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Q1(d)

Lethal and sublethal genes

UPSC Civil Services Mains 2024 · Anthropology GS 1 · 10 marks · Mendelian genetics in man-family study, single factor, multifactor, lethal, sub-lethal and polygenic inheritance in man.

9.2 Mendelian genetics in man-family study, single factor, multifactor, lethal, sub-lethal and polygenic inheritance in man.

Core demand of the question

- Define lethal and sublethal genes in terms of genotype and viability
- Explain inheritance patterns and altered Mendelian ratios
- Give precise human examples
- Relate the concepts to selection, counselling and population anthropology

Revision summary

A lethal genotype causes death before reproduction; a sublethal genotype substantially lowers viability or fertility.

Recessive lethals hidden in carriers can produce a 2:1 ratio among survivors.

Tay-Sachs illustrates a recessive lethal; homozygous FGFR3 **achondroplasia** is lethal while heterozygotes live.

Huntington persists partly because onset is often after reproduction.

HbSS is severely deleterious, while HbAS can be favoured in falciparum-malaria regions.

Endogamy changes homozygosity and health care changes the fitness effect.

Introduction

A lethal allele causes death in a particular genotype, usually before reproduction; a sublethal allele markedly lowers survival or reproductive fitness without invariably causing death. The allele itself is not lethal in every carrier: dominance, age of onset, penetrance, environment and medical care determine its effect.

Body

Genetic patterns

Most lethal alleles are recessive because a normal heterozygote can transmit them. When two heterozygotes mate, the lethal homozygote may disappear before observation, changing the surviving Mendelian ratio from 3:1 to 2:1. **Tay-Sachs disease** is an autosomal-recessive example historically lethal in early childhood without effective supportive care.

Some alleles are dominant for a visible trait but homozygous lethal. In **achondroplasia**, one altered FGFR3 allele causes short-limbed dwarfism, while two altered copies usually cause lethal skeletal dysplasia. Two affected heterozygous parents therefore face a 1/4 homozygous-lethal conception risk.

Dominant lethals can persist when expression follows reproduction. **Huntington disease**, caused by a HTT CAG expansion, reduces survival but often has adult onset; it is better described as a late-acting deleterious dominant than as an invariably pre-reproductive lethal.

Sublethal effects form a continuum. Untreated **beta-thalassaemia major**, cystic fibrosis and **HbSS sickle-cell disease** sharply reduce viability, but outcome varies with environment and treatment. Their persistence cannot be explained by lethality alone. HbS and some thalassaemia alleles are maintained in malarial regions because heterozygotes receive protection against severe *Plasmodium falciparum* malaria-**balanced polymorphism**, demonstrated for sickle-cell trait by **A. C. Allison**.

Anthropological significance

Small populations, endogamy and consanguinity can increase homozygosity of rare recessives. Pedigree analysis and population screening inform non-directive counselling, while modern treatment changes selection coefficients. Labels must not stigmatise communities or imply that carriers are diseased.

Flow diagram

Aa: viable carrier x Aa: viable carrier -> AA: viable: viable
Aa: viable carrier x Aa: viable carrier -> Aa: viable carrier: viable carrier
Aa: viable carrier x Aa: viable carrier -> aa: lethal genotype: lethal genotype
aa: lethal genotype -> Survivors often show 2 to 1 ratio
Environment and treatment -> Observed fitness

Conclusion

Lethal and sublethal describe genotype-specific fitness effects, not morally defective people or permanently fixed outcomes. Altered ratios reveal the genetics; age, malaria, endogamy and health care reveal the population-anthropological context.

Facts & figures

Achondroplasia

An FGFR3 variant is dominant for achondroplasia in heterozygotes; homozygosity usually causes lethal skeletal dysplasia.

Tay-Sachs

Biallelic HEXA variants cause progressive neurodegeneration. The classic infantile form was historically fatal in early childhood.

Modified ratio

Loss of one homozygous class from an Aa × Aa cross can leave two heterozygotes for every one normal homozygote among survivors.

A. C. Allison

Linked sickle-cell trait to protection from severe falciparum malaria, a classic human example of balancing selection.

Population context

Consanguinity increases the chance that two copies of a rare recessive allele meet; it does not create the mutation.

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