蜂窩織炎

**蜂窩織炎を診るときのポイント!**

**～壊死性皮膚軟部組織感染症を見逃すな～**

* 蜂窩織炎は臨床診断、診断基準はない
* 他疾患の除外が大事だが、ぶっちゃけムズイ
* 壊死性皮膚軟部組織感染症を見逃さない
* 蜂窩織炎を診断・治療するときに必要な検査を押さえておく
* 蜂窩織炎は兎にも角にもセファゾリンとRICEで治療する
* 特殊な菌のカバーが必要なときを覚える
* 蜂窩織炎は入院適応例以外は外来でも十分治療できる
* 治療開始後48~72時間で改善がなければ他疾患や耐性菌を考える
* コンサルテーションのタイミングを知っておく

（図：右側に配置されたフロー図の概要）

* **診断**
  + 診断基準はなく臨床診断、検査は不要
  + 皮膚の炎症4徴候（発赤、熱感、腫脹、疼痛）
  + 以下の特徴：片側下肢が多い、日の単位で増悪、バリア機能の低下（白癬、外傷など）
  + 壊死性皮膚軟部組織感染症 (NSTI)の除外（LRINECスコアも万能ではない。基本は臨床的に除外。急激な進行、激しい疼痛、壊死、血疱に注意）
* **鑑別**
  + その他の鑑別診断は深追いしない
  + うっ滞性皮膚炎、遊走性紅斑、血腫など
  + 初見での診断は困難なことが多い
  + 片側・下肢でないときにはより注意して鑑別
* **治療**
  + フィンガーテストを依頼
  + 特殊なリスクがない場合の抗菌薬治療期間：5~7日間
  + 内服：セファレキシン250mg 1回2Cap 1日3回
  + 点滴：セファゾリン2g+生理食塩液100mL 8時間ごと
  + NSTI（特に壊死性筋膜炎であればデブリードマンが重要）
  + 特殊なリスク（特殊な抗菌薬が必要）
    - ショック
    - 動物咬傷
    - 肝疾患のある人で海や川に行ったまたは水産物を食べた
  + マーキングとRICE (Rest, Icing, Compression, Elevation) 処置
* **経過**
  + RICE（安静、冷却、圧迫、挙上）
  + 治療開始48~72時間ごろまでには皮膚所見が改善傾向となることが多い
  + 皮膚炎症所見は病態改善後も残ることあり

症例 高血圧症のある肥満な68歳男性

来院2日前から左足の先が痛いことに気がついていたが様子をみていた。来院当日になって左足が腫れて赤くなり、痛みで歩けなくなったため受診した。体温38.0℃、脈拍95回/分、血圧125/80mmHg,呼吸数24回/分,SpO₂ 98% (room air) ほか、バイタルサインは安定、左足先は白癬でびらんあり、そこを中心に足関節まで背面が赤く腫れあがって、熱感があり、押すとかなりの疼痛がみられる。熱もあり、足の痛みも強く、入院を希望している。

LRINECスコア (一部)

（表）

| **項目** | **スコア** |
| --- | --- |
| CRP mg/dL |  |
| <15 | 0 |
| ≧15 | 4 |
| WBC /mm³ |  |
| <15,000 | 0 |
| 15,000-25,000 | 1 |
| >25000 | 2 |
| Hb g/dL |  |
| >13.5 | 0 |
| 11.0-13.5 | 1 |
| <11.0 | 2 |
| Na mEq/L |  |
| ≧135 | 0 |
| <135 | 2 |
| Cr mg/dL |  |
| ≦1.6 | 0 |
| >1.6 | 2 |
| Glucose mg/dL |  |
| ≦180 | 0 |
| >180 | 1 |

（文献5より）

**NSTIの除外に役立つ可能性のある所見**

* 乳酸値<18mg/dL (2mmol/L)
* WBC<15,400/µL かつ Na > 135mEq/L (Balley E, et al: Dermatol Ther, 24: 229-239,2011より)

救急外来,病棟管理で絶対マスターしたい疾患対応

**蜂窩織炎は臨床診断、診断基準はない**

* 臨床診断のポイントは、大きく以下の3つである 。
* 蜂窩織炎の診断基準はない 。 ①皮膚の炎症所見の4徴「発赤、熱感、疼痛、腫脹」がみられる。 ②バリア不全が背景にあることが多い(白癬、アトピー性皮膚炎、外傷、褥瘡など)。 ③原則として、片側で、下肢(まれに手や顔あり)、関節が中心ではないことが大事である。
* 1~数日間の経過で発赤や疼痛が広がってくることが多い [days (日の単位)の経過]。
* 炎症所見は、すべてそろわないこともある。

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（画像：左から順に、深部静脈血栓症、石灰沈着症、うっ滞性皮膚炎、血腫、遊走性紅斑、蜂窩織炎の患部の写真が6枚並んでいる。それぞれの皮膚の状態が視覚的に示されている。）

* 片側と下肢でないときは蜂窩織炎の診断は慎重に、他疾患の可能性をより丁寧に検討する。
* 発赤の分布が関節を中心としている場合には、関節炎が波及して蜂窩織炎のようにみえることも要注意である。

表1 蜂窩織炎の鑑別診断

（表）

| **カテゴリー** | **Common** | **Uncommon** |
| --- | --- | --- |
| **感染性** | 遊走性紅斑、ヘルペス、帯状疱疹、皮下膿瘍 | 化膿性関節炎、壊死性筋膜炎、丹毒、伝染性紅斑、重症熱性血小板減少症候群(SFTS)、日本紅斑熱、抗酸菌感染症 |
| **炎症性** | 痛風、接触性皮膚炎、血管性浮腫、アナフィラキシー、スウィート病、結晶性関節炎、結節性紅斑 | 固定薬疹、好酸球性筋膜炎、サルコイドーシス、脂肪織炎、好酸球性蜂窩織炎、再発性多発軟骨炎、家族性地中海熱 |
| **血管性** | うっ滞性皮膚炎、リンパ浮腫、深部静脈血栓症、血腫、表在性血栓性静脈炎 | 肢端紅痛症、カルシフィラキシス |
| **悪性** | なし | パジェット病、乳房外パジェット病、炎症性乳がん、悪性リンパ腫、白血病、丹毒様がん |
| **その他** | 虫刺症、異物反応、ルート刺入部の炎症 | コンパートメント症候群、放射線性皮膚炎、圧痕 |

(Raff AB, et al: JAMA, 316-325-337,2016より)

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救急外来,病棟管理で絶対マスターしたい疾患対応

**他疾患の除外が大事だが、ぶっちゃけムズイ**

* 非専門医が皮膚所見 (図1) だけで鑑別するのは原則無理だと思っていい。入院中の患者さんで蜂窩織炎疑いで皮膚科にコンサルテーションしても、74%に別の診断がついたという報告もある 。
* 蜂窩織炎として治療を開始するときのポイントは、以下のとおり。 ①原則的に片側、下肢(まれに上肢や顔あり)で皮膚の炎症所見を伴っている。 ②壊死性皮膚軟部組織感染症(NSTI) は必ず「らしくないか」 チェックする(後述)。 ③エコーで深部静脈血栓症を除外する。 ④関節を中心に炎症がある場合は、エコーを含めて関節炎の可能性をチェックする。 ⑤病歴からアナフィラキシーと薬疹らしくないかをチェックする。 ⑥その他の鑑別疾患らしさがないかを 病歴と検査所見で一応チェックする。 ⑦やっぱり蜂窩織炎が一番疑わしいなら蜂窩織炎として暫定診断、治療を開始する。
* 顔面や上肢、体幹部の蜂窩織炎ももちろんあるが、それらの診断はより慎重に行う必要がある。
* 治療経過が合わなければ、生検を含めて他疾患(表1)の鑑別へ進む 。

本症例の診断

①2日間の経過で、片側の足先から、皮膚の炎症所見の4徴がみられる。

②足先にバリア不全がみられていることから、蜂窩織炎と臨床的に診断した。

図1 蜂窩織炎と紛らわしい皮膚所見

(Raff AB, et al: JAMA, 315: 325-337,2016より)

（図の内容はPage2上部の6枚の写真と同様）

**壊死性皮膚軟部組織感染症を見逃さない**

* 蜂窩織炎も壊死性皮膚軟部組織感染症 (NSTI)も皮膚軟部組織の細菌感染だが、蜂窩織炎は比較的ゆるやかな経過をとる一方、NSTIは急速に悪化し命に関わることも多いため見極めが重要である 。
* NSTIとは、表皮、真皮、脂肪組織、筋膜、筋といった皮膚軟部組織の壊死性感染症全般を指す(図2) 。壊死性筋膜炎もNSTIに含まれる概念とされる 。
* 異常に進行が速い、見た目に比べ異常に痛がるまたはまったく痛くない、状態が悪すぎるときには必ず疑う 。

**1. 壊死性筋膜炎を疑うポイント**

* 古典的症状としては75%に浮腫、72%に紅斑、72%に強い疼痛、60%に発熱、38%に水疱や皮膚壊死を呈する 。
* 直近の手術歴、臨床的見た目と解離する疼痛、低血圧、皮膚壊死、血疱がリスクとされている報告もある 。
* バイタルサインや検査では、頻脈(脈拍>120回/分)、低血圧、CPK上昇、CRP>15mg/dL、LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) スコア ≧6 (表2)が参考になる所見となる 。
* 壊死性筋膜炎の診断は、「皮膚切開をして軟部組織の壊死を証明すること」以外にない 。
* 特定の検査、所見、スコアなどで確定や除外は困難と心得る 。
* 上記の臨床状況から疑った場合、否定しきれないと感じる場合には、外科医へのコンサルテーション、フィンガーテストを含めて壊死した軟部組織の確認をためらわない 。基本的に検査結果を待ってはだめ 。

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（図：NSTI（壊死性皮膚軟部組織感染症）の進行を示す模式図。4段階で描かれている。

第1段階：皮膚や皮膜の裂傷から原因菌が侵入。表皮、真皮、皮下脂肪、筋肉、深筋膜の層が描かれている。

第2段階：紅斑や腫脹が出現。局所組織のダメージと、真皮での血管拡張と白血球の浸潤が示されている。

第3段階：水疱、血疱が形成される。血管閉塞が起こる。

第4段階：多層組織の壊死と深部組織へのダメージが広がる。）

（図：もう一つのNSTIの進行を示す模式図。こちらも4段階。

第1段階：表皮、真皮の炎症。活性化した筋原細胞、白血球が描かれている。深部組織の損傷が始まる。

第2段階：ビメンチンを介してA群溶血性レンサ球菌が深筋膜へ侵入。

第3段階：白血球凝集による血管閉塞。

第4段階：水疱形成。壊死が徐々に上方向に進行し、広範囲の組織破壊が起こる。）

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表2 LRINECスコア

（表）

| **項目** | **スコア** | **項目** | **スコア** |
| --- | --- | --- | --- |
| CRP (mg/dL) |  | Na (mEq/L) |  |
| <15 | 0 | ≧135 | 0 |
| ≧15 | 4 | <135 | 2 |
| WBC (/mm³) |  | Cr (mg/dL) |  |
| <15,000 | 0 | ≦1.6 | 0 |
| 15,000~25,000 | 1 | >1.6 | 2 |
| >25,000 | 2 | Glu (mg/dL) |  |
| Hb (g/dL) |  | ≦180 | 0 |
| >13.5 | 0 | >180 | 1 |
| 11.0~13.5 | 1 |  |  |
| <11.0 | 2 |  |  |

(Wong CH, et al: Crit Care Med, 32:1535-1541,2004より)

**2. 壊死性筋膜炎診療のネクストステップ**

* 熱がない、皮膚所見がまったくない、画像検査で所見がはっきりしない、毒素性ショック症候群として消化器症状が前面に出ていることがある、といったピットフォールに注意する 。
* 以下のような補助となる検査所見も提案されているが、臨床経過・身体所見からの判断と合わせて診断・除外が必要とされている。 ①WBC > 15,400/µLかつNa < 135mEq/Lであれば、NSTIの診断に対して感度90%, 特異度76%, 陽性尤度比 (LR+)3.75, 陰性尤度比 (LR-)0.13 ②乳酸値 >2mmol/L (18mg/dL) であれば、NSTIの診断に対して感度100%, 特異度76%, LR+4.17, LR-0 ③LRINECスコア (表2) 6点以上であれば、陽性的中率 (PPV) 57~92%, 陰性的中率 (NPV) 86~96%

救急外来、病棟管理で絶対マスターしたい疾患対応

図2 NSTI

(Stevens DL, et al: N Engl J Med, 377:2253-2265、2017より)

（図の内容はPage3上部のNSTI進行図と同様）

* フィンガーテストとは、壊死性筋膜炎が疑われる部位と深筋膜まで小切開する 。そのうえで深筋膜レベルに示指を入れ、①出血しない、②悪臭を伴う滲出液が出てくる、③組織が抵抗なく剥離できる、以上の所見があれば壊死性筋膜炎と診断する 。
* 非典型的な壊死性筋膜炎の場合、初診時の評価だけで除外するのは困難 。疑いが強い場合には15分後、30分後、1時間後と何回も皮膚所見や全身状態の確認を繰り返し、疑いがやはり強い場合は再度外科医ヘコンサルテーションする 。
* 治療は、迅速な広域デブリードマン 。抗菌薬も速やかに投与するが、圧倒的にデブリードマンが重要となる 。

**蜂窩織炎を診断・治療するときに必要な検査を押さえておく**

* 原則として検査は不要である 。
* 蜂窩織炎の血液培養の陽性率は7.9%とされルーチンでの採取は推奨されないが、担がん状態、化学療法中、無顆粒球症が疑われるとき、細胞性免疫不全、リンパ浮腫、動物咬傷の場合には採取を検討する 。

**MEMO** 筆者は入院が必要な蜂窩織炎の場合にも、血液培養を採取することが多い。

* 開放創の創部感染、潰瘍病変などのスワブでの擦過培養はコンタミネーションと判断がつかなく、原因菌を反映しにくいとされ推奨されていない 。
* 皮下膿瘍や NSTIなどで皮膚切開直後の内部の滲出液を培養することは、原因菌の同定につながるので推奨される 。

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（図：化膿性、非化膿性皮膚軟部組織感染症の治療戦略を示すフローチャート「図3」）

分岐点：膿性の排液、膿疱の有無

* **あり（化膿性：癤（せつ）／癰（よう）／膿瘍）**
  + **軽度（全身性の感染徴候なし）**
    - → 切開ドレナージ
    - → 2cm以上は抗菌薬投与
  + **中等度（SIRS≧1点）**
    - → 切開ドレナージ
    - → 培養＆感受性試験＆抗菌薬
  + **重度（SIRS≧2点、切開ドレナージが無効、免疫不全、低血圧、疾患の急速進行）**
    - → 抗菌薬投与
    - → 緊急試験切開／デブリードマンの検討
    - → 壊死性筋膜炎の除外
* **なし（非化膿性：丹毒／蜂窩織炎／壊死性筋膜炎）**
  + **軽度（全身性の感染徴候なし、典型的な丹毒／蜂窩織炎）**
    - → 経口投与 セファレキシン
  + **中等度（SIRS≧1点）**
    - → 静脈投与 セファゾリン （経口投与が無効のときもこちらへ）
  + **重度（SIRS≧2点かつ免疫不全または疾患の急速進行または水疱、皮膚剥離、低血圧、臓器機能障害などの深部感染症の臨床症状）**
    - → 抗菌薬投与
    - → 緊急試験切開／デブリードマンの検討
    - → 壊死性筋膜炎の除外 SIRS：体温>38℃または<36℃、脈拍>90回/分、呼吸数>20回/分、WBC>12,000または<4,000/mm² (Stevens DL, et al: Clin Infect Dis. 59: e10-52, 2014より)

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救急外来、病棟管理で絶対マスターしたい疾患対応

特にリスクのない人の蜂窩織炎疑いの場合

検査不要

**免疫不全、担がん、入院が必要そうな蜂窩織炎疑いの場合**

* 血算(分画まで)、生化学(肝腎機能ベースライン確認目的)
* 血液培養、非開放創で膿瘍などの培養が取れそうなときは感染部位の培養
* 胸部単純X線、心電図(入院時ベースラインとして)

本症例に必要な検査

SIRS 3点(「第4章-1敗血症/敗血症性ショックの初期治療」参照)であり、歩行が困難なことから入院点滴加療適応と判断した。

入院症例として、血算、生化学、血液培養検査を提出し、入院時の胸部単純X線、心電図をとることとした。

**蜂窩織炎は兎にも角にもセファゾリンとRICEで治療する**

* 原因菌は、黄色ブドウ球菌とレンサ球菌で72%、まれにグラム陰性桿菌のこともある 。
* 抗菌薬の原則は、セファレキシンもしくはセファゾリンである 。
* 化膿性病変がある場合には、切開ドレナージと培養を提出する(図3) 。
* 治療の開始前に必ず、炎症範囲をマーキングする。
* 蜂窩織炎の治療成功の可否はRICE (Rest (安静), Icing(冷却), Compression(圧迫), Elevation (挙上)〕にかかっているといっても過言ではない。RICEができておらず悪化するケースを散見する。

**特殊な菌のカバーが必要なときを覚える**

**1. MRSA カバーが必要なとき**

* 患者さんの状態からショック状態、発熱性好中球減少症、人工物が関連してそうな場合(人工関節、カテーテルなど)、感染性心内膜炎(IE) を疑うとき、NSTIが除外しきれないとき 。
* 耐性菌のリスクなどから、メチシリン耐性黄色ブドウ球菌(methicillin-resistant Staphylococcus aureus: MRSA)をカバーしない抗菌薬に不応、過去90日以内の抗菌薬使用歴、MRSA検出歴、最近の手術歴・入院歴、血液透析中のとき 。

**MEMO** ただし、日本ではほとんどの場合MRSA カバーが不要と思われる。血液培養などから原因菌が検出できないことが多く、一度抗MRSA薬で治療を開始すると変更できなくなることも多いため、筆者らはNSTIが除外しきれない場合、ショックを含めてかなり状態が悪い場合、発熱性好中球減少症を伴う場合のみに投与している。もちろん、上記リスクがある場合に抗MRSA薬を使わないときには、より慎重な経過観察が必要なのはいうまでもない。

**2. 何かに咬まれたとき**

* 猫や犬に咬まれるとパスツレラ・ムルトシダ、カプノサイトファーガ属などが、人に咬まれるとエイケネラ属などが問題となるためスルバクタム/アンピシリン (ユナシン®S)もしくはクラブラン酸/アモキシシリン (オーグメンチン®)の投与が必須となる 。
* 創部処置も別に必要なので、必ず病歴で確認する。
* 予防的な抗菌薬投与が必要となる数少ないシチュエーションでもある。

**3. 川、池、海に行ったとき、水産物を食べたとき**

* 淡水であれば緑膿菌、エロモナス・ハイドロフィラが、海水であれば緑膿菌、ビブリオ・バルニフィカスが原因となることがあり、NSTIを呈してくることがある 。特に、肝硬変を含めた肝疾患がある場合には注意が必要となる 。
* テトラサイクリン系薬、ニューキノロン系薬が必要なこともあり、感染症科にコンサルテーションする 。

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3 蜂窩織炎 219

**蜂窩織炎は入院適応例以外は外来でも十分治療できる**

* 以下の場合は入院で治療、それ以外であれば外来でも十分治療できる 。SIRSのスコアも参考にするが、絶対ではない。 ①「広範囲、全身状態が悪い、急速に進行、免疫不全、病変近くに人工物がある、経口投与で治療したが48~72時間無効」な病態 ②「経口投与できない、RICEを守れない」患者さん

**処方例**

* **外来治療できる場合**
  + セファレキシン(ケフレックス®) 250mg 1回2Cap 1日3回
  + ペニシリンアレルギーの場合:
    - クリンダマイシン (ダラシン®) 150mg 1回 2Cap 1日3回
* **入院が必要で特殊な菌のカバーが不要な場合**
  + セファゾリン2g+生理食塩液100mL 8時間ごと 100mL/時で投与
* **動物咬傷による蜂窩織炎の場合**
  + 点滴の場合:
    - スルバクタム/アンピシリン(ユナシン®S) 3g+生理食塩液100mL 6時間ごと 100mL/時
  + 内服の場合:
    - クラブラン酸/アモキシシリン (オーグメンチン®) 250mg 1回1錠 1日3回
    - +アモキシシリン (サワシリン®) 250mg 1回1錠 1日3回
* **入院が必要でMRSAや耐性グラム陰性桿菌のカバーが必要な場合**
  + バンコマイシン15~20mg/kg+生理食塩液100mL 12時間ごと 100mL/時
  + +以下のいずれか
    - タゾバクタム/ピペラシリン(ゾシン®) 4.5g+生理食塩液100mL 6時間ごと 100mL/時
    - セフェピム2g+生理食塩液100mL 12時間ごと 100mL/時
    - メロペネム(メロペン®) 1g+生理食塩液100mL 8時間ごと 100mL/時

抗菌薬以外の指導

RICEを指示

外来通院患者さんにも、可能な限り歩き回らずRICEをするように指導

RICEができていないと治療がうまくいかないことがあることを強調

**治療開始後48~72時間で改善がなければ他疾患や耐性菌を考える**

**1. 蜂窩織炎がよくなっているかの経過観察のポイント**

* 臓器特異的な所見として、診断時にみられた発赤、熱感、腫脹、疼痛の皮膚の炎症所見4徴の改善の有無をチェックする 。
* 全身状態の所見として、診断時にみられた発熱、食思不振、倦怠感などの改善の有無をチェックする 。
* 抗菌薬治療は上記所見の改善があれば、多少所見が残存していても5~10日間で終了とする 。
* 免疫不全やリンパ浮腫が背景にある場合には、10~14日間の抗菌薬投与を考慮する 。
* 治療開始後48~72時間で改善がない場合には、他疾患や耐性菌による蜂窩織炎の可能性を考える 。

**入院時指示の出し方**

* 通常の入院時指示は、「第5章-10入院時指示の考え方・出し方・コール条件・必要時指示の出し方」を参照
* それに加えて、「患肢を可能な限り挙上してクーリング、アイスノンがぬるくなったら交換、安静度の基本はベッド上安静、トイレ歩行は可」を追加
* 血液検査は経過が問題なければ抗菌薬の副作用チェックのため週1回程度で行う
* 深部静脈血栓症 (DVT) の高リスクとなりやすいので、DVT予防も忘れずに行う

**2. 外来で経過観察する場合**

* 3日後くらいをめどに1回外来で経過観察する。
* 良くなっていれば抗菌薬治療期間を決めて、さらに1週間後に経過観察する。そこで良くなっていれば終診とする。
* いずれかのタイミングで悪化傾向があれば、入院での精査・治療に切り替えるのが定石である。

4

救急外来、病棟管理で絶対マスターしたい疾患対応

**コンサルテーションのタイミングを知っておく**

* NSTIが疑われるときは、外科にコンサルテーションする 。病院や地域、罹患部位によりコンサルテーションする科は外科、耳鼻科、整形外科、形成外科、産婦人科などさまざまである 。
* 自施設で診療経験がなければ、高次医療機関にすぐコンサルテーションする。
* 蜂窩織炎以外の皮膚疾患が疑われるときは、皮膚科にコンサルテーションを検討する。

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第4章 救急外来、病棟管理で絶対マスターしたい疾患対応

本症例の経過

歩行困難であったため入院適応と判断した。問診から特殊な菌のカバーが必要な背景疾患や状況はなく、血液検査でも肝腎機能正常であり、セファゾリン2g+生理食塩液100mL 8時間ごと100mL/時で投与開始した。炎症範囲のマーキング、RICEおよび安静度の指示をした。

入院2日目には局所の炎症所見(発赤、熱感、疼痛、腫脹)は横ばいからやや軽快のように思われ、3日目には明らかに疼痛を含め改善がみられた。経過が良好であったため皮膚炎症所見はやや残存したものの、5日間の抗菌薬投与として、入院6日目に退院となった。白癬がみられたため皮膚科で治療するよう指導した。

**文献**

1. Spelman D, et al Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis. UpToDate (last updated Dec 15, 2023)
2. Raff AB, et al: Cellulitis: A Review. JAMA, 316 325-337, 2016 [PMID: 27434444]
3. Stevens DL, et al: Necrotizing soft tissue infections. UpToDate (last updated Oct 07, 2022)
4. Stevens DL, et al Necrotizing Soft-Tissue Infections. N Engl J Med, 377 2253-2265, 2017 [PMID: 29211672]
5. Wong CH, et al The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med, 32 1535-1541, 2004 [PMID: 15241098]
6. Wall DB, et al: A simple model to help distinguish necrotizing fasciitis from nonnecrotizing soft tissue infection. J Am Coll Surg, 191: 227-231, 2000 [PMID: 10989895]
7. Murphy G, et al: Raised serum lactate: a marker of necrotizing fasciitis? J Plast Reconstr Aesthet Surg, 66: 1712-1716, 2013 [PMID: 23911720]
8. Stevens DL, et al Infectious Diseases Society of America: Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clin Infect Dis, 59: e10-e52, 2014 [PMID: 24973422]
9. Spelman D, et al: Acute cellulitis and erysipelas in adults: Treatment. UpToDate (last updated Dec 15, 2023)

**INTRODUCTION**

Necrotizing soft tissue infections (NSTIs) include necrotizing forms of fasciitis, myositis, and cellulitis [[1-4](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1-4)]. These infections are characterized clinically by fulminant tissue destruction, systemic signs of toxicity, and high mortality. Accurate diagnosis and appropriate treatment must include early surgical intervention and antibiotic therapy.

Several different names have been used to describe the various forms of necrotizing infections; this is related in part to naming based on clinical features rather than surgical or pathologic findings. The degree of suspicion should be high since the clinical presentation is variable and prompt intervention is critical. The lay press has referred to organisms that cause NSTI as "flesh-eating bacteria."

Necrotizing fasciitis, myositis, and cellulitis will be reviewed here. Clostridial infection and pyomyositis are discussed separately. (See ["Clostridial myonecrosis"](https://www.uptodate.com/contents/clostridial-myonecrosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Primary pyomyositis"](https://www.uptodate.com/contents/primary-pyomyositis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

Surgical management of NSTI is discussed separately. (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**CONDITIONS, MICROBIOLOGY, AND EPIDEMIOLOGY**

NSTI can involve the epidermis, dermis, subcutaneous tissue, fascia, and muscle [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)]. Necrotizing infection may be categorized based on microbiology and presence or absence of gas in the tissues ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

Distinguishing necrotizing fasciitis from necrotizing myositis may be difficult as skeletal muscle and fascia are involved in both syndromes [[5-7](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/5-7)]. Necrotizing myositis primarily involves skeletal muscle, whereas necrotizing fasciitis primarily involves fascia.

**Necrotizing fasciitis** — Necrotizing fasciitis is an infection of the deep soft tissues that results in progressive destruction of the muscle fascia and overlying subcutaneous fat. Infection typically spreads along the muscle fascia due to its relatively poor blood supply; muscle tissue is frequently spared because of its generous blood supply [[8](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/8)]. Development of anesthesia may precede the appearance of skin necrosis and provide a clue to the presence of necrotizing fasciitis [[9](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/9)]. Initially, the overlying tissue can appear unaffected; therefore, necrotizing fasciitis is difficult to diagnose without direct visualization of the fascia.

Necrotizing fasciitis may be divided into two microbiologic categories: polymicrobial (type I) and monomicrobial infection (type II) [[10-12](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/10-12)]:

●

Polymicrobial (type I) necrotizing infection is caused by aerobic and anaerobic bacteria.

Typically, at least one anaerobic species (most commonly *Bacteroides*, *Clostridium*, or *Peptostreptococcus*) is isolated in combination with Enterobacteriaceae (eg, *Escherichia coli*, *Enterobacter*, *Klebsiella*, *Proteus*) and one or more facultative anaerobic streptococci (other than group A *Streptococcus* [GAS]) [[13-15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13-15)]. Obligate aerobes (such as *Pseudomonas aeruginosa*) are rarely components of such mixed infections. Uncommonly, fungi (predominately *Candida* species) are recovered in polymicrobial (type I) necrotizing infection [[16](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/16)].

**Fournier gangrene** is caused by facultative organisms (*E. coli*, *Klebsiella*, enterococci) along with anaerobes (*Bacteroides*, *Fusobacterium*, *Clostridium*, anaerobic or microaerophilic streptococci) [[17](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/17)]. (See ['Involved sites'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H3846414689) below.)

**Necrotizing infection of the head and neck** is usually caused by mouth anaerobes (such as Fusobacteria, anaerobic streptococci, *Bacteroides*, and spirochetes). (See ['Involved sites'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H3846414689) below.)

Other terms for polymicrobial (type I) infection include synergistic necrotizing cellulitis and progressive bacterial synergistic gangrene.

●

Monomicrobial (type II) necrotizing infection is usually caused by GAS or other beta-hemolytic streptococci. Infection can also be caused by *Staphylococcus aureus* [[18,19](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/18,19)]. Infection with no clear portal of entry occurs in about half of cases; in such circumstances, the pathogenesis of infection likely consists of hematogenous translocation of GAS from the throat (asymptomatic or symptomatic pharyngitis) to a site of blunt trauma or muscle strain [[1,7](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,7)].

M protein is an important virulence determinant of GAS. Necrotizing infection caused by GAS strains with M types 1 and 3 is associated with streptococcal toxic shock syndrome in about 50 percent of cases [[20-22](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/20-22)]. GAS strains of these and other serotypes can produce pyrogenic exotoxins, which induce cytokine production, likely contributing to shock, tissue destruction, and organ failure [[6,23,24](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6,23,24)]. (See ["Group A streptococcus: Virulence factors and pathogenic mechanisms"](https://www.uptodate.com/contents/group-a-streptococcus-virulence-factors-and-pathogenic-mechanisms?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Invasive group A streptococcal infection and toxic shock syndrome: Epidemiology, clinical manifestations, and diagnosis"](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-epidemiology-clinical-manifestations-and-diagnosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

Numerous other pathogens can cause monomicrobial (type II) necrotizing infection less frequently; *Vibrio vulnificus* and *Aeromonas hydrophila* deserve special comment. Infections due to these pathogens typically occur in the setting of traumatic injury associated with sea water or fresh water, respectively. Other risk factors associated with necrotizing infection due to *V. vulnificus* include cirrhosis and ingestion of contaminated oysters [[25](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/25)]. (See ["Vibrio vulnificus infection"](https://www.uptodate.com/contents/vibrio-vulnificus-infection?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

The incidence of necrotizing fasciitis ranges from 0.3 to 15 cases per 100,000 population [[1,26](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,26)]:

●

Polymicrobial (type I) necrotizing fasciitis (caused by aerobic and anaerobic bacteria) usually occurs in older adults and/or in individuals with underlying comorbidities. The most important predisposing factor is diabetes, especially with associated peripheral vascular disease. (See ['Risk factors'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H3864839350) below.)

●

Monomicrobial (type II) necrotizing fasciitis (most caused by GAS) may occur in any age group and in individuals with no underlying comorbidities [[15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)]. In the United States, there are an estimated 3.5 cases of invasive GAS infections per 100,000 persons; necrotizing infections make up approximately 6 percent of these cases [[27](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/27)].

**Necrotizing myositis** — Necrotizing myositis is an infection of skeletal muscle typically caused by GAS(and other beta-hemolytic streptococci). It may be preceded by skin abrasions, blunt trauma, or heavy exercise [[5,28-32](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/5,28-32)]. Necrotizing myositis is rare. One report noted 21 cases documented between 1900 and 1985; another review of over 20,000 autopsies noted 4 cases [[28,29](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/28,29)].

Clostridial myonecrosis (gas gangrene) is discussed separately. (See ["Clostridial myonecrosis"](https://www.uptodate.com/contents/clostridial-myonecrosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**Necrotizing cellulitis** — Necrotizing cellulitis is typically caused by anaerobic pathogens and may be divided into two types: clostridial (usually caused by *Clostridium perfringens*; less frequently *Clostridium septicum*) and nonclostridial (caused by polymicrobial infection).

In both types, crepitus is observed in the skin, but there is sparing of fascia and deep muscles. Pain, swelling, and systemic toxicity are not prominent features, and the relative mildness helps distinguish cellulitis from clostridial myonecrosis (gas gangrene) in the immunocompetent host. (See ["Clostridial myonecrosis"](https://www.uptodate.com/contents/clostridial-myonecrosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**RISK FACTORS**

Necrotizing infection can occur among healthy individuals with no past medical history or clear portal of entry in any age group [[15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)].

Risk factors associated with NSTI include [[1,13,18,33-37](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,13,18,33-37)]:

●

Major penetrating trauma

●

Minor laceration or blunt trauma (muscle strain, sprain, or contusion)

●

Skin breach (varicella lesion, insect bite, injection drug use)

●

Recent surgery (including colonic, urologic, and gynecologic procedures as well as neonatal circumcision)

●

Mucosal breach (hemorrhoids, rectal fissures, episiotomy)

●

Immunosuppression (diabetes, cirrhosis, neutropenia, HIV infection)

●

Malignancy

●

Obesity

●

Alcoholism

●

In women: pregnancy, childbirth, pregnancy loss, gynecologic procedures

Diabetes is a particularly important risk factor for necrotizing infection involving the lower extremities, perineum, and head and neck region [[14,15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/14,15)]. In addition, use of sodium-glucose cotransporter 2 inhibitors (agents used for treatment of adults with type 2 diabetes) has been associated with NSTI of the perineum (Fournier gangrene) [[38](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/38)]. (See ["Sodium-glucose cotransporter 2 inhibitors for the treatment of hyperglycemia in type 2 diabetes mellitus", section on 'Genitourinary tract'](https://www.uptodate.com/contents/sodium-glucose-cotransporter-2-inhibitors-for-the-treatment-of-hyperglycemia-in-type-2-diabetes-mellitus?sectionName=Genitourinary%20tract&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H3506386806&source=see_link#H3506386806).)

Use of nonsteroidal anti-inflammatory drugs (NSAIDs) may be associated with development or progression of streptococcal necrotizing infection; data are conflicting [[1,19,39-41](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,19,39-41)]. Regardless of their role in pathogenesis, NSAIDs may mask signs and symptoms of inflammation in patients with NSTI, which may be associated with a delay in diagnosis.

**CLINICAL MANIFESTATIONS**

**Typical findings** — NSTI can include involvement of the epidermis, dermis, subcutaneous tissue, fascia, and muscle [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)]. Necrotizing infection most commonly involves the extremities (lower extremity more commonly than upper extremity), particularly in patients with diabetes and/or peripheral vascular disease. Necrotizing infection usually presents acutely (over hours); rarely, it may present subacutely (over days). Rapid progression to extensive destruction can occur, leading to systemic toxicity, limb loss, and/or death [[6,7,22](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6,7,22)]. Therefore, early recognition of necrotizing infection is critical.

Clinical manifestations of necrotizing infection include [[1,2,4,7,42,43](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,2,4,7,42,43)]:

●

Erythema (without sharp margins; 72 percent)

●

Edema that extends beyond the visible erythema (75 percent)

●

Severe pain (out of proportion to exam findings in some cases; 72 percent)

●

Fever (60 percent)

●

Crepitus (50 percent)

●

Skin bullae, necrosis, or ecchymosis (38 percent)

Fever (102 to 105°F), tachycardia, and systemic toxicity may be observed. Hypotension may be present initially or develop with progressive infection. Other symptoms include malaise, myalgias, diarrhea, and anorexia.

The subcutaneous tissue may be firm and indurated, such that the underlying muscle groups cannot be palpated distinctly [[2,4](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/2,4)]. Marked edema may produce a compartment syndrome with complicating myonecrosis requiring fasciotomy. Lymphangitis and lymphadenitis are infrequent. (See ["Acute compartment syndrome of the extremities"](https://www.uptodate.com/contents/acute-compartment-syndrome-of-the-extremities?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

The process progresses rapidly over several days, with changes in skin color from red-purple to patches of blue-gray. Within three to five days after onset, skin breakdown with bullae (containing thick pink or purple fluid) and frank cutaneous gangrene can be seen.

In the setting of surgical wound infection, NSTI is characterized by copious drainage, dusky and friable subcutaneous tissue, and pale, devitalized fascia.

In the setting of necrotizing fasciitis, diminished sensation to pain develops in the involved area, due to thrombosis of small blood vessels and destruction of superficial nerves in the subcutaneous tissue. This may precede the appearance of skin necrosis and provide a clue to the presence of necrotizing fasciitis [[9](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/9)]. Subcutaneous gas is often present in the polymicrobial (type I) form of necrotizing fasciitis, particularly in patients with diabetes [[15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)].

**Involved sites** — Necrotizing fasciitis most commonly involves the extremities, as discussed in the preceding section. Other presentations include necrotizing fasciitis of the perineum (Fournier gangrene), head and neck region, and neonatal infection:

●

**Perineum (Fournier gangrene)** – Necrotizing fasciitis of the perineum, known as Fournier gangrene, can occur as a result of a breach in the integrity of the gastrointestinal or urethral mucosa [[44,45](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/44,45)]. Fournier gangrene is a form of polymicrobial (type I) infection. Fournier gangrene typically begins abruptly with severe pain and may spread rapidly to the anterior abdominal wall and the gluteal muscles. Men are more commonly affected than women. Involvement in men may include the scrotum and penis ([picture 1](https://www.uptodate.com/contents/image?imageKey=PC%2F58093&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)); involvement in women may include involvement of the labia.

●

**Head and neck region** – Necrotizing fasciitis of the head and neck can result from a breach in oropharynx mucous membrane integrity following surgery or instrumentation or in the setting of odontogenic infection [[46](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/46)].

In one study including 45 patients with cervical necrotizing fasciitis, most were attributable to mixed aerobic and anaerobic bacteria. The majority of cases were of dental origin (78 percent); the remaining cases were of pharyngeal origin or occurred after surgery or trauma [[47](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/47)]. Fasciitis spread to the face (22 percent), lower neck (56 percent), and mediastinum (40 percent). In a separate study, 28 percent of patients with necrotizing fasciitis of the head and neck developed mediastinitis; factors that contributed to mediastinal involvement included prior corticosteroid use, infection by gas-producing microbes, and a pharyngeal focus of infection [[48](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/48)]. Cervical (head and neck) necrotizing fasciitis is usually a polymicrobial (type I) infection. However, monomicrobial (type II) infection due to group A *Streptococcus* (GAS) can also occur. (See ['Conditions, microbiology, and epidemiology'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2533911134) above.)

Other conditions that can occur in the setting of necrotizing infection involving the head and neck region include Ludwig's angina (submandibular space infection) and Lemierre syndrome (septic thrombophlebitis of the jugular vein). (See ["Ludwig angina"](https://www.uptodate.com/contents/ludwig-angina?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Lemierre syndrome: Septic thrombophlebitis of the internal jugular vein"](https://www.uptodate.com/contents/lemierre-syndrome-septic-thrombophlebitis-of-the-internal-jugular-vein?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

**Neonatal infection** – Most cases of necrotizing fasciitis in neonates present with abdominal or perineal involvement and are often due to beta-hemolytic streptococci. Polymicrobial infection occurs less often. Associated conditions include omphalitis, balanitis (related to circumcision), and hernia repair [[49-53](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/49-53)].

**Laboratory findings** — Laboratory findings are generally nonspecific. Abnormalities may include leukocytosis with left shift, acidosis, coagulopathy, hyponatremia, elevated inflammatory markers (C-reactive protein and/or erythrocyte sedimentation rate), and elevations in serum creatinine, lactate, creatine kinase (CK), and aspartate aminotransferase (AST) concentrations [[1,6,54-57](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1,6,54-57)]. Elevations in serum CK or AST concentrations suggest deep infection involving muscle or fascia (as opposed to cellulitis) [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)].

NSTI cannot be predicted reliably using laboratory parameters, particularly in the setting of early infection. A tool called the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score has been described; it is based on laboratory indicators including white cell count, hemoglobin, sodium, glucose, creatinine, and C-reactive protein [[58,59](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/58,59)]. The tool has demonstrated variable sensitivity and should **not** be used to rule out NSTI [[58,60-62](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/58,60-62)].

Blood cultures are positive in approximately 60 percent of patients with monomicrobial (type II) necrotizing fasciitis (eg, due to GAS or other beta-hemolytic streptococci) and are routinely positive in patients with necrotizing myositis [[30](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/30)]. The yield of blood cultures is lower among patients with polymicrobial (type I) necrotizing fasciitis; in one series, it was 20 percent [[15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)]. In addition, blood culture results may not reflect all organisms involved [[63](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/63)]. (See ['Conditions, microbiology, and epidemiology'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2533911134) above.)

**DIAGNOSIS**

**General approach** — NSTI should be suspected in patients with soft tissue infection (erythema, edema, warmth) and signs of systemic illness (fever, hemodynamic instability) in association with crepitus, rapid progression of clinical manifestations, and/or severe pain (out of proportion to skin findings in some cases) ([algorithm 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116424&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)). Early recognition of necrotizing infection is critical; rapid progression to extensive destruction can occur, leading to systemic toxicity, limb loss, and/or death [[6,7,22](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6,7,22)].

The diagnosis of necrotizing infection is established via surgical exploration of the soft tissues in the operating room, with physical examination of the skin, subcutaneous tissue, fascial planes, and muscle [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)]. Surgical exploration is required to establish the presence of necrotizing infection, evaluate the scope of involvement, and to debride devitalized tissue. Surgical exploration should **not** be delayed when there is clinical suspicion for a necrotizing infection while awaiting results of radiographic imaging, culture results, or other diagnostic information. (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

Intraoperative specimens should be sent for Gram stain and culture (in addition to histology) ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

Radiographic imaging studies can be useful to help determine whether necrotizing infection is present but should not delay surgical intervention when there is crepitus on examination or rapid progression of clinical manifestations [[6](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6)]. (See ['Radiographic imaging'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H1770115080) below.)

Blood cultures (two sets) should be obtained prior to administration of antimicrobial therapy. Reasonable serum laboratory testing includes complete blood count with differential, chemistries, liver function tests, creatinine concentration, coagulation studies, creatine kinase concentration, lactate concentration, and inflammatory markers (C-reactive protein and/or erythrocyte sedimentation rate). (See ['Laboratory findings'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2012028741) above.)

Clinical factors that may make diagnosis of NSTI difficult include [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)]:

●

Absence of fever – Fever may be absent; in some cases, this may be due to use of nonsteroidal anti-inflammatory drugs.

●

Absence of cutaneous manifestations – Patients presenting with no obvious portal of entry may present with infection that began deep in the soft tissues; superficial signs of infection may not appear until late in the course of disease.

●

Attribution of severe pain to alternative cause – Pain may be erroneously attributed to recent surgery or other known condition.

●

Nonspecific imaging tests – Radiographic imaging may demonstrate edema with no gas in the deep tissue; these findings may be attributed to noninfectious causes, thereby confounding the diagnosis.

●

Attributing systemic manifestations to other causes – Gastrointestinal symptoms (nausea, vomiting, diarrhea) may be early manifestations of toxemia due to group A streptococcal infection but may be wrongly attributed to other conditions.

**Surgical exploration and debridement** — Surgical exploration is the **only** way to establish the diagnosis of necrotizing infection. Findings on direct examination include swollen and dull-gray appearance of the fascia, thin exudate without clear purulence, and easy separation of tissue planes by blunt dissection ([picture 2](https://www.uptodate.com/contents/image?imageKey=SURG%2F109141&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)) [[2,4](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/2,4)].

Surgery should be performed at the center where the patient presented, provided an appropriately trained surgeon is available (rather than delaying care for transfer). Early debridement is associated with better outcomes; survival is significantly increased among patients taken to surgery within 24 hours after admission compared with those in whom surgery is delayed, and survival is further increased with earlier surgical intervention (eg, within six hours) [[43,64,65](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/43,64,65)].

Intraoperative specimens should be sent for Gram stain and culture ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

Tissue biopsy may be obtained but is not required to establish the diagnosis of necrotizing infection. Characteristic pathologic features of necrotizing fasciitis include extensive tissue destruction, thrombosis of blood vessels, abundant bacteria spreading along fascial planes, and infiltration of acute inflammatory cells [[66](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/66)]. Characteristic pathologic features of necrotizing myositis include degeneration and necrosis of skeletal muscle fibers, infiltration of granulocytes, and numerous bacteria in areas of muscle necrosis ([picture 3](https://www.uptodate.com/contents/image?imageKey=ID%2F53989&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

Issues related to surgical management of NSTIs are discussed further separately. (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**Radiographic imaging** — Radiographic imaging can be useful to help determine whether necrotizing infection is present but should not delay surgical intervention when there is crepitus on examination or rapid progression of clinical manifestations [[6](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6)].

The best initial radiographic imaging exam is computed tomography (CT) scan ([image 1](https://www.uptodate.com/contents/image?imageKey=RADIOL%2F97786&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link) and [image 2](https://www.uptodate.com/contents/image?imageKey=RADIOL%2F101588&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)). The most useful finding is presence of gas in soft tissues, which is seen most frequently in the setting of clostridial infection or polymicrobial (type I) necrotizing fasciitis ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)); this finding is highly specific for NSTI and should prompt immediate surgical intervention [[13,67,68](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13,67,68)]. Other radiographic findings may include fluid collections, absence or heterogeneity of tissue enhancement with intravenous contrast, and inflammatory changes beneath the fascia [[69](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/69)].

Magnetic resonance imaging (MRI) is not as useful as CT for detection of gas in soft tissues. In addition, MRI can be overly sensitive; it tends to overestimate deep tissue involvement and therefore cannot be used to reliably distinguish between necrotizing cellulitis and deeper infection [[70](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/70)].

Ultrasound may be used for detection of localized abscesses and gas in tissues but has not been well studied in necrotizing fasciitis.

Frequently, imaging studies demonstrate soft tissue swelling; this finding is not specific since it is not possible to distinguish between swelling caused by infection, trauma, surgery, or inflammation. Therefore, in such cases, the diagnosis of necrotizing infection can be established only by surgical exploration.

**DIFFERENTIAL DIAGNOSIS**

Conditions included in the differential diagnosis include:

●

Cellulitis – Cellulitis presents with skin erythema, edema, and warmth. Fever may be present, but cellulitis is generally not associated with hemodynamic instability or exquisite tenderness. Elevations in serum CK or AST concentrations suggest deep infection involving muscle or fascia (as opposed to cellulitis). (See ["Cellulitis and skin abscess: Epidemiology, microbiology, clinical manifestations, and diagnosis"](https://www.uptodate.com/contents/cellulitis-and-skin-abscess-epidemiology-microbiology-clinical-manifestations-and-diagnosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

Pyoderma gangrenosum – Pyoderma gangrenosum may be difficult to distinguish from necrotizing fasciitis [[63,71-74](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/63,71-74)]. Distinguishing features are summarized in the table ([table 2](https://www.uptodate.com/contents/image?imageKey=ID%2F115267&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)). The distinction is important because inappropriate surgical debridement of pyoderma gangrenosum can cause extension of the lesion, and inappropriate administration of immunosuppressive therapy may worsen necrotizing fasciitis. (See ["Pyoderma gangrenosum: Pathogenesis, clinical features, and diagnosis"](https://www.uptodate.com/contents/pyoderma-gangrenosum-pathogenesis-clinical-features-and-diagnosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

Gas gangrene (clostridial myonecrosis) – Gas gangrene (clostridial myonecrosis) is an acute invasion of healthy tissue that occurs spontaneously or as a result of traumatic injury. Both gas gangrene and polymicrobial (type I) NSTI are associated with gas in the tissues. In gas gangrene, the Gram stain typically demonstrates gram-positive rods, while, in polymicrobial necrotizing fasciitis, the Gram stain typically demonstrates mixed aerobes and anaerobes ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)). The distinction is important in that management of clostridial myonecrosis may require amputation, whereas management of necrotizing fasciitis requires debridement (but limb salvage may be possible). (See ["Clostridial myonecrosis"](https://www.uptodate.com/contents/clostridial-myonecrosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

Pyomyositis – Pyomyositis may be confused with necrotizing myositis. These conditions differ in that pyomyositis is characterized by abscess formation in skeletal muscle, while necrotizing myositis is characterized by gangrenous necrosis. These are distinguished by clinical and radiographic features. Pyomyositis is usually caused by *S. aureus* and is generally associated with less systemic toxicity than necrotizing myositis. (See ["Primary pyomyositis"](https://www.uptodate.com/contents/primary-pyomyositis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

Deep venous thrombosis – Deep venous thrombosis (DVT) is characterized by extremity swelling, pain, and warmth; the pain is less extreme than in the setting of necrotizing infection. Fever may be present in DVT but is more common in the setting of soft tissue infection. (See ["Clinical presentation and diagnosis of the nonpregnant adult with suspected deep vein thrombosis of the lower extremity"](https://www.uptodate.com/contents/clinical-presentation-and-diagnosis-of-the-nonpregnant-adult-with-suspected-deep-vein-thrombosis-of-the-lower-extremity?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**TREATMENT**

**Clinical approach** — Treatment of NSTI consists of early and aggressive surgical exploration and debridement of necrotic tissue, together with broad-spectrum empiric antibiotic therapy and hemodynamic support. Administration of antibiotic therapy in the absence of debridement is associated with a mortality rate approaching 100 percent [[13](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13)].

**Surgical debridement** — NSTI is a surgical emergency. Radiographic imaging studies should not delay surgical intervention when there is crepitus on examination or rapid progression of clinical manifestations.

The goal of operative management is to perform aggressive debridement of all necrotic tissue until healthy, viable (bleeding) tissue is reached. Inspection and debridement in the operating room should be continued every one to two days until necrotic tissue is no longer present [[42](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/42)]. For severe necrotizing infection involving the extremities, amputation may be needed to control the infection [[13](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13)].

Issues related to surgical debridement and reconstruction procedures are discussed further separately. (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**Antibiotic therapy** — In general, empiric treatment of NSTI should consist of broad-spectrum antimicrobial therapy, including activity against gram-positive, gram-negative, and anaerobic organisms [[13](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13)]. Antibiotic therapy should be initiated promptly after obtaining blood cultures ([algorithm 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116424&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

Acceptable empiric antibiotic regimens include [[2,4](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/2,4)]:

●

A carbapenem:

•

[Imipenem](https://www.uptodate.com/contents/imipenem-and-cilastatin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (adults: 1 g IV every 6 to 8 hours)

•

[Meropenem](https://www.uptodate.com/contents/meropenem-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (adults: 1 g IV every 8 hours; children and neonates with a postnatal age >7 days: 20 mg/kg per dose every eight hours),

•

[Ertapenem](https://www.uptodate.com/contents/ertapenem-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (adults: 1 g IV every 24 hours; infants ≥3 months and children: 15 mg/kg per dose IV twice daily [maximum dose 500 mg]; adolescents: 1 g IV every 24 hours)

**or**

●

[Piperacillin-tazobactam](https://www.uptodate.com/contents/piperacillin-and-tazobactam-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (adults: 3.375 g every 6 hours or 4.5 g every 8 hours; children and neonates with a postnatal age >7 days: 75 mg/kg per dose of the piperacillin component, not to exceed to a maximum of 3 g, every 6 hours)

**PLUS**

●

An agent with activity against methicillin-resistant *S. aureus* (MRSA; such as [vancomycin](https://www.uptodate.com/contents/vancomycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) or [daptomycin](https://www.uptodate.com/contents/daptomycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link)) ([table 3](https://www.uptodate.com/contents/image?imageKey=ID%2F110072&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)). In neonates and children, vancomycin (15 mg/kg/dose every six to eight hours) is the usual empiric antibiotic for MRSA; the six-hour dosing interval is employed for sicker children.

**PLUS**

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[Clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link), for its antitoxin and other effects against toxin-elaborating strains of beta-hemolytic streptococci and *S. aureus* (600 to 900 mg intravenously [IV] every eight hours in adults; 40 mg/kg per day divided every eight hours in children and neonates) [[7,75-80](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/7,75-80)] (see ["Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention", section on 'General principles'](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-treatment-and-prevention?sectionName=General%20principles&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H15604631&source=see_link#H15604631)). For patients with NSTI due to beta-hemolytic streptococci or *S. aureus* that are resistant to clindamycin, [linezolid](https://www.uptodate.com/contents/linezolid-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) or [tedizolid](https://www.uptodate.com/contents/tedizolid-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) can be used (linezolid, adults and children ≥12 years: 600 mg IV every 12 hours; children <12 years of age: 10 mg/kg IV every eight hours [maximum 600 mg/dose]) or tedizolid (adults: 200 mg IV every 24 hours; not US Food and Drug Administration [FDA] approved for use in children). (See ["Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention", section on 'General principles'](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-treatment-and-prevention?sectionName=General%20principles&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H15604631&source=see_link#H15604631) and ["Staphylococcal toxic shock syndrome", section on 'Antibiotic therapy'](https://www.uptodate.com/contents/staphylococcal-toxic-shock-syndrome?sectionName=Antibiotic%20therapy&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H23&source=see_link#H23).)

For patients who have exposures that may suggest infections with specific organisms, such as trauma in fresh water (*Aeromonas*) or sea water (*V. vulnificus*), it is appropriate to ensure that empiric therapy includes antimicrobial agents with activity against such organisms. (See ["Aeromonas infections", section on 'Therapy'](https://www.uptodate.com/contents/aeromonas-infections?sectionName=THERAPY&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H14&source=see_link#H14) and ["Vibrio vulnificus infection", section on 'Treatment'](https://www.uptodate.com/contents/vibrio-vulnificus-infection?sectionName=TREATMENT&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H12&source=see_link#H12) and ["Soft tissue infections following water exposure"](https://www.uptodate.com/contents/soft-tissue-infections-following-water-exposure?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

Due to concerns for multidrug resistance among some Enterobacteriaceaeand lack of consistent availability, [ampicillin-sulbactam](https://www.uptodate.com/contents/ampicillin-and-sulbactam-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ticarcillin-clavulanate, respectively, are no longer recommended. Patients with hypersensitivity to carbapenems or [piperacillin-tazobactam](https://www.uptodate.com/contents/piperacillin-and-tazobactam-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) may be treated with either an aminoglycoside or a fluoroquinolone, plus [metronidazole](https://www.uptodate.com/contents/metronidazole-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).

Antibiotic treatment should be tailored to Gram stain, culture, and sensitivity results when available [[2,4](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/2,4)]:

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Group A streptococcal (GAS) or other beta-hemolytic streptococcal infection – Penicillin (4 million units IV every four hours in adults >60 kg with normal renal function or 300,000 units/kg per day divided every six hours in children) **plus** [clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (600 to 900 mg IV every eight hours in adults or 40 mg/kg per day divided every eight hours in neonates and children) [[7](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/7)].

Combination therapy with penicillin and [clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) should be continued until patients are clinically and hemodynamically stable for at least 48 to 72 hours; thereafter, penicillin monotherapy may be administered.

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Clostridial infection – Penicillin plus [clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (dosing as above). (See ["Clostridial myonecrosis"](https://www.uptodate.com/contents/clostridial-myonecrosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

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*Aeromonas hydrophila* – (See ["Aeromonas infections"](https://www.uptodate.com/contents/aeromonas-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

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*Vibrio vulnificus* – (See ["Vibrio vulnificus infection"](https://www.uptodate.com/contents/vibrio-vulnificus-infection?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

●

Polymicrobial infection – [Vancomycin](https://www.uptodate.com/contents/vancomycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) ([table 3](https://www.uptodate.com/contents/image?imageKey=ID%2F110072&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)) plus a beta-lactam-beta-lactamase inhibitor or a carbapenem.

Antibiotics should be continued until no further debridement is needed and the patient's hemodynamic status has normalized; this duration often consists of at least two weeks of treatment and must be tailored to individual patient circumstances [[81](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/81)].

**Hemodynamic support** — Hemodynamic instability may require aggressive supportive care with fluids and vasopressors. Intravenous fluid requirements may be high, and albumin replacement may be required in the setting of capillary leak syndrome associated with streptococcal toxic shock syndrome (TSS) [[1](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)]. (See ["Invasive group A streptococcal infection and toxic shock syndrome: Epidemiology, clinical manifestations, and diagnosis"](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-epidemiology-clinical-manifestations-and-diagnosis?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Evaluation and management of suspected sepsis and septic shock in adults"](https://www.uptodate.com/contents/evaluation-and-management-of-suspected-sepsis-and-septic-shock-in-adults?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**Intravenous immune globulin** — We favor administration of intravenous [immune globulin](https://www.uptodate.com/contents/immune-globulin-intravenous-subcutaneous-and-intramuscular-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (IVIG) for patients with NSTI in the setting of streptococcal TSS. This approach is supported by a 2018 meta-analysis including five studies of patients with streptococcal TSS treated with [clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (one randomized and four nonrandomized), in which use of IVIG was associated with a significant reduction in 30-day mortality (33.7 to 15.7 percent) [[82](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/82)]. Similarly, in a subsequent prospective observational study of patients with NSTI due to GAS, use of IVIG was associated with reduced 90-day mortality [[83](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/83)]. Prior data from retrospective studies and statistically underpowered prospective trials have been inconclusive on the efficacy of IVIG for NSTI [[84-86](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/84-86)]. The combination of clindamycin and IVIG is likely efficacious by reducing circulating toxins produced by GAS [[82](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/82)].

Issues related to use of [IVIG](https://www.uptodate.com/contents/immune-globulin-intravenous-subcutaneous-and-intramuscular-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) in the setting of streptococcal TSS are discussed separately. (See ["Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention", section on 'Intravenous immune globulin'](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-treatment-and-prevention?sectionName=Intravenous%20immune%20globulin&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H12&source=see_link#H12).)

**Perioperative care** — Issues related to perioperative care and use of hyperbaric oxygen are discussed separately. (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Hyperbaric oxygen therapy", section on 'Infection'](https://www.uptodate.com/contents/hyperbaric-oxygen-therapy?sectionName=Infection&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H15&source=see_link#H15).)

**PREVENTION**

Close contacts of a patient with necrotizing infection due to group A *Streptococcus* (GAS) can become colonized with a virulent strain [[87,88](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/87,88)]. The likelihood of a secondary case of necrotizing fasciitis or toxic shock syndrome is very low but higher than for the general population [[89,90](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/89,90)].

**Postexposure prophylaxis** — The role of postexposure prophylaxis in reducing the likelihood of a secondary GAS infection is uncertain [[91](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/91)]. We suggest prophylaxis for highly susceptible individuals (such as immunocompromised individuals or patients with recent surgery) who are close contacts of a patient with necrotizing infection due to GAS. We use penicillin (250 mg orally 4 times daily) for 10 days in such patients. Alternative regimens have been suggested [[92](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/92)], however, the optimal antibiotic prophylaxis remains undefined.

Regardless of whether a close contact receives postexposure prophylaxis or not, it is imperative that they be educated about the signs and symptoms of invasive GAS infections and to seek immediate medical care if these clinical features develop within 30 days of diagnosis in the index case.

Evidence supporting use of postexposure prophylaxis is limited due in part to the relative rarity of necrotizing GAS infection, and it has not been studied in prospective, randomized trials. Nevertheless, we favor this approach because of the potential severity of the infection.

Issues related to prophylaxis for contacts are discussed further separately. (See ["Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention", section on 'Prophylaxis for contacts'](https://www.uptodate.com/contents/invasive-group-a-streptococcal-infection-and-toxic-shock-syndrome-treatment-and-prevention?sectionName=Prophylaxis%20for%20contacts&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&anchor=H24997268&source=see_link#H24997268).)

**Infection control** — In addition to standard precautions, patients with invasive GAS infection associated with soft tissue involvement warrant droplet precautions and contact precautions [[93](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/93)]. Droplet and contact precautions may be discontinued after the first 24 hours of antimicrobial therapy.

**OUTCOME**

Necrotizing infection is associated with considerable mortality, even with optimal therapy [[83](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/83)]. Observational studies have reported the following mortality rates:

●

Polymicrobial (type I) necrotizing fasciitis – 21 percent [[15](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)]

•

Fournier gangrene – 22 to 40 percent [[44,45,94](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/44,45,94)]

•

Cervical necrotizing fasciitis – 22 percent [[47](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/47)]

•

Neonatal necrotizing fasciitis – 59 percent [[49](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/49)]

●

Monomicrobial (type II) necrotizing fasciitis – 14 to 34 percent [[6,20,21](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6,20,21)]

Factors associated with increased mortality include [[15,21,95,96](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15,21,95,96)]:

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White blood cell count >30,000/microL; band neutrophils >10 percent

●

Serum creatinine >2.0 mg/dL (177 mmol/L)

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Age >60 years

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Streptococcal toxic shock syndrome

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Clostridial infection

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Delay in surgery for more than 24 hours

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Infection involving the head, neck, thorax, or abdomen

**SOCIETY GUIDELINE LINKS**

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See ["Society guideline links: Skin and soft tissue infections"](https://www.uptodate.com/contents/society-guideline-links-skin-and-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

**INFORMATION FOR PATIENTS**

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

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Basics topic (see ["Patient education: Gangrene (The Basics)"](https://www.uptodate.com/contents/gangrene-the-basics?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link))

**SUMMARY AND RECOMMENDATIONS**

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**Definitions** – Necrotizing soft tissue infections (NSTIs) include necrotizing forms of fasciitis, myositis, and cellulitis. They may be categorized based on microbiology and presence or absence of gas in the tissues ([table 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116305&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

•

**Necrotizing fasciitis** – Necrotizing fasciitis is an infection of the deep soft tissues that results in progressive destruction of the muscle fascia and overlying subcutaneous fat. Infection may be polymicrobial (type I) or monomicrobial (type II) (see ['Necrotizing fasciitis'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H650406663) above):

-

Polymicrobial (type I) necrotizing infection is caused by aerobic and anaerobic bacteria. It usually occurs in older adults and/or in individuals with underlying comorbidities including diabetes.

-

Monomicrobial (type II) necrotizing infection is most commonly caused by group A *Streptococcus* (GAS)(and other beta-hemolytic streptococci). It may occur in any age group and in individuals with no underlying comorbidities.

•

**Necrotizing myositis** – Necrotizing myositis is a rare, serious infection of skeletal muscle typically caused by GAS(and other beta-hemolytic streptococci). (See ['Necrotizing myositis'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H1339346879) above.)

•

**Necrotizing cellulitis** – Necrotizing cellulitis is typically caused by anaerobic pathogens and may be divided into two types: clostridial (usually caused by *Clostridium perfringens*) and nonclostridial (caused by polymicrobial infection). Unlike necrotizing fasciitis and myositis, necrotizing cellulitis is a mild illness in the immunocompetent host. (See ['Necrotizing cellulitis'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H233742482) above.)

●

**Risk factors** – Risk factors associated with NSTI include skin or mucosal breach, traumatic wounds, and diabetes or other immunosuppressing conditions. (See ['Risk factors'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H3864839350) above.)

●

**Clinical manifestations** – Clinical manifestations of NSTI include erythema, edema extending beyond the visible erythema, severe pain (out of proportion to exam findings in some cases), fever, crepitus, and skin bullae, necrosis, or ecchymosis. Systemic toxicity may be observed. Necrotizing infection most commonly involves the extremities (lower extremity more commonly than upper extremity) and usually presents acutely. Other presentations of necrotizing fasciitis include involvement of the perineum (Fournier gangrene), head and neck region, and neonatal infection. (See ['Clinical manifestations'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2371333042) above.)

●

**Diagnosis** – NSTI should be suspected in patients with soft tissue infection (erythema, edema, warmth) and signs of systemic illness (fever, hemodynamic instability) in association with crepitus, rapid progression of clinical manifestations, and/or severe pain (out of proportion to skin findings in some cases) ([algorithm 1](https://www.uptodate.com/contents/image?imageKey=ID%2F116424&topicKey=ID%2F7662&search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&rank=1%7E116&source=see_link)).

•

**Definitive diagnosis** – The diagnosis of NSTI is established via surgical exploration of the soft tissues in the operating room, with physical examination of the skin, subcutaneous tissue, fascial planes, and muscle. (See ['Diagnosis'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2611694952) above.)

•

**Role of imaging** – Radiographic imaging studies can be useful to help determine whether necrotizing infection is present **but should not delay surgical intervention** when there is crepitus on examination or rapid progression of clinical manifestations. The best initial radiographic imaging exam is computed tomography scan. Presence of gas in the tissues (seen most frequently in the setting of polymicrobial [type I] necrotizing fasciitis or clostridial infection) is highly specific for NSTI and should prompt immediate surgical intervention. (See ['Radiographic imaging'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H1770115080) above.)

●

**Treatment** – Treatment of necrotizing infection consists of early and aggressive surgical exploration and debridement of necrotic tissue, together with broad-spectrum empiric antibiotic therapy and hemodynamic support. (See ['Treatment'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H22) above.)

In general, empiric antibiotic treatment of necrotizing infection should consist of broad-spectrum antimicrobial therapy, including activity against gram-positive, gram-negative, and anaerobic organisms. Acceptable empiric antibiotic regimens include the following (see ['Antibiotic therapy'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H24) above):

•

A carbapenem or [piperacillin-tazobactam](https://www.uptodate.com/contents/piperacillin-and-tazobactam-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) **plus**

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An agent with activity against methicillin-resistant *Staphylococcus aureus* **plus**

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[Clindamycin](https://www.uptodate.com/contents/clindamycin-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) (for its antitoxin effects against toxin-elaborating strains of beta-hemolytic streptococci and *S. aureus*)

Antibiotic treatment should be tailored to Gram stain, culture, and sensitivity results when available.

For patients with NSTI and toxic shock syndrome due to beta-hemolytic streptococci, we suggest adding intravenous [immune globulin](https://www.uptodate.com/contents/immune-globulin-intravenous-subcutaneous-and-intramuscular-drug-information?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) ([**Grade 2C**](https://www.uptodate.com/contents/grade/6?title=Grade%202C&topicKey=ID%2F7662)). (See ['Intravenous immune globulin'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H2540005751) above.)

Issues related to surgical management of NSTI and hemodynamic support are discussed separately (See ["Surgical management of necrotizing soft tissue infections"](https://www.uptodate.com/contents/surgical-management-of-necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link) and ["Evaluation and management of suspected sepsis and septic shock in adults"](https://www.uptodate.com/contents/evaluation-and-management-of-suspected-sepsis-and-septic-shock-in-adults?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&topicRef=7662&source=see_link).)

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**Management of close contacts** – For highly susceptible individuals (such as immunocompromised individuals or patients with recent surgery) who are close contacts of a patient with necrotizing infection due to GAS, we suggest postexposure prophylaxis with oral penicillin ([**Grade 2C**](https://www.uptodate.com/contents/grade/6?title=Grade%202C&topicKey=ID%2F7662)). (See ['Prevention'](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections?search=%E5%A3%8A%E6%AD%BB%E6%80%A7%E7%AD%8B%E8%86%9C%E7%82%8E&source=search_result&selectedTitle=1~116&usage_type=default&display_rank=1#H3795999502) above.)

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REFERENCES

1. [Stevens DL, Bryant AE. Necrotizing Soft-Tissue Infections. N Engl J Med 2017; 377:2253.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/1)
2. [Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin Infect Dis 2014; 59:147.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/2)
3. [Bonne SL, Kadri SS. Evaluation and Management of Necrotizing Soft Tissue Infections. Infect Dis Clin North Am 2017; 31:497.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/3)
4. [Hua C, Urbina T, Bosc R, et al. Necrotising soft-tissue infections. Lancet Infect Dis 2023; 23:e81.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/4)
5. [Jahnson L, Berggren L, Björsell-Ostling E, et al. Streptococcal myositis. Scand J Infect Dis 1992; 24:661.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/5)
6. [Stevens DL, Tanner MH, Winship J, et al. Severe group A streptococcal infections associated with a toxic shock-like syndrome and scarlet fever toxin A. N Engl J Med 1989; 321:1.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/6)
7. [Stevens DL. Streptococcal toxic-shock syndrome: spectrum of disease, pathogenesis, and new concepts in treatment. Emerg Infect Dis 1995; 1:69.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/7)
8. [Gozal D, Ziser A, Shupak A, et al. Necrotizing fasciitis. Arch Surg 1986; 121:233.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/8)
9. Schwartz MN, Pasternack MS. Cellulitis, necrotizing fasciitis and subcutaneous tissue infections. In: Principles and Practice of Infectious Diseases, 9th ed, Bennett JE, Dolin R, Blaser MJ (Eds), Elsevier, Philadelphia 2005. p.1282.
10. [McLellan E, Suvarna K, Townsend R. Fatal necrotizing fasciitis caused by Haemophilus influenzae serotype f. J Med Microbiol 2008; 57:249.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/10)
11. [Resman F, Svensjö T, Ünal C, et al. Necrotizing myositis and septic shock caused by Haemophilus influenzae type f in a previously healthy man diagnosed with an IgG3 and a mannose-binding lectin deficiency. Scand J Infect Dis 2011; 43:972.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/11)
12. [Stumvoll M, Fritsche A. Necrotizing fasciitis caused by unencapsulated Haemophilus influenzae. Clin Infect Dis 1997; 25:327.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/12)
13. [Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. Clin Infect Dis 2007; 44:705.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/13)
14. [Brook I, Frazier EH. Clinical and microbiological features of necrotizing fasciitis. J Clin Microbiol 1995; 33:2382.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/14)
15. [Wong CH, Chang HC, Pasupathy S, et al. Necrotizing fasciitis: clinical presentation, microbiology, and determinants of mortality. J Bone Joint Surg Am 2003; 85-A:1454.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/15)
16. [Horn CB, Wesp BM, Fiore NB, et al. Fungal Infections Increase the Mortality Rate Three-Fold in Necrotizing Soft-Tissue Infections. Surg Infect (Larchmt) 2017; 18:793.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/16)
17. [Eke N. Fournier's gangrene: a review of 1726 cases. Br J Surg 2000; 87:718.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/17)
18. [Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles. N Engl J Med 2005; 352:1445.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/18)
19. [Bisno AL, Stevens DL. Streptococcal infections of skin and soft tissues. N Engl J Med 1996; 334:240.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/19)
20. [Kaul R, McGeer A, Low DE, et al. Population-based surveillance for group A streptococcal necrotizing fasciitis: Clinical features, prognostic indicators, and microbiologic analysis of seventy-seven cases. Ontario Group A Streptococcal Study. Am J Med 1997; 103:18.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/20)
21. [Darenberg J, Luca-Harari B, Jasir A, et al. Molecular and clinical characteristics of invasive group A streptococcal infection in Sweden. Clin Infect Dis 2007; 45:450.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/21)
22. [Chelsom J, Halstensen A, Haga T, Høiby EA. Necrotising fasciitis due to group A streptococci in western Norway: incidence and clinical features. Lancet 1994; 344:1111.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/22)
23. [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.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/23)
24. [Stevens DL, Bryant AE, Hackett SP, et al. Group A streptococcal bacteremia: the role of tumor necrosis factor in shock and organ failure. J Infect Dis 1996; 173:619.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/24)
25. [Hau V, Ho CO. Necrotising fasciitis caused by Vibrio vulnificus in the lower limb following exposure to seafood on the hand. Hong Kong Med J 2011; 17:335.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/25)
26. [Das DK, Baker MG, Venugopal K. Increasing incidence of necrotizing fasciitis in New Zealand: a nationwide study over the period 1990 to 2006. J Infect 2011; 63:429.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/26)
27. [O'Loughlin RE, Roberson A, Cieslak PR, et al. The epidemiology of invasive group A streptococcal infection and potential vaccine implications: United States, 2000-2004. Clin Infect Dis 2007; 45:853.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/27)
28. [Adams EM, Gudmundsson S, Yocum DE, et al. Streptococcal myositis. Arch Intern Med 1985; 145:1020.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/28)
29. [Svane S. Peracute spontaneous streptococcal myositis. A report on 2 fatal cases with review of literature. Acta Chir Scand 1971; 137:155.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/29)
30. [Yoder EL, Mendez J, Khatib R. Spontaneous gangrenous myositis induced by Streptococcus pyogenes: case report and review of the literature. Rev Infect Dis 1987; 9:382.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/30)
31. [Mac Laurin JP. Spontaneous streptococcal myositis associated with disseminated intravascular coagulopathy. J Am Osteopath Assoc 1977; 76:675.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/31)
32. [Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition. The Working Group on Severe Streptococcal Infections. JAMA 1993; 269:390.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/32)
33. [Hasham S, Matteucci P, Stanley PR, Hart NB. Necrotising fasciitis. BMJ 2005; 330:830.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/33)
34. [Eneli I, Davies HD. Epidemiology and outcome of necrotizing fasciitis in children: an active surveillance study of the Canadian Paediatric Surveillance Program. J Pediatr 2007; 151:79.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/34)
35. [Aebi C, Ahmed A, Ramilo O. Bacterial complications of primary varicella in children. Clin Infect Dis 1996; 23:698.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/35)
36. [Beaudoin AL, Torso L, Richards K, et al. Invasive group A Streptococcus infections associated with liposuction surgery at outpatient facilities not subject to state or federal regulation. JAMA Intern Med 2014; 174:1136.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/36)
37. [Gupta Y, Chhetry M, Pathak KR, et al. Risk Factors For Necrotizing Fasciitis And Its Outcome At A Tertiary Care Centre. J Ayub Med Coll Abbottabad 2016; 28:680.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/37)
38. US Food and Drug Administration. FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes. https://www.fda.gov/downloads/Drugs/DrugSafety/UCM618466.pdf (Accessed on October 05, 2018).
39. [Stevens DL. Could nonsteroidal antiinflammatory drugs (NSAIDs) enhance the progression of bacterial infections to toxic shock syndrome? Clin Infect Dis 1995; 21:977.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/39)
40. [Bouza E, Bernaldo de Quirós JC, Rodríguez Créixems M, Quintans A. Fulminant myonecrosis due to Streptococcus pyogenes in a previously healthy patient. Eur J Clin Microbiol Infect Dis 1988; 7:205.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/40)
41. [Aronoff DM, Bloch KC. Assessing the relationship between the use of nonsteroidal antiinflammatory drugs and necrotizing fasciitis caused by group A streptococcus. Medicine (Baltimore) 2003; 82:225.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/41)
42. [Sudarsky LA, Laschinger JC, Coppa GF, Spencer FC. Improved results from a standardized approach in treating patients with necrotizing fasciitis. Ann Surg 1987; 206:661.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/42)
43. [McHenry CR, Piotrowski JJ, Petrinic D, Malangoni MA. Determinants of mortality for necrotizing soft-tissue infections. Ann Surg 1995; 221:558.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/43)
44. [Laucks SS 2nd. Fournier's gangrene. Surg Clin North Am 1994; 74:1339.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/44)
45. [Stephens BJ, Lathrop JC, Rice WT, Gruenberg JC. Fournier's gangrene: historic (1764-1978) versus contemporary (1979-1988) differences in etiology and clinical importance. Am Surg 1993; 59:149.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/45)
46. [Gunaratne DA, Tseros EA, Hasan Z, et al. Cervical necrotizing fasciitis: Systematic review and analysis of 1235 reported cases from the literature. Head Neck 2018; 40:2094.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/46)
47. [Mathieu D, Neviere R, Teillon C, et al. Cervical necrotizing fasciitis: clinical manifestations and management. Clin Infect Dis 1995; 21:51.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/47)
48. [Petitpas F, Blancal JP, Mateo J, et al. Factors associated with the mediastinal spread of cervical necrotizing fasciitis. Ann Thorac Surg 2012; 93:234.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/48)
49. [Hsieh WS, Yang PH, Chao HC, Lai JY. Neonatal necrotizing fasciitis: a report of three cases and review of the literature. Pediatrics 1999; 103:e53.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/49)
50. [Jamal N, Teach SJ. Necrotizing fasciitis. Pediatr Emerg Care 2011; 27:1195.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/50)
51. [Walls T, Williams G, Adams S, et al. Neonatal necrotising fasciitis following superficial skin infection with community-associated methicillin-resistant Staphylococcus aureus. J Paediatr Child Health 2011; 47:918.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/51)
52. [Zundel S, Lemaréchal A, Kaiser P, Szavay P. Diagnosis and Treatment of Pediatric Necrotizing Fasciitis: A Systematic Review of the Literature. Eur J Pediatr Surg 2017; 27:127.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/52)
53. [Totapally BR. Epidemiology and Outcomes of Hospitalized Children With Necrotizing Soft-Tissue Infections. Pediatr Infect Dis J 2017; 36:641.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/53)
54. [Simonart T, Simonart JM, Derdelinckx I, et al. Value of standard laboratory tests for the early recognition of group A beta-hemolytic streptococcal necrotizing fasciitis. Clin Infect Dis 2001; 32:E9.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/54)
55. [Yaghoubian A, de Virgilio C, Dauphine C, et al. Use of admission serum lactate and sodium levels to predict mortality in necrotizing soft-tissue infections. Arch Surg 2007; 142:840.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/55)
56. [Butterworth SA, Murphy JJ. Necrotizing soft tissue infections--are they different in healthy vs immunocompromised children? J Pediatr Surg 2006; 41:935.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/56)
57. [Wall DB, Klein SR, Black S, de Virgilio C. A simple model to help distinguish necrotizing fasciitis from nonnecrotizing soft tissue infection. J Am Coll Surg 2000; 191:227.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/57)
58. [Wong CH, Khin LW, Heng KS, et al. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med 2004; 32:1535.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/58)
59. [Wu PH, Wu KH, Hsiao CT, et al. Utility of modified Laboratory Risk Indicator for Necrotizing Fasciitis (MLRINEC) score in distinguishing necrotizing from non-necrotizing soft tissue infections. World J Emerg Surg 2021; 16:26.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/59)
60. [Wilson MP, Schneir AB. A case of necrotizing fasciitis with a LRINEC score of zero: clinical suspicion should trump scoring systems. J Emerg Med 2013; 44:928.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/60)
61. [Holland MJ. Application of the Laboratory Risk Indicator in Necrotising Fasciitis (LRINEC) score to patients in a tropical tertiary referral centre. Anaesth Intensive Care 2009; 37:588.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/61)
62. [Fernando SM, Tran A, Cheng W, et al. Necrotizing Soft Tissue Infection: Diagnostic Accuracy of Physical Examination, Imaging, and LRINEC Score: A Systematic Review and Meta-Analysis. Ann Surg 2019; 269:58.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/62)
63. [Bisarya K, Azzopardi S, Lye G, Drew PJ. Necrotizing fasciitis versus pyoderma gangrenosum: securing the correct diagnosis! A case report and literature review. Eplasty 2011; 11:e24.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/63)
64. [Bucca K, Spencer R, Orford N, et al. Early diagnosis and treatment of necrotizing fasciitis can improve survival: an observational intensive care unit cohort study. ANZ J Surg 2013; 83:365.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/64)
65. [Hadeed GJ, Smith J, O'Keeffe T, et al. Early surgical intervention and its impact on patients presenting with necrotizing soft tissue infections: A single academic center experience. J Emerg Trauma Shock 2016; 9:22.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/65)
66. [Bakleh M, Wold LE, Mandrekar JN, et al. Correlation of histopathologic findings with clinical outcome in necrotizing fasciitis. Clin Infect Dis 2005; 40:410.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/66)
67. [Zacharias N, Velmahos GC, Salama A, et al. Diagnosis of necrotizing soft tissue infections by computed tomography. Arch Surg 2010; 145:452.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/67)
68. [Becker M, Zbären P, Hermans R, et al. Necrotizing fasciitis of the head and neck: role of CT in diagnosis and management. Radiology 1997; 202:471.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/68)
69. [Bruls RJM, Kwee RM. CT in necrotizing soft tissue infection: diagnostic criteria and comparison with LRINEC score. Eur Radiol 2021; 31:8536.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/69)
70. [Schmid MR, Kossmann T, Duewell S. Differentiation of necrotizing fasciitis and cellulitis using MR imaging. AJR Am J Roentgenol 1998; 170:615.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/70)
71. [Berger N, Ebenhoch M, Salzmann M. Postoperative Pyoderma Gangrenosum in Children: The Case Report of a 13-Year-Old Boy With Pyoderma Gangrenosum After Hip Reconstruction Surgery and a Review of the Literature. J Pediatr Orthop 2017; 37:e379.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/71)
72. [Touil LL, Gurusinghe DA, Sadri A, et al. Postsurgical Pyoderma Gangrenosum Versus Necrotizing Fasciitis: Can We Spot the Difference? Ann Plast Surg 2017; 78:582.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/72)
73. [Hradil E, Jeppsson C, Hamnerius N, Svensson Å. The diagnosis you wish you had never operated on: Pyoderma gangrenosum misdiagnosed as necrotizing fasciitis-a case report. Acta Orthop 2017; 88:231.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/73)
74. [Karimi K, Odhav A, Kollipara R, et al. Acute Cutaneous Necrosis: A Guide to Early Diagnosis and Treatment. J Cutan Med Surg 2017; 21:425.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/74)
75. [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.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/75)
76. [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.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/76)
77. [Stevens DL, Yan S, Bryant AE. Penicillin-binding protein expression at different growth stages determines penicillin efficacy in vitro and in vivo: an explanation for the inoculum effect. J Infect Dis 1993; 167:1401.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/77)
78. [Stevens DL, Bryant AE, Yan S. Invasive group A streptococcal infection: New concepts in antibiotic treatment. Int J Antimicrob Agents 1994; 4:297.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/78)
79. [Zimbelman J, Palmer A, Todd J. Improved outcome of clindamycin compared with beta-lactam antibiotic treatment for invasive Streptococcus pyogenes infection. Pediatr Infect Dis J 1999; 18:1096.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/79)
80. [Stevens DL, Bryant AE, Hackett SP. Antibiotic effects on bacterial viability, toxin production, and host response. Clin Infect Dis 1995; 20 Suppl 2:S154.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/80)
81. [Lauerman MH, Kolesnik O, Sethuraman K, et al. Less is more? Antibiotic duration and outcomes in Fournier's gangrene. J Trauma Acute Care Surg 2017; 83:443.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/81)
82. [Parks T, Wilson C, Curtis N, et al. Polyspecific Intravenous Immunoglobulin in Clindamycin-treated Patients With Streptococcal Toxic Shock Syndrome: A Systematic Review and Meta-analysis. Clin Infect Dis 2018; 67:1434.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/82)
83. [Bruun T, Rath E, Madsen MB, et al. Risk Factors and Predictors of Mortality in Streptococcal Necrotizing Soft-tissue Infections: A Multicenter Prospective Study. Clin Infect Dis 2021; 72:293.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/83)
84. [Madsen MB, Hjortrup PB, Hansen MB, et al. Immunoglobulin G for patients with necrotising soft tissue infection (INSTINCT): a randomised, blinded, placebo-controlled trial. Intensive Care Med 2017; 43:1585.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/84)
85. [Kadri SS, Swihart BJ, Bonne SL, et al. Impact of Intravenous Immunoglobulin on Survival in Necrotizing Fasciitis With Vasopressor-Dependent Shock: A Propensity Score-Matched Analysis From 130 US Hospitals. Clin Infect Dis 2017; 64:877.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/85)
86. [Darenberg J, Ihendyane N, Sjölin J, et al. Intravenous immunoglobulin G therapy in streptococcal toxic shock syndrome: a European randomized, double-blind, placebo-controlled trial. Clin Infect Dis 2003; 37:333.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/86)
87. [Davies HD, McGeer A, Schwartz B, et al. Invasive group A streptococcal infections in Ontario, Canada. Ontario Group A Streptococcal Study Group. N Engl J Med 1996; 335:547.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/87)
88. [Kakis A, Gibbs L, Eguia J, et al. An outbreak of group A Streptococcal infection among health care workers. Clin Infect Dis 2002; 35:1353.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/88)
89. [Prevention of Invasive Group A Streptococcal Infections Workshop Participants. Prevention of invasive group A streptococcal disease among household contacts of case patients and among postpartum and postsurgical patients: recommendations from the Centers for Disease Control and Prevention. Clin Infect Dis 2002; 35:950.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/89)
90. [Carapetis JR, Jacoby P, Carville K, et al. Effectiveness of clindamycin and intravenous immunoglobulin, and risk of disease in contacts, in invasive group a streptococcal infections. Clin Infect Dis 2014; 59:358.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/90)
91. [Sablier F, Slaouti T, Drèze PA, et al. Nosocomial transmission of necrotising fasciitis. Lancet 2010; 375:1052.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/91)
92. [Moore DL, Allen UD, Mailman T. Invasive group A streptococcal disease: Management and chemoprophylaxis. Paediatr Child Health 2019; 24:128.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/92)
93. [Siegel JD, Rhinehart E, Jackson M, et al. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Health Care Settings. Am J Infect Control 2007; 35:S65.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/93)
94. [Yeniyol CO, Suelozgen T, Arslan M, Ayder AR. Fournier's gangrene: experience with 25 patients and use of Fournier's gangrene severity index score. Urology 2004; 64:218.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/94)
95. [Anaya DA, McMahon K, Nathens AB, et al. Predictors of mortality and limb loss in necrotizing soft tissue infections. Arch Surg 2005; 140:151.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/95)
96. [Huang KF, Hung MH, Lin YS, et al. Independent predictors of mortality for necrotizing fasciitis: a retrospective analysis in a single institution. J Trauma 2011; 71:467.](https://www.uptodate.com/contents/necrotizing-soft-tissue-infections/abstract/96)

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