

6.7 Multifactorial disease and pharmacogenomics

Name: _____ Class: _____ Date: _____

Total: 23 marks

KEY WORDS liability threshold model

Objective

Quote multifactorial recurrence risks and apply pharmacogenomic screens.

1 Key knowledge and worked examples

■ The bell and its threshold

Liability (genes + environment) $\approx$ normal; disease past the threshold. Empiric 2–5 % after one affected; rising with more affected relatives, severity, and the more-affected sex ✓.

■ Worked example: the NT defect quote

One affected child: 2–4 % (folate cuts it); two: ~10 % ✓ – tables not grids, and folate regardless.

2 Practice

2.1 State the typical empiric recurrence for a multifactorial condition after ONE affected child. [3]

2.2 Which CYP variant status makes clopidogrel ineffective? [3]

2.3 Which HLA allele requires screening before abacavir? [3]

3 Exam-style questions

3.1 A couple has one child with a neural-tube defect (fictional).

Quote the recurrence risk and its modifiers (two affected $\rightarrow$ $\sim 10\%$). Explain the liability-threshold basis of the rise. State the folate prescription and why it applies regardless of risk. [7]

3.2 A psychiatric service considers routine pharmacogenomic screening (fictional).

Discuss CYP2C19/clopidogrel ($\sim 20\%$ of East-Asian allele carriers are poor metabolisers), TPMT/thiopurines, and HLA-B*57:01/abacavir: what does each screen prevent? State the general principle (genotype as dosing instruction, not diagnosis). [7]
