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Interdisciplinary Clinical Management and Nursing Care Approaches in Scarlet Fever

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Abstract

Background: Scarlet fever is an acute, toxin-mediated illness caused by Group A *Streptococcus pyogenes* (GAS), historically a major cause of childhood morbidity and mortality. It is characterized by a distinctive sandpaper-like rash, strawberry tongue, and fever, primarily affecting school-aged children. The disease has seen a global resurgence in recent decades, linked to the emergence of more virulent GAS strains.

Aim: This article aims to provide a comprehensive overview of scarlet fever, detailing its etiology, pathophysiology, clinical presentation, and the critical importance of timely diagnosis and management to prevent both acute suppurative complications and severe immune-mediated sequelae like acute rheumatic fever and poststreptococcal glomerulonephritis.

Methods: The diagnosis is primarily clinical, based on characteristic signs and symptoms, and confirmed through laboratory testing such as rapid antigen detection tests (RADT) and throat culture. Molecular methods like PCR are increasingly used for strain identification during outbreaks. Management centers on antibiotic therapy and supportive care.

Results: Penicillin remains the first-line antibiotic treatment, effectively reducing symptom duration, transmission, and complication risks. However, rising macrolide and clindamycin resistance in some regions complicates management for penicillin-allergic patients. With prompt treatment, the prognosis is excellent, though complications can arise from delayed or inadequate care.

Conclusion: Scarlet fever is a re-emerging public health concern. Its successful management relies on a coordinated, interprofessional approach involving clinicians, nurses, and pharmacists for accurate diagnosis, appropriate treatment, patient education, and infection control to optimize individual and community health outcomes.

Keywords: Scarlet Fever, Group A Streptococcus, Streptococcus pyogenes, Superantigen, Scarlatiniform Rash, Strawberry Tongue, Poststreptococcal Complications..

1. Introduction

Scarlet fever is an acute, toxin-mediated illness characterized classically by a blanching, erythematous, maculopapular rash with a distinctive “sandpaper-like” texture, a “strawberry tongue,” and exudative pharyngitis (see Image. Scarlet Fever).[1] The syndrome most often develops in the setting of pharyngeal infection, although it can also complicate other manifestations of group A streptococcal disease. The causative organism, *Streptococcus pyogenes* (group A Streptococcus or “GAS”), is a gram-positive coccus arranged in pairs and chains, strictly adapted to humans.[2] This pathogen is responsible for a wide spectrum of clinical presentations, ranging from superficial infections such as pharyngitis and impetigo to deeper tissue involvement including cellulitis, erysipelas, and necrotizing fasciitis, as well as severe invasive diseases and toxin-mediated syndromes.[2] The distinctive clinical picture of scarlet fever is primarily driven by streptococcal pyrogenic exotoxins (SPEs), which function as superantigens released during GAS infection.[5] These exotoxins bypass conventional antigen processing and presentation pathways, directly linking major histocompatibility complex class II molecules on antigen-presenting cells to specific Vβ regions of T-cell receptors. This results

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in massive, polyclonal T-cell activation and an exaggerated cytokine response.[5] The ensuing inflammatory cascade manifests clinically as the diffuse erythematous rash, circumoral pallor, and mucocutaneous changes that define scarlet fever. The strawberry tongue, for example, results from prominent, erythematous papillae on an edematous tongue surface, initially coated with a white exudate that later desquamates.[1][5]

GAS bacterial pharyngitis and scarlet fever most commonly affect school-age and adolescent children, reflecting both host susceptibility and environmental factors that favor transmission.[3] Crowded settings such as schools, daycare centers, and boarding institutions facilitate spread through respiratory droplets generated by coughing, sneezing, or close contact.[3][4] Household and community outbreaks may occur when hygiene and infection control practices are inadequate, and secondary cases among family members and caregivers are not uncommon.[4] Nonetheless, scarlet fever can occur in any age group, particularly in environments where close interpersonal contact is frequent, including households, military barracks, and nursing homes.[3][4] Although the disease is generally less common in adults, they remain susceptible, especially if they lack immunity to circulating toxigenic GAS strains. Scarlet fever is most often associated with GAS pharyngitis, but it may also complicate other invasive or noninvasive GAS infections, including erysipelas, cellulitis, or necrotizing fasciitis.[2][5] In these contexts, the same superantigen-mediated mechanisms drive the rash and systemic symptoms, even when the primary focus of infection is outside the oropharynx. Historically, GAS serotypes have exhibited cyclical epidemiological patterns, with particular emm types and toxin profiles predominating at different times.[7][8] Certain strains, especially those harboring specific superantigen genes such as *speA*, *speC*, and *ssa*, demonstrate enhanced virulence and transmissibility.[6] These genes encode potent superantigens that increase the organism's fitness within the human host and contribute to both the intensity of the toxin-mediated manifestations and the propensity for invasive disease.[5][6]

Epidemics of scarlet fever and other invasive GAS infections were common in the 19th century, often associated with substantial morbidity and mortality, particularly in children.[7][8] With improvements in living conditions, public health measures, and the advent of antimicrobial therapy, the overall prevalence and severity of scarlet fever declined markedly through the 20th century.[8] However, beginning in the 1980s, a resurgence of GAS infections was documented in several regions, linked to the emergence and global spread of more virulent epidemic strains.[8] Over the past decade, renewed increases in scarlet fever notifications have been reported in multiple countries, again associated with specific emm types and superantigen profiles that appear to confer both higher transmissibility and aggressive clinical behavior.[8] These epidemiological shifts underscore the dynamic nature of GAS as a pathogen and the importance of ongoing surveillance. Beyond its acute manifestations, scarlet fever holds clinical importance because of the potential for both suppurative and non-suppurative complications. Locally, untreated or inadequately treated GAS pharyngitis may progress to peritonsillar or retropharyngeal abscess, otitis media, or sinusitis.[2] Systemically, GAS infection can trigger immune-mediated sequelae such as acute rheumatic fever and subsequent rheumatic heart disease (RHD), as well as poststreptococcal glomerulonephritis (PSGN).[2] These conditions develop after a latent period following the initial pharyngeal or skin infection and result from host immune responses that cross-react with cardiac, renal, or other tissues. RHD, in particular, remains a major cause of cardiovascular morbidity and mortality in many low- and middle-income countries.[2] The recognition of scarlet fever as an early, treatable manifestation of GAS infection therefore has important implications for long-term health outcomes.

Prompt diagnosis and appropriate antibiotic therapy are central to the management of scarlet fever and its underlying GAS infection. Early treatment not only accelerates symptom resolution and reduces contagiousness but also substantially decreases the risk of non-suppurative complications, especially acute rheumatic fever.[2][5] From a public health perspective, identifying and managing scarlet fever cases in congregate settings can help control outbreaks, limit transmission, and protect vulnerable populations such as younger children, the elderly, and individuals with comorbidities.[3][4] In summary, scarlet fever represents a classic example of a toxin-mediated exanthem arising from a common bacterial pathogen, *Streptococcus pyogenes*.[1][2] Its characteristic clinical features reflect the action of streptococcal pyrogenic exotoxins acting as superantigens, which drive an intense host immune response and distinctive mucocutaneous findings.[5][6] Although its overall incidence declined for much of the 20th century, the emergence of more virulent epidemic GAS strains has contributed to a resurgence of scarlet fever and invasive infections in recent decades.[8] Given the potential for serious acute and delayed complications, including RHD and PSGN, timely recognition and treatment of scarlet fever remain essential components of pediatric and general clinical practice.[2][5]

Etiology

Group A Streptococcus (GAS), the etiologic agent of scarlet fever, is a gram-positive, non-spore forming coccus that is catalase- and oxidase-negative and typically grows in pairs and chains when viewed microscopically.[2] In the laboratory, GAS thrives on blood agar incubated at 35 °C to 37 °C, with optimal growth often observed in an atmosphere enriched with

approximately 10% carbon dioxide.[6] On blood agar plates, the organism forms smooth, moist, greyish-white colonies with clearly defined margins, usually measuring more than 0.5 mm in diameter.[6] These colonies are characteristically surrounded by a distinct zone of complete hemolysis (β-hemolysis), reflecting the organism's ability to completely lyse red blood cells, a key feature used for routine identification.[6] GAS is widely distributed in nature but is strictly adapted to humans as its primary reservoir. Within humans, the mucous membranes of the upper respiratory tract and the skin represent the principal ecological niches. From these sites, GAS is responsible for a broad spectrum of clinical infections, most commonly involving the upper respiratory tract and skin. These include acute pharyngitis, scarlet fever, impetigo, cellulitis, and erysipelas, spanning a continuum from mild, localized infections to severe, invasive GAS (iGAS) disease.[6][9] Invasive infections arise when the organism breaches epithelial barriers and gains access to normally sterile sites such as the bloodstream, cerebrospinal fluid, pleural cavity, or deep soft tissues.[9] Both noninvasive and invasive GAS infections have shown rising incidence globally and are associated with substantial morbidity and mortality, underscoring the clinical and public health significance of this pathogen.[6][9]

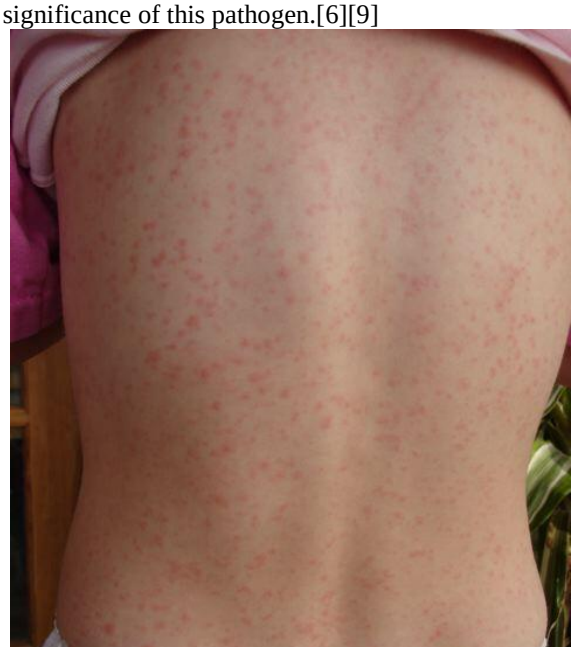

Fig. 1: Scarlet Fever.

Beyond acute infection, GAS is notable for its capacity to trigger immune-mediated sequelae, including acute rheumatic fever (ARF), poststreptococcal glomerulonephritis (PSGN), and rheumatic heart disease (RHD).[10] These conditions arise from aberrant immune responses in which antibodies or T cells directed against streptococcal antigens cross-react with host tissues in the heart, joints, kidneys, or central nervous system. In the United States, recent data suggest that approximately 1% to 3% of patients with untreated GAS infections, typically GAS pharyngitis, will go on to develop ARF, and up to 60% of those individuals may progress to chronic RHD.[10] This postinfectious burden highlights the importance of early recognition and treatment of GAS infections, including those presenting as scarlet fever. From a taxonomic and serologic standpoint, streptococci are categorized using the Lancefield classification, which groups organisms (A to O) according to cell wall carbohydrate antigens detectable by specific antisera.[11] At least 20 such serological groups have been identified, with groups A, B, and C being particularly relevant to human disease.[11] GAS belongs to Lancefield group A and is therefore designated as group A Streptococcus.[12][13] Other streptococci within different Lancefield groups can produce syndromes that clinically resemble GAS infections. A notable example is group B Streptococcus (GBS; *Streptococcus agalactiae*), which colonizes the gastrointestinal and genital tracts of humans and is an important cause of puerperal sepsis in mothers and invasive neonatal disease, including pneumonia, bacteremia, and meningitis.[14] However, scarlet fever is specifically associated with toxigenic GAS strains rather than other streptococcal groups.

The pathogenic success of GAS is attributed to a broad array of virulence determinants that collectively support adhesion, colonization, immune evasion, tissue invasion, and systemic dissemination within the human host.[15] Among the most prominent virulence factors are the M-protein, a fibrillar surface protein that interferes with phagocytosis; a hyaluronic acid capsule that mimics host connective tissue and aids immune evasion; and extracellular enzymes such as streptokinase and DNase B, which facilitate tissue spread and degradation of host defenses.[15] In the context of scarlet fever, the pyrogenic exotoxins—also termed scarlatinal or erythrogenic toxins—are particularly important. These exotoxins function as superantigens that bypass conventional antigen processing and directly link major histocompatibility complex class II molecules on antigen-presenting cells to specific regions of T-cell receptors.[6][16] The resulting massive, polyclonal T-cell activation leads to exuberant cytokine release, including tumor necrosis factor-α (TNF-α), interleukin (IL)-1, and IL-6, which contribute to fever, systemic toxicity, and the characteristic erythematous "sandpaper-like" rash and strawberry tongue seen in scarlet fever.[5][16] GAS strains are further differentiated based on the serological types of M- and T-antigens expressed on their surface.[11] Traditional serotyping methods using antisera to identify these antigens have largely been supplanted by molecular approaches, particularly sequence typing of the N-terminal region of the M-protein gene (emm). Emm typing is now widely used in epidemiologic investigations to track circulating strains and identify those associated with

outbreaks.[11][17] Whole genome sequencing (WGS) is increasingly applied to characterize epidemic clones in greater detail, facilitating more precise tracking of transmission dynamics and virulence determinants.[17] To date, more than 250 emm types have been identified based on sequence variation in the emm gene, highlighting the extensive genetic diversity of GAS.[18][11] The M-protein itself, encoded by emm, not only serves as a key virulence factor but is also an important target for vaccine development due to its immunodominant and strain-specific antigenic properties.[17]

Certain emm types appear to be disproportionately associated with invasive disease and scarlet fever outbreaks. Emm1 strains, for example, are particularly virulent and frequently implicated in severe invasive infections, including streptococcal toxic shock syndrome (STSS) and necrotizing fasciitis.[19] Additionally, emm types such as M1, M2, M3, M4, M6, M12, and M22 have been linked to recurrent scarlet fever epidemics.[20] Over the past decade, a global resurgence of scarlet fever has been documented in several regions, including the United Kingdom, Hong Kong, mainland China, and Korea, often associated with the emergence of novel emm clones that carry enhanced virulence or transmissibility traits.[20][21] These observations underscore how shifts in emm type distribution and the acquisition of particular virulence genes can influence disease patterns at the population level. A distinctive feature of GAS, highly relevant to scarlet fever, is its ability to produce superantigen exotoxins—among the most potent T-cell activators known. These superantigens, also termed erythrogenic or scarlet fever toxins, directly mediate the erythematous rash and strawberry tongue that define the clinical syndrome.[5] In severe toxin-mediated conditions such as STSS, certain superantigenic exotoxins can precipitate atypical, widespread activation of lymphocytes, leading to a fulminant cytokine storm characterized by hypotension, tissue hypoperfusion, and multiorgan failure, often with high mortality.[16] Key superantigenic exotoxins include not only the classical streptococcal pyrogenic exotoxins (e.g., SpeA, SpeC) but also toxins such as toxic shock syndrome toxin-1 (TSST-1) and enterotoxins, which play analogous roles in driving systemic inflammation.[16] In summary, the etiology of scarlet fever is rooted in the complex interplay between a highly adapted human pathogen—group A Streptococcus—and an array of virulence factors, particularly superantigenic exotoxins, that drive its characteristic clinical manifestations. The organism's global distribution, genetic diversity, and capacity to cause both localized and invasive disease, along with significant immune-mediated sequelae, render GAS a pathogen of enduring clinical and public health importance.[6][9][10]

Epidemiology

Epidemic scarlet fever, or scarlatina, is a toxin-mediated exanthematous illness caused by streptococcal pyrogenic exotoxins (SPEs) produced during group A Streptococcus (GAS) infections. It is classically associated with GAS pharyngitis but may also arise from other GAS disease foci.[1][22] Clinically, scarlet fever is characterized by a coarse, papular erythematous ("sandpaper-like") rash, strawberry tongue, and exudative pharyngitis, often occurring in the context of acute sore throat.[1] From an epidemiologic standpoint, scarlet fever is notable for its tendency to occur in cyclical epidemics approximately every 5 to 6 years, a pattern that is thought to reflect the waxing and waning of type-specific herd immunity within populations.[22] During the 19th and early 20th centuries, scarlet fever was a major cause of childhood morbidity and mortality, responsible for large-scale epidemics and significant public health burden.[22] With the advent of antibiotics and improvements in hygiene and living conditions, the incidence and lethality of scarlet fever declined markedly in the latter half of the 20th century, attenuating its impact as a classic childhood killer.[20][1] Nonetheless, the disease has resurged in recent decades in several regions, coinciding with shifts in circulating GAS emm types and the emergence of more virulent or transmissible clones.[20][21] GAS is strictly a human pathogen and can infect multiple body sites, particularly the upper respiratory tract and skin.[2] Globally, GAS infections are increasing and contribute substantially to morbidity and mortality through both acute disease and chronic sequelae.[6][9] Transmission occurs primarily via respiratory droplets generated by coughing, sneezing, or close contact with infected individuals, but it can also occur through contact with contaminated fomites and via direct skin-to-skin contact in superficial infections such as impetigo.[3][4] Although GAS can infect individuals of any age, children—especially those of school age—older adults, and immunocompromised individuals have consistently been identified as higher-risk groups for both disease acquisition and complications.[23][3] The incubation period for GAS typically ranges from 1 to 5 days, during which time infected individuals, including those who are asymptomatic or minimally symptomatic, may shed the organism and facilitate transmission.[3]

Environmental and social factors strongly influence GAS epidemiology. Crowded settings, including schools, daycare centers, households with multiple occupants, military barracks, and nursing homes, promote efficient spread of GAS.[3][4] In such environments, even a small number of symptomatic or asymptomatic carriers can drive rapid dissemination and generate outbreaks of pharyngitis and scarlet fever. Heavy shedding of GAS in classrooms or similar congregate settings can occur in the absence of overt illness, contributing to difficulty in controlling transmission.[3] Within the community, GAS causes a

broad range of infections that vary in severity and anatomic location, from superficial to invasive. These include pharyngitis and scarlet fever; impetigo, which involves the superficial keratin layer; cellulitis, affecting the subcutaneous tissue; erysipelas, involving the superficial dermis; streptococcal toxic shock syndrome (STSS); myositis and myonecrosis, involving muscle; and necrotizing fasciitis, targeting the fascia.[6][9][25] Importantly, GAS may exist as a harmless commensal in the pharynx or as a pathogenic agent causing acute pharyngitis. In many populations, approximately 5% to 15% of individuals are asymptomatic pharyngeal carriers at any given time, providing a reservoir for ongoing transmission.[15][24] Symptomatic pharyngitis generally results from person-to-person spread via oropharyngeal secretions and respiratory droplets from infected or colonized individuals.[24] In addition to localized disease, GAS infections can precipitate immune-mediated sequelae such as acute rheumatic fever (ARF) and poststreptococcal glomerulonephritis (PSGN), as well as the chronic consequences of these conditions, notably rheumatic heart disease (RHD).[26] These postinfectious complications contribute substantially to the global disease burden, particularly in low- and middle-income countries.[26][31]

The epidemiology of specific GAS-related syndromes varies by age group, season, and underlying risk factors. GAS pharyngitis is most prevalent in children aged 5 to 15 years and is the most common bacterial cause of acute pharyngitis in this age range.[3][27] It is strongly associated with close contact among children in schools and daycare facilities, where shared airspace and frequent interpersonal interaction facilitate transmission.[3][27] In adults, GAS accounts for approximately 5% to 15% of clinical visits for sore throat, whereas in children it is responsible for about 20% to 30% of pharyngitis presentations.[27][28][29] Pharyngitis caused by GAS shows clear seasonality in temperate climates, with peak incidence during winter and early spring, aligning with increased indoor crowding and overlapping viral respiratory illnesses.[27] Severe and invasive GAS infections display a bimodal age distribution, with higher rates observed in young children (especially those aged 2 years or younger) and in older adults aged 50 years or more.[24][30] Multiple risk factors for increased mortality have been identified and include advanced age, male sex, residence in a nursing home, chronic comorbid conditions (such as diabetes, cardiovascular disease, and chronic kidney disease), immunosuppression, recent surgery, septic shock, necrotizing fasciitis, concurrent viral infections (for example, influenza or varicella), isolated bacteremia, and infection with highly virulent emm1 or emm3 strains.[4][30] These factors often cluster in vulnerable populations, leading to disproportionate rates of severe outcomes and death in specific subgroups.

Global estimates underscore the substantial burden of GAS disease. Severe GAS infections are estimated to affect approximately 18.1 million people worldwide at any given time, with 1.78 million new cases of severe disease and about 616 million cases of GAS pharyngitis occurring annually.[31] Overall, severe GAS infections are thought to cause around 500,000 deaths each year, with the majority attributable to RHD and invasive infections.[31] Invasive GAS (iGAS) alone is responsible for an estimated 663,000 new cases and 163,000 deaths annually.[31] The skin and soft tissues are the most common sites of iGAS infection, with cellulitis present in roughly 32% of patients and necrotizing fasciitis developing in about 8%.[4] Notably, GAS has been reported to cause disease in young, previously healthy individuals, with one study indicating that approximately 25% of iGAS cases occur in persons without identifiable risk factors.[4] Molecular epidemiology has revealed that genetic variation among GAS strains, particularly within the emm gene encoding the M-protein, plays a central role in disease patterns. GAS emm1 strains are highly virulent, and the M-protein itself is a key virulence determinant facilitating immune evasion and resistance to phagocytosis.[32] The resurgence of severe GAS infections in the 1980s has been largely attributed to the emergence of emm1 strains as predominant causes of iGAS following specific genetic shifts.[33] These emm1 strains have been repeatedly associated with invasive infections, including necrotizing fasciitis and STSS, and are often overrepresented among severe cases.[34] In the context of scarlet fever, specific emm types—such as M1, M2, M3, M4, M6, M12, and M22—have been linked to recurrent outbreaks.[20] Over the last decade, a global reemergence of scarlet fever has been documented in the United Kingdom, Hong Kong, mainland China, and Korea, frequently associated with novel emm clones carrying enhanced toxin and resistance profiles.[20][21]

Given the rising incidence and significant burden of GAS infections, especially iGAS, robust epidemiological surveillance has become essential. Whole genome sequencing (WGS) plays a crucial role in tracking the emergence, spread, and evolution of epidemic strains, as well as in identifying virulence and resistance determinants.[9][11][18][30][31] Since the early 2000s, the dominant emm types in Europe and North America have been emm1 and emm3, with emm1 serving as the principal type associated with invasive infections in high-income settings.[32] Seven emm types—emm1, emm28, emm89, emm3, emm12, emm4, and emm6—have been found collectively responsible for 50% to 70% of iGAS infections, and these have been collectively referred to as the M1global group in the context of dominant invasive lineages.[11][35] A landmark scarlet fever outbreak

occurred in Hong Kong in 2011, where a roughly 10-fold increase in case numbers was noted relative to baseline.[36] This outbreak was associated predominantly with GAS emm12 and emm1 types, with emm12 emerging as the dominant clone among isolates.[36] Molecular analyses revealed that these strains had acquired mutations and mobile genetic elements that enhanced both virulence and transmissibility.[36] Furthermore, surveillance of emm types in Hong Kong demonstrated that these new strains exhibited increased resistance to macrolides and clindamycin, linked to the acquisition of resistance genes from commensal bacteria inhabiting the human urogenital and gastrointestinal tracts.[37]

Following the Hong Kong outbreak, WGS-based surveillance revealed a parallel increase in scarlet fever cases in mainland China, driven in large part by the expansion of emm12 clones.[21] Detailed genetic studies identified mobile elements responsible for disseminating key virulence and resistance determinants, including streptococcal toxin–encoding prophages φHKU.vir and φHKU.ssa, as well as macrolide- and tetracycline-resistant integrative and conjugative elements (ICEs), specifically ICE-emm12 and ICE-HKU397.[21] These findings highlighted the role of multiclonal emm12 isolates in expanding scarlet fever lineages both in China and internationally, reinforcing the importance of genomic surveillance in understanding and managing GAS epidemics.[21] In the United Kingdom, a new emm1 sublineage, termed "M1UK," was first identified around 2008 and was associated with increased expression of the scarlet fever toxin SPE-A (speA).[19][39] During the 2014 scarlet fever surge in the UK, epidemiological surveillance showed that regional outbreaks were caused by multiple emm types—emm3, emm12, emm1, and emm4—along with distinct phylogenetic lineages.[14] A marked increase in the prevalence of the ssa gene, which encodes another superantigen, was observed among scarlet fever cases, suggesting that enhanced superantigen expression contributed to disease severity and transmissibility.[14] The M1UK lineage was identified as a key driver of rising case numbers, outbreaks, and invasive infections between 2014 and 2018, ultimately becoming the dominant emm1 strain in the UK.[34][38][39] By 2020, M1UK accounted for approximately 91% of invasive emm1 isolates in England.[34] Interestingly, the incidence of scarlet fever declined during the COVID-19 pandemic, likely reflecting the impact of nonpharmaceutical interventions such as social distancing, school closures, and mask use on respiratory pathogen transmission.

In the post-COVID period, however, three emerging M1UK clades rapidly expanded across the UK, leading to severe outcomes in children and renewed concern about GAS disease.[32][39][40] The M1UK clone, first formally described in 2019, is associated with seasonal waves of scarlet fever and an increased incidence of iGAS, driven in part by approximately 10-fold overproduction of the speA superantigen, also known as erythrogenic toxin A or scarlet fever toxin.[39] Genomic analysis has shown that M1UK differs from the previously dominant M1T1 strain by an additional 27 single-nucleotide polymorphisms, changes that correlate with enhanced speA expression and increased virulence compared with M1T1 isolates.[19] The M1UK lineage appears to have outcompeted the globally widespread emm1 M1global strain that had predominated since the 1980s.[32][34] M1UK isolates produce substantially higher levels of speA than contemporary M1global strains, likely conferring a fitness advantage in colonization, transmission, and pathogenesis.[34] While declining population immunity may partly explain recurrent streptococcal outbreaks, the genetic attributes of M1UK suggest that this lineage is particularly well adapted to survive population bottlenecks and exploit ecological opportunities. Two additional emm1 lineages, designated M113SNPs and M123SNPs, have also been identified, further illustrating the ongoing diversification of this important serotype.[32][40] During the 2022–23 season in the UK, GAS emm1 strains, predominantly M1UK, were responsible for more than half of invasive infections in children, underscoring their substantial clinical impact.[32][34] All globally sequenced M1UK (speA-positive) isolates trace their origin back to the United Kingdom, where they first caused epidemic scarlet fever and subsequently disseminated across Europe and other regions.[32] In summary, the epidemiology of scarlet fever and related GAS infections reflects a complex interplay between host factors, environmental conditions, and dynamic bacterial population genetics. While the overall incidence of severe disease diminished in the antibiotic era, the recent global resurgence of scarlet fever and iGAS—driven by specific emm lineages such as emm12 and M1UK—highlights the continuing threat posed by GAS.[20][21][32][34][39] Ongoing epidemiological and genomic surveillance, combined with robust clinical vigilance and public health interventions, remains essential to detect emerging clones, understand transmission dynamics, and guide preventive strategies against this historically important yet persistently evolving pathogen.[9][11][18][30][31][35]

Pathophysiology

The pathophysiology of scarlet fever reflects a complex interplay between the virulence machinery of *Streptococcus pyogenes* (group A Streptococcus, GAS) and the host's immune response. GAS employs a wide array of virulence determinants that promote adhesion, colonization, immune evasion, tissue invasion, and systemic dissemination.[15] These molecular mechanisms collectively shape the clinical manifestations of scarlet fever, including its characteristic rash, fever, and mucocutaneous findings. A central virulence determinant is the M-

protein, encoded by the *emm* gene. This surface fibrillar protein remains one of the most important factors enabling GAS to resist phagocytosis by neutrophils and macrophages. By binding host regulators such as factor H, M-protein inhibits complement deposition, thereby protecting the bacterium from complement-mediated killing. It also plays a substantial role in adherence to epithelial surfaces and invasiveness, contributing to the initial establishment of infection.[17] Importantly, the M-protein is highly antigenic; variations in the *emm* gene produce numerous distinct emm types, more than 250 of which have been identified. Some emm types—particularly emm1—are strongly associated with invasive GAS disease and have been repeatedly implicated in large-scale scarlet fever outbreaks.[20][21] The emergence of novel emm clones with enhanced virulence has been linked to modern resurgences of scarlet fever in diverse regions, including Hong Kong, mainland China, Korea, and the United Kingdom. Other surface components contribute to GAS pathogenicity. The hyaluronic acid capsule mimics host connective tissue, enabling the bacterium to avoid immune detection. Enzymes such as streptokinase facilitate fibrinolysis, allowing deeper tissue spread, while DNase B degrades neutrophil extracellular traps (NETs), promoting escape from innate immune defenses.[15] These factors collectively enhance the organism's capacity to colonize and persist within the host.

The defining pathophysiologic feature of scarlet fever, however, is the action of streptococcal pyrogenic exotoxins (SPEs)—also called scarlatinal or erythrogenic toxins. These toxins function as superantigens, an unusual class of molecules capable of bypassing normal antigen processing. Instead of binding to a specific antigenic peptide, superantigens link major histocompatibility complex (MHC) class II molecules on antigen-presenting cells directly to conserved Vβ regions of T-cell receptors. This nonspecific interaction results in massive polyclonal T-cell activation.[5][16] Because superantigens activate up to 20% of the body's T-cell population—far more than the tiny fraction stimulated by conventional antigens—they trigger a powerful cytokine storm. This cytokine surge includes high levels of TNF-α, IL-1, and IL-6, which drive fever, malaise, and systemic inflammatory manifestations.[6][16] In severe toxin-mediated diseases, such as streptococcal toxic shock syndrome (STSS), these mechanisms culminate in hypotension, capillary leak, multiorgan dysfunction, and potentially death. The primary superantigenic exotoxins implicated in such severe presentations include TSST-1 and several enterotoxins.[16] The hallmark rash of scarlet fever—the diffuse, erythematous, finely papular eruption with a sandpaper-like texture—was historically attributed to direct toxin injury. However, current evidence indicates that the rash arises instead from a delayed-type host hypersensitivity reaction to streptococcal superantigens.[41][42] Individuals who develop the rash are typically pre-sensitized from prior exposure to GAS. Reactivation of memory T cells amplifies the immune response during subsequent infections, producing heightened cytokine release and infiltration of leukocytes into the skin. The strawberry tongue, Pastia lines, and circumoral pallor are likewise immunologically mediated mucocutaneous manifestations resulting from the same toxin-driven hypersensitivity pathways. Notably, the rash is largely absent in individuals with no prior immune sensitization to GAS superantigens, underscoring its immunologic basis rather than direct toxin-induced damage.[41] In summary, the pathophysiology of scarlet fever reflects both the sophisticated virulence strategies of GAS—particularly the production of superantigen toxins—and the host's immunologic history. Superantigens are central to the disease, driving the intense cytokine release that results in the characteristic rash, mucosal changes, and systemic manifestations. Variation in emm types and superantigen gene content helps explain epidemiologic patterns and the resurgence of scarlet fever linked to novel, highly virulent clones.

History and Physical

A detailed and structured clinical history remains the cornerstone of evaluating patients with suspected scarlet fever or other group A streptococcal (GAS) infections. Patients are commonly present for medical evaluation with complaints suggestive of an acute infectious process—most often pharyngitis, fever, or skin infections such as cellulitis—without immediately recognizing the characteristic rash. Although scarlet fever is classically associated with GAS-induced acute pharyngitis, it can also arise from other GAS infections, including erysipelas, impetigo, and postoperative or traumatic wound infections.[41] Understanding the typical timeline is vital: the GAS incubation period ranges from 1 to 5 days, and the signature rash generally emerges 24 to 48 hours after the onset of symptoms, particularly sore throat and fever. The onset of GAS pharyngitis is usually abrupt. Patients or caregivers often report a sudden high fever accompanied by a severe sore throat. Frequently associated symptoms include headache, chills, nausea, vomiting, abdominal pain, and malaise, reflecting the systemic inflammatory response.[43] In pediatric populations, abdominal discomfort is a common presenting feature and may occasionally be mistaken for gastrointestinal or appendiceal pathology. When eliciting exposure history, clinicians should inquire about recent contact with individuals exhibiting GAS infection, especially in environments such as schools, dormitories, military barracks, and nursing homes. These settings facilitate efficient transmission due to close proximity and shared airspace.

Physical examination for GAS pharyngitis typically reveals erythema and swelling of the tonsils

and pharyngeal tissues, with or without tonsillar exudates. The uvula may be erythematous and mildly edematous. Palatal petechiae, though not pathognomonic, are suggestive of GAS pharyngitis in the appropriate clinical context. Tender, enlarged anterior cervical lymph nodes are another characteristic finding and should be assessed through careful palpation.[43] Distinguishing GAS pharyngitis from viral etiologies based solely on physical examination is difficult. Viral infections commonly manifest with cough, conjunctivitis, rhinorrhea (coryza), hoarseness, emesis, or diarrhea, features that typically argue against GAS as the primary cause and instead support viral diagnoses such as adenovirus or rhinovirus infection.[44] Historically, tools like the Centor Criteria were developed to improve clinical prediction based on symptoms and exam findings; however, these criteria alone lack sufficient sensitivity and specificity and therefore must be supplemented with microbiological testing, such as rapid antigen detection testing (RADT) or throat culture, to ensure accurate diagnosis.[43][45] A full skin examination is crucial when evaluating patients with suspected scarlet fever. The characteristic rash is described as a fine, blanching, maculopapular erythematous eruption with a distinctly rough texture, often likened to sandpaper.[46] The rash typically begins on the trunk, axillae, and groin before spreading outward to the extremities. Notably, it spars the palms and soles, a feature that helps differentiate it from other exanthematous diseases such as hand-foot-and-mouth disease or Kawasaki disease. The rash may intensify in skin creases, where the papules coalesce into Pastia lines, prominently visible in the antecubital fossa, axillae, groin, and neck.[46]

Circumoral pallor, a pale area surrounding the mouth contrasting sharply with the flushed cheeks, is another classic finding. Examination of the oral cavity often reveals the hallmark strawberry tongue. Initially, the tongue appears coated with a white membrane through which enlarged papillae protrude, known as the "white strawberry tongue." As desquamation proceeds, the membrane peels away, leaving behind a bright red surface studded with prominent papillae, the classic "red strawberry tongue." These mucocutaneous changes are highly suggestive of scarlet fever when present in the context of recent fever and pharyngitis.[46] Following the acute phase, patients may enter a stage of a desquamation, typically beginning on the face before affecting the trunk, fingers, and toes. This peeling process can persist for up to two weeks, and while benign, it may cause concern among patients and caregivers if unexpected.[46] Importantly, clinicians must recognize that scarlet fever can develop even in the absence of classic pharyngitis symptoms, particularly when associated with skin infections such as erysipelas or impetigo. In these cases, the typical rash and mucous membrane findings remain the most reliable clues pointing toward scarlet fever. In summary, the history and physical examination in scarlet fever require careful attention to symptom onset, potential exposures, pharyngeal findings, and the full spectrum of characteristic dermatologic signs. A systematic approach ensures timely identification of scarlet fever, facilitates appropriate diagnostic testing, and helps distinguish it from viral and non-streptococcal conditions that may present similar features.

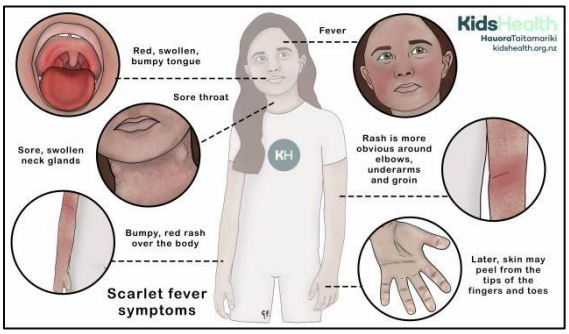

Fig. 2: Scarlet Fever symptoms.

Evaluation

Evaluating a patient with suspected scarlet fever requires a structured and comprehensive diagnostic approach that integrates clinical findings, epidemiologic clues, and targeted microbiological testing. When patients present with a blanching, maculopapular, sandpaper-like rash, strawberry tongue, or other mucocutaneous signs suggestive of toxin-mediated illness, identifying the primary source of group A Streptococcus (GAS) infection becomes central to establishing the diagnosis. Because scarlet fever most frequently arises in the context of GAS pharyngitis, clinicians should begin by assessing for signs and symptoms of streptococcal sore throat. The CENTOR criteria—which evaluate tonsillar exudates, tender anterior cervical lymphadenopathy, absence of cough, and fever—can serve as a useful initial framework for assessing the likelihood of GAS pharyngitis.[47][48][49] However, these criteria should not be used in isolation. When supported by clinical suspicion, they guide the need for confirmatory testing rather than provide a standalone diagnosis. Patients without pharyngeal symptoms or with negative testing require evaluation for alternative GAS infection sites, such as skin lesions, wounds, or deeper soft tissue infections. A thorough physical examination remains indispensable in identifying such non-pharyngeal sources. Laboratory testing for suspected GAS pharyngitis begins with a throat swab for bacterial culture, the long-standing gold standard for diagnosis.[2] GAS grows readily on sheep blood agar, producing β-hemolytic colonies, and is characteristically catalase- and oxidase-negative. Confirmation of GAS identity may be achieved using Lancefield grouping or advanced technologies such as matrix-assisted laser desorption ionization–time of flight (MALDI-TOF) mass spectrometry, which allows rapid and precise organism identification.[50] Although highly accurate, throat culture requires 24

hours or more to yield results, limiting its immediate utility in time-sensitive clinical decisions related to treatment initiation, school exclusion, or public health reporting.

Rapid clinical decisions often rely on a rapid antigen detection test (RADT). RADTs provide results within minutes and have a sensitivity of approximately 85% in children, with specificity consistently around 95%.[51] The high specificity means that a positive RADT result reliably confirms GAS pharyngitis, allowing clinicians to initiate antibiotic therapy without additional testing. For children, however, some guidelines recommend confirmatory throat cultures after negative RADT results due to the higher prevalence of GAS and the importance of preventing complications. When RADT is negative, clinicians should follow national and regional guidelines to determine whether to pursue further testing or initiate empiric management.[51] In adults, the prevalence of GAS pharyngitis is substantially lower, producing a low pretest probability. Consequently, a negative RADT is generally considered sufficient to rule out GAS in adult patients, and confirmatory cultures are not routinely required.[44] This practice reduces unnecessary testing while maintaining diagnostic accuracy. When scarlet fever is suspected to arise from non-pharyngeal GAS infections, appropriate sampling and culture of the involved site is required. GAS can be cultured from superficial skin lesions (e.g., impetigo), deeper wounds, aspirates, blood cultures in cases of suspected invasive disease, or pleural fluid in respiratory involvement. Gram staining can offer rapid clues to GAS involvement by revealing gram-positive cocci in chains, while cultures provide definitive identification.

Polymerase chain reaction (PCR) testing represents an important additional diagnostic tool, particularly for complicated cases, outbreaks, or epidemiologic surveillance. PCR can detect GAS with high sensitivity and specificity and can distinguish among different GAS emm types, which is valuable during outbreaks linked to specific virulent clones.[52] PCR testing may also be used when cultures are negative but clinical suspicion remains high or when early identification of toxin-producing strains is necessary. In summary, evaluation of suspected scarlet fever requires a balance of clinical insight and strategic microbiological testing. Identification of the primary GAS infection source—most commonly the pharynx, but potentially any skin or soft tissue site—is crucial for accurate diagnosis. While throat cultures remain the definitive diagnostic method, RADTs are vital for timely decision-making, and PCR offers advanced diagnostic clarity in complex or unusual cases. This multifaceted approach ensures early detection, appropriate therapy, and effective prevention of complications associated with scarlet fever and other GAS infections.

Treatment / Management

Timely and accurate recognition of group A streptococcal (GAS) infection in a patient with a scarlatiniform rash is essential, as early treatment reduces symptom duration, limits transmission, and helps prevent serious suppurative and nonsuppurative complications such as acute rheumatic fever and poststreptococcal glomerulonephritis.[8][43] The combination of a sandpaper-like, blanching maculopapular rash and features of acute pharyngitis should raise a strong clinical suspicion for scarlet fever and prompt microbiologic evaluation for GAS. Diagnostic testing—typically rapid antigen detection tests (RADT) and/or throat culture—should be performed as soon as feasible, but treatment should not be unduly delayed in a highly compatible clinical scenario, particularly in high-risk patients or outbreak settings.[43] Because GAS infection is associated with substantial morbidity and ranks among the top infectious causes of global mortality, empiric antibiotic therapy must reliably cover this pathogen while cultures and susceptibility data are pending.[8] Culture results remain crucial for confirming the diagnosis, distinguishing GAS from other pathogens, and monitoring the emergence of resistance. They also help refine therapy, especially in the context of increasing global resistance to macrolides and clindamycin and reports—albeit still uncommon—of reduced susceptibility to β-lactams linked to pbp2x mutations.[43][53] Despite these concerns, β-lactam antibiotics remain the cornerstone of therapy for both noninvasive and invasive GAS infections. Penicillin has maintained excellent activity against GAS, and clinically significant resistance remains rare worldwide.[43][53] Accordingly, penicillin continues to be the gold standard for treating scarlet fever and other GAS infections.[43][54] For uncomplicated GAS pharyngitis and scarlet fever, a 10-day course of oral penicillin V or amoxicillin is recommended, as this duration has been shown to eradicate GAS from the pharynx reliably, shorten symptom duration, and markedly reduce the risk of acute rheumatic fever.[43] Amoxicillin is often favored in children due to better palatability and once- or twice-daily dosing. In patients in whom adherence to a full oral course is uncertain, a single intramuscular injection of benzathine penicillin G offers an effective alternative that ensures complete therapy.[43][44]

For patients with a true penicillin allergy, alternative agents are needed. Macrolides (such as erythromycin, azithromycin, or clarithromycin) and Lincosamides (such as clindamycin) are the most notable substitutes.[43] However, macrolide and clindamycin resistance among GAS isolates has increased significantly in the past decade, with marked geographic variability.[55] Data from China have reported macrolide resistance rates approaching 90%, whereas some European regions document macrolide resistance rates of 20% to 40% and Lincosamides

resistance up to 19%; in other areas, particularly parts of Europe, resistance rates may be as low as 2%.[55][56] These patterns are largely driven by macrolide resistance mechanisms, including those encoding the MLS $_B$ phenotype, which confers cross-resistance to macrolides, lincosamides, and streptogramin B.[55][56][57] Consequently, local susceptibility data should guide the selection of macrolides or clindamycin. Where resistance rates are high or unknown, clinicians may consider non–β-lactam alternatives based on regional guidelines and expert consultation, especially in severe disease or treatment failure.[43] The choice of antibiotic regimen must also take into account the site and severity of infection, the patient's allergy profile, and local resistance patterns.[43] For uncomplicated pharyngitis-associated scarlet fever in otherwise healthy outpatients, oral penicillin V or amoxicillin for 10 days is usually sufficient.[43] Symptomatic treatment—such as acetaminophen or ibuprofen for fever and throat pain, adequate hydration, and rest—is an important adjunct. Once effective antibiotic therapy has been initiated, patients are generally considered significantly less contagious after about 24 hours, which has implications for return to school or work and for household infection control.[43][44]

In contrast, severe GAS infections such as necrotizing fasciitis, bacteremia with shock, and streptococcal toxic shock syndrome (STSS) require urgent, aggressive management. Broad-spectrum intravenous antibiotics should be started empirically to cover GAS and other possible pathogens, especially in polymicrobial or healthcare-associated infections, while awaiting culture and susceptibility results.[58] Regimens often include a β-lactam (such as high-dose penicillin or a broad-spectrum cephalosporin) in combination with agents active against gram-negative and anaerobic organisms, depending on the clinical context and local epidemiology. In these life-threatening toxin-mediated syndromes, clindamycin plays a particularly important adjunctive role.[59] Clindamycin inhibits bacterial protein synthesis, thereby reducing the production of streptococcal superantigens and other toxins that drive the systemic inflammatory response. It may also enhance phagocytosis of *S. pyogenes* by downregulating M-protein expression.[59] For these reasons, guidelines frequently recommend combining clindamycin with penicillin or another β-lactam when treating necrotizing fasciitis or STSS. Early and repeated surgical debridement is also a critical component of management in necrotizing soft tissue infections, and failure to promptly remove necrotic tissue is associated with poor outcomes.[58] Supportive care is essential in moderate to severe GAS disease, particularly in patients with systemic involvement. Management typically includes aggressive fluid resuscitation to correct hypovolemia, electrolyte correction, and close monitoring of urine output and organ function. In cases of septic shock, vasopressor agents may be required to maintain adequate mean arterial pressure and end-organ perfusion.[60][61] Admission to a high-dependency or intensive care unit is often indicated for patients with STSS, necrotizing fasciitis, or rapidly progressive iGAS, given the risk of acute respiratory distress syndrome, renal failure, and cardiovascular collapse.[60][61] In select cases of severe toxin-mediated disease, intravenous immunoglobulin (IVIG) may be considered as an adjunct to neutralize circulating superantigens and exotoxins, although practice patterns vary and evidence is evolving.

From a public health and infection control perspective, prompt identification and treatment of scarlet fever help curb transmission within schools, households, and other congregate settings. Patients should be advised to avoid close contact with others, practice meticulous hand hygiene, and refrain from attending school or work until at least 24 hours after the initiation of effective antibiotic therapy and clinical improvement begins.[43][44] During outbreaks, clinicians and public health authorities may recommend screening and treating close contacts with symptoms suggestive of GAS infection, particularly in high-risk environments such as long-term care facilities. In summary, the management of scarlet fever and related GAS infections hinges on early recognition, appropriate and timely antibiotic therapy, and careful attention to local resistance patterns. Penicillin and other β-lactams remain highly effective first-line agents, while macrolides and clindamycin serve as alternatives in penicillin-allergic patients, with the caveat of growing resistance in many regions.[43][53][55][56] Severe toxin-mediated and invasive infections require broad-spectrum coverage, combination therapy with clindamycin, intensive supportive care, and often urgent surgical intervention.[58][59][60][61] A thoughtful, evidence-based treatment strategy not only improves individual patient outcomes but also reduces the broader burden of GAS disease at the community and global levels.

Differential Diagnosis

The differential diagnosis of fever with rash is extensive, and a careful clinical assessment is essential to distinguish scarlet fever from other exanthematous illnesses. When a blanching, erythematous, sandpaper-like maculopapular rash is observed, clinicians should look for additional characteristic features that strongly support scarlet fever—particularly the presence of a strawberry tongue, Pastia lines in flexural areas, and a compatible exposure history. These findings, when combined with symptoms of acute pharyngitis, markedly increase the likelihood of scarlet fever and should prompt targeted evaluation for a group A Streptococcus (GAS) source such as GAS pharyngitis, impetigo, or erysipelas. Identifying this primary focus is crucial for both diagnosis and management. Several viral exanthems can mimic scarlet fever. Rubella and rubeola (measles) may present with fever and generalized rash, but they

are typically accompanied by characteristic features such as conjunctivitis, cough, coryza, and, in measles, Koplik spots. Infectious mononucleosis, caused by Epstein-Barr virus (EBV) or Cytomegalovirus, can cause fever, pharyngitis, lymphadenopathy, and sometimes a generalized rash, especially in the setting of aminopenicillin exposure; however, the classic sandpaper texture and Pastia lines are absent. Parvovirus B19 infection (erythema infectiosum) usually produces a "slapped cheek" appearance and lacy rash on the extremities, differing from the more diffuse truncal distribution of scarlet fever. Varicella typically presents with vesicular lesions at varying stages rather than a uniform fine papular eruption.

Other important infectious mimics include enteroviral infections, such as hand, foot, and mouth disease due to Coxsackie virus, which features vesicular lesions on the hands, feet, and oral mucosa rather than the classic scarlatiniform rash. Arcanobacterium haemolyticum pharyngitis can cause a similar sore throat and rash in adolescents and young adults and should be considered, particularly when streptococcal tests are negative. Systemic bacterial toxin-mediated conditions such as toxic shock syndrome (TSS) and staphylococcal scalded skin syndrome (SSSS) may also present with diffuse erythema and desquamation, but they are usually accompanied by more severe systemic toxicity and mucocutaneous patterns that differ from those of scarlet fever. Noninfectious causes must also be included in the differential. Kawasaki disease, especially in children, may resemble scarlet fever with fever, strawberry tongue, rash, and desquamation; however, it is typically associated with conjunctival injection, extremity changes, and coronary artery involvement. Drug eruptions can result in morbilliform rashes and systemic symptoms, but the distribution, history of new medication exposure, and absence of classic streptococcal features often help distinguish them. Ultimately, combining detailed history, thorough physical examination, and appropriate microbiological testing allows clinicians to differentiate scarlet fever from these numerous alternatives and accurately attribute the rash to a GAS-related etiology.

Prognosis

The prognosis of scarlet fever in the modern era is excellent, representing a dramatic improvement compared with the pre-antibiotic era of the early 20th century, when this disease carried high morbidity and mortality in children.[62][63] The advent of effective antimicrobial therapy and advances in rapid diagnostic methods have transformed scarlet fever from a potentially lethal epidemic illness into a largely self-limited, readily treatable infection. In most cases, once appropriate antibiotic therapy is initiated, fever and systemic symptoms begin to improve within 24 to 48 hours, and patients are usually able to resume regular activities about 24 hours after the fever resolves, assuming they feel clinically well and have completed at least one full day of therapy. For the majority of treated patients, clinical recovery occurs within 3 to 6 days, although certain manifestations, particularly cutaneous changes, may persist longer. The characteristic rash often fades over several days and is followed by desquamation, which may last up to 2 weeks or occasionally longer, especially on the hands and feet.[62] This peeling phase, while sometimes alarming to patients and families, is benign and self-limiting. In a minority of cases, infection can recur, particularly in settings of repeated exposure, incomplete adherence to the antibiotic regimen, or colonization with a different GAS strain. With contemporary therapy, the mortality rate of scarlet fever is now less than 1%, a marked contrast to historical figures.[62][63] Morbidity today primarily reflects the occurrence of complications—both suppurative and nonsuppurative—rather than the acute infection itself. Suppurative complications such as otitis media, sinusitis, and peritonsillar abscess, and nonsuppurative sequelae such as acute rheumatic fever, poststreptococcal glomerulonephritis, and, ultimately, rheumatic heart disease, are now relatively rare in high-resource settings due to prompt diagnosis and treatment.[62][63] Nevertheless, these complications still occur, particularly where access to care is limited or antibiotic courses are delayed or incomplete. The overall favorable prognosis depends heavily on timely recognition, initiation of appropriate antibiotics, and adequate treatment duration. In low- and middle-income regions where healthcare access is constrained, scarlet fever and GAS infections can still contribute to significant long-term morbidity, particularly via rheumatic heart disease. Therefore, while the individual prognosis for a treated patient is excellent, scarlet fever retains public health relevance, underscoring the importance of continued vigilance, adherence to treatment guidelines, and education aimed at preventing delayed or missed diagnoses.

Complications

Although scarlet fever itself is now considered a relatively mild and treatable illness, untreated or inadequately treated group A streptococcal infections can result in a wide range of serious complications. Historically, before the introduction of antibiotics, scarlet fever was associated with high complication rates and significant mortality in children. Today, the risk is greatly diminished, but complications still occur, particularly when therapy is delayed or incomplete. These complications are broadly divided into suppurative and non-suppurative categories, reflecting direct extension of infection versus immune-mediated sequelae. Suppurative complications arise from local spread of the primary infection or hematogenous dissemination of bacteria. For example, GAS pharyngitis may progress to peritonsillar or pharyngeal abscess, manifesting with trismus, muffled voice, and severe unilateral throat

pain. The infection can extend to the middle ear, causing otitis media, or to the paranasal sinuses, resulting in sinusitis, which may rarely progress to orbital or intracranial involvement. Hematogenous spread can lead to streptococcal bacteremia, meningitis, or even brain abscess, especially in immunocompromised hosts. In severe soft tissue infections, GAS can cause necrotizing fasciitis, a rapidly progressive and life-threatening condition that requires urgent surgical debridement and intensive care. Jugular vein septic thrombophlebitis is another severe complication, often associated with deep neck space infections.

Non-suppurative complications are typically immune-mediated and occur after the acute infection has resolved. Acute rheumatic fever (ARF) is the classic example and may develop several weeks after untreated or inadequately treated GAS pharyngitis. ARF can involve the heart, joints, skin, and central nervous system, with the most serious consequence being chronic valvular damage, leading to rheumatic heart disease and long-term cardiac morbidity. Poststreptococcal reactive arthritis represents another postinfectious inflammatory syndrome affecting the joints. Acute poststreptococcal glomerulonephritis (APSGN) arises from immune complex deposition in the glomeruli, leading to hematuria, proteinuria, edema, and hypertension. Other notable non-suppurative manifestations include streptococcal toxic shock syndrome (STSS), a fulminant toxin-mediated illness characterized by hypotension, multiorgan failure, and high mortality, and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), in which abrupt-onset obsessive-compulsive symptoms or tics may follow GAS infection in susceptible children. While scarlet fever itself does not directly cause these outcomes, it serves as a clinical marker of GAS infection and thus shares the same potential for complications if the underlying infection is not adequately treated. In modern practice, the incidence of these complications is relatively low in settings with good access to healthcare and high rates of timely antibiotic use. Nevertheless, clinicians must remain vigilant—especially when patients present late, fail to respond to therapy, or demonstrate signs suggestive of deeper infection or postinfectious syndromes.

Deterrence and Patient Education

Effective prevention of scarlet fever and other GAS-related illnesses relies heavily on public health measures and patient education focused on interrupting transmission and encouraging timely medical evaluation. Because GAS spreads primarily via respiratory droplets and contaminated fomites, basic infection control practices are central to deterrence. Patients and caregivers should be advised to practice frequent hand hygiene, using soap and water or alcohol-based hand sanitizers, particularly after coughing, sneezing, or touching the face. Covering coughs and sneezes with a tissue or the elbow, disposing of tissues promptly, and avoiding the sharing of utensils, drinking glasses, or personal items are simple yet effective strategies to reduce spread. Regular disinfection of high-touch surfaces, such as doorknobs, keyboards, and toys, is also beneficial, especially in households or institutions where cases have been identified. Public reminders via posters, educational leaflets, and media campaigns can reinforce these messages in schools, childcare centers, and healthcare facilities. Parents, teachers, and caregivers should be made aware of the typical signs and symptoms of GAS pharyngitis and scarlet fever—such as fever, sore throat, sandpaper-like rash, and strawberry tongue—and encouraged to seek medical assessment promptly when these occur. Early evaluation and treatment not only promote rapid symptom resolution but also help prevent complications and limit community spread.

Another critical educational focus is the appropriate use of antibiotics. Overuse and misuse of antibiotics contribute to the development and dissemination of antibiotic-resistant GAS strains, especially resistance to macrolides and clindamycin. Patients and families should understand that antibiotics are indicated for confirmed or strongly suspected bacterial infections like GAS pharyngitis, but not for viral sore throats or nonbacterial illnesses. Healthcare professionals should explain the importance of completing the full course of prescribed antibiotics, even when symptoms improve early, to ensure eradication of the organism and reduce the risk of relapse or selection of resistant subpopulations. Education should also include counseling about the natural course of scarlet fever, including the possibility of desquamation after the rash fades, so that this benign phase is not mistaken for a new or worsening condition. Patients should be instructed on when to return for medical evaluation—for example, if fever persists beyond 48–72 hours of therapy, if new focal symptoms develop (such as ear pain or severe headache), or if there are signs of systemic deterioration such as shortness of breath, chest pain, or decreased urine output. By promoting hygienic practices, rational antibiotic use, and early recognition of illness, patient education serves as a powerful tool to reduce the incidence of scarlet fever and its complications, protect vulnerable populations, and slow the emergence of resistant GAS strains.

Enhancing Healthcare Team Outcomes

Optimal management of scarlet fever is best achieved through a coordinated interprofessional healthcare team that integrates the expertise of physicians, nurses, pharmacists, and allied health professionals, with patient education at the center of care.[64][65] Clinicians—such as primary care physicians, pediatricians, emergency physicians, and infectious disease specialists—play a key role in early recognition, appropriate diagnostic testing, and timely initiation of therapy. They should provide clear guidance on the nature of the illness, expected clinical

course, and warning signs that warrant reevaluation. Pharmacists are vital partners in ensuring safe and effective treatment. They should verify dosing based on age and weight, screen for drug interactions and allergies, and counsel patients and caregivers on correct administration schedules. Emphasis should be placed on adherence to the full course of antibiotics, even when symptoms improve early, to maximize eradication of GAS and minimize the risk of recurrence or complications.[64] Pharmacists can also reinforce messages about the risks of unnecessary antibiotic use and the importance of not sharing leftover medications. Nurses, particularly those in primary care, school health, and community settings, are central to patient and family education. They can demonstrate hand hygiene techniques, discuss infection control measures at home, and explain the contagious period of scarlet fever. Nurses are often the first to identify changes in a patient's condition, such as persistent fever, worsening rash, or emerging signs of systemic illness, and they play a crucial role in triaging the need for reassessment.

Physical and occupational therapists may be involved in more complex or prolonged cases, especially in patients who develop complications that limit activity or require rehabilitation. School nurses and public health practitioners contribute by monitoring clusters of cases, coordinating with local health authorities, and implementing outbreak control measures in educational and institutional settings. Effective communication among all team members is critical. Shared electronic health records, clear documentation of test results and treatment plans, and timely handoffs between inpatient and outpatient providers help ensure continuity of care. Team-based case reviews and morbidity discussions can identify areas for improvement in recognition, treatment, or patient education. Finally, engaging patients and families as active partners in care—encouraging them to ask questions, report new symptoms promptly, and follow infection control measures—enhances both individual outcomes and public health. When the interprofessional team functions cohesively, scarlet fever is not only effectively treated but also more effectively prevented, with reduced complications, improved adherence, and higher overall patient satisfaction.[64][65]

Conclusion:

In conclusion, scarlet fever remains a significant clinical entity, demonstrating a dynamic interplay between a classic bacterial pathogen and the human immune system. While the advent of antibiotics transformed its prognosis from a historical killer to a readily treatable condition, the recent global resurgence driven by novel, more virulent GAS clones underscores that it is not a disease of the past. The hallmark clinical presentation—the sandpaper rash, strawberry tongue, and pharyngitis—is a direct consequence of superantigen-mediated toxin production, which triggers a massive and dysregulated immune response. The cornerstone of management is prompt diagnosis and timely administration of appropriate antibiotics, with penicillin V or amoxicillin remaining the gold standard. This approach is crucial not only for alleviating acute symptoms but, more importantly, for preventing serious suppurative and non-suppurative complications such as acute rheumatic fever and poststreptococcal glomerulonephritis. The growing challenge of antimicrobial resistance to alternative agents like macrolides highlights the need for ongoing surveillance and prudent antibiotic use. Ultimately, optimizing patient outcomes extends beyond prescription. It requires a robust, interprofessional healthcare strategy that integrates accurate diagnosis, effective treatment, and comprehensive patient and community education on hygiene and infection control. By fostering collaboration among clinicians, nurses, pharmacists, and public health officials, healthcare teams can effectively manage individual cases, control outbreaks, and mitigate the long-term sequelae of this re-emerging infectious disease, thereby protecting both individual and public health.

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