Ignaz Semmelweis made one of the most important contributions to modern medicine when he instituted handwashing in an obstetric clinic in Austria in 1847, decreasing mortality there from more than 10% to 2%. Unfortunately, puerperal sepsis remains a leading cause of maternal mortality throughout the world. Group A streptococcus (GAS), *Streptococcus pyogenes*, is an organism associated with high rates of morbidity and mortality from puerperal infections. When associated with sepsis, known as streptococcal toxic shock syndrome, mortality rates approach 30–50%. Group A streptococcus can cause invasive infections in the form of endometritis, necrotizing fasciitis, or streptococcal toxic shock syndrome. The clinical presentation of women with puerperal GAS infections is often atypical with extremes of temperature, unusual and vague pain, and pain in extremities. Toxin production by the organism may allow GAS to spread across tissue planes and cause necrosis while evading containment by the maternal immune system in the form of a discrete abscess. Endometrial aspiration in addition to blood cultures may be a useful rapid diagnostic tool. Imaging may appear normal and should not dissuade the clinician from aggressive management. When suspected, invasive GAS infections should be treated emergently with fluid resuscitation, antibiotic administration, and source control. The optimal antibiotic regimen contains penicillin and clindamycin. Source control may require extensive wound or vulvar debridement, hysterectomy, or a combination of these, which may be life-saving. The benefit of immunoglobulins in management of puerperal GAS infections is unclear.

The Hungarian physician Ignaz Semmelweis (1818–1865) is credited with one of the most important advances in the history of medicine when, in 1847, he discovered that handwashing decreased the rate of perinatal mortality among women attending his clinic. Semmelweis was bothered that his clinic in Vienna (First Clinic) had an approximately 10% rate of mortality from “childbed fever” compared with the 2% rate at Second Clinic, the clinic run by midwives. Apparently, so infamous was the site that women would beg to be admitted to Second Clinic or even opt for home birth rather than attend the First Clinic. Semmelweis knew that at the First Clinic, autopsies were performed and physicians routinely went from the autopsy room to perform a delivery. After Semmelweis instituted a policy of handwashing, the rate of death from childbed fever dropped dramatically. *Streptococcus pyogenes*, although not discovered until years later, was later thought to be the causative agent for the childbed fever in Semmelweis’ clinic.

Group A β-hemolytic *S pyogenes*, a Gram-positive coccus, may colonize the skin, pharynx, or vagina but is also known to be a pathogen. It causes millions of cases of pharyngitis annually but can cause invasive disease resulting in septic shock, necrotizing soft tissue infections, amputation, or death. Worldwide, rates of severe invasive disease, streptococcal toxic shock syndrome, and necrotizing fasciitis increased from the mid-1980s to early 1990s after decreasing incidence since the mid-1900s. The reason for the increase is not
known, but increased bacterial virulence has been theorized. Recent data from the Centers for Disease Control and Prevention demonstrate that rates of invasive disease have now been stable over the past several years in the United States. More than 10 million noninvasive group A streptococcus (GAS) infections (primarily throat and superficial skin infections) occur annually.1 Approximately 10,000 cases of invasive disease (3.2–3.9/100,000 population) are thought to occur each year in the United States; streptococcal toxic shock syndrome and necrotizing fasciitis each accounted for approximately 6–7% of cases.2 Death occurs in 10–15% of all invasive cases, more than 35% of patients with streptococcal toxic shock syndrome, and approximately 25% of necrotizing fasciitis cases. Organ system failure (streptococcal toxic shock syndrome) and amputation (necrotizing fasciitis) can also be encountered.1

Group A streptococcus infections remain of particular interest to the obstetrician. Because of the relative rarity of the condition and the varied and atypical presentation, the diagnosis of GAS infection can be elusive. Unfortunately, delay in the diagnosis of invasive GAS can have disastrous consequences because of the aggressive nature of the disease. Once shock develops, mortality approaches 40–60%.2,4 The relative importance to obstetricians is the result of the increased incidence attributable to pregnancy. Deutscher et al5 conducted a surveillance study through the Centers for Disease Control and Prevention and the Prevention Active Bacterial Core. They found that postpartum women, in particular, have a 20-fold increased incidence of GAS disease compared with nonpregnant women, 0.56 per 1,000 woman-years (range 0.42–0.70) compared with 0.019 cases per 1,000 woman-years among nonpregnant (range 0.017–0.021). They did not find, although, that disease severity, defined as hospital length of stay, was worse among pregnant or postpartum women who developed disease.3 The finding of increased incidence in the postpartum period has been borne out in scientific literature. Hamilton et al4 conducted a review of the published literature of GAS infections in pregnancy or postpartum and reported that 85% of GAS occurs postpartum, most after vaginal delivery and occurring within the first 4 days postpartum.

INCIDENCE

Incident infection may be related to ascension of the organism from the maternal vagina or transmitted from infected or colonized contacts. Occasional hospital-based outbreaks have occurred, thought to be related to nosocomial spread through health care workers. There have been reports of cases of invasive disease after identification of GAS at the time of screening for group B streptococcus.6 Such cases have sparked debate over the need to report, treat, or report and treat GAS in colonized women. Mead7,8 has reported low rates of vaginal colonization among asymptomatic pregnant women, 1 per 3,472 deliveries. Although GAS disease risk is increased 20-fold among postpartum women compared with nonpregnant women, the overall incidence is low. It is estimated that only approximately 220 cases occurred among postpartum women annually in the United States between 1995 and 2000. Of these, 64% of the women were white and 28% African American. The most common infections are bacteremia (46%), endometritis (28%), peritonitis (8%), septic abortions (7%), streptococcal toxic shock syndrome (3%), and chorioamnionitis (3%). The rate of mortality among the 87 women sampled was 3.4%.9 In a population-based study, the overall rate of invasive GAS disease between 2000 and 2004 in the United States was 3.48 per 100,000 persons. Of these, only 2.6% had recently been pregnant and had a 4.3% case-fatality rate. However, as has been reported in the obstetric literature, once toxic shock occurs, the fatality rate was 49%.8 There are estimates from a population-based study conducted in the early 1990s suggesting that this rate translates into a delivery incidence of 0.5 cases per 10,000 deliveries.10

PATHOPHYSIOLOGY

Although millions of noninvasive GAS infections occur each year, only a few become invasive. The increased risk of disease related to pregnancy suggests that there is something related to host immunity that allows for invasive GAS. There are a number of suggested theories for this increased risk. In a recent review, Hamilton et al4 suggest that this could be related to 1) damage to cutaneous barriers such as that which occurs during routine deliveries; 2) altered vaginal pH from amniotic fluid exposure; or 3) altered innate immunity resulting from pregnancy. Of these suggested theories, the third seems most likely. There is abundant literature documenting altered maternal susceptibility to certain organisms such as influenza and listeriosis during pregnancy.12 It is also established that innate immunity is altered in pregnancy.13

The M protein is the major virulence characteristic of GAS. Strains with abundant M protein are resistant to phagocytosis by leukocytes. Its presence is associated with increased ability to multiply in human blood and cause disease, and its absence is associated with decreased virulence.14 Antigenic differences in M protein account for various serotypes of the organism. Increases in the severity of disease are associated with
increases in prevalence of M-1 and M-3 serotypes (emm types 1 and 3). The emm gene encodes for the M protein and genotypic differences contribute to serotyping. There are at least 120 different serotypes and genotypes in existence. There are also a number of newer virulence antigenic proteins and genotypes that have been identified. There are a number of extracellular products and exotoxins generated by GAS that are thought to allow for its somewhat unusual presentation during invasive disease. The toxins produced by GAS stimulate T cell production of inflammatory cytokines such as interleukin-1β, interleukin-6, and tumor necrosis factor-α, which lead to profound hypotension and diffuse capillary leaking. Proteases produced by GAS cause release of bradykinin, a powerful vasodilator of both systemic and pulmonary vasculature. This, in turn, is thought to lead to widespread organ failure. Group A streptococcus toxins are thought to cause liquefaction of purulent material to evade abscess formation and allow spread of streptococci along tissue planes.

DIAGNOSTIC APPROACHES

Identification of GAS infections during pregnancy or in the postpartum period can be difficult because of the rarity of invasive GAS disease and because of atypical presentation. Typical symptoms of chorioamnionitis or postpartum endometritis may or may not be present. Nonspecific symptoms are frequently present and can progress rapidly to critical illness and death within hours or days. A review of case reports in the literature reveals a wide range of presenting symptomatology. Very high, spiking fevers frequently exceeding 40°C and uterine tenderness may be present, and nonspecific or unusual symptoms may occur in the absence of fever and may be the only indication of GAS (Box 1). Given the high mortality associated with the condition, obstetric care providers should familiarize themselves with the typical presentation of GAS disease despite its relative rarity.

Group A streptococcal disease can be categorized into invasive GAS disease or toxic shock syndrome, and the Centers for Disease Control and Prevention case definitions apply to disease in any setting and are not specific to peripartum infections (Boxes 2 and 3). Patients may first have symptoms of invasive GAS disease and progress to toxic shock syndrome. Progression is associated with a very poor prognosis. It is unclear whether early intervention can halt the progression of disease but this basic tenet of sepsis management likely holds true for GAS infection. Pregnant and particularly postpartum patients presenting with atypical symptoms should first be evaluated with consideration of eliminating GAS infection from the differential diagnosis before seeking other causes. Because identification of GAS disease is so difficult but can be life-saving, a goal of

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Box 1. Symptoms of Puerperal Infection in Group A Streptococcal Disease

**Typical**
- Fever or rigors
- Uterine pain
- Malodorous vaginal discharge

**Atypical**
- Swelling or pain in extremities or joints
- Nausea and vomiting
- Copious nonfoul smelling vaginal discharge
- Bloody secretions from wound
- General malaise
- Headache
- Myalgias
- Dyspnea
- Rash
- Pharyngitis
- Confusion or combativeness

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Box 2. Invasive Group A Streptococcal Disease (Requires Clinical and Laboratory Criteria for Diagnosis)

**Clinical syndromes**
- Pneumonia
- Bacteremia in association with cutaneous infection (eg, cellulitis, erysipelas, or infection of a surgical or nonsurgical wound)
- Deep soft tissue infection (eg, myositis or necrotizing fasciitis)
- Meningitis
- Peritonitis
- Osteomyelitis
- Septic arthritis
- Postpartum sepsis
- Neonatal sepsis
- Nonfocal bacteremia

**Laboratory criteria**
- Isolation of group A Streptococcus (Streptococcus pyogenes) by culture from a normally sterile site (eg, blood or cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid)

Data from Case definitions for infectious conditions under public health surveillance. Centers for Disease Control and Prevention. MMWR Recomm Rep 1997;46:1–55.
The presence of neutrophils and
In patients with preexisting renal disease, greater
Anderson
This aspirate can be
Disseminated intravascular coagulation, defined
Platelets 100,000/mm³ or less
Creatinine 2 mg/dL or greater
Once stabilized, transfer to
Acute onset of diffuse pulmonary infiltrates and
Puerperal Group A Streptococcal Infections
or less
Alanine aminotransferase, aspartate aminotrans-
Laboratory abnormalities are common and may be
obstetric and emergency medicine residency training
should be to routinely include GAS disease on the
differential diagnosis of anyone with atypical presenta-
tion in the peripartum period.
Laboratory abnormalities are common and may be
very abnormal even in a patient who does not appear
particularly ill. A marked bandemia (greater than 10%) may
be seen even in the absence of a leukocytosis. Marked leukocytosis or leukopenia can be seen. Hemo-
ysis or hemoconcentration can occur in addition to the
markers of streptococcal toxic shock syndrome noted in
Box 1. Because pregnant women have alteration in several
laboratory parameters as part of normal pregnancy,
these changes should be considered when making a diag-
nosis of streptococcal toxic shock syndrome. For ex-
ample, a creatinine above 1 mg/dL is considered abnormal
in pregnancy and should raise a clinician’s suspicion for
severe illness in a pregnant or postpartum woman although the Centers for Disease Control and Preven-
tion criteria use 2 mg/dL as a cutoff value. Alternatively,
because pregnancy is associated with leukocytosis, this
parameter may not be particularly reliable for evidence of
organ dysfunction. In pregnant or postpartum
women, a significant bandemia is of concern.

In patients with clinical suspicion of GAS disease,
efforts to isolate the organism and source of infection are important parts of the initial management. Blood
and urine cultures should be collected. If the uterus is a suspected source of infection, Gram stain and culture
should be conducted. If the patient is pregnant at the
time, amniocentesis can be performed. In the post-
partum patient, the endometrium can be sampled with
the use of an endometrial aspirate. Endometrial biopsy
is an effective means of diagnosing upper genital tract
infection and should be considered in any postpartum
patient with sepsis.27 The presence of neutrophils and plasma cells is considered diagnostic for endometritis.
Endometrial aspiration can be carefully collected to avoid vaginal contamination so that anaerobic and fac-
cultative bacteria may be cultured.28 This aspirate can be
used for Gram stain. The presence of Gram-positive
cocci in chains on Gram stain from endometrial aspir-
ate in a postpartum patient with sepsis should prompt
immediate intervention (Fig. 1).

Imaging is frequently performed as part of the
evaluation for the source of sepsis. In the case of GAS
infection, the findings are frequently deceptively normal.
There may be a small amount of fluid in the pelvis or
findings that may be expected to be seen shortly after
a delivery. Imaging may be helpful, however, to exclude
other causes of sepsis such as appendicitis.

THERAPEUTIC APPROACHES
Basic tenets of sepsis management hold in the case of
GAS disease. If sepsis is identified, fluid resuscitation,
prompt administration of antibiotics, and source
control are major goals.29 Once stabilized, transfer to
a facility capable of critical care in obstetric patients
may be considered. Timely recognition and intervention
have the potential to decrease morbidity and mortality in
this highly morbid condition. The commonly accepted
term of early goal-directed therapy has become the

Box 3. Streptococcal Toxic Shock Syndrome Case
Definition (Requires Clinical and Laboratory
Criteria for Diagnosis)

Clinical case definition
- Hypotension (systolic blood pressure 90 mmHg or less)
- Multigorgan involvement characterized by two or
  more of the following:
  - Renal impairment
    - Creatinine 2 mg/dL or greater
    - In patients with preexisting renal disease, greater
      than twofold elevation over the baseline level
  - Coagulopathy
    - Platelets 100,000/mm³ or less
    - Disseminated intravascular coagulation, defined
      by prolonged clotting times, low fibrinogen level,
      and the presence of fibrin degradation products
  - Liver involvement
    - Alanine aminotransferase, aspartate aminotrans-
      ferase, or total bilirubin levels twice or more the
      upper limit of normal
- Acute respiratory distress syndrome
  - Acute onset of diffuse pulmonary infiltrates and
    hypoxemia in absence of cardiac failure or by
    evidence of diffuse capillary leak manifested by
    acute onset of generalized edema
  - Generalized erythematous macular rash that may
desquamate
  - Soft tissue necrosis, including necrotizing fasciitis or
    myositis, or gangrene

Laboratory criteria for diagnosis
- Isolation of group A streptococcus

Case classification
- Probable: a case that meets the clinical case defini-
tion in the absence of another identified etiology for
the illness and with isolation of group A streptococ-
cus from a nonsterile site
- Confirmed: a case that meets the clinical case defi-
nition and with isolation of group A streptococcus
from a normally sterile site

Modified from Centers for Disease Control and Prevention.
Streptococcal toxic-shock syndrome (STSS) (Streptococcus
pyogenes). Available at: http://www.cdc.gov/nndss/script/
casedef.aspx?CondYrID=858%26DatePub=1/1/2010%
2012:00:00%20AM. Retrieved January 6, 2014.
backbone of sepsis management, because it is a bundle of care that has been shown to decrease mortality compared with conventional sepsis management.\textsuperscript{30} The premise of the early goal-directed therapy management is that it is proscribed, and there are very specific targets for success within 3–6 hours of patient presentation.

The Surviving Sepsis Campaign was revised in 2013 and is in the form of guidelines supported by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. There are four main components to this management approach on evaluation of an individual patient. They include: 1) initial resuscitation—the goal of this portion is to improve and document improvement in tissue perfusion; 2) diagnosis—this includes imaging and culture collection to identify the cause of the sepsis; 3) antimicrobial therapy—this is administration of antimicrobials with good tissue penetration directed at all likely pathogens; and 4) source control—this is identification of an anatomic source of infection and intervention undertaken to manage it within 12 hours of presentation.\textsuperscript{29} In the case of the postpartum woman, common sources of infection that may require surgical intervention generally include the uterus or a wound.

In general and in the case of GAS sepsis, initial fluid resuscitation should be accomplished with 30 mL/kg of crystalloid fluids for treatment of hypotension or a lactate level greater than 4 mmol/L. In a 70-kg patient, this results in rapid administration of more than 2 L of fluid. For sepsis management, the goal is to accomplish this level of fluid resuscitation within 3 hours of presentation. Measures of successful response to fluid resuscitation include adequate urine output, improved mean arterial pressure, and measures of tissue perfusion using a central venous pressure catheter.

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) in the setting of GAS infection is somewhat controversial. There have been reports of association with worsened clinical outcomes in the setting of NSAID use. A recent study used experimental conditions in mice to test this hypothesis.\textsuperscript{31} Hamilton et al injected mice with GAS and treated with various types of NSAIDs and antibiotics. Outcomes were compared with those in a control group. The authors found that the use of nonselective NSAIDs such as ibuprofen was associated with accelerated mortality and reduced antibiotic efficiency.\textsuperscript{31} These findings need to be evaluated systematically in humans but are worth considering when caring for women with GAS infections.

Diagnosis when GAS disease is suspected can significantly alter the acute management of a critically ill patient, so timely identification is particularly important. It is recommended that cultures be obtained before the administration of antibiotics but that this should not delay administration of antibiotics for more than 45 minutes. Two sets of blood cultures should be collected from different sites and each set should include both aerobic and anaerobic bottles.\textsuperscript{29} Additionally, as noted, when GAS is suspected as a source of endometritis, endometrial aspiration should be considered. Amniocentesis can be done for women with an ongoing pregnancy. Gram stain should be done and a discussion with an experienced microscopist should note that GAS is suspected.

ANTIMICROBIALS

"One major reason to accurately identify GAS as a potential etiologic agent on a differential diagnosis is the importance of administration of effective antibiotics to decrease the severity of disease. Consultation with an expert in infectious diseases may be considered. Penicillin is still the first-line drug for treatment of GAS because it remains nearly universally susceptible to this drug. Because it is often not clear at the time of presentation that sepsis is caused by GAS, this is usually administered in the form of a broad-spectrum antibiotic containing penicillin initially. A problem with penicillin as a sole therapy for GAS disease, however, is that there is a risk of the
The “Eagle effect.” The “Eagle effect” was described in 1952 and essentially showed that penicillin had decreased efficacy against GAS when there was a large inoculum. This is thought to occur because penicillin-binding proteins are not expressed during the stationary phase growth of GAS, resulting in an inability to be eradicated from the source of infection. The stationary phase of growth for bacteria occurs when there is exhaustion of nutrients or accumulation of toxins so that growth ceases and only cell turnover occurs. During this growth phase, total cell count increases but viable cell count remains the same, resulting in ongoing disease. A cornerstone of antibiotic therapy for treatment of GAS disease is inclusion of clindamycin in the regimen along with a penicillin, which is the treatment regimen of choice endorsed by the Infectious Diseases Society of America.

Clindamycin is thought to be so important in the management of GAS disease because it has a direct effect on toxin production and is not susceptible to the “Eagle effect.” Therefore, it continues to decrease colony counts even when penicillin has reached its maximal efficacy. Clindamycin has also demonstrated improved mortality rates over erythromycin and penicillin in an animal model of GAS disease. The rate of clindamycin resistance in the United States is only approximately 0.5%. In the case of severe penicillin hypersensitivity, there are a number of alternative drugs to which GAS is susceptible, but vancomycin has been used commonly in pregnancy (Table 1). Resistance to erythromycin has been increasing both in the United States and globally. In unusual cases, a clinician may consider the use of penicillin administered continuously rather than intermittently. Extrapolating from the recommendations for endocarditis treatment, there is a theoretical benefit to continuous therapy. When the uterus is not removed or there is deep tissue that cannot be debrided, there remain concentrated foci of microbes that may not allow adequate antibiotic penetration and may have continued slow growth. In such cases, it appears that increased duration of contact between the penicillin and the microbe is more effective in killing than increased concentration of the antibiotic. In fact, in the case of endocarditis vegetations, increasing doses of antibiotic do not improve outcome. The decision to administer and appropriately dose continuous penicillin infusions should be made in consultation with infectious diseases experts and hospital pharmacist assistance.

The use of intravenous immunoglobulin (IVIG) in the treatment of streptococcal toxic shock syndrome is controversial. The most recent Surviving Sepsis Campaign specifically recommends against the use of IVIG in adults with severe sepsis or septic shock and calls for high-quality randomized trial data. This publication, however, does not specifically address GAS disease and some have suggested that GAS may be an exception for the use of IVIG in sepsis. This is partially because the Surviving Sepsis Campaign recommendations are predominantly based on a recent Cochrane review, which found that the use of IVIG does not decrease the risk of mortality for adults with sepsis when analysis is restricted to trials with low risk of bias (relative risk 1.02, 95% confidence interval 0.84–1.24). These analyses are inclusive of all types of sepsis and are not specific to GAS. Furthermore, there are no studies restricted to pregnant and postpartum women. The few studies examining the affect of IVIG specifically in streptococcal toxic shock syndrome have conflicting results. Only one was a randomized trial. The trial was terminated prematurely because of slow recruitment and enrolled 21 patients, only 18 of whom were confirmed to have GAS as the causative organism. Of these 18 patients, the primary outcome of 28-day mortality occurred in one of eight patients in the IVIG group (12.5%) and 3 of 10 patients in the placebo group (30%) with a nonsignificant P value. At this point, there is insufficient evidence to support the routine use of IVIG in streptococcal toxic shock syndrome.

The duration of therapy for GAS disease depends on the severity of illness, and data to guide recommendations are lacking. In the case of streptococcal toxic shock syndrome, or in the setting of positive blood cultures with GAS, long-term intravenous therapy is warranted. In general, at least 2 weeks of intravenous therapy should be used for patients with bacteremia. Longer therapy may be required for those

| Table 1. Recommended Regimens for Group A Streptococcus Invasive Peripartum Infections |
|-------------------------------------------------|-----------------|
| Recommended Drug | Regimen |
|-------------------|---------|
| Penicillin        | 4 million units every 4 h intravenously |
| plus Clindamycin  | 900 mg every 8 h intravenously |
| Severe penicillin hypersensitivity Vancomycin | 30 mg/kg/d in 2 divided doses intravenously |
| plus Clindamycin  | 900 mg every 8 h intravenously |

Data from Stevens DL, Bisno AL, Chambers HF, Everett ED, Dellinger P, Goldstein EJ, et al. Practice guidelines for the diagnosis and management of skin and soft-tissue infections. Clin Infect Dis 2005;41:1373–406.
with ongoing deep tissue infection. For those with less severe infection, it may be reasonable to complete the 2-week course with an oral agent once symptoms have resolved.

**SOURCE CONTROL**

The term “source control” refers to the definitive control of an anatomic source of infection to decrease or eliminate ongoing microbial contamination. The Surviving Sepsis Campaign guidelines recommend an early search for such sources and that if a source is identified that intervention be undertaken within 12 hours. In some cases of sepsis, the cause is an abscess that can be drained percutaneously or operatively, if necessary. In the case of streptococcal toxic shock syndrome in the puerperium, the source is often a postpartum uterus. Unfortunately, conservative therapy is difficult to accomplish if the source of GAS disease is the uterus. The diagnostic measures discussed here can allow rapid intervention for the clinician with a high index of suspicion for GAS disease. If there is extensive evidence of GAS on a Gram stain obtained from endometrial sampling, surgical intervention should be pursued.

Hysterectomy may be life-saving in puerperal GAS sepsis and should be the default management in GAS puerperal sepsis because of the high mortality rate. There are no trials comparing outcomes between conservative and surgical approaches, but most experts agree that a confirmed GAS infection in the presence of organ dysfunction should be managed surgically. Occasionally, there will be abscesses in the pelvis evident on imaging. In this event, an attempt may be made at percutaneous or laparoscopic drainage and debridement if a woman desires future fertility and is not suffering from severe sepsis. In that case, hysterectomy may be avoided. Conversely, very extensive infections may require deep tissue and even retroperitoneal debridement. Therefore, consultation with experienced surgeons should be considered. Occasionally, vulvar debridement, vaginal debridement, or both may be required as a result of extension from an infected cervix or from an episiotomy site. In patients with amniotic fluid infection, it may be reasonable to proceed with delivery and then assess whether more extensive therapy such as hysterectomy is needed. Individualization is warranted in such cases.

In patients without sepsis but with invasive GAS disease such as a documented GAS endometritis, management solely with antibiotics may be possible if there is not evidence of end-organ dysfunction. If GAS disease is managed conservatively, it should be done in consultation with an expert with a plan to move to operative intervention if the condition worsens. Both penicillin and clindamycin should be administered. In such cases, continuous penicillin may be considered.

**COMPLICATIONS**

A number of long-term complications have been reported after invasive GAS disease. These include renal dysfunction, amputation, and disfiguring consequences of extensive debridement in the case of necrotizing soft tissue infections. Organisms may spread to essentially any anatomic site and result in local infection at that site. Because most women experiencing this devastating infection were previously healthy, ensuring follow-up with the appropriate medical specialists for long-term care should be done before hospital discharge. Additionally, mental health consultation should be considered because patients are at risk for situational psychiatric complications.

Fetal and neonatal complications may occur as a result of intraamniotic infection with GAS. Infection-mediated preterm labor can be the presenting sign of GAS disease. Because most preterm birth is of unclear etiology, there is often little reason to suspect GAS as an etiologic source. However, these neonates often sustain the complications of both sepsis and prematurity, leading to poor outcomes. Stillbirth can occur as well. As is the case in any patient with evidence of chorioamnionitis, antenatal broad-spectrum antibiotics should be administered and delivery should be undertaken. One clue to GAS as a source is the occurrence of “intact” chorioamnionitis, that is, chorioamnionitis occurring in women with intact membranes. More than 90% of chorioamnionitis occurs in women with ruptured membranes. Therefore, the finding of intact chorioamnionitis should prompt the clinician to evaluate the patient for unusual causes of infection such as GAS or *Listeria monocytogenes*. For women in whom the source of chorioamnionitis is thought to be related to GAS disease, the antibiotic regimen should contain a penicillin and clindamycin.

**CONCLUSIONS**

Despite significant advances in modern medicine since the time of Ignaz Semmelweis, puerperal infection with GAS remains a highly morbid condition. It causes significant morbidity and, if sepsis occurs, mortality rates remain as high as those seen in the most devastating conditions in obstetrics. Unusual complaints of malaise or fever in pregnancy, or more commonly, in the postpartum period, should prompt an emergent evaluation for GAS as a source. Basic tenets of sepsis management apply to infection
with GAS. These include restoration of adequate perfusion with crystalloid fluids, collection of blood, and, if appropriate, amniotic fluid or endometrial samples for Gram stain and culture. Antibiotic administration should occur rapidly and should include a penicillin and clindamycin. Hysterectomy may be a life-saving measure in women with streptococcal toxic shock syndrome and organ dysfunction. It can be a difficult decision for a clinician to undertake hysterectomy in a young woman who desires future fertility, but it is necessary in such cases. Because of the relative rarity of GAS disease, the optimal management approach remains unclear. Future studies should examine dose and duration of antibiotic administration as well as use of IVIG therapy. Like most forms of serious infections, time to identification of the infection, fluid resuscitation, and antibiotic administration are major determinants of prognosis. For this reason, it is imperative that emergency medicine personnel and the staff and clinicians of those providing obstetric services become familiar with GAS as an entity that can cause serious disease during and after pregnancy. A high index of suspicion at the time of the first interaction with such patients can lead to timely care and be potentially life-saving.

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