For the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy.[1]

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The first licensed biologic that inhibits IL-13 alone,[1,2] a key driver of atopic dermatitis signs and symptoms.[3]

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IL, interleukin.
*Interim analysis from ongoing open label extension study (data cut off: April 30 2021).[4] The 2-year cohort subgroup (n=86) included patients previously treated with Adtralza® monotherapy for 52 weeks in ECZTRA 1 and 2, followed by a washout period >15 weeks from last treatment in parent trial, then assigned to 104 weeks' treatment in ECZTEND study.[4] Primary endpoint was number of adverse events from baseline to last treatment visit (up to Week 268).[4]
**Data from 2-year interim safety analysis of the ECZTEND study, which included patients from parent trials ECZTRA 1, 2, 3, 4, 5 and 7.[5]

Prescribing information for Adtralza®▼ (tralokinumab) 150 mg solution for injection in pre-filled syringe
Please refer to the full Summary of Product Characteristics (SmPC) (www.medicines.org.uk/emc) before prescribing.
▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. **Indications:** Treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. **Active ingredients:** Each pre-filled syringe contains 150 mg of tralokinumab in 1 mL solution (150 mg/mL). **Dosage and administration:** *Posology:* The recommended dose of tralokinumab is an initial dose of 600 mg (four 150 mg injections) followed by 300 mg (two 150 mg injections) administered every other week as subcutaneous injection. Every fourth week dosing may be considered for patients who achieve clear or almost clear skin after 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment. Some patients with initial partial response may subsequently improve further with continued treatment every other week beyond 16 weeks. Tralokinumab can be used with or without topical corticosteroids. The use of topical corticosteroids, when appropriate, may provide an additional effect to the overall efficacy of tralokinumab. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas. If a dose is missed, the dose should be administered as soon as possible and then dosing should be resumed at the regular scheduled time. No dose adjustment is recommended for elderly patients, patients with renal impairment or patients with hepatic impairment. For patients with high body weight (>100 kg), who achieve clear or almost clear skin after 16 weeks of treatment, reducing the dosage to every fourth week might not be appropriate. The safety and efficacy of tralokinumab in children below the age of 18 years have not yet been established. *Method of administration:* Subcutaneous use. The pre-filled syringe should be not shaken. After removing the pre-filled syringes from the refrigerator, they should be allowed to reach room temperature by waiting for 30 minutes before injecting. Tralokinumab is administered by subcutaneous injection into the thigh or abdomen, except the 5 cm around the navel. If somebody else administers the injection, the upper arm can also be used. For the initial 600 mg dose, four 150 mg tralokinumab injections should be administered consecutively in different injection sites. It is recommended to rotate the injection site with each dose. Tralokinumab should not be injected into skin that is tender, damaged or has bruises or scars. A patient may self inject tralokinumab or the patient's caregiver may administer tralokinumab if their healthcare professional determines that this is appropriate. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Precautions and warnings:** If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of tralokinumab should be discontinued and appropriate therapy initiated. Patients treated with tralokinumab who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination. Patients with pre-existing helminth infections should be treated before initiating treatment with tralokinumab. If patients become infected while receiving tralokinumab and do not respond to antihelminth treatment, treatment with tralokinumab should be discontinued until infection resolves. Live and live attenuated vaccines should not be given concurrently with tralokinumab. **Fertility, pregnancy and lactation:** There is limited data from the use of tralokinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of tralokinumab during pregnancy. It is unknown whether tralokinumab is excreted in human milk or absorbed systemically after ingestion. Animal studies did not show any effects on male and female reproductive organs and on sperm count, motility and morphology. **Side effects:** *Very common (≥1/10):* Upper respiratory tract infections. *Common (≥1/100 to <1/10):* conjunctivitis, conjunctivitis allergic, eosinophilia, injection site reaction. *Uncommon (≥1/1,000 to <1/100):* keratitis. **Precautions for storage:** Store in a refrigerator (2°C-8°C). Do not freeze. Store in the original package in order to protect from light. **Legal category:** POM **Marketing authorisation number and holder:** PLGB 05293/0182, EU/1/21/1554/002. LEO Pharma A/S, Ballerup, Denmark. **Basic NHS price:** 4 pre-filled syringes: £1,070 (each syringe contains 150 mg/mL). **Last revised:** July 2021. **Reference number:** REF-19086(2)

Reporting of Suspected Adverse Reactions
Adverse events should be reported.
Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Drug Safety at LEO Pharma by calling +44 (0)1844 347333 or e-mail: medical-info.uk@leo-pharma.com

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Review article

CED
Clinical and Experimental Dermatology

CPD

Panton–Valentine leucocidin-producing *Staphylococcus aureus*: a clinical review

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Abstract

Panton–Valentine leucocidin (PVL) is a virulence factor produced by certain strains of *Staphylococcus aureus* (SA). Through its cytolytic action on the cell membranes of human polymorphonuclear neutrophils, PVL causes a range of pathologies collectively known as PVL-SA disease. The hallmark clinical signs of PVL-SA are recurrent boils and necrotizing skin and soft tissue infections (SSTIs) in otherwise healthy patients; however, it can lead to more severe and invasive presentations, including necrotizing haemorrhagic pneumonia, necrotizing fasciitis and purpura fulminans. Young adults with minimal previous exposure to healthcare settings tend to be at highest risk for acquiring PVL-SA disease, with close physical contact playing a central role in disease transmission. The prevalence of PVL-SA varies globally; however, this is often underestimated owing to a lack of routine PVL testing. In the UK, PVL-positive SA isolates have been rising over the past decade alongside an increasing prevalence of multidrug resistance in larger cities. This review article aims to raise awareness of the PVL toxin, to aid clinicians with diagnostic pointers and to provide guidance with treatment, with an emphasis on the need for further population-based studies.

Introduction

Panton–Valentine leucocidin (PVL) is an exotoxin produced by certain strains of *Staphylococcus aureus* (SA). Originally discovered by Panton and Valentine in 1932,[1] PVL is a virulence factor, which causes a range of diseases known as collectively known as PVL-SA disease, typically presenting as recurrent skin and soft tissue infections (SSTIs) despite antibiotic treatment.[2,3] PVL may be produced by different strains of SA, both methicillin-sensitive SA (MSSA) and methicillin-resistant SA (MRSA). The proportion of PVL-SA is higher in infections caused by MRSA (74–100%) than in those caused by MSSA (9–46%), with the proportion being dependent on the prevalence of MRSA in the respective regions.[4] Rarely, PVL can lead to very serious invasive infections, including necrotizing haemorrhagic pneumonia (which has a mortality of up to 75%).[2] SA is known to colonize the skin and mucosa of 20–30% of healthy adults.[2] Recent analysis of PVL-positive SA isolates in the UK have been reported at ~20%.[5] This is significantly different from the prevalence in 2005, which was < 2%.[1] With its potential for severe disease, high transmissibility and reports of antimicrobial resistance in comparison to PVL-negative strains, it is important that dermatologists worldwide are aware of the urgency of early recognition and treatment of PVL-SA infection.[3,6]

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Early clinical suspicion and diagnosis is crucial for survival; however, only a quarter of cases present with current skin infection or a history of recurrent skin infections.[7]

Epidemiology

PVL was first reported in emerging community-acquired MRSA strains in the 1990s, with the hypervirulent MRSA strain ST8/USA300 quickly becoming the main PVL-producing clone in the USA.[3,8] The documented prevalence of PVL-SA disease varies globally and is linked to strain types and lineages.[2]

The community-acquired strains are differentiated from hospital-acquired strains by the presence of the mobile genetic elements, known as staphylococcal cassette chromosomes mec (SCCmec), which code for methicillin resistance genes. Of these, SCCmec Types I, II and III are found in hospital-acquired MRSA (HA-MRSA) strains and Types IV and V (which are smaller) are found in community-acquired MRSA (CA-MRSA) strains.[9,10] Clonal complexes of CA-MRSA, which dominate in Australia, Europe and North America, contain the Type IV SCCmec element along with the PVL locus. The shorter SCCmec elements are believed to contribute to the survival of these strains and their shorter doubling time.[9,10] In the USA, the ST8-SCCmecIV USA300 clone is predominant, with other strains predominating elsewhere: ST80 in Europe and the Middle East, ST59 in Asia, ST30 in New Zealand, ST93 in Australia, ST88 in Africa, and ST22 and ST772 in Asia.[3,8,11] Following the hypervirulent USA300 strain, there are new hypervirulent strains arising in Africa, Asia and Europe, such as the ST121 strain, which has a high frequency of PVL positivity (~90%).[12]

PVL testing is not routinely carried out at local hospital microbiology laboratories unless requested by a clinician,[5] hence the prevalence is often underestimated. Specimens from severe disease are more commonly tested for PVL toxin genes rather than minor SSTIs,[2,3] leading to bias in many retrospective studies.[3] Moreover, the broad range of PVL-SA disease means it is not always suspected, further contributing to inaccuracies in epidemiological data.[2,3]

In the UK, again not withstanding ascertainment bias, data demonstrate that 20.8–46% of SA isolates from skin or soft tissue infections contain PVL-producing SA strains.[13,14] These are most commonly from skin abscesses.[12] PVL-producing community MRSA strains are rarely reported in the UK, with the majority of PVL strains reported being MSSA.[2,5,13]

However, globally the strain type and prevalence vary significantly (Table 1).[2] In the USA, the hypervirulent PVL-SA MRSA strain USA300 has a strong association with SSTIs.[15] Europe has a lower number of methicillin-resistant PVL-SA, apart from in Greece and Cyprus, where PVL-positive MRSA isolates were found have rates of 27% and 27.7% respectively.[2,16,17]

International travel is an established factor in the global dissemination of strain types of the hypervirulent USA300 clone, hence rapid diagnosis along with effective antimicrobial therapy are imperative.[18]

Risk factors

Patients with PVL-SA are often young adults with very little or no previous exposure to healthcare settings.[2,5,19,20] Factors increasing the risk of acquiring PVL-SA-related disease have been categorized into the 'Five Cs' by the US Centre for Disease Control and Prevention. These are: (i) close contact; (ii) contaminated items, (iii) crowding, (iv) cleanliness, and (v) cuts and other compromised skin integrity.[21] They can be similar to features for other cutaneous infections. There have been reported outbreaks in a variety of different communities, with certain groups being recognized as at risk.[22] These include children,[23] prisoners,[24] those who play close contact sports,[25] men who have sex with men[26] and the military.[27] Close contact dominates as an important factor in disease transmission.[2]

Pathogenesis

The pathogenesis of PVL-SA diseases arises from the cytolytic pore-forming action of the PVL toxin, which induces cell apoptosis through the intrinsic pathway of cells.[28,29] PVL is a cytotoxin composed of two proteins: LukS-PV and LukF-PV, which are encoded by two genes (*lukS-PV* and *lukF-PV*) carried on temperate bacteriophages.[3,13]

Table 1 Summary of Panton–Valentine leucocidin prevalence published globally.

Region	PVL-SA disease prevalence, %
USA	29[15]
Europe	18.6[48]
Tehran	4.6%[49]
Australia	28–54[50,51]
Western Africa	47–75[52]
Nepal	35.6–56.8[36,53]

PVL–SA, Panton–Valentine leucocidin *Staphylococcus aureus*.

These two components are secreted by SA and act synergistically to create one hetero-octameric unit, which binds to the C5AR and C5A2 human complement receptors of human polymorphonuclear neutrophils (PMNs), monocytes and macrophages.[28,29] Initially, the LukS-PV subunit binds to the human complement receptor C5AR, which then results in the secondary binding of LukF-PV to form the assembly of one bi-component toxin that creates pores in the cell membranes.[30] This eventually leads to cell membrane lysis and cell death.[28,29,31]

The mode of cell death in PVL-SA has been shown to be toxin concentration-dependent. Concentrations of 0.3–2 μg/mL result in local cell necrosis, whereas at lower sublytic concentrations, cell death occurs through apoptosis in peripheral circulating cells.[31] This indicates that direct bacterial invasion by SA is not strictly required for apoptosis to occur. Neutrophil apoptosis occurring in the peripheral circulation plays a significant role in the depletion of phagocytosis, significantly reducing the first-line defence of cells against bacteria.[31] Neutropenia is found to be significantly more frequent in cases of necrotizing pneumonia that are PVL-positive, compared with cases that are PVL-negative.[31] The additional release of proinflammatory cytokines and nuclear factor κB in neutrophils has also been reported to be a virulence factor in necrotizing infections.[3,10]

Although USA300 is a widely accepted globally hypervirulent strain, whether or not its virulence is directly related to PVL gene expression is controversial. Neutrophil lysis is widely accepted to have a role in PVL-SA disease; however, initially in trials on rabbits (in which neutrophils are highly sensitive to PVL gene expression) it was found that lysis had a limited impact on virulence and there may be a role for the expression of other virulence factors, such as the α toxin from *agr* gene expression.[32] This was further reflected in human trials, in which it was found that PVL-positive infections did not result in a worse clinical outcome regardless of methicillin resistance; in fact, other genes were also noted to produce a statistically significant clinical impact on disease response, including the aforementioned type IV SCCmec element and the *agr* group of genes.[33] Furthermore, a recent case–control study in the USA found no difference in final clinical outcomes when comparing PVL-positive cases with control cases, highlighting the role of *agr*-dependent expression of α toxins, as well as the arginine catabolic mobile element (ACME).[16] Regardless, it has been shown in both animal and human studies that there is consistently a link between PVL positivity and its hallmark clinical manifestations of SSTIs and severe pneumonia, especially in younger populations.[33,34]

Clinical presentation

PVL-SA presents as a broad range of disease, ranging from asymptomatic nasopharyngeal carriage of PVL-SA to severe necrotizing disease.[35] These can be divided into dermatological and nondermatological presentations.

Dermatological presentations

The hallmark signs of PVL-SA include recurrent boils and necrotizing SSTIs in otherwise healthy patients, particularly when other members of the same household or close community also present with similar signs (Fig. 1). The most common SSTIs seen with PVL-SA are furunculosis, carbuncles, folliculitis, cellulitis, abscesses and skin necrosis, which tend to recur despite several courses of antibiotics and delay the diagnosis of PVL-SA disease.[2,19,21] It is also important to appreciate that associated pain/erythema can be out of proportion to the severity of the clinical signs.

Nondermatological presentations

PVL-SA can lead to invasive infections in previously immunocompetent patients. In those with community-acquired pneumonia, haemoptysis should be a major alerting sign for necrotizing pneumonia[2,7] with further imaging to elucidate this. Haemoptysis is typically preceded by a period of influenza-like prodrome in these patients (typically children and young adults).[3] Around a quarter of patients have a prior history of skin lesions, either personal or in a close contact.[20]

Other invasive infections include necrotizing fasciitis and purpura fulminans. PVL-SA disease can present as severe musculoskeletal infections such as osteomyelitis, pyomyositis and septic arthritis, especially in children. Compared with PVL-negative SA infections, these musculoskeletal infections have been associated with higher complication rates, elevated levels of inflammation and prolonged hospital stay, and overall are more likely to require surgical treatment.[3,36,37]

Investigations

A bacterial swab should be taken if there is a clinical suspicion of PVL-SA, based on features such as recurrent boils/abscesses or necrotizing SSTIs, or if there is ≥ 1 case in a home or closed community.

For diagnosis of suspected cases, a swab should be taken from the infected areas of the skin and nares in all cases, including pus, exudate from a lesion or sputum

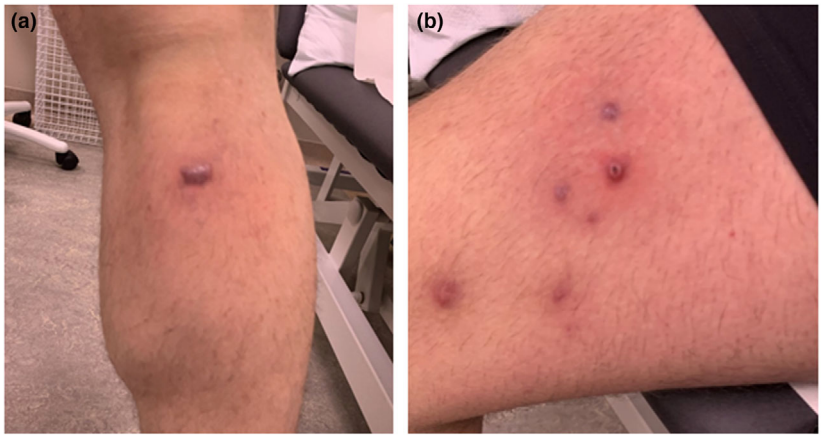

Figure 1 (a, b) A patient presenting with Panton–Valentine leucocidin-induced skin infection with violaceous nodules present on (a) the calf and (b) inner thigh with surrounding erythema and minimal discharge in a nonspecific distribution.

for invasive cases, and sent to the laboratory with a request for microscopy, culture and antimicrobial susceptibility testing. PVL should be specifically requested in the clinical details. Diagnosis of PVL-SA disease requires clinical samples from suspected cases to be sent to for molecular diagnostics.[2] This is not routinely done in many healthcare settings, hence clinical suspicion is key in the diagnosis of PVL-SA disease.[3,8] With a suspected case of necrotizing pneumonia, co-infection with influenza should also be investigated.[20,38] In hospital, if there are suspected or confirmed cases of PVL-SA, personal protective equipment (PPE) should be used, particularly if PVL necrotizing pneumonia is suspected, as this requires side room isolation.

Molecular diagnostics are often not performed in peripheral laboratories and require referral to national reference laboratories (as in the UK via Public Health England, which can introduce a significant delay in results).[22] As multiplex PCR assays become cheaper and able to be miniaturized, PVL testing should become more decentralized, particularly in high-resource countries. For use in low- and middle-income countries, there are now lateral flow assays that provide near real-time results from cultures of SAs, albeit with reduced sensitivity compared with molecular diagnostics; however, these may prove pragmatic in services where molecular diagnostics are inadequate.[39]

Treatment

Once diagnosed, PVL-SA infection must be treated appropriately, without delay. Initial empirical antimicrobial coverage generally includes an anti-staphylococcal regimen and an anti-toxin agent able to block the production of the toxin.[3] Treatment for PVL-SA disease depends on the severity of the clinical presentation (Table 2).[40]

To date, all treatment option combinations (Table 2) have been proven successful; however, antimicrobial susceptibility tests should be performed to direct the antibiotic treatment option of choice. There is no evidence suggesting that dual therapy is essential, except when using rifampicin or covering multiple pathogens in severe infection. Monotherapy with rifampicin alone should never be prescribed as monoresistance rapidly occurs after days.[3,20]

There have been reported experience of community PVL-MSSA cases failing treatment with commonly used antibiotics such as flucloxacillin.[2] This can be explained by studies showing that suboptimal tissue concentration of flucloxacillin enhances the transcription of the PVL toxin gene, thus upregulating the release of PVL increasing toxicity.[41] By contrast, clindamycin, linezolid and fusidic acid have been found to significantly downregulate the release of the PVL toxin through suppression of translation, thought to be due to better soft tissue penetration.[2,3,42]

After primary treatment of the patient's disease, preventative measures are crucial to stop infections from recurring and to interrupt the transmission through the community. Decolonization plays a key role in achieving this.[3,40] All patients (along with their close contacts and/or family members living in the same household) should undergo a 5-day course of topical decolonization with chlorhexidine 4% wash once daily and mupirocin nasal ointment applied three times

Table 2 Summary of Panton–Valentine leucocidin-producing *Staphylococcus aureus*-associated skin and soft tissue disease classified according to severity of presentation.

PVL-SA severity	Treatment
Incidental diagnosis	Requires decolonization of both patient and household members with chlorhexidine as a daily wash and shampoo on Days 1, 3 and 5, as well as mupirocin nasal ointment applied three times daily for 5 days. Personal hygiene measures, avoiding sharing fomites and regularly cleaning of shared household areas should also be followed[20]
Minor SSTI	Lesions should be appropriately covered with a clean and dry dressing. Topical antibiotics (fusidic acid three times daily for 5 days for MSSA, mupirocin three times daily for 5 days for MRSA), may be considered for localized areas or in patients who are immunocompromised or show clinical deterioration[22] Additional incision and drainage if required for presentation with abscesses[2,3,41]
Moderate SSTI (not for hospital admission)	Requires a 5–7-day course of oral antibiotic treatment[22] MSSA infection options: Clindamycin 450 mg four times daily Flucloxacillin 500 mg four times daily MRSA infection options Rifampicin 300 mg twice daily + doxycycline 100 mg twice daily (not for children < 12 years of age) Rifampicin 300 mg twice daily + fusidic acid 500 mg three times daily Rifampicin 300 mg twice daily + trimethoprim 200 mg twice daily Rifampicin 300 mg twice daily + doxycycline 100 mg twice daily Clindamycin 450 mg four times daily Additional incision and drainage if required for presentation with abscesses[2,3,41]
Severe infection or systemic upset	Empirical antibiotic therapy of parenteral clindamycin 1.2 g four times daily and linezolid 600 mg twice daily should be started and continued for 48–72 h until culture results are received from Microbiology for clindamycin sensitivity. If resistance is found, clindamycin can be replaced with linezolid.[8,29] If patient is clinically deteriorating (toxic shock, necrotizing fasciitis or purpura fulminans), consider the use of IV immunoglobulins and early surgical debridement if warranted. IV flucloxacillin (either alone or in combination with other agents) should not be given.[22] Treatment should be continued for 10–14 days until the patient has improved and is clinically stable

IV, intravenous; PVL, Panton–Valentine leucocidin; SA, *Staphylococcus aureus*; SSTI, skin and soft tissue infection.

daily, without prior PVL gene screening.[43,44] To further prevent the spread of PVL-SA, personal hygiene measures in relation to close contacts must be followed. Fomites such as toiletries, towels and clothes should be kept separately from those of others and washed frequently, while shared household areas and shared personal/household items should be regularly vacuumed and/or cleaned with a household detergent. Washing hands frequently with liquid soap and water, especially after changing plasters/dressings and touching infected skin should be encouraged. To date, there are no reports of a significant association between livestock-associated MRSA and antibiotic-resistant PVL-MRSA strains; however, standard hygiene precautions should be adhered to when dealing with animals and handling raw meat.[45]

Repeated decolonization has been found to greatly reduce the chances of reinfection, with patients being 89% less likely to be reinfected after the fifth course of topical decolonization.[46] If mupirocin resistance is found, neomycin-based nasal ointments can be used, and if there is allergy to chlorhexidine, octenidine antimicrobial wash lotion (Octenisan®; Schülke & Mayr, Norderstedt, Germany) can be used.

Conclusion

Although the discovery of PVL-SA has been in existence for almost a century, the recent increased prevalence of the disease may be attributed to a number of reasons, including wider access to PCR-based technologies in routine diagnostic laboratories, a higher index of clinical suspicion with available testing, and an increase in human–human contact and international travel. However, this remains to be fully elucidated. Large cities reflect this by demonstrating a wide and evolving genetic diversity of PVL-SA, and our centre has confirmed this with a high prevalence of multidrug resistance seen in northwest London.[47] Further work is needed to establish a more accurate representation of the global prevalence of PVL-SA and its increasing antibiotic resistance, particularly in the community, through population-based studies. Public health surveillance is crucial here, either through consolidated laboratory surveillance systems or through a sentinel surveillance programme. Future research should be prospective to avoid ascertainment biases, with a greater emphasis on network analyses to identify modes of crosstransmission with public health

measures to interrupt this. Finally, there needs to be further emphasis on those who manage SSTIs (primary care physicians, acute physicians and dermatologists), highlighting the awareness of PVL and the need to specifically liaise with microbiology colleagues to enact testing where it is suspected.

Learning points

- PVL is a virulence factor produced by certain strains of SA.
- The hallmark clinical signs of PVL-SA are recurrent boils and necrotizing SSTIs.
- Nondermatological manifestations can include necrotizing haemorrhagic pneumonia in otherwise healthy patients.
- There is no routine testing for PVL and therefore the prevalence is likely to be underestimated.
- For moderate to severe skin infections, an antitoxin antimicrobial such as clindamycin or linezolid is advised.
- After primary treatment, SA decolonization plays an important role in reducing recurrence of the condition.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Ethics statement

Ethics approval and informed consent not applicable.

Data availability

Data openly available in a public repository that issues datasets with DOIs.

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CPD questions

Learning objective

To gain up-to-date knowledge about Panton–Valentine leucocidin-producing *Staphylococcus aureus* and associated disease.

Question 1

Which of the following groups is most commonly affected by Panton–Valentine leucocidin-producing *Staphylococcus aureus* (PVL-SA) disease?

(a) Elderly patients in hospital.
(b) Immunosuppressed patients.
(c) Prisoners of any age.
(d) Women of childbearing age.
(e) Young adults with no comorbidities.

Question 2

Which of the following describes the correct preventative measures after the primary infection has been managed?

(a) A 3-day course of chlorhexidine 4% wash used once daily by the infected patient.
(b) A 5-day course of chlorhexidine 4% wash used once daily and mupirocin nasal ointment applied three times daily by the infected patient and their close contacts.
(c) A 10-day course of chlorhexidine 4% wash used once daily and mupirocin nasal ointment applied three times daily by the infected patient and their close contacts.
(d) A 5-day course of chlorhexidine 4% wash used once daily and mupirocin nasal ointment applied three times daily by the infected patient.
(e) A 5-day course of chlorhexidine 4% wash used once daily by the infected patient and their close contacts.

Question 3

Which of the following is effective in the treatment of a Panton–Valentine leucocidin-related skin and soft tissue infection?

(a) Amoxicillin.
(b) Cefalexin.
(c) Clindamycin.
(d) Trimethoprim.
(e) Doxycycline.

Question 4

Based on the literature, which of the following can be used to help identify a case of Panton–Valentine leucocidin positive necrotizing pneumonia?

(a) Eosinophilia.
(b) Neutrophilia.
(c) Haemoptysis.
(d) Neutropenia.
(e) Eosinopenia.

Question 5

Which of the following should never be used to treat a patient with severe infection with systemic symptoms?

(a) Intravenous immunoglobulins.
(b) Intravenous clindamycin and linezolid.
(c) Intravenous flucloxacillin.
(d) Early surgical debridement.
(e) IV rifampicin.

Instructions for answering questions

This learning activity is freely available online at http://www.wileyhealthlearning.com/ced

Users are encouraged to

- Read the article in print or online, paying particular attention to the learning points and any author conflict of interest disclosures.
- Reflect on the article.
- Register or login online at http://www.wileyhealthlearning.com/ced and answer the CPD questions.
- Complete the required evaluation component of the activity.

Once the test is passed, you will receive a certificate and the learning activity can be added to your RCP CPD diary as a self-certified entry.

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