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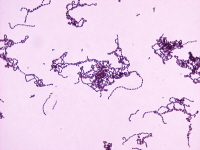
INTRODUCTION  
Group A *Streptococcus* (GAS) is a pathogen that causesacute bacterial pharyngitis in human and it can be spread through aerosols among individuals, or by eating contaminated food (Bisno *et al*., 2003) . The site of infection of GAS is in the pharyngeal mucosa, where it causes pharyngitis (Carapetis *et al*., 2005. The pathogen enters the body through the ciliated epithelium in the nose, which results in edema and hyperemia of the nasal mucous membranes. This condition induces high secretory activity of the mucous glands thus causing disruptive symptoms (Red Book, 2006). GAS pharyngitis pathogenesis is divided into three stages as follows : adherence to the pharyngeal epithelium, collection of nutrients needed for proliferation and avoidance of the host immune response as shown in (Fig. 1) below (Bisno *et al*., 2003). 

Image of Streptococcus pyogenes.(emedicine.medscape.com)

  
 Table 1, ( Journal compilation © 2008 Blackwell Publishing Ltd, *Cellular Microbiology*, **11**, 1–1)

**Survival of GAS in blood**

GAS is open to the elements of human plasma at the points of inflammation where it causes superficial infections as a result of vascular seepage, which is facilitated by the action of M protein interacting with fibrinogen and the b2-integrin adhesion molecule on the neutrophils surface. This consequently leads to an inflammatory cascade which involves the discharge of heparin-binding protein and induces vascular seepage ( Herwald, etal. 2004). Shock is underlined by the pathophysiological mechanism of vascular permeability, cross linking of the M protein and fibrinogen with b2-integrin might be instrumental in what causes or leads to the development of streptococcal toxic shock syndrome. Plasma is a rich medium that aids bacterial growth. It also contains immune system components that GAS must elude to survive, including opsonizing antibodies and complement. The normal function of hosts defences is disrupted by the several interactions between plasma proteins and GAS proteins (Walker, etal 2005). Also, GAS expresses surface proteins that have a high affinity for several human plasma proteins such as albumin, fibrinogen, a2-macroglobulin, IgG and plasminogen (McArthur, etal, 2006) which suggests that the pathogen has evolved mechanisms to capture and to use host proteins for enhanced survival in vivo.

**Epithelial cell adherence**

Recent discovery reveals that GAS pili-like cell surface structures are key factors in pharyngeal epithelial cell adherence and biofilm formation as shown in ([Fig. 1B](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full#f1)). The pili are programmed by genes found in the fibronectin, collagen-binding, T-antigen, FCT, gene region and are composed of the main pilus subunit (spy0128 in the serotype M1 strain SF370) and two ancillary proteins ([Mora et al., 2005](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full#b14)). The principal pilus subunit tallies with the T antigen of the Lancefield T serotypes, which is one of the major GAS classification scheme. Assembly of GAS pili depends on a sortase encoded by genes in the FCT region and in M3 strains, on a signal peptidase encoded upstream of the T antigen ([Zahner etal., 2007](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full" \l "b16" \o "Link to bibliographic citation)).Other GAS proteins are also involved in epithelial cell adherence. For example, the serotype M3 GAS emergence has been connected to the accumulation of a bacteriophage-encoded phospholipase A2 (SlaA) whose mechanism of action appears to involve penetrating host cells hence allowing adherence and binding to host epithelium. The The ability of A Δ*slaA* strain to cause pharyngitis in the cynomolgus macaque is impaired thus providing a significant support for the key role of SlaA in GAS pharyngeal pathogenesis ([Sitkiewicz et al., 2006](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full" \l "b18" \o "Link to bibliographic citation)).

**Intracellular invasion**

GAS is mainly an extracellular pathogen, the past decade data have shown that the organism may invade and persist within epithelial cells ([Wang et al., 2006](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full#b7)). The exact role of this event in GAS pathogenesis is yet unclear. Many of the proteins that are involved in GAS epithelial cell invasion also take part in adherence, this includes FnBPs, M protein and streptocococcal collagen-like protein. This protein is located on the cell wall and it is required for invasive infection. T cells when exposed to the M protein cross-react with similar epitopes on human cardiac myosin and laminin, leading to the pathogenesis of rheumatic heart disease, (Guilherme, etal, 2006). The signalling pathways mediating GAS invasion begin with bacterial binding to eukaryotic cell surface integrins, which results in actin cytoskeletal rearrangement and GAS internalization ([Purushothaman et al., 2003](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full" \l "b19" \o "Link to bibliographic citation)). The binding of GAS with integrin-bound Fn leads to upregulation of growth factor β1, which in turn triggers cell surface expression of 0003b15 integrin and Fn, this consequently makes the cells better targets for streptococcal binding ([Wang et al., 2006](http://onlinelibrary.wiley.com/doi/10.1111/j.1462-5822.2008.01225.x/full#b20)).

***Immune system avoidance***

For GAS to cause pharyngitis and start the colonization of the oropharynx, the host innate immune response must be overcome for a periods of time (Ashbaugh *et al*., 2000; Virtaneva *et al*., 2005). GAS has modified several mechanisms for escaping the host innate immune response as observed in M protein and hyaluronic acid capsule (Cunningham, 2000). There are other immune proteins which add to GAS pharyngitis such as streptococcal inhibitor of complement (Sic), and secreted DNases . ScpA is a cell surface serine protease that specifically cleaves C5a, thereby decreasing C5apolymorphonuclear (PMN) leucocyte binding and subsequent PMN recruitment (Brown *et al*., 2005). Sic is a protein secreted to produce protean effects on host immunity at the back of pharynx. In the course of pharyngitis, the gene that encodes Sic is quickly upregulated (Virtaneva *et al*., 2005). In addition to preventing the complement membrane attack complex, Sic gets involved with pharyngeal immune defence function such as lysozyme, b-defensins, and the cathelicidin LL-37. Due to the interaction of Sic with proteins of the immune system, the bactericidal activity against GAS is strongly reduced.

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