

# Severe Community-Onset Pneumonia in Healthy Adults Caused by Methicillin-Resistant *Staphylococcus aureus* Carrying the Panton-Valentine Leukocidin Genes

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**Background.** Recent worldwide reports of community-onset skin abscesses, outbreaks of furunculosis, and severe pneumonia associated with methicillin-resistant *Staphylococcus aureus* (MRSA) carrying Panton-Valentine leukocidin (PVL) genes and the staphylococcal cassette chromosome *mec* (SCC*mec*) type IV indicate that MRSA infections are evolving into a community-related problem. The majority of cases reported to date involve skin and soft-tissue infections, with severe pneumonia representing a relatively rare phenomenon. During a 2-month period in the winter of 2003–2004, four healthy adults presented to 1 of 2 Baltimore hospitals with severe necrotizing MRSA pneumonia in the absence of typical risk factors for MRSA infection.

**Methods.** Patients' MRSA isolates were characterized by strain typing with use of pulsed-field gel electrophoresis and SCC*mec* typing with use of a multiplex polymerase chain reaction (PCR) assay and detection of PVL genes by PCR.

**Results.** All 4 patients' MRSA isolates carried the PVL genes and the SCC*mec* type IV element and belonged to the USA300 pulsed-field type. These 3 findings are among the typical characteristics of community-onset MRSA strains. In addition, 2 of our patients had concomitant influenza A diagnosed, which likely contributed to the severity of their presentation.

**Conclusions.** To our knowledge, these patients represent the first reported North American adults with severe community-onset MRSA pneumonia caused by strains carrying the PVL genes.

In 1882, the Scottish surgeon Sir Alexander Ogston named the organism "*Staphylococcus*" [1], which is now recognized as an extremely successful human pathogen. Resistance to methicillin emerged shortly after the drug's introduction and is a factor that has helped *Staphylococcus aureus* become established as a nosocomial pathogen [2]. The prevalence of methicillin-resistant *S. aureus* (MRSA) in the community was relatively rare until the past decade, during which there

was a substantial increase in prevalence, representing a mix of health care-associated strains and distinctive genotypes that appear to have originated in the community [3, 4]. These latter strains have been implicated in reports of severe MRSA infections in children and young adults [5–10], suggesting unique virulence.

Methicillin resistance is determined by the presence of a penicillin-binding protein with decreased affinity to penicillin. The *mecA* gene encodes this protein and is located on the staphylococcal cassette chromosome *mec* (SCC*mec*). Types I–V and additional SCC*mec* elements have been described elsewhere; however, community-onset MRSA (CO-MRSA) infections have mostly been associated with type IV [3, 11–15].

In 1932, Panton and Valentine [16] described leukocidin as a virulence factor. Production of the Panton-Valentine leukocidin (PVL) is now known to be asso-

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ciated with tissue necrosis. Lina et al. [17] screened 172 staphylococcal isolates submitted to a reference laboratory in France during the period of 1985–1998 to correlate toxin production with disease states. They found PVL genes in isolates from 27 (93%) of 30 cases of furunculosis and 23 (85%) of 27 cases of community-onset pneumonia. Fourteen (61%) of the 23 cases of pneumonia were fatal, and autopsies revealed diffuse, bilateral necrotic hemorrhagic pneumonia.

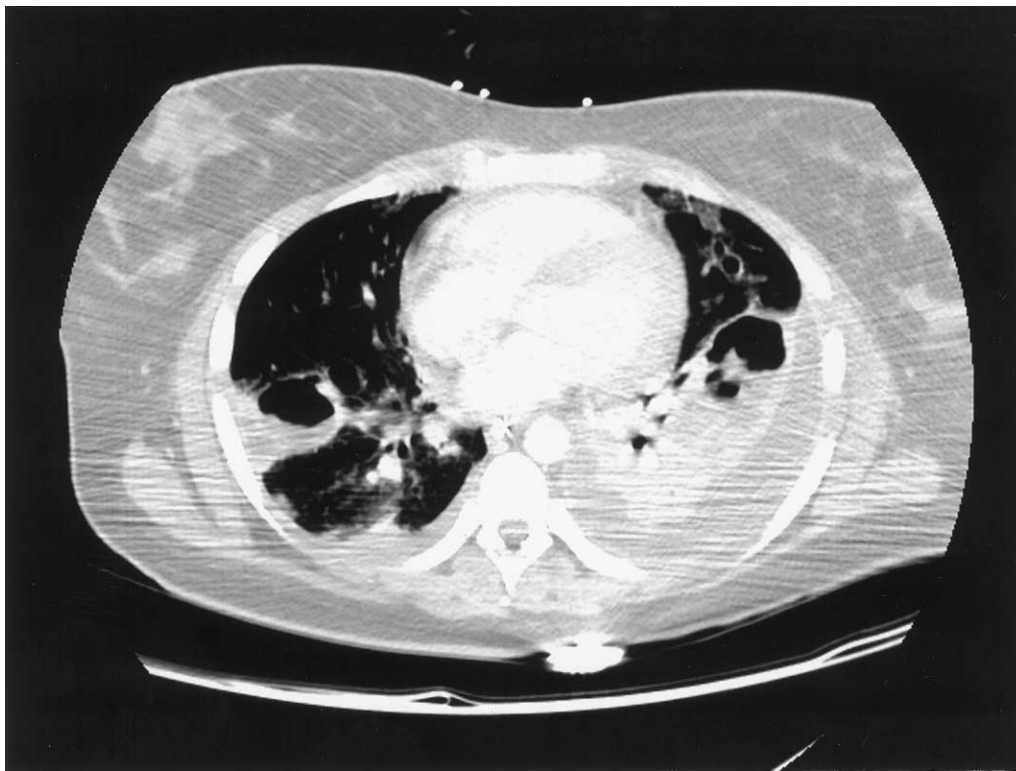
We describe 4 previously healthy adults who developed severe necrotizing pneumonia caused by MRSA in the absence of known risk factors for MRSA infection. All 4 patients' MRSA isolates belonged to the USA300 pulsed-field type and carried the genes for PVL and the SCC $mec$  type IV element. To our knowledge, this is the first report from North America of severe necrotizing community-onset pneumonia in adults caused by MRSA carrying the PVL genes.

## CASE REPORTS

**Patient 1.** A 31-year-old woman with a history of smoking 6 cigarettes per day for 10 years and of eczema developed fever, cough, headache, and myalgia 7 days after contact with a friend who had influenza-like symptoms. Despite receiving azithromycin, she developed shortness of breath and hemoptysis. At presentation, the patient's vital signs were as follows: temper-

ature, 37.3°C; heart rate, 128 beats/min; respiratory rate, 35 breaths/min; blood pressure, 123/70 mm Hg; and oxygen saturation on room air, 94%. Her WBC count was 10,320 cells/mm<sup>3</sup> (48% bands and 38% polymorphonuclear cells). Subsequent arterial blood gas analysis revealed a pH of 7.37, partial pressure of carbon dioxide (Pco<sub>2</sub>) of 35 mm Hg, and a partial pressure of oxygen, arterial (Pao<sub>2</sub>) of 58 mm Hg on room air. CT revealed multiple bilateral cavitory lung lesions, the largest of which was 4 × 2.8 cm (figure 1). Cultures of blood and sputum samples obtained on the day of hospital admission yielded MRSA, and serologic testing demonstrated evidence of acute influenza A (table 1). Treatment with vancomycin, gatifloxacin, and meropenem was initiated (the latter was changed to rifampin on the basis of culture results), as well as therapy with activated protein C and vasopressors. The patient required mechanical ventilation and drainage of an empyema before ultimately being discharged from the hospital receiving oral gatifloxacin and rifampin after 4 weeks in the intensive care unit (ICU).

**Patient 2.** A 52-year-old man who smoked 2 packs of cigarettes per day for 30 years presented with a 2-day history of fever, cough, hemoptysis, and dyspnea. Physical examination revealed the following values: temperature, 39.2°C; heart rate, 104 beats/min; respiratory rate, 24 breaths/min; blood pressure,



**Figure 1.** Necrotizing pneumonia on a chest CT with intravenous contrast, obtained on hospital day 3 from patient 1. The CT shows multiple bilateral nodular and cavitory lesions (some of which have surrounding ground glass halos that are likely to represent hemorrhages) and left lower lobe consolidation, with small left-side pleural effusion.

**Table 1. Clinical characteristics of patients with severe community-onset methicillin-resistant *Staphylococcus aureus* pneumonia.**

Patient	Age, years	Peak temperature, °C	Hemoptysis	Shock	Cavitary lesions	Duration of hospitalization, days	Nadir WBC count, cells/mm <sup>3</sup>	Influenza A titer <sup>a</sup>
1	31	39.7	+	+	+	41	7400	<1:10 to 1:80
2	52	41.0	+	+	+	2 <sup>b</sup>	1020	ND
3	20	39.9	—	+	+	108	380	1:32 to 1:512
4	33	40.2	+	+	+	102	800	ND

**NOTE.** ND, not determined; +, present; —, absent.

<sup>a</sup> Semiquantitative detection of antibodies to influenza A virus in acute-phase (first titer) and convalescent-phase (second titer) serum samples, determined by hemagglutination inhibition.

<sup>b</sup> Patient died on day 2 of hospitalization.

123/68 mm Hg; and oxygen saturation on room air, 97%. The examination also revealed wheezing on lung auscultation and subcutaneous abscesses on the arms and back. The patient's WBC count was 11,750 cells/mm<sup>3</sup> (25% bands and 68% polymorphonuclear cells). Subsequent arterial blood gas analysis revealed a pH of 7.33, Pco<sub>2</sub> of 42 mm Hg, and Pao<sub>2</sub> of 70 mm Hg on 4 L nasal cannula. Chest CT demonstrated 2 cavitary lesions (size, 3.9 × 2 and 2.8 × 2 cm), with nodular opacities in the right middle lobe and bilateral lower lobes. Cultures of sputum samples obtained at admission subsequently grew MRSA. Treatment with gatifloxacin, vancomycin, and meropenem was initiated, but the patient developed progressive hypotension and hypoxia, requiring aggressive hydration and increased oxygenation. On day 2 of hospitalization, he developed pulseless electrical activity and died, despite resuscitation efforts.

**Patient 3.** A 20-year-old woman with no significant past medical history presented with a 6-day history of fever, myalgia, and dry cough and a 1-day history of vomiting and dyspnea. At presentation, her vital signs were as follows: temperature, 39.9°C; heart rate, 130 beats/min; respiratory rate, 40–50 breaths/min; blood pressure, 120/63 mm Hg; and oxygen saturation on room air, 75%. Laboratory studies revealed an arterial blood gas pH of 7.46, Pco<sub>2</sub> of 27 mm Hg, Pao<sub>2</sub> of 45 mm Hg on room air, and a WBC count of 700 cells/mm<sup>3</sup> (24% bands and 56% polymorphonuclear cells). CT revealed dense consolidation of bilateral mid- and lower-lung zones; serologic testing demonstrated evidence of acute influenza A (table 1), and cultures of blood and bronchoalveolar lavage (BAL) fluid samples obtained at hospital admission yielded MRSA. Treatment with cefepime, gatifloxacin, vancomycin, and oseltamivir (antibiotics narrowed to vancomycin and clindamycin after culture result) was initiated, but the patient's condition deteriorated, requiring mechanical ventilation, vasopressors, and activated protein C therapy. Her course was complicated by cavitary pneumonia, disseminated intravascular coagulation, bilateral pneumothoraces, mitral valve endocarditis, digital and

lower extremity necrosis (requiring below-the-knee amputation), embolic strokes, and an episode of pulseless electrical activity with successful resuscitation. She was discharged to a rehabilitation center after a 3-month hospitalization.

**Patient 4.** A 33-year-old woman with no significant past medical history presented to an emergency department with fever, sore throat, rhinorrhea, nasal congestion, productive cough, arthralgia, myalgia, vomiting, and hemoptysis. She received amoxicillin, but that evening, she developed pleuritic chest pain and dyspnea, and she returned to the emergency department by ambulance. Vital signs at hospital admission were as follows: temperature, 37°C; heart rate, 136 beats/min; respiratory rate, 28 breaths/min; blood pressure, 123/78 mm Hg; and oxygen saturation on room air, ~80%. Laboratory studies revealed a WBC count of 1200 cells/mm<sup>3</sup> (28% bands and 20% polymorphonuclear cells). Chest radiography revealed infiltrates in the left lower lobe and right middle and lower lobe. BAL cultures from hospital day 3 yielded MRSA. The patient was treated with levofloxacin, clindamycin, vancomycin, mechanical ventilation, vasopressors, and a brief trial of activated protein C. The patient was transferred to Johns Hopkins Hospital (Baltimore, MD), where her antibiotic therapy was changed to vancomycin, linezolid, and rifampin (subsequently narrowed to vancomycin and linezolid). Her hospital stay was complicated by refractory hypoxemia, cavitary pneumonia, deep venous thrombosis (on hospital day 10), digital and lower-extremity necrosis (requiring bilateral below-the-knee amputations), and use of multiple chest tubes for pneumothoraces. After 3 months, the patient was discharged to a rehabilitation center.

## PATIENTS, MATERIALS, AND METHODS

**Patient selection.** All 4 patients with severe community-onset pneumonia caused by MRSA were identified on referral to the infectious diseases consultation service at Johns Hopkins Hospital or Johns Hopkins Bayview Medical Center. No systematic

attempt was made to identify additional cases. All patients were previously healthy and lacked typical risk factors for MRSA (e.g., recent surgery, recent hospitalization, residence in long-term care facilities, injection drug abuse, hemodialysis, and percutaneous catheterization).

**Definitions.** A community-onset staphylococcal infection was defined as an infection in which an isolate was cultured from a patient <72 h after hospital admission. Nosocomial staphylococcal isolates were defined by culture collection dates  $\geq$ 72 h after admission.

**Identification and characterization of MRSA.** *S. aureus* was identified by standard microbiologic methods. Susceptibility testing was performed by agar dilution, in accordance with NCCLS guidelines [18]. Staphylococcal isolates were analyzed by the Johns Hopkins Hospital Division of Medical Microbiology and were sent to the Centers for Disease Control and Prevention (CDC; Atlanta, GA) for confirmatory PCR detection of PVL genes and SCCmec typing with use of methods described by Lina et al. [17] and Okuma et al. [12], respectively.

**Detection of virulence factors.** Genomic DNA was obtained by a Qiamp DNA mini kit protocol (Qiagen). PCR was then performed on the genomic DNA for a 433-bp overlap-region segment of the *lukS-PV* and *lukF-PV* genes (encoding the PVL gene products LukS and LukF, respectively) and for internal control 16S rDNA. Primers for PVL genes were described by Lina et al. [17]. Primers for 16S rDNA (16S-F1, 5'-GCAAGCGTTATCCGGAATTATTG-3'; and 16S-R1, 5'-GGC-GGAGTGCTTAATGCGTTAG-3') were used to generate an internal control with an amplicon size of 341 bp. Amplifications were performed with the following parameters: predenaturation for 2 min at 94°, followed by 25 cycles of 94° for 15 s, 55° for 15 s, and 72° for 15 s. Samples were analyzed in an ethidium bromide-stained 2% agarose gel. *S. aureus* strains 43300 and 49775 (American Type Culture Collection [ATCC]) were used as PVL-negative and PVL-positive controls, respectively. In ad-

dition, each patients' MRSA isolates were evaluated at the CDC for the presence of staphylococcal enterotoxins A–D and Toxic Shock Syndrome Toxin-1 (TSST-1) by Oxoid LTD Reverse Passive Latex Agglutination (RPLA) assays (Key Scientific Products).

**SCCmec typing.** Genomic DNA from each patient's MRSA isolate was obtained as described above. SCCmec typing was performed by multiplex PCR strategy [19], with the modifications described below. DNA was amplified using a Gene Amp PCR system 9600 apparatus (Perkin-Elmer) with the following parameters: predenaturation for 2 min at 94°, followed by 30 cycles of 94° for 15 s, 62° for 15 s, and 72° for 15 s. Amplified DNA were separated by electrophoresis in a 2% agarose gel then stained with ethidium bromide. Control strains for SCCmec elements type I–IV (I-COL, II-N315, III-ANS46, and IV-HDE288) were obtained from Oliveira and de Lencastre [19]. ATCC *S. aureus* strain 25923 was used as a *mecA*-negative control.

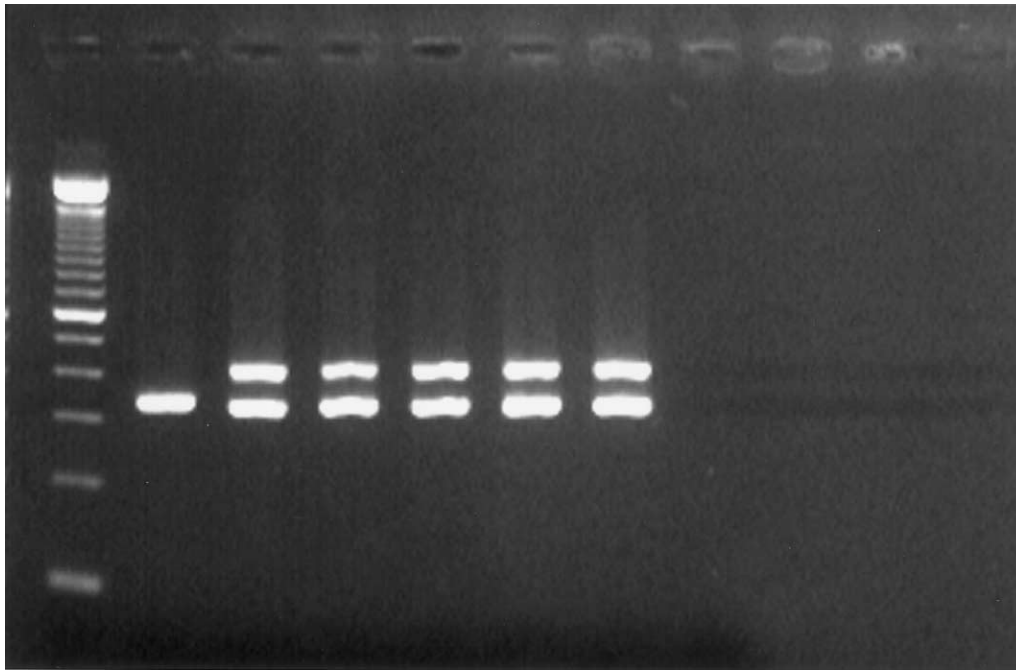
**PFGE.** PFGE was performed using a protocol developed in the Johns Hopkins Hospital Division of Medical Microbiology. For controls, 2 nosocomial isolates were selected from MRSA known to circulate among Johns Hopkins Hospital patients. A CO-MRSA isolate obtained from McDougal et al. [20], with known USA300 pulsed-field type, was used as a positive control. Overnight broth cultures of *S. aureus* were pelleted; bacterial DNA was extracted in agarose plugs with a solution containing lysostaphin and lysozyme. Restriction enzyme digestion was performed with *Sma* I. Restriction endonuclease fragments were analyzed by PFGE using a contour-clamped homogeneous electric field DR-II apparatus (BioRad Laboratories) set at 14°C; initial switch, 5 s; final switch, 50 s; and time, 23.5 h. After electrophoresis, gels were stained with ethidium bromide. Macrorestriction DNA banding patterns were digitized and analyzed using Molecular Analyst DNA Fingerprinting software

**Table 2. Characteristics of patients' community-onset methicillin-resistant *Staphylococcus aureus* (MRSA) isolates.**

Patient	Source of MRSA	DNA analysis			Antibacterial susceptibility <sup>a</sup>						
		PFGE pattern	SCCmec type IV	PVL	Vm	C	Em	TMP-SMZ	Tet	Gm	Gat
1	Blood, sputum	Same	+	+	S	S	R	S	S	S	S
2	Sputum	Similar	+	+	S	S	R	S	R	S	I
3	BAL, blood	Same	+	+	S	S	R	S	R	S	I
4	BAL, blood	Same	+	+	S	S	R	S	S	S	I

**NOTE.** BAL, bronchoalveolar lavage; Cm, clindamycin; Em, erythromycin; Gat, gatifloxacin; Gm, gentamicin; I, intermediate; PFGE, pulsed field gel electrophoresis of *Sma*I-digested genomic DNA; PVL, Panton-Valentine leukocidin; R, resistant; S, susceptible; SCCmec type IV, staphylococcal cassette chromosome *mec* type IV element; Tet, tetracycline; TMP-SMZ, trimethoprim-sulfamethoxazole; Vm, vancomycin; +, present.

<sup>a</sup> Each patient's MRSA isolate was evaluated for inducible macrolide-lincosamide-streptogramin B resistance by double-disk diffusion test (D test) before reporting clindamycin susceptibility.



**Figure 2.** PCR detection of overlap region of Pantone-Valentine leukocidin (PVL) genes in community-onset methicillin-resistant *Staphylococcus aureus* isolates. *Lane 1*, 100-bp molecular weight marker (middle bright band, 600-bp); *lane 2*, PVL-negative American Type Culture Collection (ATCC) strain 43300; *lane 3*, PVL-positive ATCC strain 49775; *lane 4*, isolate recovered from patient 2; *lane 5*, isolate recovered from patient 1; *lane 6*, isolate recovered from patient 3; *lane 7*, isolate recovered from patient 4; *lane 8*, no genomic DNA (template negative control). PVL-positive control and patient isolates all show the predicted 433-bp amplicon from the overlap region of the PVL genes. Internal control to confirm the quality of each DNA extract revealed that the PVL-negative control and all samples with genomic DNA show the predicted 341-bp amplicon from 16S rDNA.

(BioRad). Patterns were compared and interpreted using the criteria of Tenover et al. [21].

## RESULTS

**Patient selection.** Four patients were identified with severe CO-MRSA pneumonia (table 1). Three patients were female, and 1 was male. All patients required ICU admissions. For 3 patients, MRSA was isolated from cultures of samples obtained on the day of hospital admission. For the fourth patient, MRSA was isolated from cultures of samples obtained on hospital day 3 (table 2). Two patients received a diagnosis of concomitant influenza A. The remaining 2 patients were admitted to the hospital with an influenza-like prodrome; however, acute-phase and convalescent-phase serologic testing were not performed.

**Detection of virulence factors.** Each MRSA isolate carried the PVL genes (figure 2) and SCC*mec* type IV element (data not shown). Staphylococcal enterotoxins A–D and TSST-1 were not detected by RPLA.

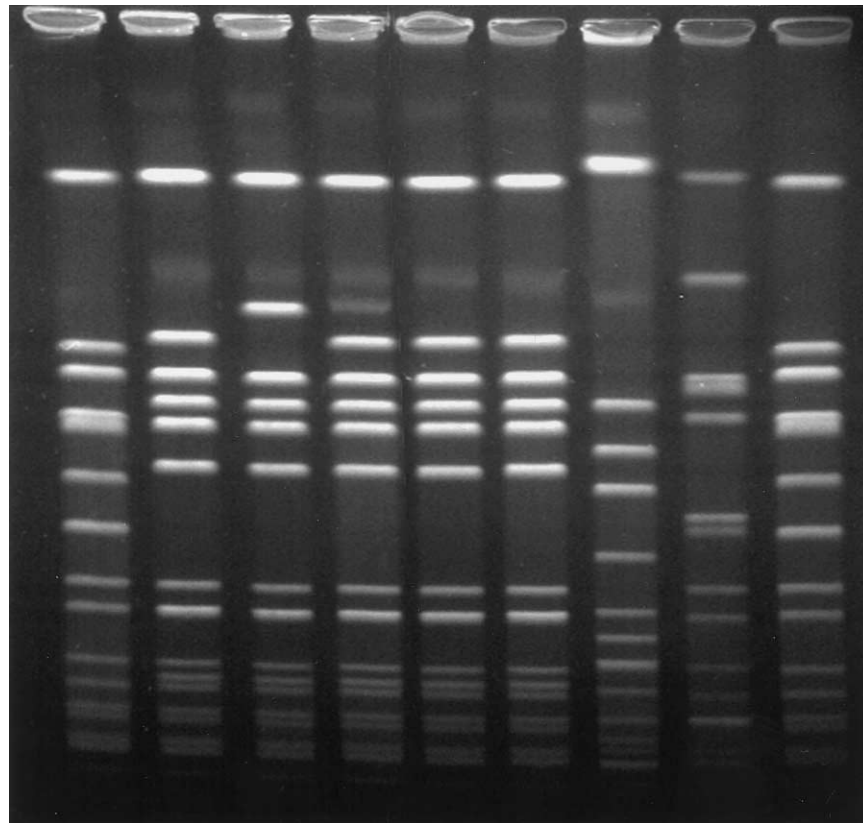
**PFGE.** Genomic DNA from patients' MRSA isolates was digested with *Sma*I, and the restriction-fragment patterns (figure 3) were compared visually. Isolates recovered from patients 1, 3, and 4 showed the same banding pattern, whereas the isolate recovered from patient 2 had a 2-band difference, representing a closely related strain, on the basis of the criteria of Tenover

et al. [21]. All isolates had banding patterns consistent with the USA300 pulsed-field type [20].

## DISCUSSION

MRSA is well known to physicians as a cause of hospital-acquired infections and is now emerging as an important pathogen in the community. First reported in 1961 [2], MRSA accounts for 30%–40% of current nosocomial staphylococcal infections [22]. CO-MRSA has been recognized by careful epidemiologic evaluation; it is characterized by the presence of a type IV SCC*mec* element, susceptibility to multiple antibiotics (other than  $\beta$ -lactams), and the presence of PVL genes [23]. These CO-MRSA strains are globally distributed and clonally disseminated [11, 12]. Although these strains are clearly documented in community-onset infections, they have also been associated with nosocomial outbreaks [24].

CO-MRSA strains have been increasingly associated with skin and soft-tissue infections, especially furunculosis, both in isolated cases and in epidemics [17, 25–27]. Approximately 12,000 MRSA infections were recently reported in the Georgia, California, and Texas prison systems, most of which involved skin and soft tissues [25]. The prevalence of MRSA increased from 29% to 74% in California jails between 1997 and 2002; 91% of these strains were determined to carry the type IV



**Figure 3.** PFGE of *Sma*I-digested DNA from community-onset methicillin-resistant *Staphylococcus aureus* (MRSA) isolates. Lanes 1 and 9, molecular weight marker NCTC 8325; lane 2, sputum isolate recovered from patient 1; lane 3, sputum isolate recovered from patient 2; lane 4, blood isolate recovered from patient 3; lane 5, sputum isolate recovered from patient 4 from an outside hospital; lane 6, USA300 positive control; lanes 7 and 8, nosocomial MRSA isolates from 2 different sources.

SCC*mec* element [28]. Outbreaks of CO-MRSA skin infections were reported in 34 individuals in Alaska [26] and 235 military recruits in Virginia [27]. The role of CO-MRSA as a cause of serious pneumonia in children and young healthy adults is far less common, with at least 10 reported cases [5–10], 2 of which were documented in adults (age,  $\geq 18$  years) in France [9, 10]. Seven of these patients presented with evidence of necrotizing pneumonia, 3 with frank hemoptysis. The fatal outcome of 6 of these cases illustrates the lethal potential of CO-MRSA pneumonia [6, 9, 10].

We describe 4 previously healthy adults without typical risk factors for MRSA infection who presented with severe pneumonia caused by MRSA during a 2-month period in the winter of 2003–2004. These infections were associated with a syndrome characterized by an influenza or influenza-like prodrome, high fever, severe necrotizing pneumonia, leukopenia, respiratory failure, and shock. Three patients recovered but had significant morbidities and required 1–3 months in an ICU.

In each case, MRSA was the only bacterial pathogen identified that was associated with their initial presentation. Each MRSA isolate carried the PVL genes (figure 2) and SCC*mec* type IV element (data not shown). These results were congruent

with the results of independent tests performed on our patients' MRSA strains at the CDC. Although our patients were not epidemiologically linked, we demonstrated that their isolates were of the USA300 pulsed-field type (figure 3), a pulsed-field type that has documented association with CO-MRSA outbreaks of skin and soft-tissue infections in the prison system, athletic teams, and nurseries [20]. In addition, all of their isolates were susceptible to clindamycin, trimethoprim-sulfamethoxazole, and gentamicin (table 2). These are among the features that distinguish CO-MRSA from the more familiar health care-associated MRSA.

Of interest, the 2003–2004 United States influenza season began earlier than in most other years and was moderately severe. The association between influenza and severe staphylococcal pneumonia is well recognized [29, 30]. Influenza and other viral syndromes can damage the respiratory epithelium and predispose to staphylococcal infections. Two of our patients had evidence of concomitant influenza. The others presented with an influenza-like prodrome; however, they did not undergo serologic testing. The current shortage of influenza vaccine for the 2004–2005 influenza season may result in an increase in CO-MRSA pneumonia in high prevalence areas.

The production of PVL may contribute to the unique pathogenicity of CO-MRSA [7, 9, 17, 31]. PVL belongs to the synergohymenotropic class of toxins (synergistic proteins directed towards cell membranes). It is assembled from 2 components that are secreted separately but combine to create lytic pores in cell membranes of neutrophils. The binding of PVL components to neutrophils induces release of the neutrophil chemotactic factors IL-8 and leukotriene B<sub>4</sub>, as well as a variety of inflammatory mediators, before bringing about cell death [32]. The combination of neutrophil chemotaxis, release of inflammatory mediators, and karyorrhexis promotes tissue necrosis and abscess formation. Purified PVL protein injected intradermally into rabbits leads to severe inflammation and necrosis [33]. Gillet et al. [7] showed that hemoptysis was found in 6 (38%) of 16 patients with severe pneumonia associated with *S. aureus* strains carrying PVL genes, compared with 1 (3%) of 33 PVL-negative patients. Interestingly, the action of PVL on neutrophils in vitro may be blocked by specific anti-PVL antibodies found in commercial preparations of intravenous immunoglobulin [34].

Our patients' severe necrotizing community-onset pneumonia is consistent with the recognized association of PVL with severe staphylococcal pneumonia in young, healthy adults. Over a 15-year period, 2 French studies identified 18 cases of severe necrotizing pneumonia caused by *S. aureus* carrying PVL genes referred to the French Reference Center for Staphylococcal Toxemia [7, 9]. However, most strains were not clonally related, and only 3 of the 18 isolates were methicillin-resistant. Together with recent case reports in children and adults [5–10], our cluster of 4 patients identified within a 2-month period raises the possibility for emergence of severe community-onset necrotizing MRSA pneumonia in other communities.

To date, severe CO-MRSA pneumonia has been rare; however, if the prevalence of this pathogen continues to increase, MRSA will become an important consideration in the differential diagnosis of severe community-onset pneumonia, especially when associated with necrotizing pneumonia, shock, high fever, hemoptysis, leukopenia, and/or an influenza-like prodrome. For such patients, MRSA should be considered as a cause, even in the absence of previously described risk factors for MRSA infection. An etiologic agent should be aggressively pursued, contact isolation should be considered, and empirical antimicrobial therapy regimens should include an agent with anticipated activity against CO-MRSA strains.

With regard to initial antibiotic therapy in severe infections, the current recommendations for empirical antimicrobial selection for patients with community-acquired pneumonia may be inadequate in areas where CO-MRSA is highly prevalent. CO-MRSA strains have universal resistance to  $\beta$ -lactams and pockets of fluoroquinolone resistance, and *S. aureus* is known to have variable susceptibility to macrolides. Alternative agents

for inclusion with standard empirical therapy, on the basis of predicted in vitro activity, may include vancomycin, linezolid, trimethoprim-sulfamethoxazole, and clindamycin—and possibly combinations of these, with or without rifampin. We suspect additional data are required before more definitive recommendations can be made. Rapid institution of antibiotics and in vitro susceptibility testing are of obvious importance. Nevertheless, the extent to which our patients' complicated clinical courses resulted from the inherent virulence of the organism versus the limited activity of initial therapeutic regimens cannot be determined. All 4 patients received initial treatment with  $\geq 1$  antibiotic with activity against this organism, suggesting that adequate antibiotic selection alone will not prevent a protracted and complicated clinical course. With regard to prevention, use of mupirocin to attempt decolonization is controversial, but it can be considered for patients and intimate contacts who are determined to be carriers of CO-MRSA strains, because nosocomial [24] and intrafamilial [9, 35] spread have been documented.

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**Potential conflicts of interest.** T.P. is a member of the advisory board for Cubist and GlaxoSmithKline and is a member of the speakers' bureaus for GlaxoSmithKline and Wyeth. E.N. has received research funding from Pfizer. All other authors: no conflicts.

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