

8.6 Antimicrobials and resistance

Name: _____ Class: _____ Date: _____ **Total: 24 marks**

KEY WORDS selective toxicity • horizontal gene transfer

Objective

Reason from targets to resistance arithmetic (no regimens).

1 Key knowledge and worked examples

■ **Four targets**

Selective toxicity needs a target human cells lack: wall (β -lactams $\rightarrow$ penicillin-binding proteins), ribosome (30S/50S vs our 40S/60S), DNA enzymes (gyrase, RNA polymerase), folate (bacteria make it; we import it) ✓.

■ **Worked example: the resistance clock**

Mutations supply resistance at 10^{-7} – 10^{-9} per cell per generation; $\sim 10^9$ cells per mL overnight $\rightarrow$ every culture carries mutants against any single drug. Two independent hits multiply to 10^{-14} – 10^{-18} ✓.

2 Practice

2.1 Why is an anti-folate selectively toxic? [3]

2.2 A 1 mL culture holds 10^9 cells; resistance arises at 10^{-8} per cell per generation – expected resistant mutants? [3]

2.3 β -lactamase resistance vs PBP2a resistance: one difference. [3]

3 Exam-style questions

3.1 A fictional broth culture of 4×10^9 cells faces drug X; resistance mutations arise at 10^{-8} per cell per generation.

Calculate the expected resistant mutants ($4 \times 10^9 \times 10^{-8} \approx 40$). For a two-drug combination with independent targets at 10^{-8} each, calculate the double-mutant expectation (10^{-16} per cell pair – effectively zero in the culture) and explain in one line why combinations exist. [8]

3.2 A fictional ward sees rising resistance tracked to broad spectrum use.

Explain the mechanism chain from drug pressure to a resistant ward flora (selection of the pre-existing 10^{-7} – 10^{-9} fraction, then plasmid spread between species). Explain why narrowing the drug to the reported susceptibility reduces selective pressure. [7]

Solutions

2.1

- Bacteria synthesise folate; humans import it in the diet – the pathway is the difference ✓.

2.2

- $10^9 \times 10^{-8} = 10^1 \approx 10$ mutants ✓.

2.3

- β -lactamase hydrolyses (opens) the drug ring; PBP2a is an altered target that still builds the wall ✓.

3.1

- $4 \times 10^9 \times 10^{-8} = 40$ resistant mutants expected ✓.
- Double mutant: $10^{-8} \times 10^{-8} = 10^{-16}$ per cell pair ✓.
- $4 \times 10^9 \times 10^{-16} = 4 \times 10^{-7}$ – effectively zero in the culture ✓.
- Combinations exist because two independent probabilities multiply: the resistant fraction collapses ✓.

3.2

- Every large population already carries the resistant fraction (10^{-7} – 10^{-9} per cell per generation) ✓.
- The drug SELECTS it: sensitive cells die, resistant cells fill the niche; plasmids then move genes between species ✓.
- Narrowing to the reported susceptibility removes needless pressure on the rest of the ward flora – stewardship is the mechanism applied ✓.