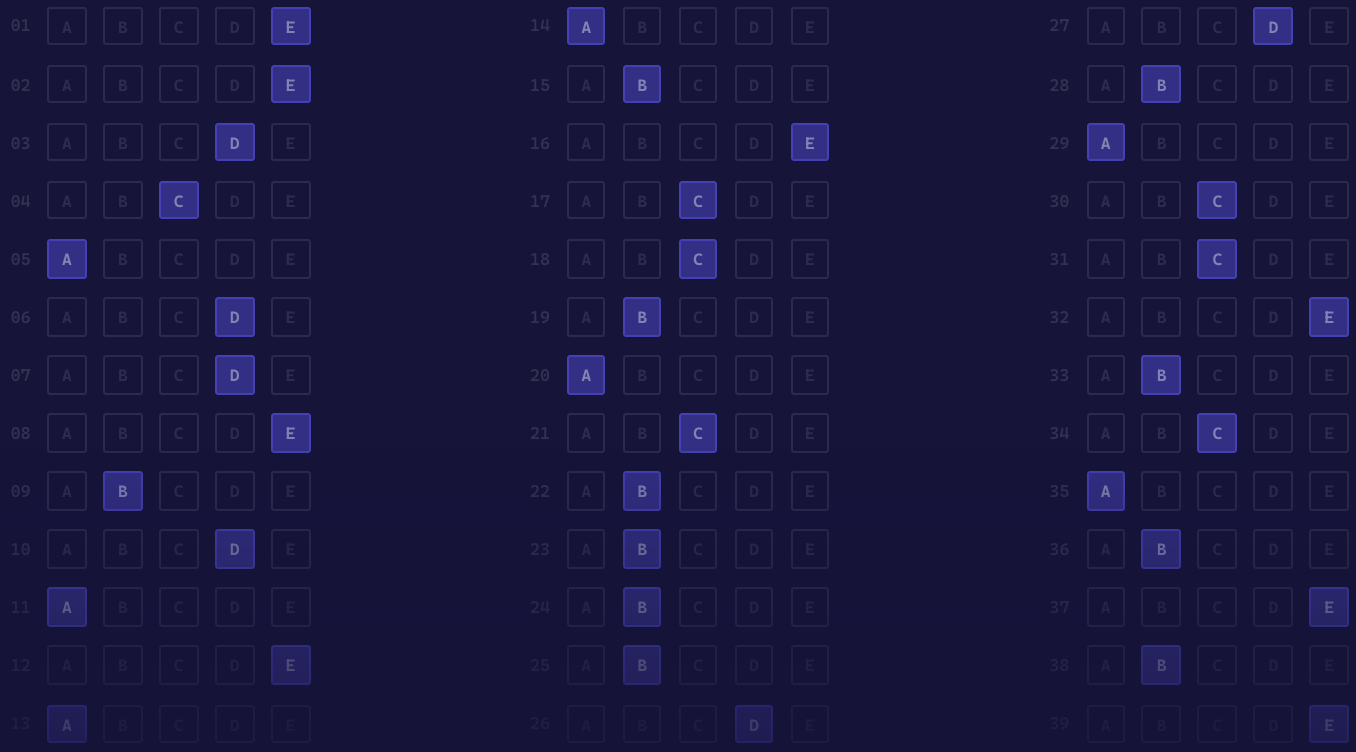

PRACTICE QUESTIONS

American Board of Medical Genetics And Genomics (ABMGG)

MG–CG

Clinical Genetics & Genomics Exam

EDITION	QUESTIONS	FORMAT
Demo	9	Limited Edition PDF

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Before you begin

What this is

9 practice questions for American Board of Medical Genetics And Genomics (ABMGG) `MG-CG`, each with its answer key and an explanation. Answer a question before you read its key — the explanation is worth more once you have committed.

If something looks wrong

Send us three things and we will check it:

- the exam code, `MG-CG`
- the question number
- the email address on your order

Write to **support@mometrix.net**. We reply within one business day.

QUESTION 1 MULTIPLE CHOICE

A couple presents for genetic counseling. The partner has achondroplasia (autosomal dominant, FGFR3), and the partner does not. Both have unaffected parents and no family history. Which of the following recurrence risks apply for their offspring? (Choose two.)

A **50% risk of achondroplasia**

B **25% risk of homozygous achondroplasia, which is typically lethal in the perinatal period**

C 50% risk of homozygous achondroplasia

D 25% risk of heterozygous achondroplasia

ANSWER **A** · **B**

WHY Because both parents are unaffected with achondroplasia yet one has it (due to a de novo or heterozygous parental mutation ~80% de novo rate), the affected parent is heterozygous. Each child therefore has a 50% risk of inheriting the FGFR3 allele (heterozygous achondroplasia) and a separate, independent probability of inheriting two copies (homozygous achondroplasia), which is essentially lethal perinatally due to respiratory failure from a small thoracic cage. The de novo origin of the parental mutation does not change these Mendelian probabilities.

QUESTION 2 MULTIPLE CHOICE

Which of the following karyotype findings are consistent with a balanced structural rearrangement that is typically not associated with an abnormal phenotype? (Choose two.)

A 46,XX,t(11;22)(q23;q11.2)

B 46,XY,inv(9)(p11q13)

C 45,XX,der(14;21)(q10;q10)

D 46,XY,rob(13;14)(q10;q10)

ANSWER B · D

WHY Pericentric inversion of chromosome 9, inv(9)(p11q13), is a common, well-recognized benign variant with no clinical consequence. Robertsonian translocations between acrocentric chromosomes (e.g., rob(13;14)) are also frequently balanced carriers without phenotype, although they confer risk for unbalanced offspring (trisomy 13 or 14). In contrast, t(11;22)(q23;q11.2) is a recurrent reciprocal translocation associated with a high risk of unbalanced offspring (Emanuel syndrome) and 45,der(14;21)(q10;q10) is a clinically significant Robertsonian translocation associated with recurrent pregnancy loss and risk of trisomy 21 offspring.

QUESTION 3 TRUE FALSE

Anticipation, defined as earlier age of onset and/or increased severity in successive generations, is a hallmark feature of trinucleotide repeat expansion disorders such as Huntington disease, myotonic dystrophy, and fragile X syndrome.

A True

B False

ANSWER A

WHY True. Anticipation is a classic feature of trinucleotide repeat expansion disorders, attributable to intergenerational instability and expansion of the repeat tract during gametogenesis. It is observed in Huntington disease (CAG), myotonic dystrophy type 1 (CTG in DMPK), and fragile X syndrome (CGG in FMR1), among others. Note that the molecular basis and parental origin of expansion differ among these conditions (e.g., congenital myotonic dystrophy type 1 is associated with very large expansions transmitted by the mother).

QUESTION 4 SINGLE CHOICE

A newborn with an elevated C5-OH acylcarnitine on dried blood spot screening most likely has which of the following conditions?

A **Phenylketonuria**

B Maple syrup urine disease

C 3-Methylcrotonyl-CoA carboxylase deficiency

D Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

ANSWER **A**

WHY C5-OH (3-hydroxypalmitoylcarnitine / hydroxy-C5 acylcarnitine) is elevated in holocarboxylase synthetase deficiency and biotinidase deficiency, and historically the C5-OH marker is associated with 3-methylcrotonyl-CoA carboxylase (3-MCC) deficiency on newborn screening. Phenylketonuria is detected by elevated phenylalanine. Maple syrup urine disease is detected by elevated leucine and the leucine/isoleucine ratio. MCAD deficiency is detected by elevated C8 (octanoylcarnitine). Therefore the C5-OH elevation is most consistent with 3-MCC deficiency.

QUESTION 5 SINGLE CHOICE

A 35-year-old woman with a strong family history of breast and ovarian cancer is found to carry a pathogenic BRCA1 frameshift variant. What is the recommended breast cancer risk-reducing management based on NCCN-style hereditary breast/ovarian cancer syndrome guidelines?

A Begin annual mammography starting at age 25

B **Begin annual breast MRI starting at age 25 and add annual mammography starting at age 30**

C Begin combined annual breast MRI and mammography starting at age 40

D No imaging is recommended until age 50

ANSWER **B**

WHY For women with BRCA1 pathogenic variants, annual breast MRI is recommended starting at age 25, with the addition of annual mammography at age 30. This is because BRCA1-associated tumors more often lack calcifications and are harder to detect by mammography alone in younger women, and mammographic sensitivity is reduced in dense breast tissue. Risk-reducing bilateral salpingo-oophorectomy is also recommended, typically between ages 35–40.

QUESTION 6 SINGLE CHOICE

A child presents with seizures, developmental delay, and a distinctive 'happy puppet' phenotype with ataxic gait and inappropriate laughter. Methylation-specific MLPA testing of the 15q11-q13 region demonstrates a maternal deletion. What is the diagnosis?

A Prader-Willi syndrome

B Angelman syndrome

C Fragile X syndrome

D Rett syndrome

ANSWER B

WHY Angelman syndrome is caused by loss of the maternally expressed UBE3A allele on 15q11-q13. Mechanisms include maternal deletion (most common, ~70%), paternal uniparental disomy, imprinting defects, and UBE3A mutations. The classic features include severe intellectual disability, ataxia, seizures, and a happy affect with frequent laughter. Prader-Willi syndrome results from loss of the paternally expressed genes in the same region and presents with neonatal hypotonia, hyperphagia, obesity, and hypogonadism. Rett syndrome is caused by MECP2 mutations and is almost exclusively seen in females.

QUESTION 7 SINGLE CHOICE

A 25-year-old tall, thin man with ectopia lentis, pectus carinatum, joint hypermobility, and a family history of aortic dissection is suspected to have Marfan syndrome. Which of the following is most consistent with the diagnosis on FBN1 molecular testing?

A **A pathogenic missense variant affecting a cysteine residue in an EGF-like domain of fibrillin-1**

B A large deletion of the entire COL3A1 gene

C A repeat expansion in the DMPK gene

D A pathogenic variant in the FBN1 3' untranslated region only

ANSWER **A**

WHY Marfan syndrome is caused by FBN1 mutations, the majority of which are missense variants substituting or creating cysteine residues within EGF-like (cb-EGF) domains of fibrillin-1, disrupting disulfide bonding and calcium binding. COL3A1 mutations cause vascular Ehlers-Danlos syndrome. DMPK repeat expansions cause myotonic dystrophy type 1. Variants limited to the 3' UTR of FBN1 are not a recognized major molecular mechanism.

QUESTION 8 SINGLE CHOICE

Which of the following best describes a limitation of whole-exome sequencing (WES) compared with chromosomal microarray analysis (CMA)?

A WES cannot detect single nucleotide variants

B **WES has limited ability to detect copy number variants and is insensitive to intronic variants outside canonical splice sites**

C WES cannot detect variants in mitochondrial DNA

D WES detects only variants in coding regions and misses all splicing variants

ANSWER **B**

WHY WES targets the coding regions of known genes and is therefore insensitive to deep intronic variants and most regulatory non-coding variation. While WES can detect some copy number variants (especially with exon-level read depth analysis), its sensitivity is much lower than CMA, which is specifically designed to detect microdeletions and microduplications genome-wide. WES also typically does not include the mitochondrial genome. WES does, however, detect SNVs and indels in coding regions, including canonical splice sites.

QUESTION 9 SINGLE CHOICE

A patient with acute lymphoblastic leukemia is found to be homozygous for TPMT*3A. What is the most appropriate dose adjustment for 6-mercaptopurine (6-MP)?

A Standard dose

B Double the standard dose

C **Significantly reduced dose (approximately 10% of standard) or alternative agent**

D Discontinue 6-MP permanently regardless of clinical need

ANSWER **C**

WHY Patients who are homozygous for nonfunctional TPMT alleles (including TPMT*3A, *3B, *3C, *2) have very high risk of severe and potentially fatal myelosuppression when given standard doses of 6-mercaptopurine or azathioprine. CPIC guidelines recommend either using a much-reduced dose (typically ~10% of the standard dose, with subsequent titration based on tolerance) or selecting an alternative agent. Complete discontinuation is not necessarily required if the drug is essential for therapy.