Summer 2017

Connections

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POLQM Quality Conference: Laboratory Quality in Challenging Times

On October 1-3, 2017 our sister program: Program Office for Laboratory Quality Management will host the 2017 Fall Quality Conference with the special theme: "Laboratory Quality in Challenging Times".

The conference will be held at the Paetzold Health Education Centre at Vancouver General Hospital and will feature more than 18 speakers.

Laboratory Leadership

Patient Centered Care

POLQM conferences are well known for its participative nature; there will be six roundtable discussions and three breakout sessions that are designed for more active participation.

Make sure to register early, please check the conference's website:

http://conference.polqm.ca/

This years some of the topics covered are:

Quality Initiatives
Quality Professionals for the Medical Laboratory
Patient Centered Care
ISO9001:2015
Antimicrobial Stewardship
Extending the scope of EQA
Laboratory developed tests
Quality education
Laboratory leadership
And more...

Macrolide and Lincosamide Resistance

By Veronica Restelli

Macrolides are composed of 2 or more amino or neutral sugars attached to a lactone ring of variable size. Commercially available macrolides have a 14-membered (clarithromycin, erythromycin, and roxithromycin) or 15-membered (azithromycin) lactone ring. Lincosamides (clindamycin and lincomycin) are devoid of a lactone ring. [1]

Mechanism of action

Macrolides and lincosamides are considered bacteriostatic antibiotics. They inhibit RNA-dependent protein synthesis by binding to the 50S ribosomal subunit where the peptide bond formation occurs, thus, inhibiting protein elongation. [2,3]

Lincosamides specifically inhibit the peptidyl transferase reaction while macrolides block the exit tunnel inducing premature dissociation of peptidyl-tRNAs from the ribosome. [3,4]

The binding sites for macrolides and lincosamide antibiotics lay in or near the active site of the peptide bond formation called peptidyl transferase center (PTC).[3] Because the binding sites for macrolides and lincosamides overlap, modification of any of these binding sites usually confers cross resistance to these antibiotics. [4,5]

Spectrum of activity

Macrolides are active against gram positive bacteria and are effective against many of the pathogens associated with sexually transmitted diseases: *Neisseria gonorrhoeae, Haemophilus ducreyi, Chlamydia trachomatis,* and *Ureaplasma urealyticum*.

Gram negative bacilli are generally resistant; some exceptions include *Bordetella perstusis, Campylobacter, Helicobacter,* and *Legionella.*

The vast majority of methicillin resistant *Staphylococcus aureus* are resistant to all macrolides and resistance among *Streptococcus pneumoniae* is increasing.

Lincosamides are also active against gram positive bacteria although *Enterococcus faecalis* is intrinsically resistant. Clindamycin is particularly active against anaerobic bacteria. [1,5]

Mechanisms of resistance

Resistance to macrolides occurs by three main mechanisms: target modification, enzymatic drug inactivation, and active efflux. [5,6]

Target modification

Methylation of the binding site in the ribosome is the most prevalent of the resistance mechanisms and confers resistance to both macrolides and lincosamides by preventing their binding to their target sites.[7,8]

Methylation is carried out by enzymes (methylases) encoded by different *erm* (erythromycin ribosome methylase) genes.

The expression of the methylases is normally inhibited by the ability of the encoding mRNA to adopt a conformation that blocks the initiation of the translation. In the presence of an inducer (macrolide) and its binding to the ribosome, the mRNA rearranges unmasking the initiation sequences for the translation of the methylase allowing for its expression and conferring resistance to macrolides (Figure 1). [7,9,10]

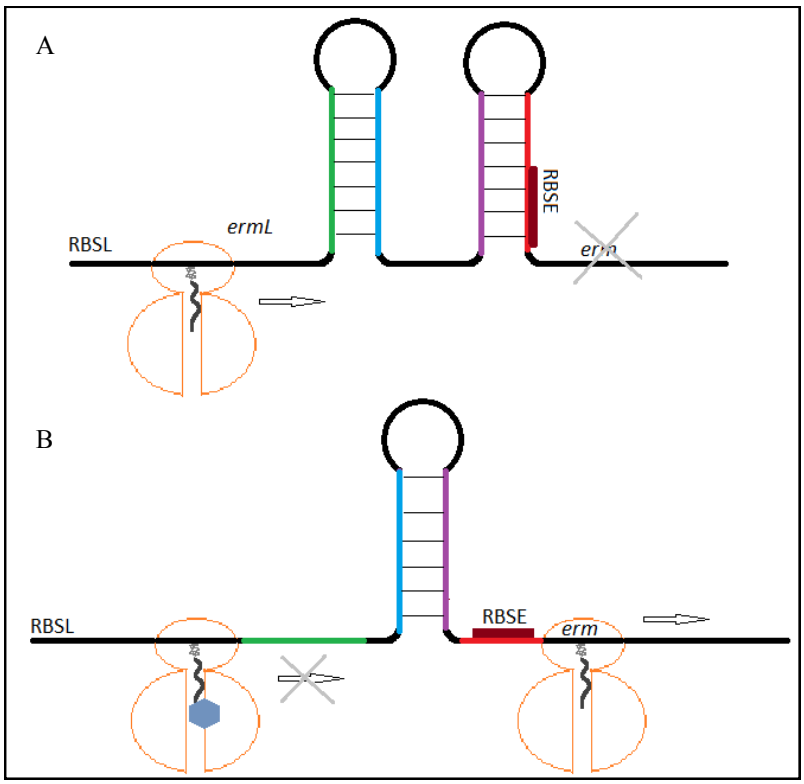

Figure 1. Schematic representation of *erm* expression regulation. In the absence of an inducer (A), the methylase gene *erm* is not translated because its ribosome binding site (RBSE) is sequestered in mRNA secondary structure. During induction (B), an erythromycin-bound ribosome stalls at the *erm*L leading to a change in the mRNA conformation allowing translation of *erm*.

This inducible resistance leads to a dissociated phenotype that is resistant to inducers (erythromycin) and susceptible to non-inducers (clindamycin).

Detection of inducible resistance is important in *Staphylococcus* and beta-hemolytic streptococci. This is achieved by placing an erythromycin disk near to a clindamycin disk on a MH agar plate. [11,12] A D-shaped zone around the clindamycin disk (D-test positive) reveals the presence of this type of resistance mechanism (Figure 2).[9]

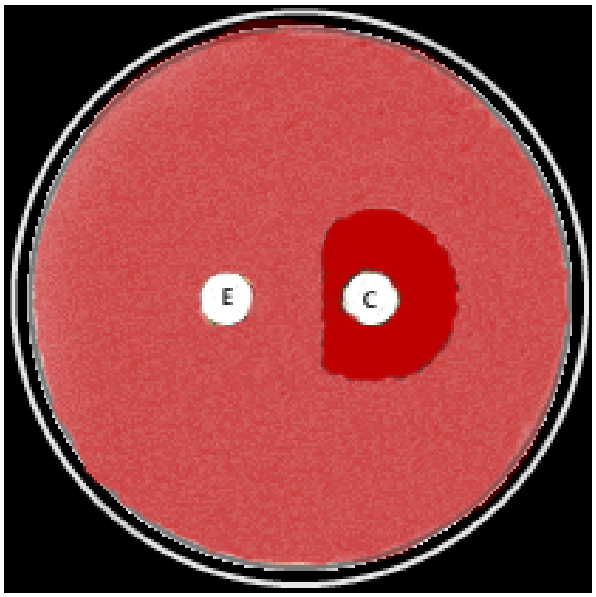

Figure 2. Schematic representation D-test. Organisms with inducible methylase expression are phenotypically resistant to erythromycin (inducer) but may appear susceptible to non-inducers (clindamycin). The D-test allows for the detection of inducible resistance by the modification of the inhibition zone around the clindamycin disk © when tested close to an erythromycin disk (E).

Isolates with inducible resistance to macrolides should also be reported resistant to clindamycin by the laboratory.[13]

In some strains, expression of methylase enzymes occurs in the absence of an inducer (constitutive expression) due to deletions or mutations in the *erm* gene conferring resistance to macrolides and clindamycin.

Enzymatic drug modification

Several enzymes produced by bacteria have been identified to have the ability to modify these antibiotics.

Esterases and phosphotransferases produced by Enterobacteriaceae inactivate the lactone ring of macrolides conferring resistance.

Phosphotransferases and nucleotidyltransferases have been associated with resistance to lincosamides in *Streptomyces, Staphylococcus, Bacteroides,* and *Streptococcus agalactiae*. [5,6]

Efflux

Active efflux of antibiotics by the expression of efflux pumps has been linked to resistance in gram positive organisms and it is responsible for the intrinsic resistance to macrolides and lincosamides of *Escherichia coli* and *Enterococcus faecalis.* [14]

Macrolides have been in use since the early 1950s and are a major alternative to the use of penicillins and cephalosporins for the treatment of infections due to gram-positive microorganisms (mostly b-hemolytic streptococci and pneumococci). Additionally, erythromycin is one of the safest antibiotics in clinical use.

However, resistance to erythromycin was reported shortly after this antibiotic was introduced and a rapid increase in macrolide resistance was observed in the 1980s. Surveillance of macrolide resistance is necessary and important as the incidence of macrolide resistance is highly variable with regard to the country and type of infection.

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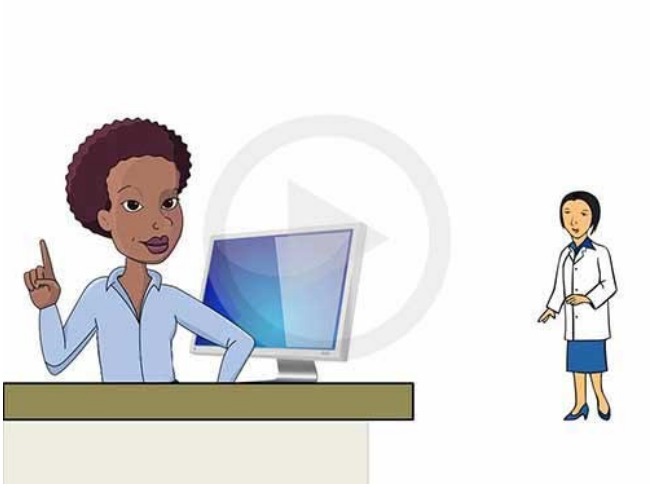
Professional Development Course

The 2016-2017 course is nearing its end. The 2018 course will start in January 2018.

Registration for the course will start in October 2017.

Stay tuned for more news!



Video Challenges

In 2017, CMPT implemented a new tool in an effort to extend EQA to the extra-analytical processes in the total laboratory testing. Two Video Challenges were sent (VC164 and VC172) with the Clinical Bacteriology Surveys. The videos and questionnaires can be accessed through the CMPT's website or through the CMPT's YouTube channel:

https://www.youtube.com/channel/UCrUFfJjsjUcjSjAUlyKKysQ/featured

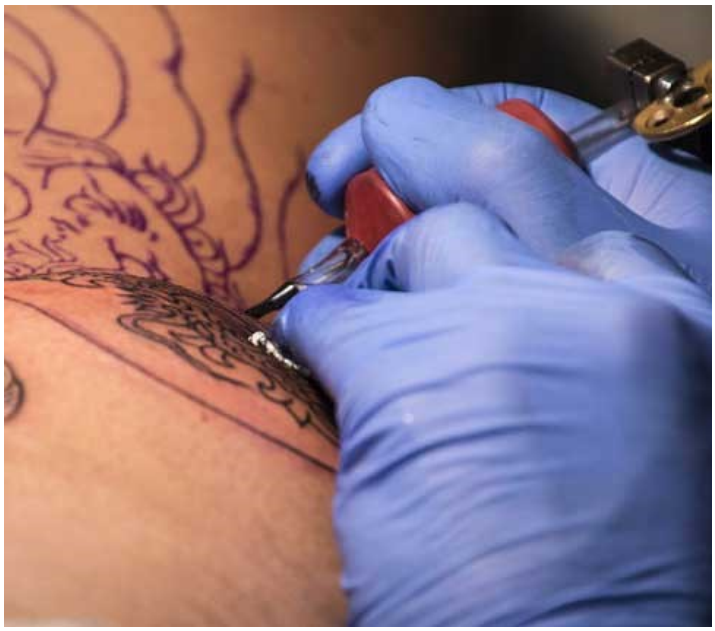
Case report

In November 2016, CMPT sent the Clinical Bacteriology PT sample, M163-3, with the survey M163. Sample M163-3 as a simulated wound sample collected from a 50 year old naval diver with an arm wound injury and cellulitis. The sample contained a strain of *Vibrio vulnificus*. The critique addressed identification and clinical relevance of this type of infection.

In June 2017, an article in the medical journal BMJ Case Reports, reported a fatal case of *Vibrio vulnificus* infection in a man with an infected tattoo.

You can access CMPT's critique: http://cmpt.ca/m163-3/

and the news report: http://www.cbsnews.com/news/man-dies-after-flesh-eating-bacteria-vibrio-infects-new-tattoo/



Upcoming Events

OCTOBER 2017

POLQM - 2017 Quality Management Conference for Medical Laboratories
October 1 - 3, 2017 Vancouver, Canada
More info: http://conference.polqm.ca/

CMPT Annual General Meeting
October 16, 2017 Vancouver, BC
More info: info@cmpt.ca

APRIL 2018

28th European Congress of Clinical Microbiology and Infectious Diseases
April 21 - 24, 2018 Madrid, Spain
More info: http://www.eccmid.org/

ABOUT CONNECTIONS

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