Invasive Group A Streptococcal Infections at Chulalongkorn University Hospital

CHUSANA SUANKRATAY, M.D., Ph.D.*,
PONGPUN NUNTHAPISUD, M.Sc.**,
HENRY WILDE, M.D.***

Abstract

To determine whether the incidence and pattern of group A Streptococcal (GAS) infections in Thailand have paralleled those in the United States and Europe, we conducted a retrospective study of invasive GAS infections at Chulalongkorn University Hospital from 1995 to 1999. A total of 42 cases were identified. There were 18 males and 24 females (median age of 59 and 46 years, respectively). Most patients were in two age groups: 20-39 (33%) and 60-79 (38%). Underlying conditions were present in 34 patients (81%), including mostly chronic system diseases (50%), alcohol abuse (19%), diabetes mellitus (14%), connective tissue diseases (12%), immunosuppressive illnesses (12%), and human immunodeficiency virus infection (10%). The most common clinical presentations were skin and soft-tissue infections (31%), primary bacteremia (29%), and arthritis (14%). Of these, 24 (57%) presented with toxic shock syndrome (TSS). Overall mortality rate was 33 per cent. All GAS but one isolate were susceptible to penicillin.

Key word : Group A Streptococcal Infection, Toxic Shock Syndrome, Bacteremia

SUANKRATAY C,
NUNTHAPISUD P, WILDE H
J Med Assoc Thai 2001; 84: 1594-1603

* Division of Infectious Diseases, Department of Medicine,
** National Streptococcal Reference Center, Department of Microbiology, Faculty of Medicine, Chulalongkorn University,
*** Queen Saovabha Memorial Institute, Bangkok 10330, Thailand.

An increased prevalence of severe infections caused by group A streptococci (GAS) has been noted throughout the United States and Europe since the late 1980's[1-5]. These were often of a fulminant nature characterized by shock, multiorgan involvement and death[1,2,6,7]. The clinical entity, known as streptococcal toxic shock syndrome (TSS), was often associated with GAS bacteremia and/or rapidly progressive soft tissue infection (usually, necrotizing fasciitis or myositis)[1,2,7-9]. Patients with this syndrome appeared to be younger and less likely to have underlying diseases. Two virulence factors, M protein and streptococcal pyrogenic exotoxins (SPEs), have been postulated to be involved in the pathogenesis of clinical manifestations of streptococcal TSS[8-10]. An increased prevalence of certain M-protein serotypes, such as M1 and M3, and an increase in the number of strains producing streptococcal pyrogenic exotoxin A (SPEA) has also been observed[2,10-15]. Decreased host immunity to these serotypes is one possible reason that could also explain the resurgence of GAS[16].

During the past two years, we have observed an apparent increase in the virulence of GAS manifesting as TSS or as other invasive GAS infections. In order to determine whether the pattern of invasive GAS infections in Thailand has paralleled the increasingly frequent and aggressive pattern seen in the United States and Europe, we conducted a 5-year review of all cases of GAS bacteremia and other invasive GAS infections seen at Chulalongkorn University Hospital (CUH).

METHOD

Patients

The authors retrospectively studied all invasive GAS infections in patients admitted to CUH from January 1, 1995 to December 31, 1999. Invasive GAS was defined by the isolation of *Streptococcus pyogenes* from blood, normally sterile body fluids, abscesses, or tissue. Two patients, one with acute pharyngitis and TSS and a throat culture positive for GAS, and another with pneumonia and GAS were isolated in predominant numbers from sputum, were also included.

A thorough medical chart review was performed for all patients in this study, categorizing patient age, site of infection, site where organism was isolated and the presence of necrotizing fasciitis, myositis, TSS or death. Cases of TSS were defined by previously published criteria[17]. Necrotizing fasciitis was diagnosed surgically, and was defined as an infection of subcutaneous tissue resulting in destruction of fascia. Medical records were also examined to assess conditions that may have predisposed patients to invasive disease such as trauma, surgery, or decreased body defenses (malignancy, AIDS, diabetes, alcoholism, cirrhosis, chronic renal failure, corticosteroid therapy etc.).

Antibiotic Susceptibility

The isolated bacteria were tested by the Kirby-Bauer method for antibiotic susceptibility.

RESULTS

Patient Characteristics

A total of 42 cases of invasive GAS infection were identified during the study period. There were 18 males and 24 females with a median age of 59 and 46 years, respectively (range, 6-83 years). Most of the patients were in two age groups: 20-39 (33%) and 60-79 (38%) years (Table 1).

Factors Associated with GAS Infections

The majority (34, 81%) of cases occurred in persons with at least 1 chronic underlying illness (Table 2). The most common underlying cause was chronic system disease (21, 50%), followed by alcohol abuse (8, 19%), diabetes mellitus (6, 14%), rheumatologic diseases (5, 12%), miscellaneous immunosuppressive illnesses (5, 12%), human immunodeficiency virus infection (4, 10%), intravenous drug use (3, 7%), malignancy (3, 7%), and predisposing chronic skin diseases (2, 5%). Most cases (40, 95%) were community-acquired and only 2 cases were nosocomial infections.

Table 1. Age groups of patients with invasive GAS infections.

Age (years)	Number of patients	%
0-1	0	
>1-19	3	7
20-39	14	33
40-59	7	17
60-79	16	38
> 80	2	5
Total	42	100

Table 2. Predisposing illness in 42 patients with invasive GAS infections.

Predisposing illness	Number of patients	%
Chronic system disease[a]	21	50
Alcohol abuse	8	19
Diabetes mellitus	6	14
Rheumatologic disease	5	12
Immunosuppressive illness[b]	5	12
Human immunodeficiency virus	4	10
Intravenous drug use	3	7
Malignancy	3	7
Predisposing chronic skin disease	2	5
Others[c]	6	14

[a] Included: chronic heart disease (6), hypertension (5), cerebrovascular disease (3), cirrhosis (3), chronic renal failure (3), and chronic obstructive pulmonary disease (3).
[b] Included: steroid abuse (3), systemic lupus erythematosus (1), vasculitis (1), and autoimmune hemolytic anemia (1).
[c] Included: thallassemia (3), hyper- and hypothyroidism (2), and endometriosis (1).

The suspected portal of entry was the skin in 15 (36%) patients, and mucous membrane in 11 (26%) patients (Table 3). Of the former group, 6 (40%) had recent minor trauma at the site of infection and 9 (60%) had antecedent skin lesions (ulcers in 4, chronic skin disease in 2, tophaceous gout in 2, and warfarin-induced cutaneous bleeding in 1). Of the latter group, 5 (45%) had recent acute diarrhea, and 2 (18%) had upper gastrointestinal or vaginal bleeding. The portal of entry was unknown in 16 (38%) patients.

Clinical Presentation

The most common clinical presentations were skin or soft-tissue infection (13, 31%), bacteremia with no identified septic focus (primary bacteremia) (12, 29%), arthritis (6, 14%), pneumonia or pleural effusion (5, 12%), primary peritonitis (4, 10%) and meningitis (3, 7%) (Table 4). Of these, 24 (57%) presented with TSS. Eight (62%) of the 13 patients with soft-tissue infections had necrotizing fasciitis or myositis. The clinical characteristics of 42 patients are summarized in Table 5.

Bacteriologic Cultures

GAS were grown from blood in 31 (74%) patients, body fluid in 8 (19%), abscess in 11 (26%) and lung tissue in 1 (2%). In addition, GAS were grown from pharyngeal specimen from one patient with scarlet fever and TSS, and from sputum specimens from one patient with pneumonia.

Clinical Course

Fourteen (33%) of the 42 patients died. Of these, 7 died within 3 days of admission, 10 died within 7 days, and 4 died beyond 7 days. The morbidity among patients in this series was high (Table

Table 3. Probable portal of entry in 42 patients with invasive GAS infections.

Portal of entry	Number of patients	%
Skin		
Local trauma	6	14
Leg ulcer	4	10
Preexisting chronic skin disease	2	5
Chronic tophaceous gout	2	5
Warfarin-induced cutaneous bleeding	1	2
Total	15	36
Mucous membrane		
Previous acute diarrhea	5	12
Upper gastrointestinal bleeding	2	5
Vaginal bleeding	2	5
Pharynx	2	5
Total	11	26
Unknown	16	38

Table 4. Clinical features of 42 patients with invasive GAS infections.

Diagnosis	Number of patients	%	Toxic shock syndrome		Fatal outcome	%
			Yes	No		
Primary bacteremia	12	29	5	7	5	42
Focal infections						
Skin and soft tissue infections	13	31	10	3	5	38
Cellulitis	5	12	2	3	2	40
Necrotizing fasciitis/myositis	7	17	7	0	2	29
Necrotizing fasciitis+pneumonia	1	2	1	0	1	100
Septic arthritis	5	12	3	2	0	-
Meningitis	3	7	1	2	1	33
Peritonitis	3	7	2	1	1	33
Pneumonia	2	5	1	1	1	50
Pleural effusion	2	5	0	2	0	-
Arthritis+peritonitis	1	2	1	0	1	100
Malignant scarlet fever	1	2	1	0	0	-
Total	42	100	24	18	14	33

6); 19 (45%) were in shock, 18 (43%) had renal failure, 2 (5%) had adult respiratory distress syndrome, 2 (5%) had disseminated intravascular coagulation, 2 (5%) had rhabdomyolysis, and 1 (2%) had abnormal liver function tests. Of 42 patients, 15 (36%) underwent major surgical procedures. These included fasciotomy (8 patients), exploratory laparotomy (4 patients), and arthroscopy/open drainage of joints (3 patients).

Shock was apparent at the time of admission or within hours thereafter in 19 patients. Adult respiratory distress syndrome developed in 2 patients. Both required intubation, supplemental oxygen, and mechanical ventilation. Renal impairment was apparent at admission or within hours thereafter in 18 patients, and persisted or progressed in all 18 patients over 48 to 72 hours. In all of the patients who survived, serum creatinine values returned to normal within four to six weeks.

Antibiotic Susceptibility

Antibiotic susceptibility of GAS was recorded in 30 of 31 blood isolates, 16 of 19 body fluids and abscesses, 1 of 1 lung tissue, and 1 of 1 throat swab culture isolates (Table 7). All but one isolate were susceptible to penicillin. All isolates were susceptible to vancomycin. Susceptibility of GAS in blood culture isolates to erythromycin, clindamycin, or tetracycline was observed in 25 (83%), 23 (77%), and 5 (17%), cases respectively. Susceptibility of GAS in body fluid and abscess culture isolates to different antibiotics was observed in 11 (69%), 13 (81%), and 1 (6%), respectively.

DISCUSSION

This study suggests that the incidence of invasive GAS infections in CUH may have increased from 1995 to 1999, compared with the previous data (unpublished data). The explanation for this finding is not clearly known, but this parallels with the increasing incidence of invasive GAS infections in the United States and Europe during the past 20 years. In our study, the higher incidence was observed in 2 age groups: patients aged 20-39 and those more than 60 years of age. The presence of underlying chronic system diseases, alcoholism, diabetes, and drug abuse was often observed among patients who were more than 60 years old. This finding is similar to earlier studies[18-22]. In contrast to the older age group, those who were 20-39 years of age, appeared to be otherwise healthy. This was also in accordance with other studies[2-7,23-27]. Thus, these results may reflect the heterogeneity of our patients with invasive GAS infections during the observed period.

In our study, approximately two-thirds of the patients had obvious portals of entry. The suspected portal of entry was the skin in 15 patients (36%), and the mucous membrane in 11 patients (26%). There was an association between minor

Table 5. Clinical characteristics and courses of 42 patients with invasive GAS infections.

Patients No.	Age/Sex	Clinical presentation	Clinical course				Bacteremia	Outcome
			Shock	ARDS*	Renal impairment	Surgery		
1.	63/F	Necrotizing fasciitis	+	-	+	-	+	Died
2.	30/F	Primary peritonitis	+	-	+	Laparotomy	+	Survived
3.	82/F	Upper gastrointestinal bleeding, primary bacteremia	+	-	-	-	+	Died
4.	39/F	Cellulitis	+	-	+	-	+	Died
5.	83/M	Pneumonia	-	-	-	-	-	Survived
6.	59/F	Primary bacteremia	+	-	-	-	+	Died
7.	67/M	Pneumonia	+	+	-	-	-	Died
8.	63/F	Primary bacteremia	+	-	+	-	+	Died
9.	32/F	Primary peritonitis	-	-	-	Laparotomy	+	Survived
10.	19/M	Empyema thoracis	-	-	-	-	+	Survived
11.	24/M	Empyema thoracis	-	-	-	-	-	Survived
12.	40/M	Arthritis	+	-	+	Open drainage	+	Survived
13.	35/F	Infected pemphigus	-	-	-	-	-	Survived
14.	69/F	Primary bacteremia	-	-	-	-	+	Survived
15.	39/M	Arthritis, primary peritonitis	+	+	+	Laparotomy	+	Died
16.	38/F	Necrotozing fasciitis	+	-	-	Debridement	+	Survived
17.	50/M	Meningitis	-	-	+	-	+	Survived
18.	35/M	Primary bacteremia	-	-	-	-	+	Survived
19.	19/M	Meningitis	-	-	-	-	+	Died
20.	63/F	Arthritis	-	-	-	Debridement, open drainage	+	Survived
21.	30/F	Celulitis	+	-	+	-	-	Died
22.	70/F	Necrotizing fasciitis	+	-	+	-	+	Survived
23.	6/M	Meningitis	-	-	-	-	-	Survived
24.	78/M	Arthritis	-	-	+	Open drainage	-	Survived
25.	60/F	Necrotizing fasciitis, hypothyroidism	+	-	+	Fasciotomy	+	Survived
26.	64/M	Myositis	+	-	+	Debridement	-	Survived
27.	64/M	Necrotizing fasciitis, pneumonia	+	-	+	Debridement	+	Died
28.	71/F	Primary bacteremia	-	-	-	-	+	Survived
29.	65/M	Primary bacteremia	-	-	+	-	+	Died
30.	72/M	Necrotizing fasciitis	+	-	+	Debridement	+	Survived
31.	35/M	Arthritis, osteomyelitis	-	-	-	Debridement	+	Survived
32.	25/F	Primary bacteremia	-	-	-	-	+	Survived
33.	52/F	Cellulitis	-	-	-	-	-	Survived
34.	46/F	Primary bacteremia	+	-	+	-	+	Died
35.	72/M	Primary bacteremia, primary peritonitis	+	-	+	-	+	Died
36.	38/F	Arthritis	+	-	-	-	+	Survived
37.	68/F	Necrotizing fasciitis	-	-	+	Debridement	-	Survived
38.	20/F	Primary bacteremia	-	-	-	-	+	Survived
39.	60/F	Primary bacteremia	-	-	-	Laparotomy	+	Survived
40.	62/M	Primary bacteremia, upper gastrointestinal bleeding	-	-	-	-	+	Survived
41.	46/F	Primary bacteremia	-	-	-	-	+	Survived
42.	23/F	Scarlet fever, toxic shock syndrome	-	-	-	-	-	Survived

* ARDS: adult respiratory distress syndrome.

trauma and the occurrence of invasive GAS infections. This is also in accordance with previous studies(2). No patient with recent varicella infection was observed and there was only one child who was younger than 10 years of age. The portal of entry was unknown in approximately 38 per cent of all patients. This percentage is close to findings of previous studies which showed approximately 50 per cent of cases with undetermined portals of entry(2).

Approximately 30 per cent of all patients in our series presented with skin and soft tissue infection (necrotizing fasciitis/myositis/cellulitis), and 57 per cent had coexistent GAS TSS, characterized by an acute fulminant disease with shock, disseminated intravascular coagulopathy, adult respiratory distress syndrome, acute renal failure and/or multisystem failure. In contrast to prior studies in which healthy young adults were found to be at risk for

Table 6. Complications of invasive GAS infections.

Complication	Number of patients	%
Shock	19	45
Adult respiratory distress syndrome	2	5
Renal impairment	18	43
Disseminated intravascular coagulation	2	5
Rhabdomyolysis	2	5
Abnormal liver function test	1	2
Surgery		
Fasciotomy + graft	8	19
Exploratory laparotomy	4	10
Arthroscopy/open drainage of the joint	3	7
Death	14	33

Table 7. Antibiotic susceptibility of GAS isolates from different culture specimens.

Specimen	N	Pen[a]		Van[b]	Ery[c]			Cli[d]			Tet[e]		
		S	I	S	S	I	R	S	I	R	S	I	R
Blood	30	29	1	29	25	1	3	23	5	2	5	0	23
Body fluid/Abscess	16	15	0	15	11	2	2	13	1	1	1	0	15
Tissue	1	1	0	1	1	0	0	1	0	0	0	0	1
Throat	1	1	0	1	1	0	0	0	1	0	0	0	1

[a] Pen : penicillin
[b] Van : vancomycin
[c] Ery : erythromycin
[d] Cli : clindamycin
[e] Tet : tetracycline

GAS TSS, those at greatest risk in our study were older and had underlying illnesses (data not shown). This difference may reflect a reduction in ascertainment bias in population-based data compared with previous case series(1,2,7). Conversely, our case definition for GAS TSS may identify patients who are debilitated and more likely to have multisystem failure when subjected to the stress of infection. Geographic, climatic and socio-cultural factors may also be involved.

There were 12 patients with primary GAS bacteremia. They accounted for 29 per cent of all invasive GAS infections. Of these, 3 (23%) and 7 (54%) were 20-39 and more than 60 years of age, respectively. This rate of primary bacteremia is different from that of most reported cases of GAS infections(7). However, it was similar to the result of Burket and Watanakunakorn who found that 33 per cent of patients had primary bacteremia(20). This predominance may be the result of a bias in our study which was retrospective, and case selection was based on patients with GAS isolated from culture specimens. Clinically, it is important to note that patients with primary GAS bacteremia often presented with nonspecific flu like symptoms, making early clinical diagnosis difficult. This observation is in accordance with previous studies of invasive GAS infections(2,24). A high mortality rate (43%) was observed in patients who were older than 60 years, and this also corresponds to previous studies(7,22,24).

Focal GAS infections such as meningitis, pneumonia with and without empyema thoracis, peritonitis, suppurative arthritis and osteomyelitis were also observed in this series. GAS meningitis is rare beyond the neonatal period. We reported 3 patients with GAS meningitis, 2 had bacteremia and all but one survived. No association with contiguous

foci of infection such as sinusitis, otitis media, mastoiditis was observed in our patients. This is in contrast to most previous studies[20,28,29]. Peritonitis was relatively rare before the reemergence of invasive GAS infections in the 1980s. There were 4 patients with GAS peritonitis in our series: 3 and 1 were 20-39 and more than 60 years of age. All of them seemed to have primary peritonitis without any gut-related foci, corresponding to the study of Francis and Warren[30]. GAS pneumonia or empyema thoracis was observed in 3 and 2 patients, respectively in this series. It was very rare in previous studies of invasive GAS infections[21]. However, Pongrithsukda reported GAS pneumonia as the most common primary site of infection in patients admitted to Maharaj Nakhon Ratchasima Hospital, Northeastern Thailand, during the 1986-1991 period [31]. Septic arthritis was observed in 6 patients, and one of these had associated osteomyelitis. GAS arthritis was relatively rare before the reemergence of GAS in the 1980s, and most patients had associated skin and soft tissue infections including necrotizing fasciitis/myositis[7,21,26]. This is in contrast to our results where no such association was observed. There was one healthy adult female who presented with GAS sore throat, scarletiniform rash, TSS, and desquamation of the skin during the recovery period. This case should be categorized as malignant scarlet fever.

In our study, all isolates were susceptible to vancomycin, and only one isolate was resistant to penicillin. These findings are similar to those of previous studies[21,22,30,31]. There was a trend toward increasing resistance to macrolides. 4 isolates of GAS were intermediately resistant or resistant to erythromycin. This finding is in accordance with the study by Santanirand et al from Ramathibodi Hospital, Bangkok during the 1990-1992 period[32].

The overall case fatality rate was 33 per cent. This is in accordance with other series in which it varied from 30 per cent to 70 per cent[2,5, 7,22-24]. It was higher (42%) in patients without a demonstrable source of infection (primary bacteremia). This can be explained by delay in diagnosis and in administration of adequate therapy. A high mortality rate was also observed in patients with skin and soft tissue infections (38%). Our patients required intensive fluid replacement, invasive monitoring, and timely surgical debridement. The antibiotics used were mostly penicillin and cephalosporins, and no conclusions about optimal antibiotic selection can be drawn from this study. Yet, failure to respond to penicillin was observed in experimental mice infected with fulminant forms of GAS, and with a large burden of bacteria[33]. Other approaches to therapy including the use of antibiotics that inhibit toxin synthesis[34] or protein that neutralizes the activity of toxin such as immunoglobulin[35] were not used in this series.

The importance of aggressive surgical treatment with adequate debridement and/or amputation has been emphasized previously for patients with necrotizing fasciitis/myositis[7,26,36]. In our series, the mortality rate approached 100 per cent for those patients without surgical treatment.

The role of M serotypes associated with increased virulence of GAS infections was not elucidated in this study. However, in previous studies of GAS isolates in Chulalongkorn Hospital, these did not show the presence of M1, 3 or 8 serotypes[37, 38]. This is in marked contrast to reports from the United States and Europe[38-41]. Unfortunately, in our study, the sequencing of M protein was not carried out.

SUMMARY

The present study describes 42 patients admitted to Chulalongkorn Hospital from 1995 to 1999 who had invasive GAS infections with and without TSS. The striking finding in this series was the bimodal incidence of invasive GAS infections; in otherwise healthy young adult patients (20-39 years of age) and in older patients (more than 60 years of age) with underlying illnesses. In addition, invasive GAS infections in our center during the past 5 years exhibited many of the characteristics of other recently reported series. There was a variety of clinical features such as skin and soft tissue infections, followed by primary bacteremia, localized suppurative infection and malignant scarlet fever. These were associated with significant morbidity and mortality. Primary GAS bacteremia is observed in increasing numbers (unpublished data), and most are community-acquired. GAS must be included in the differential diagnosis of patients presenting with primary bacteremia particularly those associated with the sepsis syndrome.

(Received for publication on April 23, 2001)

REFERENCES

1. Cone LA, Woodard DR, Schlievert PM, Tomory GS. Clinical and bacteriologic observations of a toxic shock-like syndrome due to Streptococcus pyogenes. N Engl J Med 1987; 317: 146-9.
2. Stevens DL, Tanner MH, Winship J, et al. Severe group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin. N Engl J Med 1989; 321: 1-7.
3. Wheeler MC, Roe MH, Kaplan EL, Schlievert PM, Todd JK. Outbreak of group A streptococcus septicemia in children: Clinical, epidemiologic, and microbiological correlates. JAMA 1991; 266: 533-7.
4. Holm SE, Norrby A, Bergholm AM, Norgren M. Aspects of pathogenesis of serious group A streptococcal infections in Sweden, 1988-1989. J Infect Dis 1992; 166: 31-7.
5. Demers B, Simor AE, Vellend H, et al. Severe invasive group A streptococcal infections in Ontario, Canada: 1987-1991. Clin Infect Dis 1993; 16: 792-800.
6. Bartter T, Dascal A, Carroll K, Curley FJ. "Toxic step syndrome": A manifestation of group A streptococcal infection. Arch Intern Med 1988; 148: 1421-4.
7. Stevens DL. Invasive group A streptococcal infections. Clin Infect Dis 1992; 4: 2-13.
8. Bohach GA, Fast DJ, Nelson RD, Schlievert PM. Staphylococcal and streptococcal pyrogenic toxins involved in toxic shock syndrome and related illnesses. Crit Rev Microbiol 1990; 17: 251-72.
9. Musser JM. Clinical relevance of streptococcal pyrogenic exotoxins in streptococcal toxic shock-like syndrome and other severe invasive infections. Pediatr Ann 1992; 21: 821-8.
10. Hauser AR, Stevens DL, Kaplan EL, Schlievert PM. Molecular analysis of pyrogenic exotoxins from Streptococcus pyogenes isolates associated with toxic shock-like syndrome. J Clin Microbiol 1991; 29: 1562-7.
11. Schwartz B, Facklam RR, Breiman RF. Changing epidemiology of group A streptococcal infection in the USA. Lancet 1990; 336: 1167-71.
12. Johnson DR, Stevens DL, Kaplan EL. Epidemiologic analysis of group A streptococcal serotypes associated with severe systemic infections, rheumatic fever on uncomplicated pharyngitis. J Infect Dis 1992; 166: 374-82.
13. Cleary PP, Kaplan EL, Hadley JP, et al. Clonal basis for resurgence of serious Streptococcal pyogenes disease in the 1980s. Lancet 1992; 339: 518-21.
14. Colman G, Tanna A, Efstration A, Gaworzewska ET. The serotypes of Streptococcus pyogenes present in Britain during 1980-1990 and their association with disease. J Med Microbiol 1993; 39: 165-78.
15. Kiska DL, Thiede B, Caracciolo J, et al. Invasive group A streptococcal infections in North Carolina: Epidemiology, clinical features, and genetic and serotype analysis of causative organisms. Clin Infect Dis 1997; 176: 992-1000.
16. Musser JM, Kapur V, Kanjilal S, et al. Geographic and temporal distribution and molecular characterization of two highly pathogenic clones of Streptococcus pyogenes expressing allelic variants of pyrogenic exotoxin A (scarlet fever toxin). J Infect Dis 1993; 167: 337-46.
17. The Working Group on Severe Streptococcal Infections. Defining the group A streptococcal toxic shock syndrome: Rationale and consensus definition. JAMA 1993; 269: 390-1.
18. Bibler MR, Rouan GW. Cryptogenic group A streptococcal bacteremia: experience at an urban general hospital and review of the literature. Rev Infect Dis 1986; 8: 941-51.
19. Adams EM, Gudmundsson S, Yocum DE, Haselby RC, Craig WA, Sundstrom WR. Streptococcal myositis. Arch Intern Med 1985; 145: 1020-3.
20. Burket T, Watanakunakorn C. Group A streptococcal bacteremia in a community teaching hospital 1980-1989. Clin Infect Dis 1992; 94: 29-37.
21. Dan M, Maximaia S, Siegman-Igra Y, Gutman R, Rotmensch HH. Varied presentations of sporadic group A streptococcal bacteremia: clinical experience and attempt at classification. Rev Infect Dis 1990; 12: 537-42.
22. Livni G, Ashkenazi S, Leibovici L, et al. Incidence and severity of group A streptococcal bacteremia in a Medical Center in Israel, 1981-1994. Scand J Infect Dis 1996; 28: 139-42.
23. Katz AR, Morens DM. Severe streptococcal infections in historical perspective. Clin Infect Dis 1992; 14: 298-307.
24. Bronze MS, Dale JB. The reemergence of serious group A streptococcal infections and acute rheumatic fever. Am J Med Sci 1996; 311: 41-54.
25. Low DE, Schwartz B, McGeer A. The reemergence of severe group A streptococcal disease; an evolutionary perspective. In: Scheld WM, Armstrong D, Hughes JM, eds. 1st ed. Emerging infections 1. Washington DC: ASM Press, 1998: 93-123.
26. Kaul R, McGeer A, Low D, Green K, Schwartz B. Population-based surveillance for group A streptococcal necrotizing fasciitis: Clinical features, prognostic indicators, and microbiologic analysis of seventy-seven cases. Am J Med 1997; 103: 18-24.
27. Davies HD, McGeer A, Schwartz B, et al. Invasive group A streptococcal infections in Ontario,

Canada. N Engl J Med 1996; 335: 547-54.
28. Swartz MN, Dodge PR. Bacterial meningitis-a review of selected aspects. N Engl J Med 1965; 272: 725-1010.
29. Lerner PI. Bacterial infections of the nervous system. Cleve Clin Q 1975; 42: 83-99.
30. Francis J, Warren RE. Streptococcal pyogenes bacteremia in Cambridge-a review of 67 episodes. Q J Med 1988; 256: 603-13.
31. Pongrithsukda W. Group A streptococcal bacteremia in Maharaj Nakhon Ratchasima Hospital. J Infect Dis Antimicrob Agents 1993; 10: 67-75.
32. Santanirand P, Jayanetra P. Erythromycin-resistant group A streptococcus (ERGAS) at Ramathibodi Hospial, Bangkok. J Infect Dis Antimicrob Agents 1993; 10: 125-9.
33. Eagle H. Experimental approach to the problem of treatment failure with penicillin. I. Group A streptococcal infection in mice. Am J Med 1952; 13: 389-99.
34. Stevens DL, Gibbons AE, Bergstrom R, Winn V. The Eagle effect revisited: Efficacy of clindamycin, erythromycin, and penicillin in the treatment of streptococcal myositis. J Infect Dis 1988; 158: 23-8.
35. Lamothe F, D'Amico P, Ghosn P, Tremblay C, Braidy J, Patenaude JV. Clinical usefulness of intravenous human immunoglobulins in invasive group A streptococcal infections: Case report and review. Clin Infect Dis 1995; 21: 1469-70.
36. Wilson GJ, Talkington DF, Gruber W, Edwards K, Dermody TS. Group A streptococcal necrotizing fasciitis following varicella in children: Case reports and review. Clin Infect Dis 1995; 20: 1333-8.
37. Bisno AL, Stevens DL. Streptococcal infections of skin and soft tissue. N Engl J Med 1996; 334: 340-5.
38. Nunthapisud P, Sirilertpanrana S, Reinprayoon S, Tanna A. Detection of the erythrogenic toxin A, B, and C genes in group A streptococci isolated from clinical specimens. In: Horaud T, Bouvet A, Leclercq R, eds. Streptococci and the host. New York: Plenum Press, 1997: 729-31.
39. Kaplan EL, Johnson DR, Nanthapisud P, Sirilertpanrana S, Chumdermpadetsuk S. A comparison of group A streptococcal serotypes isolated from the upper respiratory tract in the USA and Thailand: implications. Bull World Health Organ 1992; 70: 433-7.
40. Tran POT, Johnson DR, Kaplan EL. The presence of M protein in nontypeable group A streptococcal upper respiratory tract isolates from Southeast Asia. J Infect Dis 1994; 169: 658-61.
41. Pruksakorn S, Sittisombut N, Phornphutkul C, Pruksachatkunakorn C, Good MF, Brandt E. Epidemiological analysis of non-M-typeable group A streptococcus isolates from a Thai population in Northern Thailand. J Clin Microbiol 2000; 38: 1250-4.

การติดเชื้อแบบลุกลามของสเตร็พโตค็อคคัสกรุพ เอ ที่โรงพยาบาลจุฬาลงกรณ์

*ชุษณา สวนกระต่าย, พ.บ., ปร.ด.**
*ผ่องพรรณ นันทาภิสุทธิ์, วท.ม.**, เฮนรี่ ไวลด์, พ.บ.****

การศึกษาย้อนกลับของการติดเชื้อแบบลุกลามของสเตร็พโตค็อคคัสกรุพ เอ ที่โรงพยาบาลจุฬาลงกรณ์ในปี พ.ศ. 2538–2542 เพื่อเปรียบเทียบกับการศึกษาในสหรัฐอเมริกาและยุโรป มีผู้ป่วยที่รับไว้ในโรงพยาบาล 42 ราย เป็นผู้ชาย 18 ราย และผู้หญิง 24 ราย (ค่ามัธยฐานของอายุ 59 และ 49 ปี ตามลำดับ) ส่วนใหญ่ของผู้ป่วยอยู่ใน 2 ช่วงอายุ คือ 20–39 ปี (33%) และ 60–79 ปี (38%) พบมีโรคประจำตัว 34 ราย (81%) ได้แก่โรคเรื้อรังของระบบต่าง ๆ (50%), โรคพิษสุราเรื้อรัง (19%), เบาหวาน (14%), โรคเนื้อเยื่อเกี่ยวพัน (12%), ภาวะภูมิคุ้มกันบกพร่อง (12%), และติดเชื้อเอ็ชไอวี (10%) อาการทางคลินิกที่พบบ่อยสุดคือ การติดเชื้อของผิวหนังและเนื้อเยื่อ (31%), การติดเชื้อในกระแสเลือดที่ไม่มีจุดกำเนิด (29%) และข้ออักเสบ (14%) มีผู้ป่วย 24 ราย (57%) ที่มีอาการ toxic shock syndrome (TSS) ร่วมด้วย อัตราตายทั้งหมด 33% แบคทีเรียที่แยกได้จากผู้ป่วยทั้งหมดยกเว้น 1 คน ยังไวต่อเพนนิซิลลิน

คำสำคัญ : การติดเชื้อสเตร็พโตค็อคคัสกรุพ เอ, กลุ่มอาการ toxic shock syndrome, การติดเชื้อแบคทีเรียในกระแสเลือด

ชุษณา สวนกระต่าย, ผ่องพรรณ นันทาภิสุทธิ์, เฮนรี่ ไวลด์
จดหมายเหตุทางแพทย์ ฯ 2544; 84: 1594–1603

* สาขาโรคติดเชื้อ, ภาควิชาอายุรศาสตร์,
** ภาควิชาจุลชีววิทยา, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย,
*** สถานเสาวภา, กรุงเทพ ฯ 10330