



Bacteremic *Streptococcus Pyogenes* Pneumonia in Adults in the 21st Century. Report of 9 Cases at a Large Community Teaching Hospital and Review of the Literature

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Abstract

Purpose: To review the current epidemiology and incidence of Group A streptococcal (GAS) pneumonia in our community teaching hospital as part of our quality improvement project for care of patients with GAS bacteremia.

Methods: We reviewed the blood culture logs for all patients for the twelve-year period from January 1, 2006 to December 31, 2017. All patients with positive blood cultures for *Streptococcus pyogenes* were recorded and all charts were reviewed to determine age, sex, date, comorbid conditions, radiographic findings, complications, treatment and outcome.

Results: We identified 68 patients with GAS bacteremia, nine of whom were diagnosed with pneumonia. Pneumonia was the second most common identifiable cause of GAS bacteremia behind only skin and soft tissue infections identified in 29 patients. Patients with GAS pneumonia ranged in age from 31 to 86 years with a mean of 64.9 years and a median of 68 years. There were 5 men (56%) and 4 women (44%). Cases occurred in January (1 case), March (1 case), April (3 cases), May (1 case), June (1 case), November (1 case), and December (1 case). GAS was isolated from the blood only in 7 patients and from both blood and sputum in 2 patients. The most commonly observed comorbidities were: hypertension (4 cases), chronic obstructive pulmonary disease (3 cases), coronary artery disease (3 cases), diabetes mellitus (2 cases) and intravenous drug use (2 cases). One patient had influenza just preceding the episode of GAS pneumonia. One patient had influenza just preceding the episode of GAS pneumonia. Radiographic findings included lower lobe infiltrates in 7 patients: 3 bilateral, 3 right-sided, and 1 left-side.

One patient had right upper lobe infiltrates and one patient had bilateral interstitial infiltrates. Two patients developed empyema requiring tube thoracostomy and one of these two required lobectomy and pleural peel procedure. Because of severity of illness at time of presentation, all 9 patients received almost immediate appropriate parenteral antimicrobial therapy before definitive diagnosis was made. 7 patients received piperacillin/tazobactam, 1 patient received ceftriaxone, and 1 patient received moxifloxacin. 7 patients survived and 2 died (72 years and 82 years old) for a mortality rate of 22.2%.

Conclusions: Bacteremic GAS pneumonia was observed throughout the study period, presented with clinical illness indistinguishable from other acute bacterial pneumonias, and had a significant complication rate: empyema in 2 patients who survived and death in 2 other patients (overall severe complication rate = 44.4%). We review the literature and compare our patients with those reported in isolated intermittent GAS pneumonia case reports, to those reported in longitudinal studies similar to ours, to those reported in post-influenza pneumonia outbreaks, and to those in closed-population outbreaks such as in military bases and special residential homes. *Streptococcus pyogenes* (GAS) remains a significant pathogen in patients with bacteremic, primarily lobar pneumonia and causes significant morbidity and mortality despite early and appropriate antimicrobial therapy. It also is an organism without a vaccine thereby making it a potential pathogen for influenza-related or closed-population-related pneumonia far into the future.

Keywords: *Streptococcus pyogenes*; Group A *Streptococcus*; Pneumonia; Bacteremia; Empyema

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Introduction

In the pre-antibiotic era, pneumonia caused by hemolytic streptococci accounted for 2- 5 percent of all lobar or lobular pneumonias [1]. Pneumonia caused by *Streptococcus pyogenes* in adults is now less frequently diagnosed [1]. In a recent review of community-acquired pneumonia, *S. pyogenes* was not even mentioned in the “less common causes” or “uncommon causes” of pneumonia [2]. As part of a recent quality improvement study reviewing the care provided for patients with Group A *Streptococcus* bacteremia over a 12-year period at our institution, we identified 9 patients with *Streptococcus pyogenes* pneumonia (SPP). We present the epidemiologic, clinical, radiographic, microbiologic and therapeutic findings of these patients and review the recent literature for adults with SPP. We also review the medical literature for recently published articles regarding SPP.

Patient Identification

As part of a quality improvement project evaluating the care of patients at our institution with Group A streptococcal bacteremia, we reviewed the charts of 68 patients identified from our Microbiology Laboratory data base who had positive blood cultures for *Streptococcus pyogenes*. Pneumonia was the source of bacteremia in 9 of our 68 bacteremic patients. Pertinent clinical, epidemiologic, diagnostic and therapeutic information was then extracted from the patient’s chart by one of the authors (JAH).

Microbiologic Identification

Streptococcus pyogenes (Group A *Streptococcus*) was identified from clinical specimens by standard microbiologic techniques [3]. Results of positive blood cultures were called immediately by laboratory personnel to the nurse caring for the patient. The nurse immediately notified the responsible physician about positive blood culture results.

Review of the Literature

PubMed, Google, Google Scholar and Cochrane Library searches were performed using all combinations of the following key words/phrases: *Streptococcus pyogenes*, Group A *Streptococcus*, pneumonia, respiratory infection, empyema, bacteremia. Articles and their bibliographies were reviewed to identify other patients with *Streptococcus pyogenes* pneumonia in adult patients (18 years of age and older).

Case Presentation

Case 1

An 83 year old man was seen in the Emergency Department (ED) with a 24-hour history of worsening dyspnea. Review of systems (ROS) was positive for severe dyspnea, audible wheezing, and severe weakness. ROS was negative for chest pain, fever, chills, cough and sputum production. Past medical history (PMH) was significant for a history of chronic obstructive lung disease (COLD) and prior coronary artery disease. Vital signs were: BP = 156/98 mm HG, pulse = 131/min., respirations = 22/min, and temperature = 99.7°F with 95% oxygen saturation on 3 liters/min. supplemental oxygen. Lungs revealed bilateral inspiratory and expiratory sibilant rhonchi; Heart revealed tachycardia. There was bilateral lower extremity edema. Remainder of the exam was normal. Chest x-ray revealed old right upper lobe scarring and a new right upper lobe infiltrate. WBC = 20,000/ mm³ with 77% PMN and 10% band forms. CT scan of chest

showed right upper lobe consolidation. Blood cultures were obtained and the patient was begun on intravenous moxifloxacin. 2 of 2 sets of blood cultures revealed *Streptococcus pyogenes*. The patient survived.

Case 2

A 68 year old man was seen in the ED with a one-week history of cough and dyspnea and a 12-hour history of sharp, right-sided back pain, nausea, emesis, diarrhea and fever to 103.0°F. PMH is significant for diabetes mellitus, hypertension and coronary artery disease. Vital signs were: blood pressure = 90/53 mmHg; pulse = 73/ min.; respirations = 20/min.; temperature = 98.8°F; oxygen saturation = 97% on room air. Chest exam showed right-sided inspiratory rales. Cardiac exam was negative for murmur, gallop or rub. Abdominal exam was normal. Chest x-ray showed confluent infiltration of right lung base with focal infiltrate in the left lower lung zone. CT of Chest showed large right-sided pleural effusion with atelectasis of the right lower lobe and a small amount of left-sided pleural fluid with left lower lung infiltrate. The patient was treated with intravenous ceftriaxone, azithromycin and vancomycin and required right-sided tube thoracostomy with eventual pleural peel and right lower lobe wedge resection. Both sets of blood cultures revealed Group A *Streptococcus* (GAS). The patient survived to leave the hospital.

Case 3

An 81 year old man came to the ED for worsening dyspnea. He had complained of sudden onset of dyspnea, fever and chills. He was noted to have decreased oxygen saturation (70%) by Emergency Medical Service (EMS) at home. He had a past medical history of congestive heart failure and hypertension. Vital signs were: blood pressure = 242/79 mmHg; respiratory rate = 24/min.; pulse rate = 92/ min.; temperature = 101.4°F; oxygen saturation was 100% with non-rebreather oxygen mask. The patient was lethargic and in moderate respiratory distress. Lungs showed bilateral inspiratory rhonchi. Cardiac exam revealed tachycardia without murmur, gallop or rub. Abdominal exam was normal. Chest x-ray showed bilateral basilar infiltrates and cardiomegaly. WBC = 20,900/mm³ with left shift. *Streptococcus pyogenes* was isolated from both sets of blood cultures. The patient was treated with intravenous ceftriaxone and intravenous azithromycin and survived.

Case 4

A 72 year old man came to ED for sudden onset of severe shortness of breath the night prior to admission. He stated that he “recently had the flu” and was getting over his “fevers” when the new shortness of breath began. This occurred during the month of January just after a seasonal influenza outbreak had begun. He had a cough productive of purulent sputum. His past medical history was significant for adenocarcinoma of the lung status post right upper lobectomy one year previously. He had a remote history of vocal cord carcinoma. Vital signs were: temperature = 99.8°F; blood pressure = 110/84; pulse = 155/ min.; respiratory rate = 32/ min. The patient was in moderate respiratory distress and had coarse bilateral inspiratory rhonchi on chest auscultation. Cardiac exam showed tachycardia without murmur, gallop or rub. Abdominal examination was normal. Neck exam showed use of accessory respiratory muscles. Chest x-ray revealed right lower lobe infiltrate. White blood count was 24,000/ mm³ and blood cultures were drawn. While awaiting admission to the intensive care unit from the ED, he was intubated, received fluid and pressure resuscitation as well as intravenous vancomycin and piperacillin/tazobactam. Shortly after transfer to the intensive care unit, he experienced a cardiopulmonary arrest and could not be

Table 1: Our Patients with Pneumonia Due to *Streptococcus pyogenes*.

Case No	Age	Sex	Positive Cultures For Gas	Comorbid Conditions	Complications	Radiographic Findings	Surgical Intervention	Antimicrobial Therapy	Outcome
1	83	M	Blood	COPD; CAD	None	Right upper lobe infiltrate in complex pattern	None	Appropriate	Lived
2	68	M	Blood and Tracheal Aspirate	DM; CAD; HTN	Empyema	Right and left lower lobe infiltrates	Tube thoracostomy then pleural peel with wedge resection	Appropriate	Lived
3	86	M	Blood	HTN; Oseoarthritis	None	Bilateral basilar infiltrates	None	Appropriate	Lived
4	72	M	Blood	HTN; Oseoarthritis of lung	Death	Large right lower lobe infiltrate	None	Appropriate	Died
5	33	F	Blood	Intravenous drug use	Empyema; Septic arthritis of shoulder joint	Large right lower lobe infiltrate with evolving pleural effusion; Septic emboli in other lobes	Tube thoracostomy of right empyema	Appropriate	Lived
6	82	F	Blood	HTN; DM; CAD; CKD; COPD; Atrial fibrillation	Death	Left lower lobe infiltrate	None	Appropriate	Died
7	63	M	Blood	COPD; CHF; OSA; Prostatism	None	Left lower lobe infiltrate with small effusion; streaky right lower lobe infiltrate	None	Appropriate	Lived
8	66	F	Blood and Sputum	CVA; Hemiplegia	None	Bilateral interstitial densities	None	Appropriate	Lived
9	31	F	Blood	IV Substance Abuse	None	Right lower lobe infiltrate	None	Appropriate	Lived

Abbreviations Used: GAS=Group A Streptococcus; M=Male; F=Female; COPD=Chronic Obstructive Pulmonary Disease; CAD=Coronary Artery Disease; DM=Diabetes Mellitus; HTN=Hypertension; CKD=Chronic Kidney Disease; OSA=Obstructive Sleep Apnea; CVA=Cerebrovascular Accident (Stroke)

resuscitated. The following day, both of the blood cultures drawn in the ED were positive for *Streptococcus pyogenes*.

Case 5

A 33 year old woman presented to the ED with a 3 day history of chest pain, cough, dyspnea, chills and intermittent diaphoresis. Chest pain was sharp and worse with deep inspiration, with coughing and while lying in the supine position. She had a past medical history of intravenous cocaine use and tobacco abuse. Two weeks previously had been admitted to the hospital for incision and drainage of multiple cutaneous abscesses at the drug injection sites on her arms. Vital signs were: blood pressure = 107/56 mmHg; pulse rate = 94/min.; respiratory rate = 20/min.; and temperature = 97.5°F. She was awake, alert and oriented to person, place and time with moderate chest pain during deep inspiration. She was non-toxic-appearing but appeared cachectic. Neck was supple without use of accessory muscles. Chest was clear to auscultation bilaterally. Cardiac examination was significant for a new holosystolic murmur compared to the exam two weeks earlier. Abdomen was soft and non-tender without palpable organomegaly. There were multiple superficial ulcers and furuncles over right and left upper extremities with surrounding erythema and purulent drainage. Laboratory exam showed a white blood cell count of only 5,300/mm³ but the differential showed 49% band forms and 35% segmented neutrophils. Chest x-ray revealed bibasilar infiltrates, right > left, with a small right pleural effusion. CT scan of the chest showed a 2.5 cm diameter mass in the right middle lobe, a 3.6 cm-diameter infra-hilar mass in right lower lobe and a 2.0 cm-diameter peripheral mass in the right lower lobe. There was also consolidation in the right lower lobe and left upper lobe as well as cavitation of the right lower lobe lesions. On the second hospital day she developed left shoulder pain and a large right pleural effusion requiring thoracentesis followed by tube thoracostomy. She also underwent needle aspiration then arthroscopic drainage of an infected left shoulder joint. Blood cultures revealed *Streptococcus pyogenes*. Transesophageal echocardiogram revealed a tricuspid valve

vegetation. She was initially treated with intravenous vancomycin, piperacillin/tazobactam and clindamycin. 4 weeks of treatment was completed with once daily intravenous ertapenem. She survived her illness.

Case 6

An 82 year old man was brought to ED from an extended care facility (ECF) complaining of severe dyspnea. He had a chronic tracheostomy and PEG tube but was not on a ventilator at the ECF. His oxygen saturation was 83% on 12 liters of oxygen via trach mask. His PMH was significant for diabetes mellitus, hypertension, COLD, chronic renal failure, and the presence of a permanent cardiac pacemaker. Vital signs were: blood pressure = 144/64; temperature = 100.4°F; pulse rate = 85/min.; respiratory rate = 18/min. The patient was severely dyspneic and was immediately placed on the ventilator. Lung auscultation revealed bilateral lower lobe rhonchi. Cardiac and abdominal exams were normal. Chest x-ray showed bilateral lower lobe infiltrates. White blood count was 14,000/mm³. The patient was initially treated with intravenous piperacillin/tazobactam and vancomycin. His condition deteriorated rapidly and he was then placed on the palliative care service after admission to the hospital where he subsequently expired. *Streptococcus pyogenes* was isolated from both blood cultures draw upon admission.

Case 7

A 63 year old man was brought to the ED from an ECF. The patient experienced the acute onset of severe dyspnea that morning and was lethargic and barely arousable when seen in ECF by EMS. In the ED, the patient was immediately intubated and given fluid resuscitation. He had a past history of COLD, congestive heart failure, coronary artery disease and obstructive sleep apnea. Vital signs were: blood pressure = 134/79 mmHg; temperature of 101.3°F; heart rate = 131/min.; respiratory rate = 34/min. Pulse oximetry was 87% on 15 liters oxygen via mask just before intubation. Patient was noted to be in severe respiratory distress using accessory respiratory

Table 2: *Streptococcus pyogenes* Pneumonia—Literature Review of Case Reports.

Case No.	Ref. No.	First Author	Year Published	Age	Sex	Comorbidities	Complications	Antibiotic Therapy	Positive Blood Culture	Lived Or Died
1	4	Barnham	1981	55	Male	Kyphoscoliosis; Paraplegia	Fulminant sepsis	Amoxicillin	Yes	Died
2	4	Barnham	1981	92	Female	Dementia	None	Ampicillin	Yes	Lived
3	6	McMurray	1987	33	Female	None	Pleural effusion	Ampicillin/Sulbactam + Erythromycin + Flucloxacillin + Gentamicin	No	Died
4	7	McIntyre	1989	30	Female	Bronchial Asthma	Lung abscess	Penicillin G	Yes	Lived
5	8	McWhinney	1991	26	Male	Injection drug user	Pleural effusion; lung abscess	Erythromycin + Flucloxacillin	Yes	Lived
6	9	Hamour	1994	53	Male	Herpes labialis; Oral candidiasis	Pleural effusion; Atrial fibrillation; Desquamating skin rash	Ceftriaxone + Erythromycin + Ciprofloxacin	No	Lived
7	10	Brusch	1996	51	Male	None	Supraventricular tachycardia; multiple organ failure	Vancomycin + Erythromycin + Doxycycline	No	Died
8	11	Kalima	1998	35	Female	Influenza A	Pneumothorax; Bronchopleural fistula	Ampicillin + Clindamycin	Yes	Lived
9	12	Birch	2000	33	Male	None	Pleural effusion; Multiple organ failure; DIC	Ceftriaxone + Erythromycin	Yes	Lived
10	13	Taylor	2002	89	Male	COPD; Stroke	None	Ceftriaxone	Yes	Died
11	14	Papadas	2008	24	Female	Tonsillitis	None	Amoxicillin/Clavulanate Clarithromycin	Yes	Lived
12	15	Saldias	2008	35	Female	Thyroid cancer	Acute respiratory failure; Septic shock	Ceftriaxone + Clindamycin	Yes	Lived
13	16	Izumiyama	2008	30	Female	None	Acute respiratory failure; Septic shock	Meropenem + Minocycline	Yes	Died
14	17	Weinblatt	2009	54	Female	Rheumatoid arthritis	Acute respiratory failure; Septic shock; Pneumothorax	Ceftriaxone + Vancomycin+ Clindamycin	No	Died
15	18	Aebi	2010	39	Female	Influenza B	Acute respiratory failure; Septic shock	Piperacillin/Tazobactam + Clindamycin	Yes	Alive
16	18	Aebi	2010	27	Female	Influenza B	Acute respiratory failure; Septic shock; Pulmonary hemorrhage	Amoxicillin/Clavulanate + Clarithromycin	Yes	Died
17	19	Lam	2013	34	Male	Influenza B	Septic shock; Multiple organ failure	Meropenem + Azithromycin + Vancomycin	Yes	Lived
18	20	Siegel	2013	41	Female	HIV disease; Injection drug user	Empyema; Lung abscess	Vancomycin + Clindamycin	Yes	Lived
19	21	Martin	2015	57	Male	Adenocarcinoma of stomach	Respiratory failure; Severe sepsis	Ceftriaxone + Azithromycin	Yes	Died
20	22	Akuzawa	2016	78	Male	Remote pulmonary tuberculosis	None	Ampicillin/Sulbactam	Yes	Lived

muscles. He had bilateral diffuse wheezing on auscultation of lungs. Cardiac auscultation showed no murmur, gallop or rub. Abdominal examination was normal. Arterial blood gases showed carbon dioxide retention. Chest x-ray showed bilateral lower lobe infiltrates, left>right. Patient was begun on intravenous vancomycin and piperacillin/tazobactam. Both blood cultures obtained in ED before the start of antimicrobial therapy revealed *Streptococcus pyogenes*. He eventually completed a course of intravenous ceftriaxone and was discharged to his ECF.

Case 8

A 66 year woman with history of prior stroke was brought to the ED by EMS. She had been ill for two days with nausea, vomiting and

cough productive of thick green sputum. In the ED, the patient had mild respiratory distress. Vital signs were: temperature = 104.1°F; respiratory rate = 36/min.; pulse rate = 125/min.; blood pressure = 140/54. Pulse oximetry showed oxygen saturation of 85% on room air. She had left-sided weakness due to prior stroke. Neck was supple and revealed no use of accessory respiratory muscles. Cardiac auscultation showed no murmur, gallop or rub. Chest auscultation revealed bibasilar inspiratory rales. Abdominal examination showed the PEG-tube in left upper quadrant without erythema, drainage or tenderness. Remainder of abdominal examination was normal. White blood cell count = 19,600/mm³ with 95% neutrophils. Chest x-ray revealed diffuse bilateral interstitial densities. Cultures of the sputum and of

Table 3: *Streptococcus pyogenes* Pneumonia in Prospective Pneumonia Studies: 1972-2015.

Reference	Year Published	First Author	No. Patients	No. <i>S. pyogenes</i>	% <i>S. pyogenes</i>	Length of Study
36	1972	Sullivan	167	0	0	12mos.
27	1973	Dorff	148	0	0	6 mos.
31	1981	Klimek	204	2	0.9	12 mos.
26	1985	Berntsson	77	2	2.6	12 mos.
28	1990	Fang	183	0	0	12 mos.
33	1994	Moine	92	9	9.8	19 mos.
32	1997	Marston	2776	17	0	12 mos.
35	1999	Sopena	392	0	0	22 mos.
30	2012	Huijskens	408	0	0	12 mos.
34	2013	Musher	259	0	0	12 mos.
29	2015	Holter	267	1	0.4	36 mos.
Total	1972-2015	All	4973	31	0.6	6-36 mos.

Table 4: Published Series of *Streptococcus pyogenes* Pneumonia.

Reference	First Author	Year Published	Time Frame	Location	No. Cases <i>S. pyogenes</i> Pneumonia	Mortality Rate	Percent Bacteremic
23	Barnham	1999	1987-1997	United Kingdom	17	47%	88%
24	Muller	2003	1992-1999	Canada	222	38%	80%
25	Tamayo	2016	2006-2015	Spain	40	20%	No Data

Table 5: Pneumonia in Patients with Group A Streptococcal Bacteremia.

Reference	Year Published	First Author	No. with Group A Streptococcal Bacteremia	No. with Pneumonia	Percent with Pneumonia
37	1970	Henkel	49	8	16.3
38	1988	Ispahani	40	8	20
39	1989	Barnham	20	6	30
40	1990	Dan	26	1	3.8
41	1991	Braunstein	58	7	12.1
42	1992	Burkert	45	8	17.8
43	1993	Navarro	95	10	10.5
Total	All	All	333	48	14.4

both sets of blood cultures were positive for *Streptococcus pyogenes*. Patient was started on intravenous vancomycin and piperacillin/tazobactam in the ED. She survived following administration of a two-week course of intravenous ertapenem.

Case 9

A 31 year old woman with a history of intravenous substance abuse was brought to the ED by EMS because of an acute change in her mental status, combativeness and development of a new cough. She had a recent mitral valve replacement for *Staphylococcus aureus* endocarditis. Vital signs were: pulse = 116/min.; respirations = 20/min.; blood pressure = 121/61 mmHg; temperature = 100.3°F. She was oriented only to name and knew that she was at the hospital. Neck was supple. Lungs were clear to auscultation. Cardiac examination revealed no audible murmur. Abdominal exam was benign. Chest x-ray showed a new right lower lobe infiltrate. Urine drug screen was positive for cocaine and opiates. WBC was 14,500/μL. *Streptococcus pyogenes* was isolated from two blood cultures draw in the ED. Echocardiogram showed no evidence of vegetation on either the prosthetic mitral valve or any other valve. Patient was treated initially with intravenous vancomycin and piperacillin-tazobactam. This was

changed to intravenous ampicillin- sulbactam until the fifth hospital day after which the patient left the hospital against medical advice. She was seen in follow-up 2 weeks later and was well with no further cough or fever.

Results

Table 1 is a summary of our nine patients with SPP. Patients ranged in age from 31 to 86 years with a mean age of 64.9 years and a median age of 68 years. There were five men and four women. *Streptococcus pyogenes* was isolated from the blood cultures of all nine patients and from sputum specimens in 2 patients. The chest x-ray showed involvement of the right upper lobe alone in one patient, right lower lobe alone in 3 patients, left lower lobe alone in one patient, right and left lower lobes in 3 patients, and bilateral interstitial infiltrates in one patient. The most common comorbidities were hypertension (4 patients), chronic obstructive lung disease (3 patients), coronary artery disease (3 patients), diabetes mellitus (2 patients), and intravenous drug use (2 patients). The two youngest patients were intravenous drug users. All patients were treated immediately after blood cultures were obtained because of the severity of their illnesses upon presentation to the hospital’s emergency department. 7 of 9

patients received piperacillin-tazobactam with at least one other antimicrobial agent, one patient received ceftriaxone + azithromycin + vancomycin, and one patient received moxifloxacin alone. Two of the 9 patients died for a mortality rate of 22 percent. Only one of these patients had what appeared to be post-influenza pneumonia.

Literature Review

Streptococcus pyogenes pneumonia has been described in case reports [4-22], in series of patients with GAS pneumonia [23-25], in prospective studies of community-acquired pneumonia [26-36], in studies of group A streptococcal bacteremia [37-43], as a pathogen causing outbreaks of pneumonia in closed populations such as military barracks [44,45] and nursing homes [46-48] and in the setting of post-influenza bacterial pneumonia [49-51]. In the individual case reports of SPP, the authors often comment that SPP is unusual or rare. Indeed, given the relatively uncommon occurrence in series of true community-acquired pneumonia [26,28-29,31-33], a single physician may see few if any patients with SPP. However, if one includes all of the above settings, SPP is neither unusual nor rare. One of the potential issues in determining the frequency of SPP is that, in the absence of bacteremia, SPP may be very difficult to diagnose. Only in those situations where SPP occurs in epidemic proportions (military outbreaks, influenza outbreaks, nursing home outbreaks) is the patient care team more likely to think of the diagnosis and truly believe that a sputum culture with *S. pyogenes* is reflective of SPP. In order to gain a better perspective for the occurrence of SPP in each of these clinical arenas, we will review the recent literature associated with each scenario.

SPP in Case Reports

Table 2 summarizes the 20 case reports found in our review of the literature from 1981 to 2017. The average age was 45.8 years. There were 9 men and 11 women. Prior influenza infection and injection drug use were the two most common comorbid conditions. 16 of 20 patients had Group A *Streptococcus bacteremia*. 8 of 20 (40%) patients with SPP died.

SPP in Prospective Studies of Community-Acquired Pneumonia

Table 3 summarizes SPP found in 11 prospective studies of community-acquired pneumonia (CAP) published from 1972 to 2015. There were 29 patients (0.6%) with SPP among 4,973 patients with CAP. 6 of the 11 studies did not record a single patient with SPP. Duration of these studies ranged from 6 months to 3 years. In the largest prospective pneumonia series [32], 17 of 2776 (0.6%) patients had SPP. Thus, it is relatively unlikely that any single medical provider will be confronted with a patient with SPP in the routine care of patients with CAP.

SPP in Series of Patients with Group A Streptococcal Pneumonia

We found three published studies of group A streptococcal pneumonia [23-25]. (Table 4) summarizes these studies. One study includes patients from 1987-1997 [23]; one from 1992- 1999 [24]; and one from 2006-2015 [25]. There were a total of 289 patients in these 3 series. Mortality ranged from 20% [25] to 38% [24] to 47% [25]. The percentage of patients with bacteremia was determined in two [23,24] of the three studies and bacteremia was documented in 80% of one study [24] and 88% of patients in the other [23].

SPP in Patients with Group A Streptococcal Bacteremia

Table 5 summarizes the published studies of *Streptococcus pyogenes* bacteremia from 1970 to present [37-43]. Each of these 7 retrospective studies had at least one patient with SPP. The percentage of bacteremic patients diagnosed with pneumonia ranged from 3.8% to 30.0% of reported patients. There was a total of 48 patients (14.4%) with SPP among 333 patients reported with *S. pyogenes* bacteremia [37-43].

SPP in Patients with Post-Influenza Bacterial Pneumonia

Since the 1918 Spanish influenza epidemic, *S. pyogenes* has been recognized as a potential cause for post-influenza bacterial pneumonia. Bacterial culture results from several autopsy series from that pandemic show that 11.8% to 20.0% of these victims succumbed to infection caused by *S. pyogenes* [49,51]. More recently, *S. pyogenes* has been reported as the etiologic agent for post-influenza bacterial pneumonia in 2.1% of adult patients during the 2003- 2004 influenza season [50] and as a significant pathogen complicating patients in the 2009 H1N1 influenza epidemic [52].

SPP Outbreaks from Military Training Facilities

Epidemics of SPP associated with military training facilities have been described since World War I. Investigations suggest that SPP was even a factor in Civil War epidemics [45]. In 1968, Basiliere and colleagues reported 95 patients with SPP from a 1964-1966 outbreak at the US Naval Hospital in San Diego, California [45]. 55 (58%) of 95 patients had empyema and the primary presenting manifestation for most of these military recruits was severe pleuritic chest pain [45]. In 2005, Crum and colleagues reported an outbreak of 127 patients with SPP from a Marine Corps Recruit Depot in San Diego, California [44]. Many patients were co-infected with other pathogens including *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, et al. and Adenovirus. This was the largest reported outbreak of SPP since the Basiliere group report in 1968 [39,45].

SPP Outbreaks in Long-Term Care Facilities

Jordan et al reviewed the epidemiology of Group A streptococcal disease in Long-Term Care Facilities (LTCF) in 2007 [47]. They summarized the 15 published studies of Group A streptococcal LTCF outbreaks published between 1981 and 2006. Pneumonia due to *S. pyogenes* was one of the principal presenting syndromes in 9 of these 15 outbreaks [47].

Discussion

In analyzing the data obtained from our patients with *S. pyogenes* bacteremia, we were initially surprised to see that pneumonia was the second most common cause for bacteremia. However, after reviewing the literature and seeing the data presented in (Table 5), we were less surprised. Of note is that our nine patients were identified by reviewing the records of patients with group A streptococcal bacteremia. Since approximately 80% of patients with SPP in published series are bacteremic [24,39] , there may have been a few other patients at our institution with SPP during the study period who could not be identified by review of results of positive blood culture records.

Streptococcus pyogenes remains a pathogen causing bacterial

pneumonia with severe symptomatology and significant morbidity and mortality. Initial symptoms are non-specific but pleural involvement and empyema are common complications. *S. pyogenes* strains remain susceptible to penicillin G, ampicillin, cefotaxime and ceftriaxone as well as to the respiratory fluoroquinolones (moxifloxacin, levofloxacin) [53]. Current community-acquired pneumonia treatment protocols have excellent activity against *S. pyogenes*. Future outbreaks of SPP remain a distinct possibility, primarily in long-term care facilities, in military barracks and among patients with post-influenza bacterial pneumonia. Physicians should remain vigilant for patients with SPP.

Conclusion

Pneumonia caused by *Streptococcus pyogenes* is more frequently encountered than suggested by published case reports. It may occur spontaneously but is frequently seen as a complication of influenza virus infection or in institutional settings such as long-term care facilities or military barracks. Most but not all patients with SPP have concurrent *S. pyogenes* bacteremia. Patients with SPP are often severely ill, commonly present with pleuritic chest pain, and frequently are complicated by thoracic empyema. The mortality rate of SPP remains high despite early and appropriate antimicrobial therapy.

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