

## Systematic Review

### \*Corresponding author

**Sydney C. Leão, MD**  
Department of Pathology  
Paulista School of Medicine  
Federal University of São Paulo  
São Paulo, SP, Brazil  
E-mail: [sydneyleao@hotmail.com](mailto:sydneyleao@hotmail.com)

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# The Relationship Between Different Types of Streptococci and Pharyngotonsillitis: A Systematic Review

**Sydney Correia Leão, MD<sup>1\*</sup>; Tania Maria de Andrade Rodrigues, MD<sup>2</sup>**

<sup>1</sup>Medical Pathology Assistant, Department of Pathology, Federal University of São Paulo, São Paulo, SP, Brazil

<sup>2</sup>Full Professor, Department of Morphology, Federal University of Sergipe, São Cristóvão, SE, Brazil

### ABSTRACT

**Introduction:** Streptococci were initially viewed by Louis Pasteur in 1879. Brown, in 1919, created the first systematized classification of streptococci in  $\alpha$ ,  $\beta$  and  $\gamma$ . Rebecca Lancefield contributed for knowledge of streptococcal polysaccharides discovering groups and M cell wall protein. Streptococci are gram positive, catalase and oxidase negative. *Streptococci* related to pathogenesis of acute sore throat are *Streptococcus*  $\beta$ -hemolytic of the groups A, B, C, F and G. **Objective:** Our objective was to make a review of the different types of streptococcus that can cause infection in the oropharynx.

**Review:** *Streptococcus pyogenes* is belonging to the Lancefield grouping. Skin and mucous membranes of humans are the only known reservoir in the nature of streptococcus group A. *Streptococcus* of Group B (SGB) was originally isolated by Nocard in 1887. The primary habitat of these bacteria is the human colon, although it may colonize the oropharynx and especially, the vagina. For this reason, in mid-1960, the SGB has become a major cause of perinatal bacterial infection, including bacteremia and urinary tract infection in pregnant women. Group C is involved in purulent pharyngitis outbreaks. According to Fox et al, *Streptococcus anginosus* is the most common isolate  $\beta$ -hemolytic group C in the oropharynx. *Streptococcus* Group C (SGC) is reported as “pyogenes-like” because it shares important virulence factors such as hemolysins, extracellular enzymes and M proteins as well as the SGA.

**Conclusion:** We conclude that it's important to have knowledge about the different types of streptococci to better treat patients with sore throats and problems associated with this condition.

### INTRODUCTION

Streptococci were initially viewed by Louis Pasteur in 1879. He had observed under the microscope “some chain account”, which in 1884 was named *Streptococcus* by Rosenbach. Brown, in 1919, created the first systematized classification of streptococci in  $\alpha$ ,  $\beta$  and  $\gamma$ , from standard hemolysis checked on blood agar plates. Colonies of streptococci that produce a clear halo around due to complete lysis of erythrocytes were called  $\beta$ -hemolytic. Strains of streptococci that produce partial hemolysis give a greenish aspect, bright; around the colony are the  $\alpha$ -hemolytic. Colonies that are not capable of producing hemolysis are identified as  $\gamma$  or non-hemolytic and rarely cause infection in man.

Streptococci are gram positive, catalase and oxidase negative. They tend to grow in pairs or chains. They are anaerobic optional, although some species grow best aerobically. The cell wall composition is similar to other Gram-positive bacteria, although richer in peptidoglycans, where are inserted various carbohydrates, lipoproteins and surface protein antigen.<sup>1</sup>

Rebecca Lancefield contributed for knowledge of streptococcal polysaccharides discovering groups and M cell wall protein whose antigenic molecules are considered to become

the basis for grouping these micro-organisms.<sup>2,3</sup> The antigens detected in the group of Lancefield consisting of cell wall polysaccharides (groups A, B, C, F and G in humans), and cell wall lipoteichoic acids (group D enterococci). Other Streptococcus, such as viridans group, have no cell wall antigen, and cannot be included in any of these groups.<sup>4</sup>

Streptococci related to pathogenesis of acute sore throat are Streptococcus  $\beta$ -hemolytic of the groups A, B, C, F and G. In bacterial pharyngotonsillitis (PT), the main single agent is *Streptococcus pyogenes*, although in the last 50 years, an increased number of human infections caused by  $\beta$ -hemolytic Streptococcus in groups B, C, and G, have been observed worldwide.<sup>5,6</sup>

## OBJECTIVE

Our goal was to make a review of the different types of streptococcus that can cause infection in the oropharynx.

## REVIEW

### *Streptococcus pyogenes* (SGA)

*Streptococcus pyogenes* is belonging to the Lancefield grouping. Skin and mucous membranes of humans are the only known reservoir in the nature of streptococcus group A. Its pathogenicity is associated with at least two surface molecules, conferring resistance factor: The M protein and the capsular hyaluronic acid.<sup>1</sup>

The M protein is a flexible and fibrillar structure situated on the surface of the bacterial cell wall, which provides resistance and anti-phagocytic polymorphonuclear leukocytes protective against. Molecularly, they are dimeric and designed in a carboxyl-terminal portion. In their amino-terminal hypervariable portion is the specific nature of their serotype. Currently, there are about 170 types of M protein, found in "emm" patterns with more than 750 subtypes.<sup>7-9</sup>

The capsule is another antiphagocytic hialuronic structure, offering a protection, interfering in the setting of phagocytes. There are other so-called virulence factors such as the opacity factor, hemolysin, streptolysins, streptococcal pyrogenic exotoxin, C5a peptidase and deoxyribonuclease, all with specific activities of antigenic protection.<sup>4,10</sup>

### *Streptococcus agalactiae* (SGB)

$\beta$ -hemolytic streptococcus or streptococcus of group B (SGB) was originally isolated by Nocard in 1887 and described as the causative agent of bovine mastitis. They are encapsulated microorganisms, diplococcus gram-positive  $\beta$ -hemolytic on blood agar, with most of its strains resistant to bacitracin. Differentiation among the other Lancefield groups is given by capsular polysaccharides and specific antigenic proteins. They include serotypes Ia, Ib, Ia/c, II, III, IV, V, VI, VII and VIII. The SGB produces many virulence factors, including hemolysins, encap-

sulated polysaccharides, C5a peptidase (only in human pathogenic strains) and some strains produce hyaluronidase and various surface proteins which stimulates the secretion of IgA and act as adhesins.<sup>11</sup>

The primary habitat of this bacterium is the human colon, although it may colonize the oropharynx and especially, the vagina. For this reason, in mid-1960, the SGB has become a major cause of perinatal bacterial infection, including bacteremia, amniotites, endometritis and urinary tract infection in pregnant women, as well as focal or systemic infections in newborns. The SGB also cause infections in nonpregnant adults including meningitis, endocarditis and septic arthritis.<sup>12,13</sup>

The PT by SGB is reported, mostly in young adults and adults with any immunosuppressive underlying disease. There were no reports of acute SGB pharyngotonsillitis in children of school age.

### *Streptococcus anginosus* (SGC)

Group C is involved in purulent pharyngitis outbreaks. According to Fox et al, *Streptococcus anginosus* is the most common isolate  $\beta$ -hemolytic group C in the oropharynx, while the *Streptococcus equisimilis* has been associated with PT. Turner et al<sup>14</sup> reported that *Streptococcus equisimilis* showed strong evidence of being causative agent in patients with PT as *Streptococcus anginosus* appears to be part of the microbiota of the oropharynx. Al-Charrakh et al<sup>15</sup> in their study of the prevalence of Streptococcus  $\beta$ -hemolytic groups C and F in patients with acute pharyngitis, report that these groups are involved in acute PT at 6.2% of cases. Detected yet, many of these isolates showed ability to produce more than a virulence factor. According Zaoutis et al<sup>16</sup>, Group C Streptococcus (SGC) and Group G Streptococci (SGG) are reported as "pyogenes-like" because they share important virulence factors such as hemolysins, extracellular enzymes and M proteins as well as the SGA.

Regarding the similarity between the SGC and the SGA, Shah et al<sup>17</sup> reported that although the  $\beta$ -hemolytic group C is not a common cause of acute PT, comprises similar characteristics to Group A Streptococcus, as both cause isolated exudative, PT and the like cellulitis, making them clinically indistinguishable.

Strains of Streptococcus Group C contains fibrinolysin and streptolysin, such as streptolysin O (ASO). Given this proven by Johnson et al<sup>18</sup> who demonstrated in their studies that the group C Streptococcus showed a strong immune response via high titer antibody against ASO (ASO), and that this increase concomitantly persisted in the presence of streptococcus in the oropharynx of the patient.

Although the microbiological characteristics and similar virulence between the GSC and EMS, compared to non-suppurative complications, Killian<sup>11</sup> reports that the GSC may is

Complications of acute pharyngotonsillitis	
Suppurative	Non-suppurative
Peritonsillar and retropharyngeal abscess	Rheumatic fever
Sinusitis	Post-streptococci glomerulonephritis
	Scarlet fever

Table 1: Some complications of acute PT.

Drug	Dosage
Amoxicillin	500 mg, 3x each day, for 10 days
Amoxicillin/Clavulanate	500+125 mg, 3x each day, for 10 days
Benzathine penicillin G	1.200.000UI, IM, one dose
Erythromycin	250 mg, 4x each day, for 10 days
Clindamycin	300 mg, 4x each day, for 10 days

Table 2: Treatment for acute pharyngotonsillitis.

The major criteria for diagnosis includes	The minor criteria includes
Arthritis in several joints (polyarthritis)	Fever
Heart inflammation (carditis)	High ESR (erythrocyte sedimentation rate, an laboratory sign of inflammation)
Nodules under the skin (subcutaneous nodules or Aschoff bodies)	Joint pain (arthralgia)
Rapid, jerky movements (Sydenham's chorea)	EKG changes (electrocardiogram)
Skin rash (erythemamarginatum)	Other laboratory findings (elevated c-reactive protein, elevated or rising streptococcal antigen test)

Table 3: The Jones criteria for diagnosis of rheumatic fever.

related to acute glomerulonephritis but not with the FR. This fact contradicted a study by Haidan et al<sup>19</sup>, who searched PT by SGC and SGG an aboriginal population, which reported that there was a high incidence of rheumatic fever *versus* low incidence of SGA infection, leading them to investigate the correlation of a group non-A, FR, suggesting in that results *in vitro*, the SGC and SGG in those conditions have the potential for initiating an autoimmune response, triggering acute rheumatic fever.

**SYSTEMIC EFFECTS**

Streptococcal PT, if not adequately addressed, can lead to non-suppurative complications such as rheumatic fever and glomerulonephritis (Tables 1 and 2).<sup>1,4</sup>

Rheumatic Fever (RF) is a rheumatic and inflammatory disease, consequence of an untreated upper airway infection for  $\beta$ -hemolytic streptococcus of group A, usually with immunological basis. It is a disease with significant prevalence in the population of school age, manifested as polyarthritis, carditis, chorea, erythema marginatum and/or subcutaneous nodules and is considered the leading cause of chronic valvular heart disease in young adults in developing countries.<sup>9</sup> The Jones Criteria guides doctors to clinically diagnose of Rheumatic fever (Table 3). According to American Heart Association (AHA), two major criteria, or one major and two minor criteria plus a previous his-

tory of sore throat infection are necessary to diagnosis.<sup>20</sup>

The M protein is intrinsically linked to the development of rheumatic fever, which postulated involves molecular mimicry between proteins of the host and streptococcus, where the host antibodies against streptococcal antigens, do not recognize their own structures, converging in the humoral and cellular cross-recognition. This phenomenon occurs between the M protein and myosin in cardiac tissue, resulting in aggression and cell damage.<sup>10</sup>

**CONCLUSION**

It is important to have knowledge about the different types of streptococci to better treat patients with sore throats and problems associated with this condition.

**CONFLICTS OF INTEREST:** None.

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