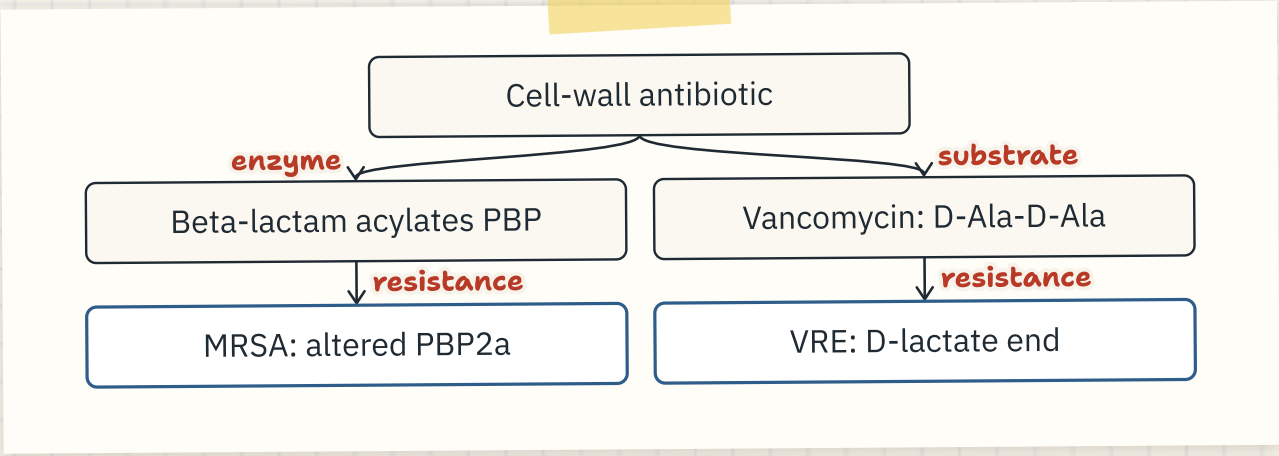
Beta-lactams and vancomycin

Enzyme versus substrate in cell-wall synthesis



Step by step

1. Peptidoglycan: sugar chains with peptides ending D-Ala-D-Ala
2. PBPs cross-link the peptides; the wall is strong
3. Block cross-linking and the wall fails
4. Vancomycin: IV for bloodstream infection; oral stays in the gut

	Beta-lactams	Vancomycin
Target	PBP (enzyme)	D-Ala-D-Ala (substrate)
Binding	Ring mimics D-Ala-D-Ala; acylates PBP serine	Large glycopeptide covers the end
Effect	Cross-linking stops; cell lyses (bactericidal)	Precursor not cross-linked
Gram-negatives	Usually via porins	Too large for outer membrane
Resistance	MRSA: altered PBP2a	VRE: D-lactate, ~1,000-fold lower affinity

Two ways to stop cross-linking

Rule of thumb

Beta-lactams target the enzyme

Vancomycin targets the substrate

Enzyme versus substrate explains the resistance patterns

Exam traps

- ! An altered PBP (MRSA) does not affect vancomycin.
- ! Vancomycin is too large for gram-negative outer membranes.
- ! VRE alter the substrate (D-lactate), not the enzyme.

Beta-lactams and vancomycin: enzyme versus substrate
Video, written lesson, practice question and sources: medservatory.com/usmle-step-1/pharmacology-principles-autonomic/cell-wall-antibiotics-beta-lactams-vancomycin

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