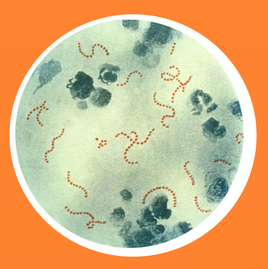

Streptococcus pyogenes: molecular basis of pathogenia and the emergence of antibiotic resistance

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INTRODUCTION

Streptococcus pyogenes is a grampositive human pathogen with a high clinical, been able to cause acute infections. It is named as Group A Streptococcus (GAS) because it has the serogroup A carbohydrates, besides produces β-hemolysis in blood agar medium.

In 2005, the estimated number of people suffering from a serious GAS disease was approximately 18,1 million, with a further 1,78 million new cases occurring each year, accounting for 517.000 deaths annually. The real burden of GAS is underestimated because it isn't universally notifiable, so this data are not entirely real. The majority of deaths are attributable to RHD and its complications, followed by invasive group A streptococcal diseases (iGAS), then acute post-streptococcal glomerulonephritis (ASPGN). Also contributing to morbidity and healthcare expenditure is the highly prevalent condition of pharingitis and tonsillitis. In figure 1 are shown the different symptoms that can produce the bacteria.

The objective is to determine what is currently known about the mechanisms of *S. pyogenes* for infect the human and it has been analyzed the importance of the emerge of antibiotic resistance in this pathogen.

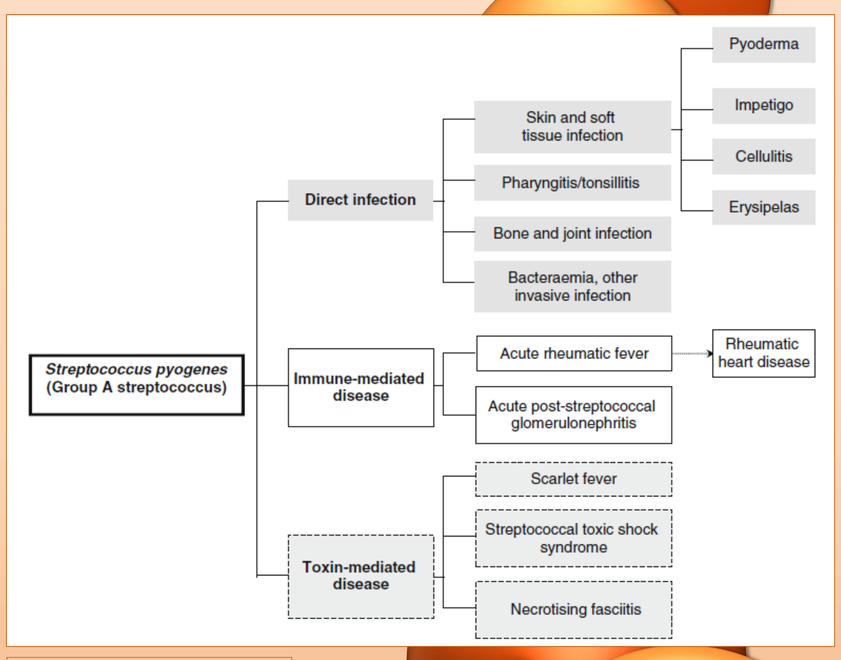

Figure 1. Clincal of *S. pyogenes*

MOLECULAR BASIS OF PATHOGENIA

First, it was thought that these bacteria were extracellular but finally was discovered that they could enter to host cell and stay there. *S. pyogenes* firstly adhere to different epithelial cells, and subsequently occurs the internalization. The bacteria can also disseminate to secure regions and persistence with different mechanisms. There are also extracellular products contributing to streptococcal pathogenia, the exotoxins.

For each step there are important molecules, essential for the appearance of the illness. Some of them are shown below.

1. Adhesion

Different adhesins to attach at the host cell:

- **Hialuronic acid Capsule (HA)**
- **Lipoteichoic acid (LTA)**
- **Pili**
- **Protein M** → *emm* gene
- **Fibronectin-binding protein**

Some of them have antifagocitary ability (HA, M protein)

2. Internalization

Most important invasins for enter to host cells:

- **SfbI/F1**
- **Protein M**

3. Dissemination and persistence

Production of acute and recurrent infections.

Dissemination:

-Troya horse theory, secure dissemination

Persistence:

-Hide in extracellular matrix

-Remain in cytoplasm or intracellular compartment

4. Exotoxins

- **Streptolisyn O (SLO)**
- **Streptolisyn S (SLS)**
- **STSS exotoxins → superantigens**

ANTIBIOTIC RESISTANCE

Now a days, the treatment is based on the use of antibiotics to eliminate the bacteria. The most habitual used are penicillin, but also have been used macrolides, like erythromycin. *S. pyogenes* is still susceptible to penicillin but not for macrolides, there have been notified resistant strains for it. There are two mechanisms for its resistance:

-Alteration of target site: modification of rRNA 23S, avoiding the action of the antibiotic.

-Efflux pump: through this mechanism the antibiotic is expulsed outside.

There are more resistances to other antibiotics, like tetracycline but not with the same percentage, so the most important are the macrolides.

Besides, have been reported the appearance of tolerant strains to penicillin, is not the same as the previous resistances. These strains maintain quiescent until penicillin is retired, this occurs due to *stk* gene.

Susceptible

- β-lactams → Penicillin

Resistance

- Macrolides → Erythromycin	32.8 %
- Tetracyclines →Tetracycline	6.8 %
- Lincodamides → Clindamycin	6.5 %

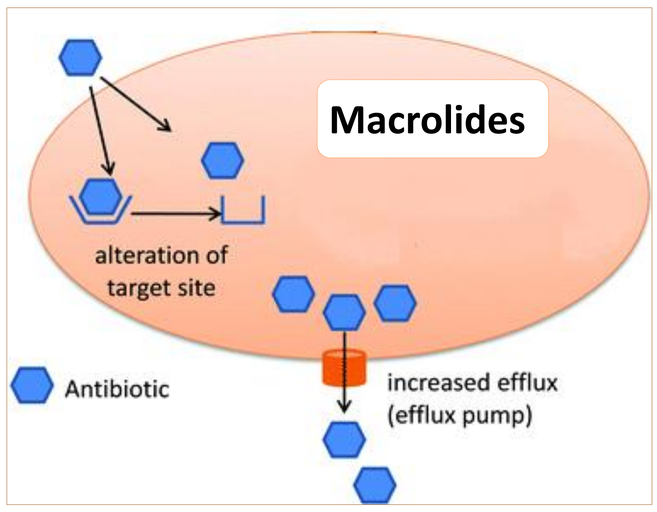

Figure 2. Mechanisms of antibiotic resistance

CONCLUSIONS

Through the entirely project we can observe that the capability of the bacteria to adhere and the internalization in secure zones, avoid the host immune system and antibiotic treatment. Together with the ability to invade PMNs and disseminate through the human body makes this pathogen so versatile and not easy to eradicate.

The use of penicillin not eliminates the intracellular bacteria so fail in completely eradication. Instead of that, macrolides have this capability, but there is an important problem, the emerging resistances.

Because of all that, is necessarily an extensive study to find out how avoid this persistence and dissemination to prevent this acute infections. Also it's important to find out new targets to attack the bacteria and finally eradicate this pathogen efficiently.

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