Answer 1: The differential diagnosis includes the toxin mediated Staphylococcal and Streptococcal diseases, which are the following:

1. Localized Staphylococcal infections with diffuse skin rash, including staphylococcal scalded skin syndrome (SSSS) and Toxic shock syndrome (syn. Staphylococcal scarlet fever). Toxic shock syndrome can be of menstrual or non-menstrual sub-types.
2. Streptococcal toxic shock syndrome (syn. Scarlet fever)
3. Kawasaki’s disease

Localized Staphylococcal infections with diffuse skin rash

**Staphylococcal scalded skin syndrome (SSSS):** Mostly found in children under 5 years of age, it can rarely present in adults. The spectrum of clinical manifestations can range from localized bullous impetigo to Ritter’s disease (SSSS in children) with generalized skin involvement by exfoliative toxins. Fever, irritability, cutaneous tenderness and scarlantiform eruption often with flexural accentuation, followed by generalized desquamation are hallmarks of the disease. S. Aureus phage II group 71 is the major pathogen isolated in the U.S. The early manifestations of TSS can mimic SSSS. Thus SSSS is possible but less likely in the presented case.

**Toxic shock syndrome:** This is the most likely diagnosis in this case. The criteria for the diagnosis of TSS are presented in the following table.

TSS is probable
- when 3 major criteria (in bold) are met in the presence of desquamation or
- 5 criteria are met in the absence of desquamation

<table>
<thead>
<tr>
<th>TABLE 1 -- Criteria for the Diagnosis of Toxic Shock Syndrome</th>
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<tbody>
<tr>
<td>Temperature $&gt;38.9^\circ$C</td>
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<tr>
<td>Systolic blood pressure $&lt;90$ mmHg</td>
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<tr>
<td>Rash with subsequent desquamation, especially on the palms and soles</td>
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</table>
**Involvement of 3 of the following organ systems:**

- Gastrointestinal: vomiting, profuse diarrhea
- Muscular: severe myalgias or >5-fold increase in CPK
- Mucous membranes (vagina, conjunctivae, or pharynx): frank hyperemia
- Renal insufficiency: BUN or creatinine at least twice the upper limit of normal with pyuria in the absence of urinary tract infection
- Liver (hepatitis): bilirubin, AST, ALT at least twice the upper limit of normal
- Blood: thrombocytopenia <100,000/mm$^3$
- Central nervous system: disorientation without focal neurologic signs

**Negative results of serologic tests for Rocky Mountain spotted fever, leptospirosis, and measles**

*Abbreviations:* ALT, Alanine transaminase; AST, aspartate transaminase; BUN, blood urea nitrogen; CPK, creatinine phosphokinase.

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**Menstrual toxic Shock Syndrome:** 96% involving women and 92% having their onset during menstruation, menstrual TSS is 96-99% associated with the use of hyperabsorbable tampons. The incidence of the disease has declined remarkably after the removal of the causative tampons and application of the federal regulations in 1981$^{1,2}$.

**Non-menstrual Toxic Shock syndrome:** After the decline of menstrual TSS, non-menstrual toxic shock syndrome has gained much more epidemiologic importance. Occurring in a male to female ratio of 1:3, about 40% cases are associated with apparently benign looking surgical wounds$^5$. However, some cases are associated with the vaginal colonization during vaginal infection, contraceptive devices use, abortion, childbirth or during 12 hours to 8-weeks post-partum period$^6$. Only 50% cases are caused by TSST-1 whereas rest are caused by enterotoxins B and C. The syndrome
usually starts 2 days after a trauma and the signs of obvious skin infections are absent, necessitating the need for culturing the benign appearing wounds in case of suspicion. It is more often acquired in the hospital and patients are more prone to developing renal and central nervous system complications.

**Streptococcal toxic shock syndrome**: Strep TSS is caused by a streptococcal infection associated with sudden onset of shock and organ failure caused by streptococcal pyrogenic exotoxins A, B and C. Proposed case definition has been shown below. Any age can be affected and the prevalence has been reported to be about 5 to 10 cases per 100,000 population. Pharynx, skin and vagina have been implicated around 50% of the times as portal of entry, rest being the surgical procedures, and rarely streptococcal pharyngitis being the cause. It is an important entity to recognize as the development of shock and death can be dramatic and rapid.

**Proposed Case Definition for the Streptococcal Toxic Shock Syndrome**

I. Isolation of group A streptococci (Streptococcus pyogenes)
   A. From a normally sterile site (e.g., blood, cerebrospinal, pleural, or peritoneal fluid, tissue biopsy, surgical wound, etc.)
   B. From a non-sterile site (e.g. throat, sputum, vagina, superficial skin lesion, etc.)

II. Clinical signs of severity
   A. Hypotension: systolic blood pressure <90 mm Hg in adults or <5th percentile for age in children

   And

   B. >2 of the following signs:

   1. Renal impairment: creatinine >177 umol/L (≥2 mg/dL) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a ≥2-fold elevation over the baseline level
   2. Coagulopathy: platelets ≤100X10^9/L (≤100,000/mm^3) or disseminated intravascular coagulation defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products
   3. Liver involvement: alanine aminotransferase (SGOT), aspartate aminotransferase (SGPT), or total bilirubin levels greater than or equal to twice the upper limit of normal for age. In patients with preexisting liver disease, a ≥2-fold elevation over the baseline level
   4. Adult respiratory distress syndrome defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure, or evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia
   5. A generalized erythematous macular rash that may desquamate
   6. Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene

* An illness fulfilling criteria IA and II (A & B) can be defined as definite case.
An illness fulfilling criteria IB and II (A &B) can be defined as probable case if no other etiology for the illness is identified.

### TABLE 2 -- Factors That Increase Likelihood of Developing Streptococcal Toxic Shock Syndrome

<table>
<thead>
<tr>
<th>Factor</th>
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<tbody>
<tr>
<td>Age (neonates and elderly)</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Alcoholism</td>
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<tr>
<td>Surgical procedures</td>
</tr>
<tr>
<td>Trauma</td>
</tr>
<tr>
<td>Penetrating (insect bites, lacerations, slivers, abrasions, burns)</td>
</tr>
<tr>
<td>Nonpenetrating (hematoma, bruise, muscle strain, hemarthrosis)</td>
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<tr>
<td>Varicella</td>
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<tr>
<td>Contact with a patient</td>
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<tr>
<td>High prevalence of invasive strains in the community</td>
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<tr>
<td>Nonsteroidal anti-inflammatory agents*</td>
</tr>
</tbody>
</table>
*Based on limited evidence.

**Answer 2**: The laboratory tests needed to confirm the diagnosis should include the vaginal and/or cervical cultures, culture of the wound on the forearm, throat culture and ASO titer. Blood cultures in the case of Staph TSS are exceptionally positive\(^{10}\) (10-15\%) as opposed to the Streptococcal TSS in which it can be positive about 50\% of the times\(^{1}\). Platelet count can be helpful in differentiating the streptococcal and staphylococcal toxic shock syndromes from Kawasaki’s disease. Thrombocytopenia is evident in toxic shock syndromes, whereas thrombocytosis is seen in Kawasaki’s disease.

**Answer 3**: Since the hypovolemic shock secondary to loss of colloids and fluids can result in acute tubular necrosis or renal insufficiency, a close observation of BUN and creatinine is warranted. LFTs and CBC should be routinely followed as periportal inflammation (hepatitis) and thrombocytopenia may ensue. Elevated CPK my indicate the muscle involvement which is of even more importance in case of suspected narcotizing faciitis, which may or may not be associated with streptococcal TSS. Serum albumin and calcium levels can fall rapidly owing to the development of capillary leak syndrome. Later in the course of streptococcal TSS, thrombocytopenia can herald the onset of DIC\(^{11}\).

**REFERENCES**
After several decades of seemingly decreasing virulence, streptococcal and staphylococcal infections have reemerged as a major source of morbidity and mortality. Within the past 2 decades, not only have well-established diseases such as rheumatic fever begun to reappear but also many new entities, such as toxic shock syndrome, streptococcal toxic shock syndrome, recurrent toxin-mediated perineal erythema, and recalcitrant erythematosus desquamating disorder have been described. Central to the renewed importance of these bacteria has been the production of circulating toxins, which often function as superantigens in causing the clinical manifestations, morbidity and mortality associated with these diseases.


8 Defining the streptococcal group A toxic shock syndrome: Rationale and consensus definition. JAMA 269:390-391, 1993
