OTHER ANTI MICROBIAL'S ACTING ON THE CELL WALLS

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Describe the mechanism of action of vancomycin

Describe the antibacterial spectrum of Monobactams

Describe the clinical uses of vancomycin

Describe the antibacterial spectrum of Carbepenems

Describe the use of vancomycin in MRSA

Describe the clinical uses of Monobactams

Describe the side effects of vancomycin

Describe the clinical uses of Carbepenems

Carbapenems are synthetic β-lactam antibiotics that differ in structure from the penicillins in that the sulfur atom of the thiazolidine ring has been externalized and replaced by a carbon atom.

Imepenem

Meropenem

Ertapenem

Dorepenem

Imepenem

It is a semisynthetic beta lactam antibiotic

Resistant to most of the beta lactamases
But
Vulnerable to Mettalo beta lactamase

Wide antibacterial spectrum
Covers **gm+**

- Strep
- Staph.A (MSSA)
- Enterococci
- Listeria .M
- C.Def

gm –ive

- P. auriginosa
- Enetrobactericiae
- B.fragalis

imepenem + cilastatin

The rate limiting factor of it is that it readily undergoes hydrolysis by dehydropeptidase 1enzyme present at the brush borders of the renal tubulular cells

It order to overcome this limitation it is added with *cilastatin*. ***Cilastatin*** is a dehydrpeptidase 1 inhibitor (reversible inhibitor).

Pharmacokinetics

Both ***cilastatin*** and ***imipenem*** are also comfortably compounded together as they also have same $t_{1/2}$ i.e., 1hour.

Imipenem +cilastatin is given 0.5g i/v 6hourly(max4g/day).

It is very well distributed in the body & can reach CSF in meningitis.

it is readily excreted by the kidneys.

Clinical uses

- Soft tissue infections
- UTI
- RTI
- GIT infections
- Bone infections
- Skin infections
- (caused by mixed bacteria)

Imipenem +cilastatin is given 0.5g i/v 6hourly (max4g/day).
It as shown very good results in a wide range of hospital acquired infections even in AIDS

Adverse effects

Nausea
Vomiting
Diarrhea
Seizures

MEROPENEM

It is not hydrolysed by dehydropeptidases 1 .

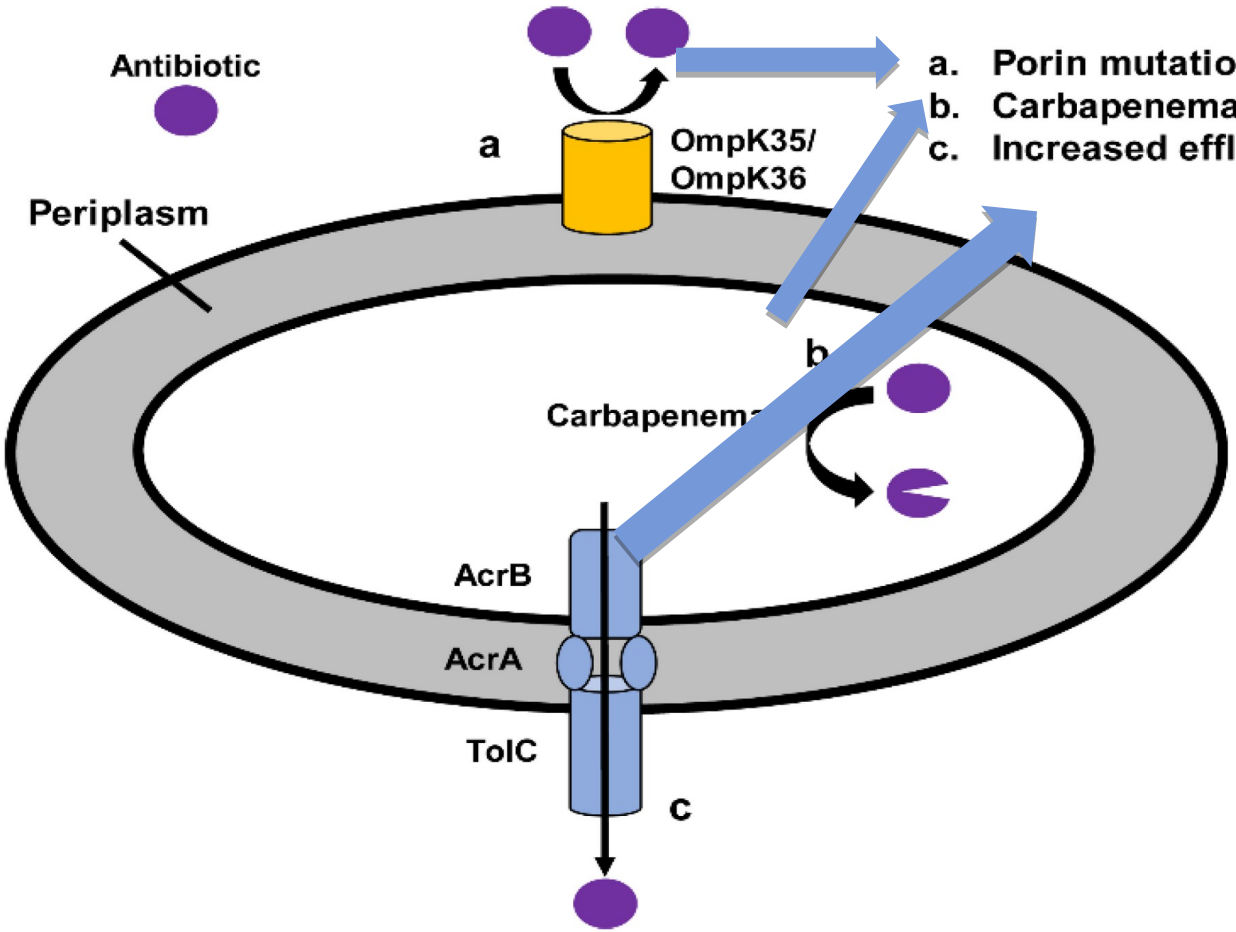
It has almost the same antibacterial spectrum as that of Imipenem except that it has comparatively lesser activity against gm +ive

It is specially effective against infections caused by cephalosporin-resistant bacteria.

Meropenem is usually combined with aminoglycosides for the treatment of infections caused by Ps. Aeruginosa

Carbapenems

	Meropenem (Merem®)	Ertapenem (Invanz®)	Imipenem - Cilastatin (Primaxin®)	Doripenem (Doribax®)
Mechanism of Action	Inhibit cell wall synthesis			
Spectrum of Activity	Broad Spectrum: Gram (+), Gram (-), ESBL, Anaerobes NOT: MRSA			
	--	NOT: Pseudomonas, Enterococcus, Acinetobacter	--	--
Adverse Effects	↓ Platelets Drug Fever		Seizure	↓ Platelets Drug Fever
Common Use	Meningitis	Intra-abdominal	Nocardia	NOT: Pneumonia



Mechanism of resistance to Carbapenems

Monobactams

It is a cell wall inhibitor

It is unique as it has only one ring (β-lactum ring) not fused to the other ring as the name “ mono” shows

Aztreonam

Antimicrobial activity

- Enterobacteriaceae
- aerobic gram-negative rods, including
- P. aeruginosa

Aztreonam is resistant to the action of β-lactamases.

Adverse effects

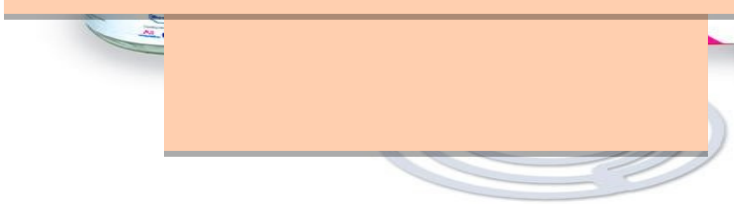
phlebitis, skin rash,
and occasionally,
abnormal liver function tests

Monobactams

Anti bacterial spectrum

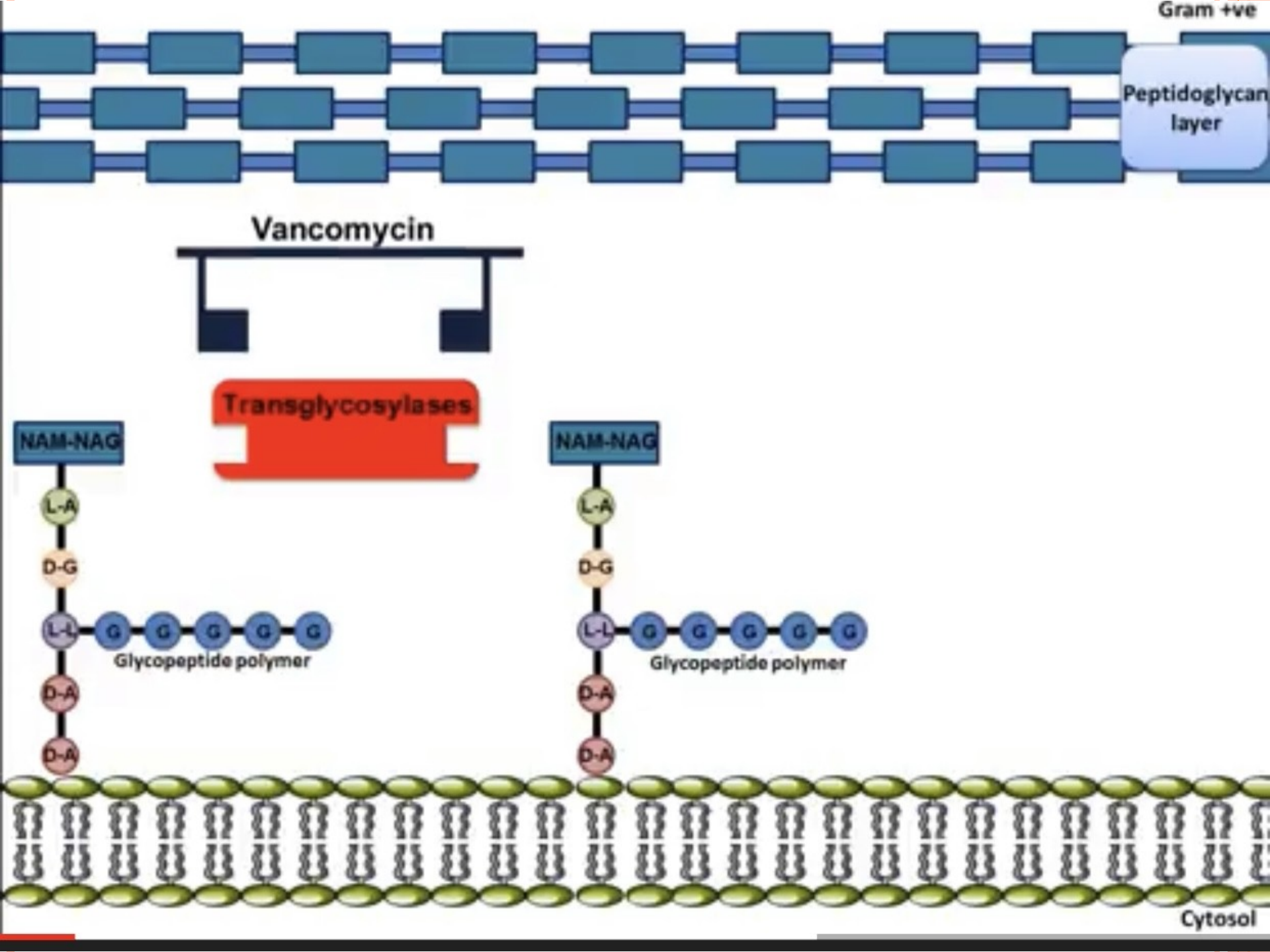
This drug may offer a safe alternative for treating patients who are allergic to penicillins and/or cephalosporins.

It is administered either IV or IM and is excreted in the urine. It can accumulate in patients with renal failure



VANCOMYCIN

- Vancomycin is a tricyclic glycopeptide with the molecular weight 1500 that has become increasingly important because of its effectiveness against multiple drug-resistant organisms, such as MRSA and enterococci. The medical community is presently concerned with emergence of vancomycin resistance in these organisms.
- Vancomycin is an antibiotic produced by Streptococcus orientalis, it is active only against gram-positive bacteria, particularly staphylococci.
- It is water-soluble and quite stable.


Gram +ve
Peptidoglycan layer
Vancomycin
Transglycosylases
NAM-NAG
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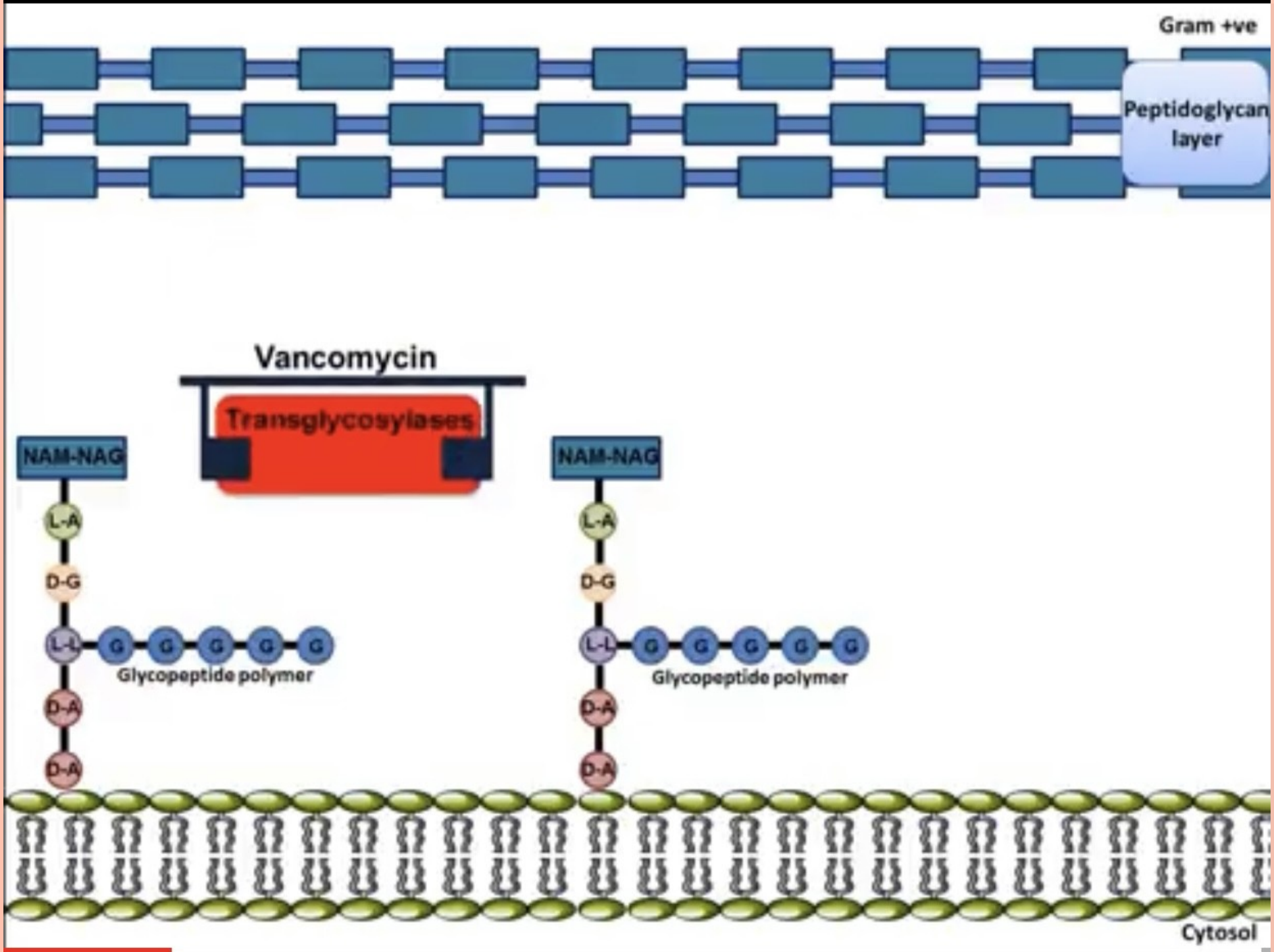
Cytosol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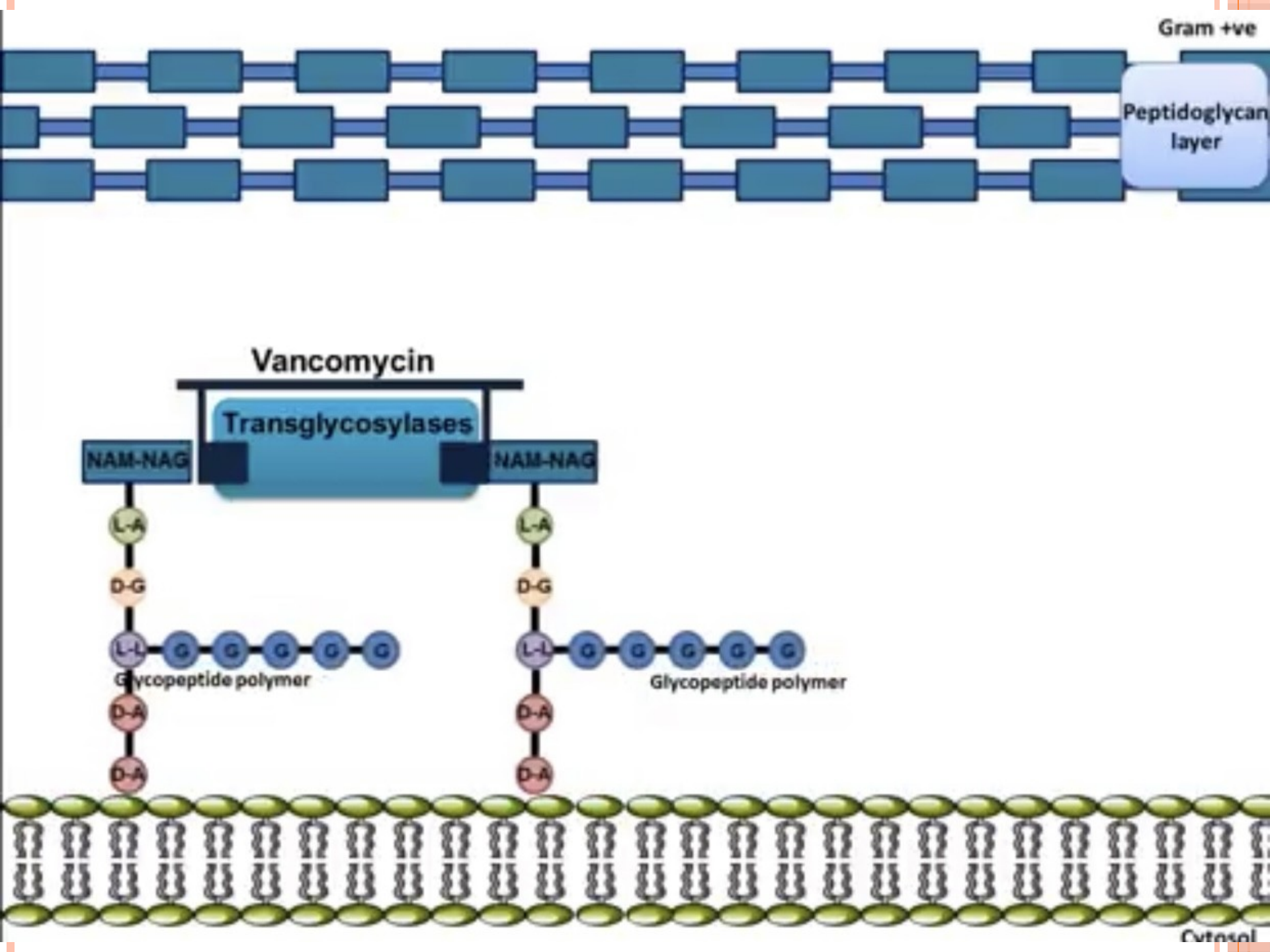
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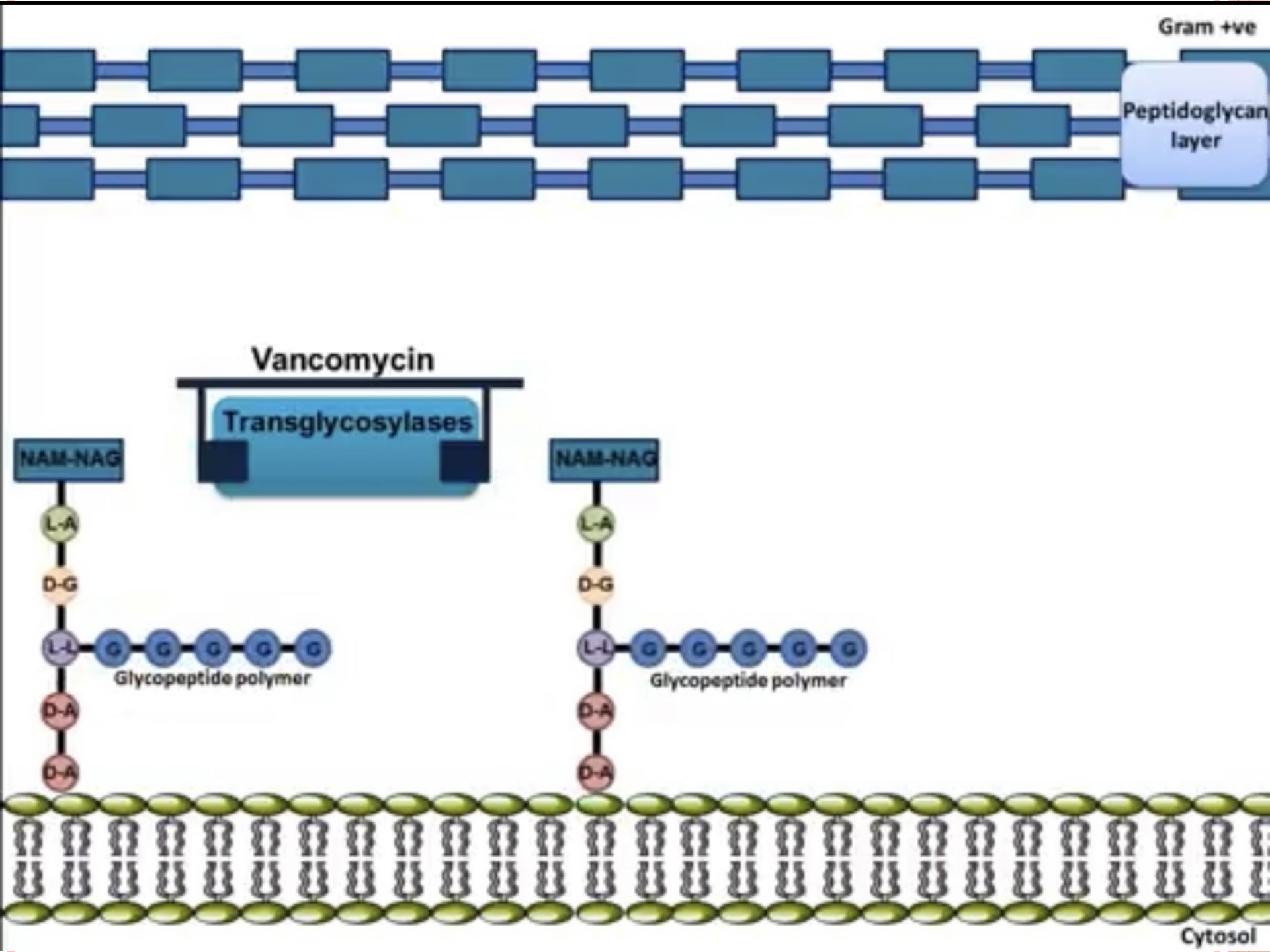
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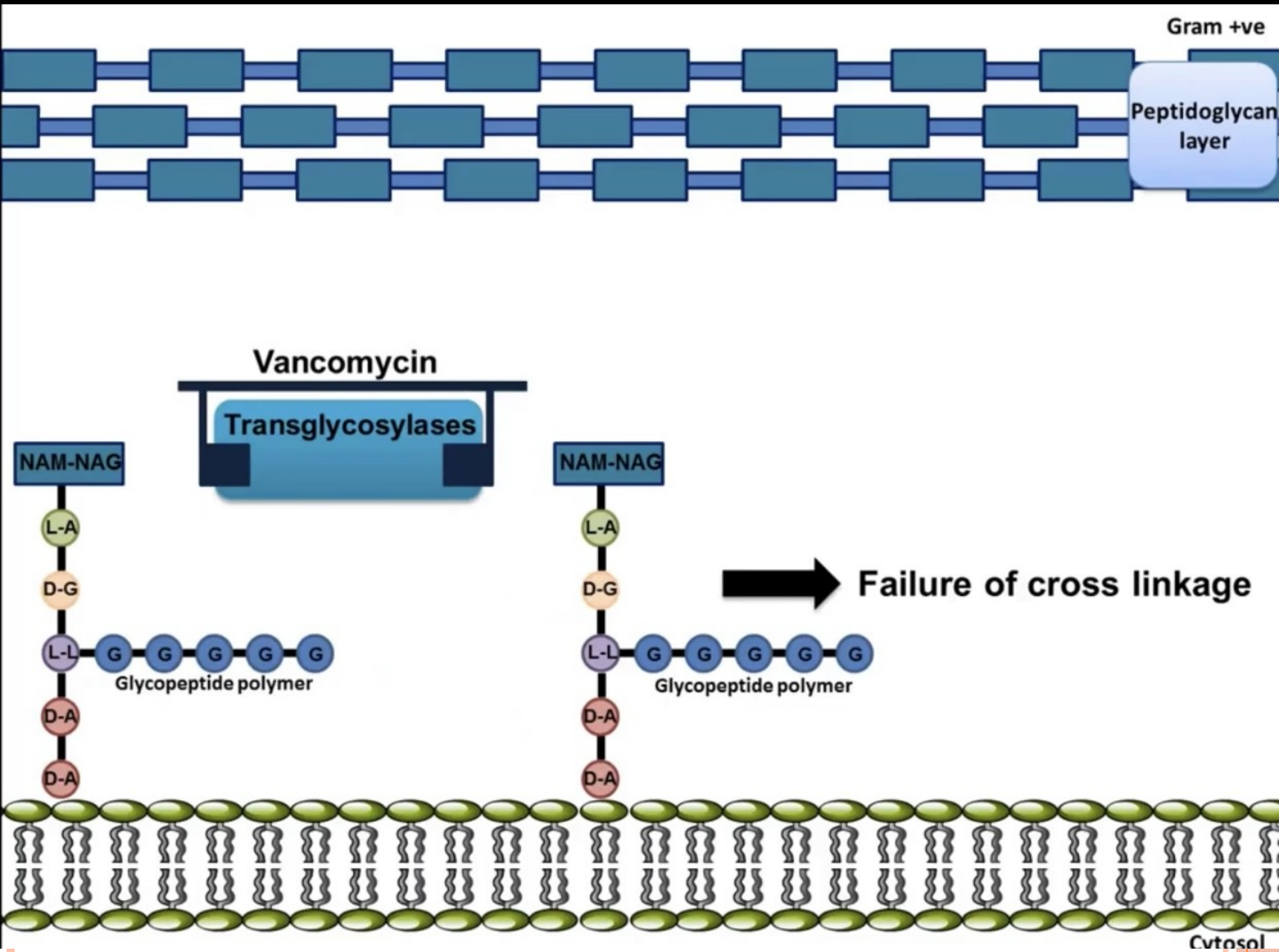
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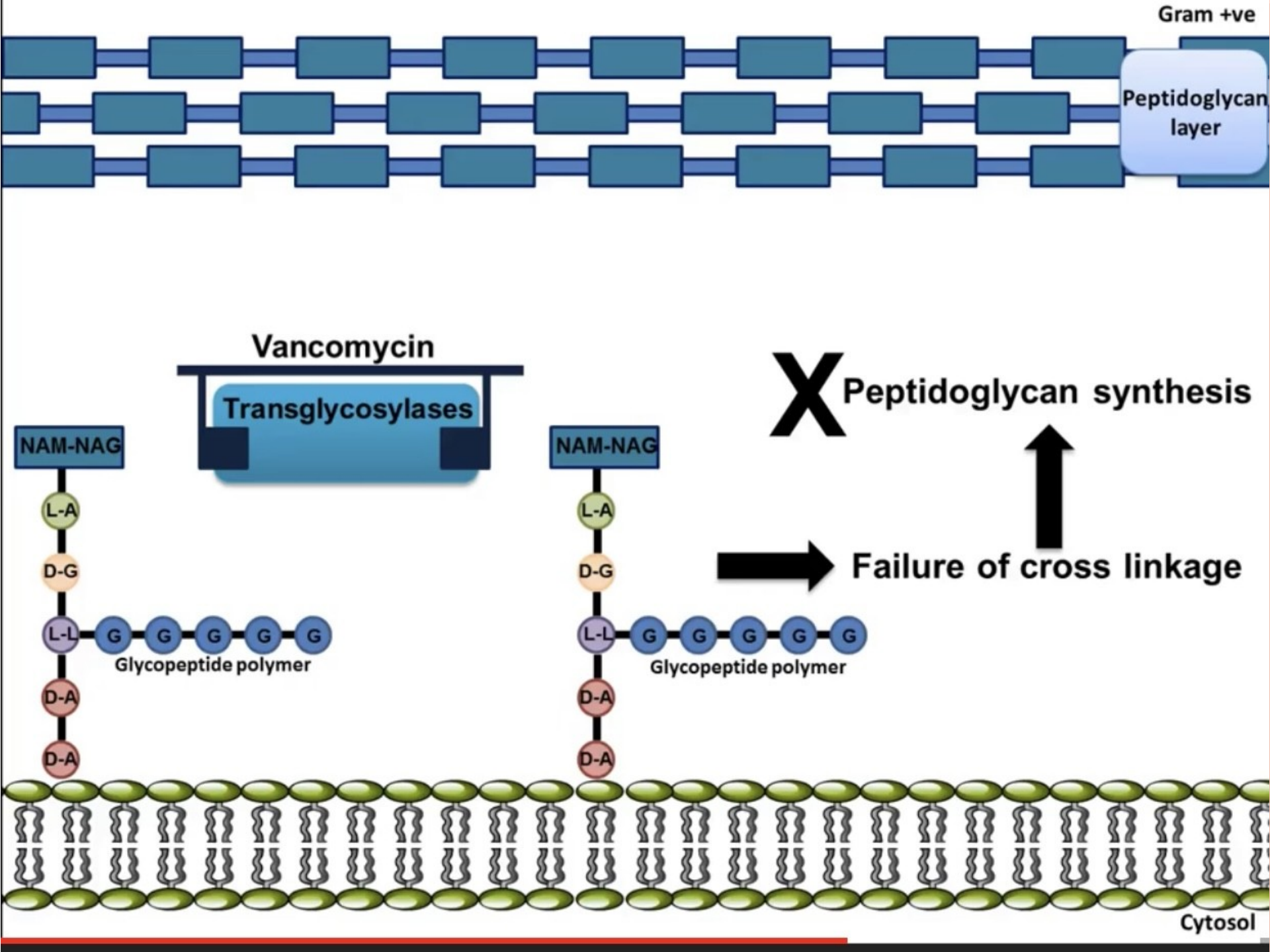
Failure of cross linkage
Cytosol


Gram +ve
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Failure of cross linkage
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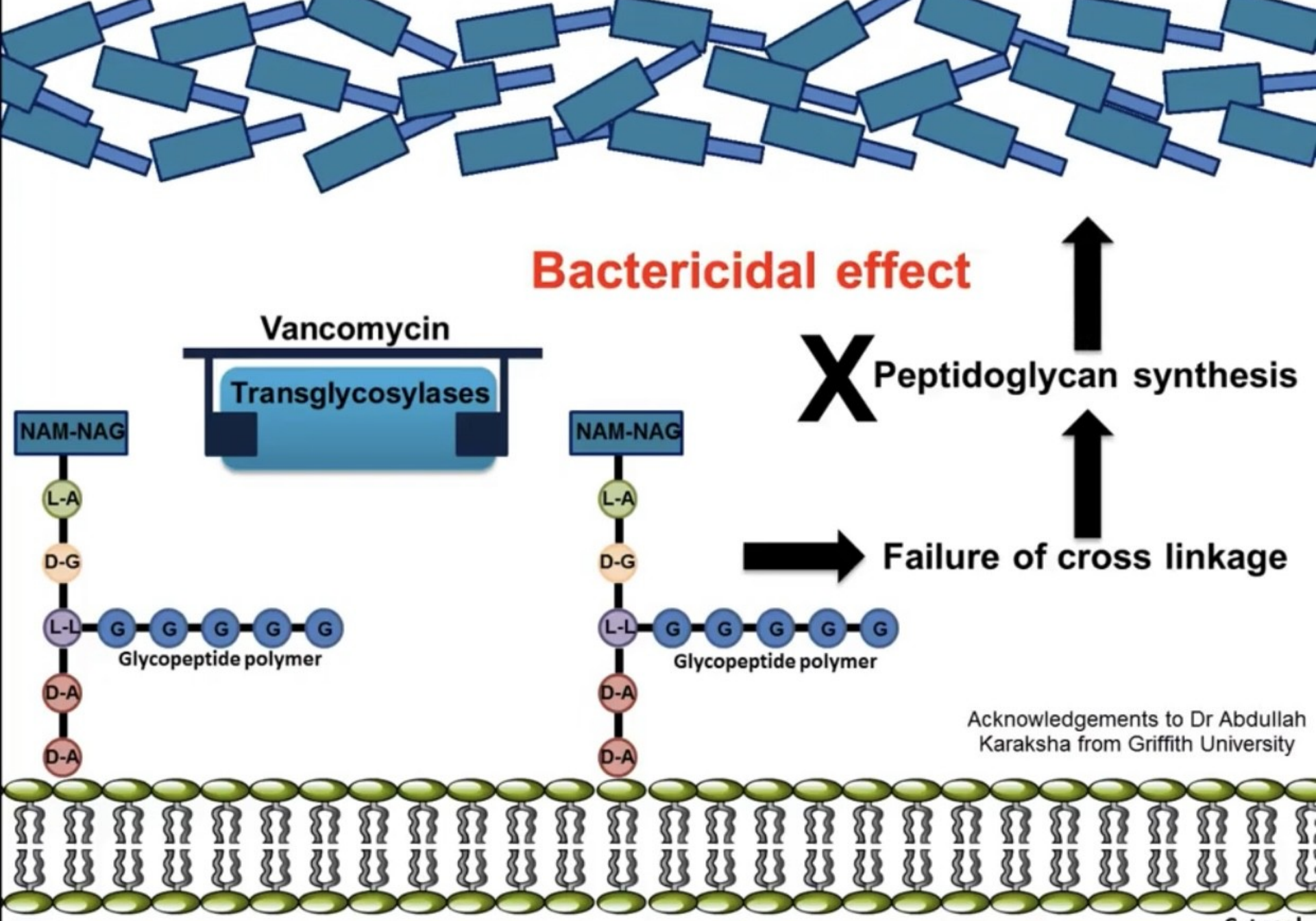
Bactericidal effect
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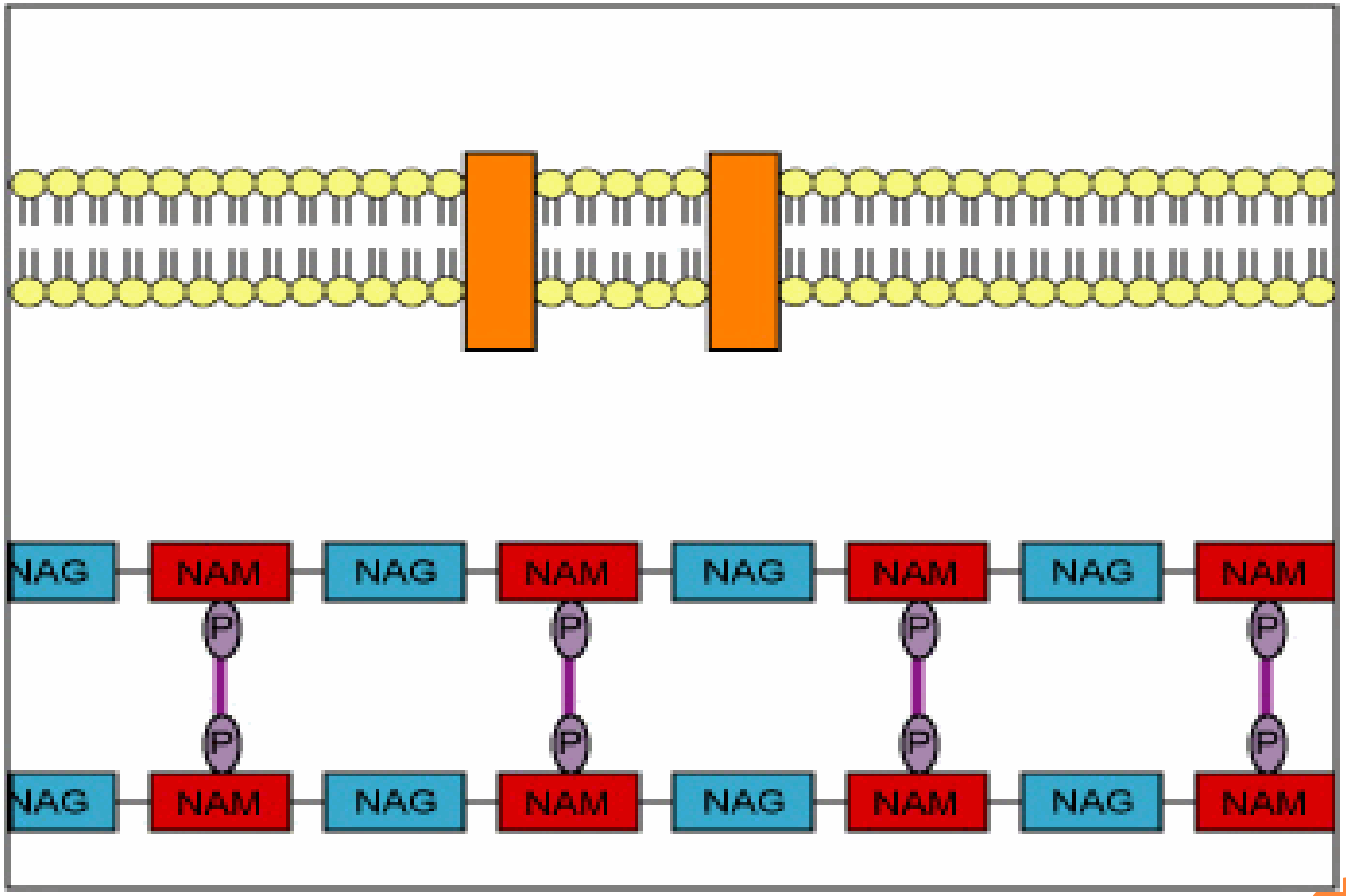
Failure of cross linkage
Acknowledgements to Dr Abdullah Karaksha from Griffith University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RESISTANCE

- *Vancomycin resistance can be caused by plasmid-mediated changes in permeability to the drug or by decreased* binding of *vancomycin to receptor molecules. An example of the latter is caused by the replacement of a* D-Ala by D-lactate in resistant organisms.
- Resistant strains are
- Vancomycin –resistant – staphlococci
- Vancomycin – resistant – enterococci (VRE) like *enterococcus faecium & enterococcas faecalis.*

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ANTI BACTERIAL SPECTRUM

- *Vancomycin is effective primarily against gram-positive organisms.*
- *It is effective against*
- *MRSA*
- *Enterococci*
- *Clostridium defficile.*

THERAPEUTIC USES

- **PARENTERAL** vancomycin is used in sepsis or endocarditis caused by MRSA.
- Vancomycin in combination with gentamicin is an alternative regimen for treatment of enterococcal endocarditis in a patient with serious penicillin allergy.
- Vancomycin (in combination with cefotaxime, ceftriaxone, or rifampin) is also recommended for treatment of meningitis suspected or known to be caused by a highly penicillin-resistant strain of pneumococcus.
- Vancomycin is used in individuals with prosthetic heart valves and in patients undergoing implantation with prosthetic devices
- **ORAL** *vancomycin is used to treat antibiotic-associated enterocolitis*
- *caused by* ***Clostridium difficile*** *although Metronidazole is a better option.*

PHARMACOKINETICS

- For serious infections/ systemic infections given I/v (60-90min)
- Poor oral absorption due very high molecular wt (>1500daltons)
- For *clostridium defficile* colitis (anti-biotic induced) it is given orally as it stays in the intestine and not readily absorbed via this route.
- In case of meningitis it is given I/V in combination with Ceftrixone both having synergistic effect.
- Mainly eliminated via kidneys so in renal compromised the dos should be recalculated..
- $t_{1/2}$ is 6-10 which may be increased to 200 hrs in end stage renal disease

ADVERSE EFFECTS

- Fever , chills and phlebitis.
- Red man syndrome due to rapid infusion. This is characterized flusing and shock due to release of histamine.
- If such a condition starts appearing slow down the rate of infusion (2hrs) and also increase the dilution of vancomycin, you may also pretreat the patient with anti-histamine
- Dose related hearing loss may occur specially in renal compromised patients.
- Ototoxicity and nephrotoxicity is more pronounced when given aminoglycosides.

REFERENCES

- https://youtu.be/fOCXqYYDCqA
- Lippincot
- Long katzung

the end.