

Genetics Patterns of Defects – Short High-Yield Summary

Penetrance: Disease present or absent.

Example: Retinoblastoma (RB1) 90% penetrance, Waardenburg syndrome (PAX3) 20% penetrance of hearing loss.

Variable Expressivity: Disease present in everyone but severity varies.

Example: Neurofibromatosis (NF1), Myotonic dystrophy (DMPK).

Variable Age of Onset: Same mutation, different ages of disease onset.

Example: Huntington disease (HTT).

Pleiotropy: One gene affects multiple organs.

Examples: Marfan syndrome (FBN1) CT abnormalities and cardiovascular problems, Cystic fibrosis (CFTR) GI, Respiratory, etc manifestation.

Allelic Heterogeneity: Different mutations in the same gene cause disease.

Example: CFTR locus on 7q mutations in cystic fibrosis : a1=F50

Locus Heterogeneity: Different genes cause the same disease.

Example: Congenital hearing loss (PAX3 on 2q, GJB2 on 13q).

Anticipation: Earlier onset and greater severity in successive generations due to repeat expansion. Examples: Fragile X (FMR1, CGG), Huntington (HTT, CAG), Myotonic dystrophy (DMPK, CTG). premature carrier state : females= POF, Males =FXTAS.

Genomic Imprinting: Expression depends on parent of origin.

Paternal deletion 15q11-q13 → Prader-Willi syndrome.

Maternal deletion 15q11-q13 → Angelman syndrome (UBE3A).

Sex-Limited: Gene present in both sexes but expressed in one sex only.

Example: Male precocious puberty.

Sex-Influenced: Disease occurs in both sexes but differs in frequency/severity.

Example: Hemochromatosis (HFE).

Mitochondrial Inheritance: Maternal inheritance only.

Examples: LHON, mitochondrial myopathies.