Antibiotics in Laboratory Medicine
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Table 12.4
Cross-links in the Peptidoglycans of Bacteria[a]

	Amino Acid 3, Chain 1[b]	Bridge[b]	Amino Acid 4, Chain 2[b]
S. aureus	L-Lys	$(Gly)_5$	D-Ala
Staphylococcus epidermidis	L-Lys	$(Gly)_{4-5}$—L-Ala	D-Ala
Staphylococcus agalacticae	L-Lys	L-Ala (or L-Ser)—L-Ala	D-Ala
Streptococcus group G	L-Lys	L-Ala (or L-Ser)—L-Ala	D-Ala
Streptococcus salivarius	L-Lys	Gly—L-Thr	D-Ala
Streptococcus bovis	L-Lys	L-Ser—L-Ala—L-Thr	D-Ala
E. facium	L-Lys	D-Asn	D-Ala
E. faecalis	L-Lys	$(L\text{-}Ala)_{2-3}$	D-Ala
Peptostreptococcus spp.	L-Lys	Gly—L-Ala	D-Ala
All Gram-negative bacilli	*m*-Dap[c]	Direct; no bridge	D-Ala

[a]Data are from Reference 454.
[b]The positions of amino acids 3 and 4 and of the bridge are indicated in Figure 12.3.
[c]*m*-DAP, *m*-diaminopimelic acid.

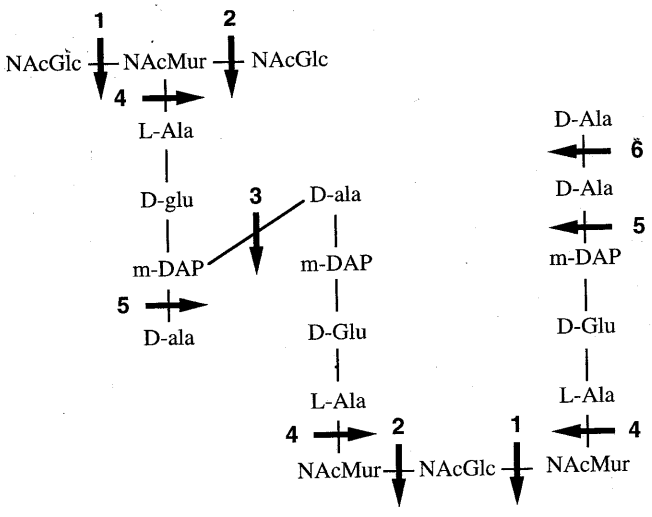

Figure 12.4. Actions of autolysins. *1*, β-*N*-Acetylglucosaminidase; *2*, lytic transglycosylase and β-*N*-acetylmuraminidase (lysozyme); *3*, D,D-endopeptidase; *4*, *N*-acetylmuramyl-L-alanine amidase; *5*, L,D-carboxypeptidase; *6*, D,D-carboxypeptidase. (Based on Reference 209.)

Although lytic transglycosylase and β-*N*-acetylmuraminidase (lysozyme) cleave the same target bond, the former enzyme additionally catalyzes transfer of the glycosyl bond to the 6′-hydroxyl group of the same muramic acid, yielding 1,6-anhydromuramic acid. *NAcGlc*, *N*-acetylglucosamine; *NAcMur*, *N*-acetylmuramic acid; *m-DAP*, *m*-diaminopimelic acid.

transpeptidation (Fig. 12.3). Transglycosylation extends sugar chains, by attaching the muramyl residue of a new precursor to a free *N*-acetylglucosamine residue on the existing peptidoglycan. Transpeptidation cross-links adjacent sugar chains via their pentapeptides (Fig. 12.3). Peptidoglycan transglycosylase and D-alanyl-D-alanine transpeptidase activities often reside at separate sites on the same proteins, and most bacteria possess multiple peptidoglycan transglycosylases/transpeptidases, each with a different role (see below) (170, 548). These enzymes contain lipophilic sequences, which anchor them to the cytoplasmic membrane and allow particular activities to be localized. Their interplay ensures the maintenance of cell shape (171, 548) and their relative amounts may vary with the growth rate (513).

Additional enzymes hydrolyze cross-linked peptidoglycan and are collectively called autolysins or peptidoglycan hydrolases (506). D-Alanyl-D-alanine carboxypeptidases hydrolyze D-alanine groups from pentapeptides that have served as amino donors (Fig. 12.4) and probably have a regulatory role in peptidoglycan synthesis. More-drastic hydrolyses of peptidoglycan are undertaken by (*a*) D,D-endopeptidases, which cleave the cross-links synthesized by D-alanyl-D-alanine transpeptidases, (*b*) *N*-acetylmuramyl-L-alanine amidase, which cleaves peptides from muramyl residues, and (*c*) lytic glycosylases, β-*N*-acetylglucosaminidases, and β-*N*-acetylmuramidases, all of which hydrolyze the sugar backbone of the peptidoglycan (Fig. 12.4). Many species have multiple autolysins (41, 464) (Table 12.5); for example, *E. coli* has at least 11 such enzymes (209), catalyzing five modes of cleavage. Like peptidoglycan transglycosylases and transpeptidases, autolysins are often (but not always) membrane-bound, allowing their activities to be localized. Their main role is to provide sites for insertion of new peptidoglycan (123), but they may also assist in daughter cell cleavage, autolysis, and flagellar extrusion. Degraded peptidoglycan fragments are absorbed and recycled (see below).

Action of β-Lactams

β-Lactams inhibit D-alanyl-D-alanine transpeptidase activity by acylation, forming stable esters with the opened lactam ring attached to the hydroxyl group of the