Infectious Etiologies of Rhabdomyolysis: Three Case Reports and Review

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Rhabdomyolysis can be precipitated by trauma, ischemia, metabolic defects, electrolyte abnormalities, drugs, and a wide variety of infectious diseases. At our institution, recent cases of rhabdomyolysis induced by influenza prompted us to review the infectious etiologies of this entity. In addition, a thorough literature search revealed numerous case reports but no general review on this subject. This study describes representative recent cases from our institution and details the wide variety of infections that can cause muscle damage. The pathophysiological mechanisms, muscle histology, and correlation with renal dysfunction are also discussed.

Materials and Methods

A retrospective chart review of inpatients treated at the University of Virginia Health Sciences Center (Charlottesville) since 1988 was conducted on the basis of discharge diagnosis codes. Patients with hypotension (systolic blood pressure, < 90 mm Hg), severe acidosis (serum pH, < 7.15), electrolyte imbalances (potassium level, < 2.5 mEq/L; or phosphorus level, < 1.5 mEq/L), drug ingestion, or other known precipitants of rhabdomyolysis were excluded from our analysis.

We did a thorough search of the literature from 1966 via MEDLINE with use of the terms rhabdomyolysis and myoglobinuria. References in primary articles that pertained to our topic were also used in the analysis. Only English-language articles were reviewed in detail; information from these articles was utilized to create tables 1, 2, and 3. Pertinent demographics (e.g., patient age, peak CPK level, and renal function) were extracted from the reported cases, where available.

Case Reports

Case 1

A 68-year-old woman presented to our center on 4 September 1988 because of respiratory failure. One week before admission she had had anorexia, malaise, cough productive of white sputum, and shortness of breath. She had a history of smoking (100 packs per year) but denied a history of diabetes mellitus, hypertension, coronary artery disease, or renal insufficiency; she was not receiving any medications.

Her temperature was 37.6°C, systolic blood pressure was 90 mm Hg, respiratory rate was 44, and pulse rate was 130. Physical examination revealed decreased breath sounds on the right and bilateral rales. Laboratory studies disclosed the following significant data: serum sodium, 136 mEq/L; potassium, 5.7 mEq/L; chloride, 110 mEq/L; bicarbonate, 19 mEq/L; blood urea nitrogen (BUN), 46 mg/dL; creatinine, 5.6 mg/dL; WBCs, 9,200/μL; hematocrit, 51.2%; platelets, 144,000/μL; CPK, 6,538 U/L; lactate dehydrogenase (LDH), 1,705 U/L; aspartate aminotransferase (AST), 280 U/L; alanine aminotransferase (ALT), 44 U/L; alkaline phosphatase (ALP), 19 U/L; prothrombin time, 13.3 seconds; and partial thromboplastin time, 44.6 seconds. An arterial blood gas determination while the patient was breathing 50% FIO₂ revealed a pH of 7.18, Pco₂ of 47, and Po₂ of 60. The urine was positive for myoglobin, and a chest radiograph showed multilobar infiltrates on the right with a possible right hilar mass. Gram staining of a sputum specimen...
demonstrated more than three polymorphonuclear cells and more than three gram-positive cocci.

The patient was intubated, and empirical therapy with broad-spectrum antibiotics (ticarcillin/clavulanic acid, erythromycin, and clindamycin) was started for presumed sepsis secondary to post-obstructive pneumonia. She required therapeutic support with pressor agents, and her condition deteriorated rapidly with the development of anuric renal failure, disseminated intravascular coagulation, abdominal distension with ileus, and possible mesenteric ischemia. In concordance with the wishes of her family, further aggressive care was not pursued, and she died the day after admission.

Subsequently, sputum and blood cultures (one of two bottles on day 2) became positive for Streptococcus pneumoniae and Clostridium perfringens, respectively.

Case 2

A 57-year-old woman with a medical history of insulin-dependent diabetes mellitus and mild chronic renal insufficiency presented to our center with a chief complaint of shortness of breath. Five days before admission she had had a cough, shortness of breath, fatigue, myalgias, nausea, and vomiting. Her medications included insulin, acetaminophen, and furosemide.

Physical examination revealed a temperature of 36.7°C, blood pressure of 133/99 mm Hg, pulse rate of 104, and respiratory rate of 40. Tachypnea with paradoxical abdominal movement was noted with respiration, and she had bilateral rales. Laboratory studies disclosed the following significant data: serum sodium, 142 mEq/L; potassium, 6.7 mEq/L; chloride, 114 mEq/L; bicarbonate, 23 mEq/L; BUN, 60 mg/dL; creatinine, 4.7 mg/dL; glucose, 173 mg/dL; WBCs, 14,200/μL; hematocrit, 25%; platelets, 347,000/μL; lactic acid, 0.9 mmol/L; AST, 146 U/L; ALT, 60 U/L; ALP, 169 U/L; LDH, 459 U/L; and CPK, 1,263 U/L. The chest radiograph revealed bilateral pulmonary infiltrates. The initial arterial blood gas determination while the patient was breathing 4 L of oxygen was remarkable for a pH of 7.20, PaO2 of 47, and PaCO2 of 65.

The patient was intubated, and empirical antibiotic therapy with cefuroxime and erythromycin was started after appropriate culture was performed. A renal ultrasonogram and a cardiac echocardiogram were unremarkable. Nasopharyngeal cultures became positive for influenza virus type A H3N2. The patient subsequently had renal failure requiring hemodialysis, disseminated intravascular coagulation, and unstable ventricular arrhythmias. In compliance with the wishes of his family, no further intervention measures were taken, and he died. An autopsy was not performed.

Case 3

A 74-year-old man with a history of metastatic prostate cancer, inferior myocardial infarction, and chronic obstructive pulmonary disease presented to another institution because of a 3-day history of shortness of breath, cough, myalgias, and fever. His wife had recently had a "flu-like" illness.

At the time of admission, his CPK level was 1,365 U/L, and his LDH level was 1,150 U/L; arterial blood gas determination at this time revealed a pH of 7.25, PaCO2 of 40, and PaO2 of 92. Gram staining of sputum demonstrated more than two gram-positive cocci in clusters, and empirical therapy with intravenous cefotaxime and erythromycin was started. Upon transfer to our center, physical examination showed vital signs of blood pressure of 120/70 mm Hg, pulse rate of 110, and respiratory rate of 16 and bilateral rales. Laboratory studies disclosed the following significant data: serum sodium, 145 mEq/L; potassium, 4.5 mEq/L; chloride, 96 mEq/L; bicarbonate, 32 mEq/L; BUN, 93 mg/dL; creatinine, 7.9 mg/dL; WBCs, 10,500/μL; hematocrit, 32%; platelets, 204,000/μL; AST, 3,605 U/L; ALT, 2,246 U/L; ALP, 186 U/L; LDH, 10,885 U/L; and CPK, 3,324 U/L. The chest radiograph revealed bilateral lower-lobe infiltrates.

He was admitted to the medical intensive care unit, and therapy with cefotaxime, erythromycin, and metronidazole was started. Blood cultures became positive for Pseudomonas species, and nasopharyngeal cultures became positive for influenza virus type A H3N2. The patient subsequently had renal failure requiring hemodialysis, disseminated intravascular coagulation, and unstable ventricular arrhythmias. In compliance with the wishes of his family, no further intervention measures were taken, and he died. An autopsy was not performed.

Literature Review and Discussion

Viral Infections

Table 1 [2–69] lists the spectrum of viral infections that have been reported to cause rhabdomyolysis. Influenza is the most common viral etiology followed by HIV infection and enteroviral infection. The presenting symptoms in the patients whose cases are reported in table 1 included myalgias, weakness, muscle tenderness, and edema. A review of viral causes of rhabdomyolysis by Tanaka et al. [61] in 1989 revealed a similar preponderance of influenza virus infections; 42 cases of virus-induced rhabdomyolysis were documented in the English-language and Japanese-language literature, and influenza accounted for 14 (33%) of 42 of these reported cases.

In our review of the literature, influenza virus was the etiologic agent in 25 (42%) of 59 cases associated with a viral infection. For each period (1966–1975, 1976–1983, 1984–1988, and 1989 to present) studied in the MEDLINE search of the literature, influenza was repeatedly one of the most common infectious precipitants of rhabdomyolysis with the exception of 1984–1988, during which surprisingly few cases
were reported. Although these time categories are arbitrary, the continued preponderance of influenza virus infections causing rhabdomyolysis is significant. From 1984 to 1988 a decrease in reported cases may have been secondary to improved preventive public health measures, such as successful large-scale vaccinations or increasing physician familiarity with the association of influenza with rhabdomyolysis. Annual global epidemics, physician vigilance, and ease of diagnosis probably all contribute to the reported predominance of this agent.

Although the precise pathophysiology underlying virus-induced myoglobinuria is unknown, two mechanisms have been postulated: direct viral invasion and toxin generation. Some authors have suggested that direct viral invasion of muscle fibers causes muscle necrosis. In 1977 Frankova et al. [14] were able to demonstrate influenza virus type A by tissue culture of specimens of the trachea, lung, liver, spleen, pancreas, and brains from patients who died of influenza virus type A infections, but no isolates were obtained from muscle. However, in 1978 Armstrong et al. [2] did show that human skeletal muscle cells in tissue culture were susceptible to influenza virus infection, and, in fact, infectious progeny were produced. Muscle biopsies of patients with rhabdomyolysis that have shown a lymphocytic infiltrate [13, 21, 42, 52, 63] support the hypothesis of direct viral invasion. More compelling evidence is present in some cases: muscle biopsies of affected individuals have revealed viral inclusions, and, recently, DNA from varicella-zoster virus was identified by PCR analysis of muscle specimens from patients with rhabdomyolysis [69]. In 1977 Fukuyama et al. [50] found picornavirus-like crystals by electron microscopy (EM) of muscle fiber samples from an 11-month-old girl thought to be infected with Coxsackie B6 virus. Porter et al. [52] described a 67-year-old man with concomitant infection with Streptococcus pyogenes and picornavirus; both viral particles and S. pyogenes were seen within muscle biopsy specimens. Greco et al. [16] documented myxovirus-like particles by EM of a muscle specimen from a patient with myositis secondary to influenza. However, viral particles are occasionally difficult to differentiate from glycogen by EM; therefore, there is some doubt about these observations.

Influenza virus was subsequently demonstrated by hemagglutination and by direct EM of cultured specimens of the liver, CSF, and muscle from a patient with Reye's syndrome [25]. In 1979 Gamboa et al. [15] definitively documented influenza virus in a skeletal muscle specimen from a patient with influenza virus infection. Light microscopy revealed necrotic muscle fibers in large clusters surrounded by morphologically normal appearing muscle. Influenza virus type B was isolated from homogenized muscle by cell culture techniques. Cytopathic changes consisting of granularity and vacuolization of the cytoplasm, retraction, and rounding of cell processes with swelling of the cell body occurred in the infected cell lines. Viral presence was confirmed by immunofluorescence and EM. Subsequently, Kessler et al. [31] also cultured influenza virus type A from a muscle specimen from a 72-year-old man with virus-induced rhabdomyolysis. Recently, Poels et al. [57] reported isolation of echovirus 6 in a tissue culture of the muscle specimen from a patient with simultaneous infection with Epstein-Barr virus and echovirus.

This evidence strongly suggests that direct viral invasion may have a causative role in precipitating rhabdomyolysis. Various reports documenting normal results of muscle biopsies or hyaline degeneration and myonecrosis but no viral particles by immunofluorescence [56] and EM [66] are used to refute this theory. Biopsies of clinically affected musculature that are essentially unremarkable raise the possibility of a circulating “toxin” or cytokine causing rhabdomyolysis. However, to date no putative toxins have been isolated in cases of virus-induced rhabdomyolysis.

We believe that HIV-associated rhabdomyolysis deserves special mention as it adds to the spectrum of clinical presentations of HIV infection. A variety of musculoskeletal syndromes associated with HIV infection have been documented [37],

### Table 1. Viral causes of rhabdomyolysis.

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of cases reported</th>
<th>Age range</th>
<th>Range of CPK levels (U/L)</th>
<th>No. with ARF/total no. (%)</th>
<th>No. of deaths/total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>8</td>
<td>18–29 y</td>
<td>2,359–398,000</td>
<td>0/8</td>
<td>0/8</td>
</tr>
<tr>
<td>Coxsackie virus</td>
<td>8</td>
<td>11 mo to 67 y</td>
<td>8,500–600,900</td>
<td>4/8 (50)</td>
<td>2/8 (25)</td>
</tr>
<tr>
<td>Epstein-Barr virus</td>
<td>5</td>
<td>6–23 y</td>
<td>4,500–482,000</td>
<td>1/5 (20)</td>
<td>0/5</td>
</tr>
<tr>
<td>Echovirus</td>
<td>4</td>
<td>17–30 y</td>
<td>19,600–890,000</td>
<td>1/4 (25)</td>
<td>0/4</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>2</td>
<td>21–27 y</td>
<td>4,800–74,850</td>
<td>1/2 (50)</td>
<td>0/2</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>2</td>
<td>20–46 y</td>
<td>57,800–133,000</td>
<td>0/2</td>
<td>0/2</td>
</tr>
<tr>
<td>Herpes simplex virus</td>
<td>1</td>
<td>20 y</td>
<td>126,600</td>
<td>1/1 (100)</td>
<td>0/1</td>
</tr>
<tr>
<td>Parainfluenza virus</td>
<td>1</td>
<td>38 y</td>
<td>66,000</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td>Varicella-zoster virus</td>
<td>3</td>
<td>15–22 y</td>
<td>84,000–1,977,600</td>
<td>1/3 (33)</td>
<td>0/3</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
<td></td>
<td></td>
<td>20/59 (34)</td>
<td>5/59 (8)</td>
</tr>
</tbody>
</table>

**NOTE.** ARF = acute renal failure; CPK = creatine phosphokinase.

* Three series with 10, 17, and 14 patients, respectively, were not included because of lack of clinical data.
ranging from myopathy to polymyositis [36] to rhabdomyolysis. Mahe et al. [41] and del Rio et al. [35] described patients in whom rhabdomyolysis developed in association with acute HIV infection and antigenemia. Clinical symptoms such as malaise and myalgias were present in these patients, similar to patients with primary viral infections with Epstein-Barr virus and cytomegalovirus. Other cases of myoglobinuria in patients with HIV infection have also been documented [32, 39, 40, 42, 45, 46].

Dalakas et al. [34] reported two cases of polymyositis associated with HIV infection. A muscle biopsy revealed OKT4 and human T cell leukemia virus type III-positive inflammatory cells surrounding myofibrils, thus suggesting that direct viral invasion or an associated immunologic mechanism is responsible for muscle damage. EM did not show any viral particles, and, to date, the virus has not been isolated from human muscle fibers. However, animal studies of monkeys infected with SAIDS D retrovirus (SRV-1) have shown myotropic tendencies of the virus and its ability to directly infect muscles [33]. Muscle biopsies of patients with HIV-induced rhabdomyolysis revealed nonspecific inflammatory myopathy with focal necrotic areas and regenerating fibers [40].

The renal dysfunction associated with rhabdomyolysis arises from a variety of factors. Myoglobin obstructs tubules and is a direct renal toxin. Cortical ischemia and decreased glomerular filtration are also injurious, and when these conditions are combined with hypovolemia, oliguric renal failure can result [70, 71]. In the previously mentioned review by Tanaka et al. [61], 15 (36%) of 42 patients with virus-induced rhabdomyolysis had acute renal failure. The long-term outcome and possible recovery of renal function were not documented. It is interesting that although influenza virus accounted for only 33% of cases of rhabdomyolysis, 53% of patients with renal failure had this infection. In addition, the conditions of 57% of patients with influenza virus infection progressed to renal failure; these patients had CPK concentrations ranging from 261 U/L to >50,000 U/L. However, most of these patients (11 of 14) had CPK levels of <20,000 U/L.

We found similar results in our review; renal failure occurred in 20 (34%) of 59 cases. Although influenza accounted for only 42% of cases, it was associated with renal failure in 55% of patients; 44% of patients with influenza had renal failure. This rate is less than the rate (57%) of renal failure with influenza reported by Tanaka et al. [61], which may be because less-severe cases of disease are now diagnosed and management techniques have improved. Renal biopsies of these patients showed acute tubular necrosis and myoglobin casts obstructing tubules. Again, the range of CPK values in influenza virus–infected patients was variable, but nine (82%) of 11 patients who had renal failure due to influenza virus infection had peak CPK levels of <20,000 U/L. Gabow et al. [1] reported earlier that peak CPK levels did not correlate with the development of renal failure. The tendency of influenza virus to cause renal dysfunction irrespective of measurable muscle injury is interesting and clinically significant. Although the specific nephrotoxic mechanism is not known, aggressive measures should be taken to protect renal function. Clinical data addressing other concomitant renal toxins (volume status, etc.) was not addressed.

Numerous viral infections can therefore cause rhabdomyolysis. The virus most commonly associated with this syndrome is influenza virus. Viral isolation from infected muscles points to direct viral invasion as the pathogenic mechanism. The high incidence of renal failure due to influenza virus–induced rhabdomyolysis is intriguing.

**Bacterial Infections**

Various bacteria have been reported to cause rhabdomyolysis (table 2) [72–121]. *Legionella* species are the most common organisms followed by *Streptococcus* species, *Francisella tularensis*, and *Salmonella* species. In earlier reviews of rhabdomyolysis by Grossman et al. [17] in 1974 and by Chugh et al. [9] in 1979, no bacterial etiologies were identified. However, by 1982 Gabow et al. [1] did note that “sepsis” accounted for 2% of cases of rhabdomyolysis. The possible bacterial agents involved in these cases were not identified.

Our review documented only one report of bacterial infection resulting in rhabdomyolysis in the 1966–1977 period (patient with *Herbicola lathyri [Enterobacter agglomerans]*) sepsis). From 1976 to 1983, 14 cases were reported, most of which were due to *Legionella* species. After 1983 the frequency and variety of bacteria reported increased markedly. This apparent increase in the number of bacterial infections causing rhabdomyolysis is probably due to a variety of factors. Culture and identification of bacteria may be improving. More patients with sepsis are therapeutically supported through their illnesses, and subsequent complications (rhabdomyolysis and acute renal failure) are increasingly apparent. The number of immunocompromised patients who are susceptible to a wide range of infections is also increasing. Physician awareness of the link between bacterial infection and rhabdomyolysis is undoubtedly improving as well. It is interesting to note that although Enterobacteriaceae frequently cause bacteremia and sepsis, they are not commonly associated with rhabdomyolysis. In our literature review *Enterobacter* species were implicated in only nine cases (15%).

The first documented association between *Legionella* and rhabdomyolysis was reported in 1980 by Posner et al. [80] who described a 61-year-old man with a CPK level of 10,700 U/L and myoglobinuria. In the 14 case reports we reviewed, the CPK level ranged from 606 U/L to >400,000 U/L; in most of the cases (10 [71%] of 14), the CPK levels were <20,000 U/L. Eleven (79%) of 14 of these patients had renal failure, and four (29%) of 14 died. Thirteen cases of *Streptococcus* species causing rhabdomyolysis were found: 8 due to *S. pneumoniae*, 2 due to group B streptococci, 2 due to *S. pyogenes*, and 1 due to viridans streptococci. Of these patients, 54% had
Table 2. Bacterial causes of rhabdomyolysis.

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of cases</th>
<th>Age range</th>
<th>Range of CPK levels (U/L)</th>
<th>No. with ARF/total no. (%)</th>
<th>No. of deaths/total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Legionella</em> species</td>
<td>14</td>
<td>26–61 y</td>
<td>1,850 to &gt;400,000</td>
<td>14/14 (79)</td>
<td>4/14 (29)</td>
</tr>
<tr>
<td><em>Franciscella tularensis</em></td>
<td>9</td>
<td>31–71 y</td>
<td>1,049–474,000</td>
<td>3/9 (33)</td>
<td>3/9 (33)</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>8</td>
<td>36–81 y</td>
<td>244–105,700</td>
<td>4/8 (50)</td>
<td>2/8 (25)</td>
</tr>
<tr>
<td><em>Salmonella</em> species</td>
<td>6</td>
<td>32–84 y</td>
<td>1,870–24,360</td>
<td>4/6 (67)</td>
<td>0/6</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>5</td>
<td>15–70 y</td>
<td>14,046–83,000</td>
<td>2/5 (40)</td>
<td>2/5 (40)</td>
</tr>
<tr>
<td>Group B <em>Streptococcus</em></td>
<td>2</td>
<td>17 d to 11 w</td>
<td>4,110–22,000</td>
<td>1/2 (50)</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>2</td>
<td>27–67 y</td>
<td>33,000–151,000</td>
<td>1/2 (50)</td>
<td>1/2 (50)</td>
</tr>
<tr>
<td><em>Listeria</em> species</td>
<td>2</td>
<td>38–51 y</td>
<td>5,000–149,500</td>
<td>1/2 (50)</td>
<td>0/2</td>
</tr>
<tr>
<td><em>Vibrio</em> species</td>
<td>2</td>
<td>38–51 y</td>
<td>9,260</td>
<td>NA</td>
<td>2/2 (100)</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>1</td>
<td>18 y</td>
<td>13,600</td>
<td>1/1 (100)</td>
<td>NA</td>
</tr>
<tr>
<td><em>Brucella</em> species</td>
<td>1</td>
<td>25 y</td>
<td>337,000</td>
<td>1/1 (100)</td>
<td>0/1</td>
</tr>
<tr>
<td><em>Bacillus</em> species</td>
<td>1</td>
<td>50 y</td>
<td>14,130</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1</td>
<td>86 y</td>
<td>11,440</td>
<td>0/1</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td><em>Herbicola lathyri</em></td>
<td>1</td>
<td>42 y</td>
<td>21,980</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>(Entrobacter agglomerans)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Lepthospira</em> species</td>
<td>1</td>
<td>19 y</td>
<td>420,000</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td><em>Polymicrobes</em> (E. coli, Clostridium species, Klebsiella species)</td>
<td>1</td>
<td>80 y</td>
<td>754</td>
<td>0/1</td>
<td>0/1</td>
</tr>
<tr>
<td><em>Borrelia burgdorferi</em></td>
<td>1</td>
<td>81 y</td>
<td>29,988</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td><em>Clostridium perfringens</em></td>
<td>1</td>
<td>35 y</td>
<td>&gt;14,000</td>
<td>NA</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td><em>Viridans streptococci</em></td>
<td>1</td>
<td>20 y</td>
<td>3,100</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td></td>
<td></td>
<td>34/60 (57)</td>
<td>23/60 (38)</td>
</tr>
</tbody>
</table>

NOTE. ARF = acute renal failure; CPK = creatine phosphokinase; NA = not available.

Renal failure and 46% died. In 1985 Chun and Raff [89] reviewed bacterial causes of rhabdomyolysis and found that four (33%) of 12 cases were caused by *Streptococcus* species. Salmonella infections accounted for six cases in our review; four of six patients had acute renal failure, and there were no deaths.

The proposed mechanisms of muscle injury by bacteria include toxin generation and direct bacterial invasion. *Legionella* is believed to release an endotoxin or exotoxin [82, 85] that causes rhabdomyolysis. Biopsy specimens that are negative for the organism [75, 80, 81] by immunofluorescence support this hypothesis. Organisms such as *Streptococcus* and *Salmonella* cause muscle damage by direct bacterial invasion as well as by decreasing the oxidative and glycolytic enzyme activity of skeletal muscle and by activating lysosomal enzymes [54]. *Staphylococcus aureus* [25, 103], *S. pyogenes* [52], *Vibrio* species [111], and *Bacillus* species [114] have all been demonstrated in muscle biopsy specimens.

Renal failure occurs secondary to decreased glomerular perfusion and the toxic effects of myoglobin on tubules. Renal biopsies reveal acute tubular necrosis and pigment casts. In 1992 Shah et al. [82] reviewed 45 cases of legionnaires’ disease and acute renal failure. Of these 45 patients, seven had rhabdomyolysis causing acute renal failure; other renal pathological findings included acute tubulointerstitial nephritis, acute pyelonephritis, mesangiogluomerulonephritis, and rapidly progressive glomerulonephritis. These investigators were able to demonstrate *Legionella pneumophila* by EM and indirect immunofluorescence of renal tissue, thus raising the possibility that direct involvement by the organism results in renal dysfunction. Whether this possibility also applies to muscle damage remains to be determined.

Rhabdomyolysis is caused by a variety of bacteria, with *Legionella* species being the most frequently cited agent. Direct bacterial invasion and release of endotoxin are proposed patho-
physiological mechanisms. Significant morbidity (57% of cases with acute renal failure) and mortality (death in 38% of cases) are associated with bacterial causes of rhabdomyolysis. Other infectious etiologies of rhabdomyolysis are listed in table 3.

Conclusion

Rhabdomyolysis can be precipitated by many conditions, including viral and bacterial infections. Influenza virus and HIV are the most common viral etiologies, and Legionella species, Streptococcus species, and Salmonella species are the most common bacterial precipitants. The proposed pathophysiological mechanisms include direct viral or bacterial invasion of skeletal muscle and toxin generation. Physicians should be aware of the association between these infections and rhabdomyolysis to facilitate optimal treatment of these patients.

References


