

6.6 Genetic testing and counselling

Name: _____ Class: _____ Date: _____ **Total: 23 marks**

KEY WORDS fluorescence in situ hybridization

Objective

Choose the right test for the question and counsel cascade results.

1 Key knowledge and worked examples

■ The windows

Karyotype $\geq 5\text{--}10$ Mb (balanced seen); CMA CNVs $\sim 50\text{--}100$ kb (balanced missed); FISH targeted; sequencing base-level in chosen scope ✓.

■ Worked example: the mapping

Aneuploidy $\rightarrow$ karyotype/FISH; developmental delay $\rightarrow$ CMA; known familial variant $\rightarrow$ targeted Sanger ✓ – the question chooses the window.

2 Practice

2.1 Which method detects balanced translocations? [3]

2.2 First-line test for unexplained developmental delay? [3]

2.3 What does a negative familial-variant test return a relative to? [3]

3 Exam-style questions

3.1 A familial pathogenic variant is found in a proband (fictional).

State each first-degree relative's a-priori risk (1/2). Explain how cascade testing converts uncertainty into binary results. State two considerations before testing a healthy 19-year-old relative (autonomy; insurance/psychological). [7]

3.2 A genome sequencing test for a child's developmental delay finds an incidental adult-onset predisposition (fictional).

State the general policy (defer adult-onset results in children). Explain why consent before testing matters here. State what changes if the finding is childhood-actionable. [7]

Solutions

2.1

- Karyotype (microscopy of metaphase spreads).

2.2

- Chromosomal microarray.

2.3

- Population risk for that syndrome.

3.1

- Each sibling and each parent: $1/2$ a priori.
- Cascade testing: relatives tested for THE familial variant $\rightarrow$ positives enter screening, negatives return to population risk – uncertainty becomes binary.
- Considerations: autonomy (the 19-year-old decides); implications for insurability and psychological burden; timing.

3.2

- Defer the adult-onset result until the child can consent.
- Consent before testing sets the return-of-results menu (opt in/out); after the fact, the choice is already gone.
- If childhood-actionable (treatable/preventable now), return it - the child's health benefit overrides deferral.