REVIEW ARTICLE

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Recurrent furunculosis: a review of the literature

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Summary

Background Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasing in incidence and manifests as skin and soft tissue infections including furuncles. The majority of studies have focused on the epidemiology of single furuncles and not recurrent disease. There is a lack of data concerning the incidence of furunculosis outside the U.S.A.

Objectives This report reviews the literature of recurrent furunculosis and the impact of CA-MRSA on the disease.

Methods Article citations were searched within PubMed. Search terms used were 'furunculosis', 'recurrent furunculosis', 'skin abscess' and 'recurrent boils'. Articles were discarded if they did not refer to furunculosis secondary to *S. aureus*.

Results A total of 1515 articles were initially retrieved with the term 'furunculosis', 77 with the term 'recurrent furunculosis', 2778 with the term 'skin abscess', and 1526 with the term 'recurrent boils'. After excluding articles not referring to *S. aureus* furunculosis, 86 articles were included for this review.

Conclusions Furunculosis is increasing within the U.S.A. secondary to the CA-MRSA epidemic and the resistant organism's close association with the Panton–Valentine leucocidin (PVL) virulence factor. PVL is associated with follicular infections in general, having its strongest association with furunculosis and its recurrence. The majority of furuncles in the U.S.A. are caused by CA-MRSA, while elsewhere in the world they are caused by methicillin-sensitive *S. aureus*. Nasal carriage of *S. aureus* is the primary risk factor for recurrent furunculosis and occurs in 60% of individuals.

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A furuncle is a primary deep infection of the hair follicle that leads to abscess formation, and is generally caused by *Staphylococcus aureus*. It is a distinct type of skin abscess appearing only on hair-bearing skin and is unrelated to secondary causes of abscesses such as trauma, surgery or the presence of a foreign body. Furthermore, furuncles do not share the pathophysiology of other primary abscess conditions including hidradenitis suppurativa, and anorectal or breast abscesses. Healthy young adults develop furuncles that usually resolve without sequelae. However, some patients suffer recurrence. Recurrent furunculosis is not defined explicitly in the literature, although it is easily perceptible as the sequential occurrence of many furuncles over a period of months, and in some cases years, in the same patient. This is to be contrasted with epidemic furunculosis, which is an outbreak of furuncles in a limited period of time affecting several patients who were in close contact with one another.

The significance of recurrent furunculosis is that in the worldwide epidemic of community-associated methicillin-resistant *S. aureus* (CA-MRSA), infections manifest primarily in the skin and soft tissues and most commonly as furuncles.[1–10] However, the exact definition of CA-MRSA remains controversial, and at least eight different definitions have been put forth in the literature.[11] Originally described epidemiologically, the Center for Disease Control and Prevention's widely accepted definition is a methicillin-resistant *S. aureus* (MRSA) strain isolated from a patient within 48 h of hospitalization, who has none of the known risk factors for a resistant infection, such as hospital, nursing home or hospice admission, dialysis or surgery within the past year, a previous record of colonization, or the permanent presence of a medical device or catheter. Presentation of any of these factors defines healthcare-associated MRSA (HA-MRSA). On the other hand, CA-MRSA's strong association with types IV and V of a particular genetic unit designated the staphylococcal cassette chromosome (SCC) *mec* permits a microbiological definition. HA-MRSA usually carries SCC*mec* types I, II or III.[12]

The cassette chromosome is a mobile unit of DNA carried by *S. aureus* that confers methicillin resistance by the presence of the *mecA* gene. This gene encodes penicillin binding protein 2a (PBP2a), a peptidase that catalyses transpeptidation reactions occurring during cell wall synthesis. PBP2a has low affinity for

β-lactam antibiotics, resulting in methicillin resistance. SCC*mec* types I, II and III are larger than types IV and V and frequently accommodate additional resistance genes that confer multidrug resistance for HA-MRSA. Conversely, CA-MRSA is normally susceptible to many non-β-lactam antibiotics. The smaller SCC*mec* types are also more mobile than the larger ones,[13] and given the scope of CA-MRSA's genetic diversity around the world[14,15] horizontal spread of these SCC*mec* types to different *S. aureus* strains has been proposed as one of the forces behind the epidemic. As MRSA strains harbouring SCC*mec* type IV have also been found to replicate faster than HA-MRSA,[16] it is easy to see how CA-MRSA has outgrown and overtaken HA-MRSA as a public health threat and even as a cause for hospital-acquired infections in some places.[17]

Although the centre of the epidemic is the U.S.A.,[12] the numbers of CA-MRSA cases reported in the U.K.[18] and throughout the world[2,3,5,6] are also rising. The growth of CA-MRSA may indicate an increase in the incidence of furunculosis and of recurrent furunculosis and, because of the pathogen's greater virulence, an increase in the rate of severe complications such as sepsis. In this paper, recurrent furunculosis and CA-MRSA's impact on this disease will be reviewed.

Increasing incidence of community-associated methicillin-resistant *Staphylococcus aureus* furunculosis in North America

The incidence of furunculosis is increasing in the U.S.A., and most new cases are caused by CA-MRSA. In a national surveillance study of U.S.A. ambulatory visits for skin and soft tissue infections, there was an increase in diagnoses of abscesses or cellulitis from 4·6 million in 1997 to 9·6 million in 2005, which accounted for 95% of the total observed increase in skin and soft tissue infections during the study period.[19] The greatest increase was found among patients under 18 years of age followed by the 18–44-year-old age group.[19] Another survey examining only U.S. emergency department (ED) visits discovered that the number of annual visits for skin abscesses or cellulitis rose from 935 000 to 2 950 000 during the years 1993–2005.[20] This change represented more than simply an increase in ED utilization, after it was noted that the proportion of ED visits for skin and soft tissue infections also rose significantly. In both reports, CA-MRSA was suspected to be the cause after the discovery of significant increases in the prescription of CA-MRSA-active antibiotics during each observation period. Orscheln *et al.*, who specifically reviewed skin abscess cultures from 1997 to 2007 taken at a children's hospital in St Louis, MO, U.S.A. measured the change and discovered a 250-fold increase in the incidence of CA-MRSA. During the same time span, the incidence of methicillin-sensitive *S. aureus* (MSSA) increased fivefold.[21] As a result of such growth, three reports now suggest that there is a high prevalence of CA-MRSA among furunculosis cases within the U.S.A. In a Los Angeles ED, Frazee *et al.*[22] found that 19 of 20 (95%) furuncles were caused by CA-MRSA, while Magilner *et al.*[23] determined that 51 of 60 (85%) furuncles from a paediatric ED in North Carolina were caused by CA-MRSA. A large prevalence study with data gathered from eleven urban EDs across the U.S.A. confirmed that the findings of Frazee and Magilner represent much of the country. In that report, 78% of all *S. aureus* skin and soft tissue infections were caused by MRSA, and 99% fit the definition of CA-MRSA based on the presence of the SCC*mec* type IV genetic unit.[24] However, outside the U.S.A., where the CA-MRSA epidemic is less aggressive, the prevalence of CA-MRSA in furunculosis is understandably low (see Table 1), and no data suggest that there is a similar ongoing furuncle epidemic.

Panton–Valentine leucocidin and its association with community-associated methicillin-resistant *Staphylococcus aureus*, furunculosis and recurrent furunculosis

S. aureus possesses a variety of virulence factors that assist the organism in evasion of immune defences and govern the clinical spectrum of disease. However, only one virulence factor, Panton–Valentine leucocidin (PVL) is linked to furunculosis, its recurrence in the same individual and CA-MRSA, helping to explain the organism's role in the growing furunculosis epidemic. PVL is a phage-encoded pore-forming protein that lyses

Table 1 Community-acquired methicillin-resistant *Staphylococcus aureus* prevalence in furunculosis

U.S.A.	Prevalence	Europe	Prevalence	Asia	Prevalence
2003–2004; Frazee *et al.*;[22] Los Angeles, California, U.S.A.; Emergency department	19/20 (95%)	2002–2008; Masiuk *et al.*;[30] Poland	1/74 (1·4%)	1987–1988; Ohana *et al.*;[81] Israel	1/136 (0·7%)[a]
2005–2006; Magilner *et al.*;[23] North Carolina, U.S.A.; Paediatric emergency department	51/60 (85%)	2004–2005; Durupt *et al.*;[31] France	1/31 (3·2%)	1997–2002; Yamasaki *et al.*;[37] Japan	7/40 (17·5%)
		1999–2004; Nolte *et al.*;[80] Germany	0/48 (0%)	1995–1996; Tan *et al.*;[6] Singapore	1/54 (1·9%)[b]

[a]An estimate, 1% of all infections were methicillin resistant. [b]Primary pyoderma was methicillin resistant. It is unknown if it was a furuncle.

neutrophils[25] and causes tissue necrosis in rabbits.[26] Neutrophils pour into the base of a hair follicle to phagocytose *S. aureus* bacteria and are destroyed in the process. Their lysosomal enzymes spill into the surrounding tissues leading to necrosis and abscess formation. Original epidemiological studies led by Cribier *et al.*[26] and Lina *et al.*[27] demonstrated that PVL was associated with deep primary skin infections, and the greatest association was with furuncles. Cribier *et al.*[26] found that six of seven furuncles had *S. aureus* isolates that produced PVL, whereas none of the 10 isolates from impetigo or folliculitis produced the toxin. Likewise, Lina *et al.*[27] determined that 28 of 30 furuncles possessed *S. aureus* with PVL genes, but identified the toxin in only five of nine cases of cellulitis ($P = 0{\cdot}01$) and in none of the 14 isolates from impetigo or folliculitis. Recent research by del Giudice's group[28,29] suggests that PVL is critical in furunculosis, playing a lesser part in the pathogenesis of skin abscesses in general. PVL was detected in 38 of 41 primary skin abscesses defined as occurring on previously healthy skin, compared with just two of 16 secondary skin abscesses.[28] This group then went on to confirm PVL's strong relationship with furuncles, detecting the toxin in 30 of 35 specimens, but they also recovered it from eight of 17 specimens of folliculitis, suggesting a propensity for the toxin to cause follicular skin infections in general.[29] Del Giudice's work as a whole shows that PVL equips *S. aureus* to penetrate the hair follicles of healthy skin and to progress from a superficial infection, folliculitis, to a deeper one in furunculosis. In this review, 83% (246/296)[26–33] of furuncles from eight molecular epidemiological studies possessed *S. aureus* isolates harbouring PVL genes, suggesting a major role for the toxin in causing furunculosis. Lina *et al.*[27] also found PVL to be prevalent in cases of *S. aureus* community-acquired necrotizing pneumonias, and with the emergence of several case reports describing PVL-producing MSSA and CA-MRSA necrotizing fasciitis,[34–36] the full scope of PVL-associated infections can be seen with their propensity for inducing tissue necrosis.

The clinical effects of PVL and its relationship to both disease severity and recurrence have been studied. In addition to finding the toxin to be associated with larger, more erythematous and more painful furuncles, Yamasaki *et al.*[37] uncovered the link to recurrent furunculosis; 10 of 16 (63%) patients with PVL-positive furunculosis had recurrent lesions compared with only four of 24 (17%) in PVL-negative furunculosis ($P < 0{\cdot}01$). Durupt *et al.*[31] carried out a similar study but did not achieve statistical significance in demonstrating an association with chronic furunculosis. Instead, the toxin was associated with a more communicable disease, which was called epidemic furunculosis and was defined as affecting patients who had at least one family member with the disease.[31] However, Durupt *et al.* did find an association between nasal colonization with *S. aureus* and recurrence. Of 16 patients with recurrent furunculosis, 14 (88%) were nasal carriers compared with just two of seven (29%) patients with simple furunculosis ($P = 0{\cdot}007$).[31]

The associative evidence between PVL, furunculosis and its recurrence is substantial but nevertheless has failed to stop the controversy surrounding the toxin's direct function in these processes, because of conflicting experimental data in animals. In one study, mice infected with CA-MRSA strains with PVL genes fared no worse than those without in both skin abscess and sepsis models.[38] However, in another investigation it was observed that higher production of PVL was associated with larger skin abscesses in mice infected with both community MSSA and MRSA strains.[39] Repeated inquiries into PVL's action during infection have not yielded a consensus, as the majority of animal studies support only a limited role if any at all in the pathogenesis of *S. aureus* infection.[40–43] As a result, it has been suggested that PVL-mediated *S. aureus* disease might require a susceptible host genetic background, or that animal models fail to account for a range of human factors such as target molecules for the toxin, which are still unknown.[44,45]

With regard to CA-MRSA, most studies indicate that PVL is a consistent marker for these strains within the U.S.A. with a prevalence ranging from 65% to 100%.[1,24,46] Among CA-MRSA skin and soft tissue infections, it has near universal association.[24] In Australia and Europe, a few CA-MRSA clones are circulating, practically all of which possess PVL genes, including one designated by multilocus sequence typing as ST80, which, described 10 years ago, was originally responsible for Europe's CA-MRSA epidemic,[47] and two strains prevalent in Eastern Australia named Queensland and South-West Pacific.[10] Del Giudice's team[48] followed a cohort of patients with CA-MRSA ST80 skin infections over a decade and observed their chronic nature and resistance to treatment. From 1999 to 2009 in a group of 20 people, of whom 19 had primary skin abscesses, eight of which were furuncles, recurrent infections occurred in four patients despite multiple antibiotic regimens coupled with strict hygiene measures and application of nasal mupirocin.[48]

However, the overall association between CA-MRSA and PVL in Europe and Australia is weaker than in North America, likely in part due to the strain diversification that was recently documented in France,[49] with estimates of overall PVL prevalence ranging from 25% to 50%.[50–53] In Ireland, a recent analysis deemed PVL to be a poor marker for CA-MRSA, which was reported in only two of 30 specimens, but this is the exception.[54] In contrast, PVL has no significant association with MSSA. PVL-producing MSSA strains accounted for < 5% of clinical MSSA infections in one study.[30] Therefore, the strong association between PVL and CA-MRSA in the U.S.A. has helped furunculosis become the primary manifestation of the CA-MRSA epidemic there. In the U.K., the rest of Europe and abroad, PVL is prevalent among, and indeed a marker for, certain CA-MRSA strains, but furunculosis is not yet an epidemic because of the lesser overall occurrence of CA-MRSA in these areas.

The molecular epidemiology of *Staphylococcus aureus* in furunculosis

In the U.S.A., a limited number of *S. aureus* clones have driven the current furuncle epidemic. Using pulsed field gel

electrophoresis, the pulsed field type of CA-MRSA underlying the majority of U.S.A. furuncle infections has been labelled U.S.A.300. Moran *et al.*'s multicity report demonstrated that CA-MRSA skin and soft tissue infections were caused by U.S.A.300 in 97% of cases, and 98% possessed PVL genes.[24] Further analysis with pulsed field gel electrophoresis showed that of the U.S.A.300 isolates, 74% were of a single strain designated U.S.A.300-0114. In a series of 20 furuncles from a Los Angeles ED, documenting 19 as resistant to methicillin, the use of multilocus sequence typing found the type ST8, of which U.S.A.300 is a member, to be the causative agent in close to 90% of cases, and it also carried PVL genes.[22]

PVL is the only virulence factor of *S. aureus* found to consistently correlate with furunculosis and recurrence. However, no evidence suggests that PVL-carrying MSSA strains outside of North America, which outnumber CA-MRSA strains clinically causing furunculosis (Table 1), are multiplying in the way that has been witnessed with PVL-carrying CA-MRSA in the U.S.A. Nevertheless, it would be desirable for epidemiological studies from Europe and other continents to be performed in order to evaluate this trend. At least one investigation shows the fitness of MSSA strains in Europe to be either comparable with or superior to two local CA-MRSA strains, as determined by the measurement of generation times,[55] frustrating efforts to discern the specific advantages that CA-MRSA possesses over MSSA in its dominant role in the furunculosis epidemic.

As such, the evidence affirms that, in addition to methicillin resistance, the core genetic background of *S. aureus* is vital to its fitness and ability to increase within a population. Acquisition of the DNA cassette SCC*mec* type IV and PVL into these well-adapted core genomes acts synergistically towards the generation of a superadapted clone with the ability to rapidly disseminate through a community causing furunculosis. The epidemiological findings by Orscheln and colleagues support this view.[21] MSSA contributed slightly to the large increase in skin abscesses in a St Louis, MO, U.S.A., ED with a fivefold rise from 1997 to 2007. From a sample of 31 isolates, nearly all were identified as the multilocus sequence type ST8, which contains the virulent U.S.A.300 as a member.[10] However, a 250-fold increase was observed in abscesses caused by CA-MRSA that were also largely represented by the U.S.A.300 clone.

In Europe, the clonal designation of most furuncle isolates is unknown because no multicentre epidemiological studies have been performed, but the data available suggest that a limited number of separate MSSA clones are largely responsible. Masiuk *et al.*[30] showed that 70% of all furuncle isolates collected in Poland were due to the clonal cluster designations 121 and 30, defined by protein A sequencing, while a familial outbreak in France was caused by the multilocus sequence type ST159. A valid concern raised by Masiuk's team is whether a furuncle epidemic will arise in Europe following acquisition of SCC*mec* type IV by a well-adapted PVL-carrying *S. aureus* clone.

Community-associated methicillin-resistant *Staphylococcus aureus* in the U.K.

Early data showing CA-MRSA in the U.K. surfaced from Health Protection Agency records of 2001, which was well after CA-MRSA's expansion in Australia and the U.S.A. in the 1990s.[10,16,56] In the first published reports, the prevailing PVL-equipped European clone ST80 and a strain from Australia were observed spreading through England and Wales.[57,58] Both strains were recovered from many different geographical locales, but while a community of injection drug users provided an epidemiological link for the spread of one Australian clone, no such link was uncovered among the many healthy community dwellers infected with the CA-MRSA clone ST80 who had various 'skin lesions' and abscesses including furuncles. By 2005, genetic diversification as a result of strain importation, which involved U.S.A. 300,[59] genetic shifts and horizontal transfers of the SCC*mec* type IV unit, took hold of the CA-MRSA epidemic in the U.K. Cities and hospitals developed characteristic profiles of the clones spreading through their populations. In a London teaching hospital from 2000 to 2006, CA-MRSA increased as a proportion of total MRSA isolates every year, and PVL-positive CA-MRSA increased from 12% of the isolates collected from 2000 to 2004 to 40% of those collected in 2005 and 2006.[53] The most common clone was WA-MRSA-1, originally classified in Western Australia, but U.S.A.300 and ST80 were also present along with many other types, as determined by protein A sequencing. In East Yorkshire from 2005 to 2007, the same three clones were present, but in different proportions, as ST80 and U.S.A.300 dominated, both of which carry PVL genes.[18]

Unlike in the U.S.A., there is a multiplicity of clones circulating in Great Britain's healthcare and community settings. Witnessed transfers of PVL and SCC*mec* type IV to healthcare-associated strains have placed Great Britain at the forefront of the discussion concerning the increasingly blurring lines between the epidemiological and molecular definitions of HA-MRSA and CA-MRSA.[60–62] With the importance of such distinctions being the ability to plan public health measures and correctly propose empirical antibiotic regimens, such work could become much more difficult as CA-MRSA clones present in the hospital setting are afforded the opportunity to develop further antibiotic resistance determinants, and are then passed on back to the community.

Risk factors for recurrent furunculosis

Despite the distinction from recurrent furunculosis, furunculosis outbreaks offer an insight into populations that are at risk from the disease by showing their predilection for healthy patient populations. Of six furunculosis outbreaks, three occurred in athletes, one in a family and two in villages (Table 2). Likewise, the hallmark of CA-MRSA infections is their indiscriminate targeting of a variety of healthy patient populations including athletes, military personnel and children.[12] Nevertheless, within seemingly healthy populations

Table 2 Outbreaks and case reports of furunculosis

Reference	Population	Risk factors identified using control	Outcome
1980s and earlier			
Bartlett *et al.*[82]	High school football team (Illinois, U.S.A.)	Skin trauma, exposure	55 furuncles, 26 people, 4 months; methicillin-sensitive; 3·2 furuncles/person-6 months
Sosin *et al.*[83]	High school football and basketball team (Kentucky, U.S.A.)	Skin trauma, exposure	71 furuncles, 31 people, 6 months; antibiotic resistance not tested; 2·3 furuncles/person-6 months
1990s			
Landen *et al.*[76]	Alaskan village	Exposure	186 boils, 115 people, 12 months; CA-MRSA; 0·8 furuncles/person-6 months
2000–present			
Pérez-Roth *et al.*[75]	Family in Spain	Exposure	10 furuncles, 6 people, 17 months; methicillin-sensitive; 0·6 furuncles/person-6 months
Müller-Premru *et al.*[84]	Europe, football team	Skin trauma, exposure	Undetermined amount of furuncles numbering at least 10, 10 people, 4 months; CA-MRSA
Embil *et al.*[85]	Canada, case report	Exposure	3 furuncles, 39 days, CA-MRSA; 13·8 furuncles/person-6 months
Wiese-Posselt *et al.*[86]	German village	Exposure	101 furuncles, 42 people, 6 years; 11 months; methicillin-sensitive; 0·2 furuncles/person-6 months

CA-MRSA, community-associated methicillin-resistant *Staphylococcus aureus*.

both endogenous risk factors, such as acquired immunodeficiencies, and exogenous risk factors, such as *S. aureus* skin colonization, play a role in the promotion of recurrent furunculosis.

Endogenous risk factors

Recurrent furunculosis can be a manifestation of underlying acquired immune dysfunctions. These include diabetes mellitus, human immunodeficiency virus infection, alcoholism and malnutrition.[63] However, even among the seemingly healthy, in the absence of these common risk factors, different defective immune system functions have been unexpectedly uncovered as promoters of infection. Kars *et al.*[64] described a severe familial outbreak of furunculosis and showed that deficiency of mannose-binding lectin in the complement system was an unknown, underlying risk factor. Research carried out in an elderly cohort from the Netherlands revealed specific polymorphisms in C-reactive protein, an acute-phase reactant, while both opsonin and complement factor H, a negative regulator of complement against self-antigens, were overrepresented in patients with boils.[65]

Neutrophils play a critical role in combating bacterial infections, and their defectiveness has been observed in several studies of patients with recurrent furunculosis. Among a group of mentally retarded adults, mostly due to Down syndrome, those with recurrent furunculosis were more likely to demonstrate impaired neutrophil chemotaxis.[66] Neutrophilic production of nitric oxide, an important cytokine-regulating molecule and bactericidal agent, was shown by Hamaliaka *et al.*[67] to be deficient in patients with recurrent furunculosis. In a separate report by Demirçay *et al.*,[68] other key neutrophil activities such as phagocytosis and generation of the respiratory burst were also impaired, but only in an iron-deficient subgroup of patients with recurrent furunculosis. Interestingly, iron deficiency has been associated with reduced activity of myeloperoxidase, among other respiratory enzymes,[69,70] and was a risk factor for recurrent furunculosis in the absence of anaemia in a study conducted by Weijmer *et al.*[71] All but one of 16 patients supplemented with iron over 3–4 weeks were cleared of further infection.

Exogenous risk factors

As evidence exists for both PVL toxin production[37] and nasal carriage of *S. aureus*[31] being separate risk factors for recurrent furunculosis, two studies, one headed by Couppie[33] and the other by Prevost,[32] have gone on to demonstrate that both factors together strongly correlate with the recurrence of furuncles. PVL-carrying *S. aureus* strains harboured in the nares appear to provide a reservoir for efficient toxin-mediated invasion of the hair follicle. Combining the results from both studies, all 15 patients with recurrent furunculosis were nasal carriers of PVL-positive *S. aureus*.[32,33] PVL-positive *S. aureus* nasal carriage among healthy persons was found to be rare. Masiuk *et al.*[30] and Prevost *et al.*[32] both detected the toxin in only one of 149 (0·1%) healthy nasal carriers.

It is important to consider modifiable exogenous risk factors when considering treatment in a patient with recurrent furunculosis. Dahl[72] noted that a group of his patients with recurrent furunculosis suffered from hyperhidrosis, and surmised that local moisture and occlusion, which may occur from tight clothing or obesity, promote local bacterial growth and injury to the hair follicle contributing to repeat infection. El-Gilany and Fathy[73] performed a case–control study between patients with recurrent furuncles and single furuncles, highlighting many modifiable endogenous and exogenous risk factors. The strongest independent factor for recurrence was family history, which could represent either an exposure risk to an infected individual or a genetic impairment. Other risk factors described in the study were poor personal hygiene, obesity, immunosuppressant therapy, antibiotic therapy, previous hospitalization, anaemia, diabetes mellitus and skin disease.[73] A case report by Levine[74] highlighted the risk of immunosuppressive therapy by reporting a carbuncle developing in the setting of antitumour necrosis factor therapy for Crohn disease.

The most important risk factor for recurrence is continued exposure to an infection source, with the most likely source being oneself in the form of skin colonization. The source can also be a family member, as noted in both El-Gilany and Fathy's[73] case–control study and the report of a familial outbreak.[75] A review of furuncle outbreaks indicates that sources may be fellow members of a sports team, the community, or shared communal facilities such as Alaskan steam baths as noted in one study.[76] A key source for return of the infection is skin colonization of the affected individual, especially of the anterior nares, the most common site of *S. aureus* skin colonization.[77] Summation of data from four reports demonstrated nasal colonization in patients with recurrent furunculosis in 79 of 131 (60%) cases.[31–33,78] In comparison, 20% of asymptomatic adults have persistent colonization.[77] 'Skin condition' was also found to be a risk factor by El-Gilany and Fathy,[73] and most likely represents a predisposition from local colonization and damage to the hair follicle. However, it should be noted that in skin conditions such as atopic dermatitis, the rate of nasal carriage of *S. aureus* is higher than in the general public, and provides an additional bacterial source for the development of furuncles.[79]

In conclusion, the incidence of CA-MRSA in the U.S.A. continues to increase, and the main manifestation of the epidemic is follicular infection, which most commonly is folliculitis followed by furunculosis after considering selection bias towards more severe disease. The acquisition of PVL and SCC*mec* type IV genes by a fit clone, U.S.A.300, is playing a dominant role and shows no signs of slowing. In comparison, the epidemiological data outside the U.S.A. suggest that CA-MRSA is causing furunculosis and is increasing, but its overall prevalence compared with the U.S.A. is still low. PVL is associated with the progression of follicular skin infections ranging from folliculitis to furunculosis and also with recurrence. Colonization of oneself, the anterior nares in particular, with PVL-producing *S. aureus* strains is likely the strongest risk factor behind recurrence. However, in some apparently healthy patients without acquired immunodeficiencies such as diabetes mellitus, skin colonization cannot be detected. In such instances, neutrophil dysfunctions have been reported as an underlying cause and should be investigated in these persons.

What's already known about this topic?

- Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is increasing in incidence.
- Panton–Valentine leucocidin (PVL) is the primary virulence factor of CA-MRSA and is associated with skin abscesses as well as necrotizing pneumonia.

What does this study add?

- CA-MRSA furuncles are increasing in incidence, with the sharpest rise in the U.S.A.
- PVL is associated with recurrent furunculosis.
- Nasal colonization with MRSA bearing the PVL toxin is a very strong risk factor for recurrent furunculosis.

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