Q3(a)

What is meant by karyotype? How does its analysis help in diagnosis of the chromosomal aberrations in man?

UPSC Civil Services Mains 2024 · Anthropology GS 1 · 20 marks · Numerical and structural aberrations (disorders).

(a) Numerical and structural aberrations (disorders).

Core demand of the question

- Define karyotype and distinguish it from the laboratory karyogram
- Describe preparation and analysis of chromosomes
- Explain diagnosis of numerical and structural aberrations with examples
- State resolution, mosaicism and single-gene limits

Revision summary

Karyotype means chromosome complement; karyogram is its ordered image.

Metaphase arrest, hypotonic spreading and G-banding permit homologous pairing and notation.

It diagnoses trisomy 21, Turner, Klinefelter and other numerical aberrations.

It also finds large deletions, inversions and balanced or unbalanced translocations.

Multiple cells must be examined for mosaicism.

A normal karyotype does not exclude microdeletions or single-gene disease; use FISH, microarray or sequencing appropriately.

Introduction

A karyotype is an individual's chromosome complement described by number, size, centromere position and banding pattern; a karyogram is its ordered visual display. Conventional analysis examines condensed metaphase chromosomes and is especially useful for whole-chromosome changes and large structural rearrangements.

Body

Preparation and reading

Dividing cells from blood, amniotic fluid, chorionic villi, marrow or tumour are cultured where necessary. Colchicine/colcemid arrests metaphase; hypotonic treatment spreads chromosomes; fixation, staining and microscopy follow. G-banding produces reproducible light and dark bands. Homologues are paired from chromosome 1 to 22 plus sex chromosomes, producing notations such as 46,XX or 46,XY.

Analysis checks:

1. total chromosome number;

2. homologous size and centromere position;
3. missing, duplicated or rearranged bands;
4. several cells to identify mosaicism.

Diagnostic value

• **Numerical aberrations:** meiotic nondisjunction may produce trisomy 21 (47,XX,+21), trisomy 18, trisomy 13, Turner syndrome (45,X) or Klinefelter syndrome (47,XXY). Polyploid conceptions can also be recognised.

• **Structural aberrations:** large deletions such as 5p deletion in cri-du-chat syndrome, duplications, inversions, ring chromosomes and reciprocal or Robertsonian translocations are visible when above the banding resolution.

• **Reproductive diagnosis:** A phenotypically normal parent may carry a balanced translocation. Karyotyping can explain recurrent miscarriage or a child with an unbalanced rearrangement and guide recurrence-risk counselling.

• **Cancer cytogenetics:** acquired rearrangements, classically the Philadelphia chromosome t(9;22) in chronic myeloid leukaemia, can classify disease.

Targeted **FISH** detects specified loci and rearrangements; chromosomal microarray detects smaller copy-number changes; sequencing detects nucleotide variants. These complement rather than make every karyotype obsolete.

Limits

Conventional resolution is usually several megabases and depends on band quality. It misses most single-gene mutations, small copy-number variants and many low-level mosaics. A normal karyotype therefore does not mean a normal genome, while a prenatal abnormality requires careful, non-directive interpretation rather than deterministic prediction.

Flow diagram

Dividing cells -> Metaphase arrest

Metaphase arrest -> Spread stain band

Spread stain band -> Ordered karyogram

Ordered karyogram -> Numerical change

Ordered karyogram -> Large rearrangement

Ordered karyogram -> FISH microarray sequencing if needed

Conclusion

Karyotyping converts chromosome morphology into a diagnosis of aneuploidy and major rearrangement. Its strength is the genome-wide view of large changes; its limit is resolution. Sound diagnosis combines clinical findings, adequate cell sampling and the appropriate molecular follow-up.

Facts & figures

Standard complements

46,XX and 46,XY are conventional chromosome notations; notation describes chromosomes and should not be treated as a complete account of sex or development.

G-banding

Giemsa produces reproducible band patterns that identify homologues and localise large structural breakpoints.

Robertsonian translocation

Fusion involving acrocentric chromosomes may be balanced in a parent but create aneuploid gametes, including translocation Down syndrome.

Mosaicism

Two or more cell lines require analysis of multiple cells and sometimes multiple tissues; low-level mosaicism may be missed.

Resolution limit

Conventional karyotyping sees megabase-scale change, not most sequence variants. Microarray detects smaller imbalances but not all balanced rearrangements.