

Report

Colonization with community-acquired methicillin-resistant *Staphylococcus aureus* in children with atopic dermatitis: a cross-sectional study

Alexandra Balma-Mena¹, MD, Irene Lara-Corrales¹, MD, MSc, Jeanne Zeller¹, MD, Susan Richardson², MD, Martin J. McGavin³, PhD, Miriam Weinstein¹, BSc, MD, and Elena Pope¹, MD, MSc

¹Division of Pediatric Dermatology, Department of Pediatrics and ²Pediatric Laboratory Medicine, Division of Microbiology, Hospital for Sick Children, Toronto, and ³Department of Microbiology and Immunology, University of Western Ontario, London, ON, Canada

Correspondence

Irene Lara-Corrales, MD, MSc
Hospital for Sick Children and
University of Toronto
555 University Avenue
Toronto
ON M5G 1X8 Canada
E-mail: Irene.lara-corrales@sickkids.ca

Conflicts of interest: None.

Funding: Canadian Dermatology Foundation.

Abstract

Background Bacterial infection with *Staphylococcus aureus* is a common complication of atopic dermatitis (AD). The incidence of community-acquired methicillin-resistant *S. aureus* infection (MRSA) in the AD population is unknown.

Objectives This study aimed to assess the prevalence of *S. aureus* and MRSA in pediatric patients with AD, to compare disease severity, and to characterize the clonal diversity of the isolates.

Methods We carried out a prospective, cross-sectional study of 200 patients with AD. The severity of AD was defined as mild, moderate, or severe depending on a composite AD severity score. A swab was taken from the nares of each patient and another from affected skin or folds. Genotyping of all *S. aureus* isolates was conducted by polymerase chain reaction (PCR) amplification of the *S. aureus* protein A (*spa*) gene.

Results According to the severity score, 66.5% of subjects were ranked as having mild AD, 29.5% as having moderate and 4% as having severe AD. *Staphylococcus aureus* colonization was seen in 61.5% of all patients, represented by 43.7% of skin swabs and 48% of nares swabs. Only one of the isolations represented MRSA. Older age and higher AD severity scores were associated with *S. aureus* colonization ($P = 0.03$ and $P < 0.001$, respectively). No significant associations were noted for attendance at day care, family members with frequent skin infections, or family members working in healthcare. Isolates from *spa* CC015 were cultured in 19.2% of patient samples. The single MRSA culture showed a new *spa* type that belonged to CC127.

Conclusions The results of this study confirm a high rate of *S. aureus* colonization of pediatric patients with AD. The low rate of MRSA requires further proof from larger prospective studies.

Introduction

Atopic dermatitis (AD) is the most common inflammatory skin condition in pediatric patients, affecting 5–20% of children worldwide.¹ In Canada, its prevalence is approximately 8.5%.² Atopic dermatitis usually presents at an early age, with pruritus, xerosis, and dermatitis, and has a chronic, relapsing course.^{3,4} Moderate to severe AD has an impact on the quality of life of affected patients and their families as a result of associated sleep disturbances, psychological distress, and financial burden.³

The pathogenesis of AD involves interactions between susceptible genes, immunological factors, defects in the

skin barrier, skin infection, and environmental factors.⁵ Although there is currently no cure for AD, a multimodal treatment strategy is helpful in alleviating symptoms of the disease and normalizing the lives of affected patients and their families.⁶

Patients with AD are highly susceptible to cutaneous bacterial, viral, and fungal infections. Bacterial infection with *Staphylococcus aureus* is the most common complication of AD. The incidence of community-acquired methicillin-resistant *S. aureus* infection (CA-MRSA) in the pediatric population with AD is increasing, mirroring the increase in the general population. A recent study of pediatric patients with AD in the USA showed that 80% were

carriers of *S. aureus* and 13% were colonized with MRSA.⁷ There are no Canadian prevalence data for MRSA available to date; however, from clinical experience, we expect to find a lower incidence of MRSA in the Canadian pediatric AD population.

The objectives of this study were to determine the prevalence of MRSA and *S. aureus* colonization in the pediatric AD population, and to evaluate the genotypic diversity of the *S. aureus* isolates.

Materials and methods

This paper reports a prospective, cross-sectional study conducted in the Dermatology Clinic, Hospital for Sick Children, Toronto, between October 2008 and February 2009. The study was approved by the institution's Research Ethics Board. The Dermatology Clinic is a tertiary referral center with 7000 annual visits, 50% of which consist of new and follow-up visits for AD. Patients, aged one month to 18 years, with a diagnosis of AD made by a pediatric dermatologist, were approached to participate in the study. Patients were included if they and/or their guardians signed a consent/assent form.

Patients were excluded from the study if they had another chronic dermatological condition in which the skin barrier is compromised (e.g. psoriasis, ichthyosis, seborrheic dermatitis, epidermolysis bullosa, etc.), if they had a diagnosis of any other chronic condition that increases the risk for MRSA colonization (e.g. cystic fibrosis, immunodeficiency, asthma, diabetes, etc.), if they had used oral or IV antibiotic treatment in the previous two weeks, if they had a history of hospitalization, surgery, dialysis or residence in a long-term facility in the past year, and if they had an indwelling catheter or a percutaneous device at the time of enrollment.

Two swabs were taken from each study subject, one from the nares and one from an open area of the skin; in patients with intact skin, the second swab was taken from a body fold. All samples were sent to the Hospital for Sick Children's microbiology laboratory for culture and sensitivity. Genotyping of all *S. aureus* isolates was conducted by polymerase chain reaction (PCR) amplification of the repetitive X-region of the *S. aureus* protein A (spa) gene.⁸ Nucleotide sequence determination was performed by the Robarts Research Institute London Regional Genomics Centre at the University of Western Ontario. Automated spa type analysis was performed through access to the eGenomics server, courtesy of Dr. Barry Kreiswirth. The spa types identified by eGenomics were converted to numerical codes using the European spa type database server (spa.ridom.de) and assigned to previously determined spa-clonal complexes (spa-CC) that were constructed by BURP (based upon repeat) analysis of the repetitive X-region of the spa gene.^{9,10} Cross-referencing with existing online databases that describe the *S. aureus* genotype and antibiotic resistance/susceptibility and the

published hypervirulent genotypes of CA-MRSA was performed.

Data collected included information on demographic data (age, gender), prior use of antibiotics, the existence of family members working in healthcare facilities, and the existence of frequent skin infections in family members. In addition, a composite AD severity score (0–25) was designed. This was based on information on age at diagnosis of AD, frequency of use of topical medications, frequency of use of systemic antibiotics, hospital admissions, and patient/family impressions of disease severity. Mild AD was defined by a score of 0–12, moderate AD by a score of 13–18, and severe AD by a score of ≥ 19 (Table 1).

Statistical analysis

Continuous variables were reported as means with standard deviations (SDs) and analyzed using analysis of variance (ANOVA). Categorical data were reported as percentages and analyzed using Chi-squared test. A *P*-value of < 0.05 was considered significant. The analysis was conducted using MINITAB software Version 9 (Minitab, Inc., State College, PA, USA).

Table 1 Scoring a composite score for severity of atopic dermatitis

Characteristic	Score
Age at diagnosis	
< 2 months	5
2–12 months	3
> 1 year	1
Frequency of topical treatments in the past year	
b.i.d./t.i.d., year round	5
Once daily, year round	4
b.i.d./t.i.d. for flare-ups several times per year	3
Few times per week, year round	2
Few times per month, year round	1
Need for oral antibiotics in the past year	
Every month	5
Few times per year	4
Once	3
Never	0
Admissions for flare-up in the past year	
Several	5
One	3
None	0
Family assessment of disease severity	
Severe	5
Moderate	3
Mild	1

Maximum score: 25; scores of 19–25, 13–18 and 0–12 indicate severe, moderate and mild disease, respectively.

Table 2 Breakdown of atopic dermatitis composite severity score

Severity score parameters	Score	Total n (%)	MSSA+ n (%)	MSSA- n (%)	P-value
Age at diagnosis					
< 2 months	5	52 (26)	30 (24)	22 (29)	0.755
2–12 months	3	105 (53)	65 (53)	40 (52)	
> 1 year	1	43 (21)	28 (23)	15 (19)	
Frequency of topical treatments in the past year					
b.i.d./t.i.d., year round	5	106 (53)	74 (60)	32 (42)	0.078
Once daily, year round	4	26 (13)	15 (12)	11 (14)	
b.i.d./t.i.d. for flare-ups several times per year	3	48 (24)	26 (21)	22 (29)	
Few times per week, year round	2	14 (7)	6 (5)	8 (10)	
Few times per month, year round	1	6 (3)	2 (2)	4 (5)	
Need for oral antibiotics in the past year					
Every month	5	0 (0)	0 (0)	0 (0)	< 0.001
Few times per year	4	29 (14)	26 (21)	3 (4)	
Once	3	32 (16)	24 (20)	8 (10)	
Never	0	139 (70)	73 (59)	66 (86)	
Admissions for flare-up in the past year					
Several	5	2 (1)	1 (1)	1 (1)	0.487
One	3	7 (3)	6 (5)	1 (1)	
None	0	191 (96)	116 (94)	75 (98)	
Family assessment of disease severity					
Severe	5	38 (19)	31 (25)	7 (9)	0.003
Moderate	3	88 (44)	56 (46)	32 (42)	
Mild	1	74 (37)	36 (29)	38 (49)	

MSSA, methicillin-susceptible *Staphylococcus aureus*.

Results

Clinical and demographic data

Two hundred patients met the inclusion criteria and were enrolled in the study. A total of 56.5% (113/200) of subjects were male. The mean $\pm$ SD age of the patients was 5.0 ± 4.1 years. The mean $\pm$ SD severity score of the study patients was 11.0 ± 3.6 (maximum score of 25). According to severity scores for the 200 subjects, 133 (66.5%) were ranked as having mild AD, 59 (29.5%) as having moderate AD, and eight (4.0%) as having severe AD. Table 2 shows the AD score breakdown in the study subjects. The score showed that antibiotic use was significantly higher in patients with methicillin-susceptible *S. aureus* infection (MSSA) ($P < 0.001$) and that family assessments of disease severity were significantly higher in colonized patients versus non-colonized patients ($P = 0.003$).

A total of 26 of the 200 enrolled patients (13.0%) reported having used antibiotics for their AD (excluding during the previous month). Of the 200 subjects, 64 attended daycare (32%). Only 22 (11%) patients had a family member working in a healthcare scenario. Frequent skin infections in family members were reported in only one of the study subjects (0.5%).

Microbiological characteristics

Skin swabs were taken in 199 patients, a fold swab in one, and nose swabs in all patients. *Staphylococcus aureus* was reported in 87 of 199 (43.7%) skin swabs. Only one of the 87 positive swabs for *S. aureus* indicated MRSA (0.5%). The only fold swab taken was negative for *S. aureus*. Of the 200 nose swabs, 96 (48%) were positive for *S. aureus* and none were positive for MRSA. A comparison of MSSA-positive patients ($n = 123$) with MSSA-negative patients ($n = 77$) showed no significant differences in gender ($P = 0.88$), daycare attendance ($P = 0.69$), or the existence of family members working in healthcare ($P = 0.83$). However, a significant difference was seen with regard to mean age, with older age being more commonly associated with MSSA colonization ($P = 0.03$). In addition, higher AD severity scores were seen in MSSA patients ($P < 0.001$) (Table 3).

Genotypic analysis

We found that six established spa-CCs accounted for 79% of the *S. aureus* isolates obtained from 120 pediatric AD patients (Table 4). The multilocus sequence typed (MLST)-CCs that associate with each spa-CC group are provided for cross-reference. Isolates from 23 of 120 (19.2%) patients were spa-CC015 (ST45), and

Table 3 Comparison of MSSA-colonized versus non-colonized atopic dermatitis population

	MSSA+	MSSA–	P-value
Age, years, mean (SD)	5.5 (4.3)	4.2 (3.7)	0.03
Male gender, %	56.9	55.8	0.88
AD score, mean (SD)	11.8 (3.7)	9.7 (2.9)	< 0.001
Daycare attendance, %	34.2	28.6	0.69
Health care workers in the family, %	11.4	10.4	0.83

MSSA, methicillin-susceptible *Staphylococcus aureus*; AD, atopic dermatitis; SD, standard deviation.

spa-CC008 (ST8), spa-CC045 (ST5) and spa-CC127 (ST1 and ST97) were each identified in 16 of 120 (13.3%) patients. The least abundant of the major clusters was spa-CC012, identified in eight of 120 patients, corresponding to MLST-CC30. Moreover, spa-CC045 included isolates from five patients with spa type 002. The single MRSA identified in our study possessed a new spa type associated with spa-CC127.

Discussion

This study, the largest prospective study in the pediatric AD population, provides further evidence of the high prevalence of *S. aureus* and reassurance of the low prevalence of MRSA in the Canadian AD pediatric population.

Rate of colonization by MSSA

The rate of *S. aureus* colonization in normal individuals is estimated to be 5–30%, with anterior nares and intertriginous areas being the most common sites.^{11,12} The loss of integrity of the skin barrier seen in patients with AD makes the stratum corneum more susceptible to colonization by *S. aureus*. In addition, AD patients may have increased bacterial adhesion, defective bacterial clearance, and decreased innate immune response.¹³ Previous publications have reported that *S. aureus* carriage in AD patients is as high as 80–97.5%.^{7,14–16} This is higher than the 61.5% found in our study; the difference may in part be explained by geographical factors, a lower prevalence of *S. aureus* colonization in the Canadian population, or overestimations of true prevalences in previous studies caused by smaller sample sizes.^{7,14,16}

Another notable difference from previous studies is that older patients were more likely to be *S. aureus* carriers than younger patients (mean $\pm$ SD age 5.5 $\pm$ 4.3 years in the MSSA group versus 4.2 $\pm$ 3.7 years in the non-colonized group; $P = 0.03$). This suggests that *S. aureus* may play a more significant role in the inflammatory cascade seen in the older patients; therefore, the eradication of colonized status may reduce the severity and frequency of flare-ups. *Staphylococcus aureus* maintains skin inflammation by the production of toxins that act as superantigens, eliciting a strong immune response that stimulates T cells, macrophages, and eosinophils.^{13,17} A correlation

Table 4 Major spa-CC groups and associated MLST-CC designations of *Staphylococcus aureus* isolates ($n = 95$) from pediatric atopic dermatitis patients

spa-CC	spa types, n	MLST-CC
spa-CC015 ($n = 23$)	t004, t031, t050 ($n = 3$), t065 ($n = 6$), t116, t132, t180, t589, t772, t908, t1321, t4506, t5497, t5599, new1 ^a ; 09-02-16-34-13-17-34-16, new2; 09-34-17-13-16-13	CC45
spa-CC008 ($n = 16$)	t008 ($n = 5$), t304, t400 ($n = 2$), t656, t701 ($n = 2$), t723, t818, new3; 11-19-12-21-17-34-24-34-22-25-24 new4; 11-10-21-17-34-24-34-17-34-24-34-22-25 new5; 11-19-12-NEW-17-34-24-34-22-25	CC8
spa-CC045 ($n = 16$)	t002 ($n = 5$), t045, t105, t179, t442 ($n = 2$), t548 ($n = 2$), t688 ($n = 2$), t1265, new6; 26-23-17-34-NEW ^b -20-17-12-17-17-16	CC5
spa-CC084 ($n = 16$)	t084 ($n = 5$), t091, t094, t335, t346, t491, t547, t774, t1204, t1243, t1492, new7; 07-23-12-34-NEW-12-12-23-02-12-23	CC15/7
spa-CC127 ($n = 16$)	t127 ($n = 2$), t189 ($n = 3$), t267 ($n = 3$), t359 ($n = 2$), t1046, t2188, t2883, t3798 new8 ^c ; 07-23-12-20-12-21-17-34-34-33-34; new9; 07-23-12-21-17-34-13-34-33-34	CC1/97
spa-CC012 ($n = 8$)	t012 ($n = 2$), t318, t338 ($n = 2$), t342, t433, new10; 08-16-02-16-02-25-02-16-02-25-17-24-24	CC30

^aNew spa types are defined by numerical spa cassette codes, identified by the Ridom spa server.

^bWhen a new spa cassette code contains a previously unknown cassette, the cassette is identified as NEW.

^cThis new spa type was associated with the only MRSA strain identified.

MLST-CC, multilocus sequence typed clonal complex; MRSA, methicillin-resistant *Staphylococcus aureus*.

between the severity of AD and colonization with *S. aureus* as a mechanism for aggravating skin lesions has been previously demonstrated.^{18–20} A study by Farajzadeh *et al.*²¹ showed that 90% of severe cases and 66.7% of mild cases of AD had *S. aureus* colonization, suggesting that the more severe the dermatitis, the higher the rate of colonization ($P = 0.05$); this study evaluated severity using the SCORing Atopic Dermatitis (SCORAD) index.²² Our study substantiated this finding (11.8% in the MSSA+ group versus 7.9% in the MSSA– group; $P < 0.001$), which again underscores the significance of *S. aureus* eradication as part of the management of AD. Of interest, a recent study of healthy infants found that colonization by *S. aureus* at the age of six months and/or frequent colonization by *S. aureus* in the first year of life are associated with the development of AD and its severity in young children.²³

MRSA prevalence

The incidence of MRSA in this study was very low, at only 0.5% of affected patients. In Canada, MRSA was first reported in 1981.²⁴ National surveillance has taken place since 1995, and the rate of MRSA increased from one detection per 100 *S. aureus* colonizations in 1995 to six detections per 100 *S. aureus* colonizations in 1999.²⁵ A study of 104 patients conducted at the Hospital for Sick Children showed that the number of new MRSA cases has increased annually in a linear fashion since 2000, initially as a result of hospital acquired-MRSA (HA-MRSA) but from 2002 as a result of CA-MRSA.²⁶ However, despite the trend data, the true prevalence of MRSA in Canada is still unknown.

Community acquired-MRSA is genotypically distinct from HA-MRSA; it preferentially infects children and young adults, and its spectrum of disease is similar to that of MSSA. Generally, CA-MRSA is susceptible to clindamycin and less often shows resistance to other non-B-lactam antibiotics.²⁷ Atopic dermatitis patients are rarely admitted to hospital and are therefore more likely to become colonized or infected with CA-MRSA. Community-acquired MRSA can carry a gene encoding Pantone–Valentine leukotoxin (PVL), which has been associated with severe or fatal infections in otherwise healthy children and adults.^{28–33} In addition, more than 50% of PVL-positive MRSA are resistant to mupirocin,³⁴ which has changed the way MRSA-colonized patients are managed. Knowing the genotypic traits of the MRSA isolates has direct implications for clinical management.

In the USA, where CA-MRSA is now the most common pathogen cultured from patients with skin and soft-tissue infections in emergency departments,^{35,36} the colonization rate of AD patients is as high as 18.3%.³⁷ The higher rate of MRSA in the AD population may reflect higher overall

prevalence rates and/or different management strategies, such as antibiotic use. Our data do not support the current management strategies employed regarding choices of empiric therapies in AD patients requiring oral antibiotics, including cephalexin, before culture results become available.

Spa-CC015 was most frequently encountered (19.2%) in the pediatric AD population, including spa type 004, which is associated with the CA-MRSA-1 strain of hospital-associated MRSA that is epidemic in Canadian hospitals.³⁸ Although spa-CC045 (ST5) represents a minor group associated with nasal carriage,^{9,39,40} it was one of the major spa-CCs associated with pediatric AD patients. Spa-CC045 accounted for 13.3% of isolates, including five with spa 002, which is associated with the CA-MRSA-2 strain of epidemic HA-MRSA in Canadian hospitals,³⁸ known globally as either USA100 or the “pediatric clone” of *S. aureus*.^{41,42} Spa-CC008 accounted for 13.3% of isolates, among which spa 008 was most common ($n = 5$); this spa type defines the CA-MRSA-10 strain of CA-MRSA in Canada, and USA300, the major cause of CA-MRSA infections in the USA. Therefore, although the spa types and clonal complexes identified in association with pediatric AD overlap with common HA- and CA-MRSA, these have not yet become entrenched within the significant sector of the population afflicted with AD. Just one other study conducted spa typing of *S. aureus* isolates from AD patients ($n = 35$) but did not report the predominance of spa-CC015 identified in our study.⁴³ However, that study identified spa t189 as being most frequently encountered ($n = 7$, 19%), and we identified spa t189 in three isolates belonging to spa-CC127, which accounted for 13.3% of total isolates. Importantly, the spa-CC127 group contained the only MRSA we identified, and the sequence of spa cassettes from this strain resembled spa types in the spa-CC127 group (i.e. t267 and t359) associated with MLST-ST97⁴⁴ (Table 4). ST97 *S. aureus* is usually of animal origin,^{44–46} but has recently been reported as CA-MRSA in both animals and humans.^{45–48} Potentially, this is a newly emergent strain of CA-MRSA. In our study, the least abundant strain was spa-CC012, which is a major lineage associated with both nasal carriage and invasive bloodstream infections.^{9,40,49,50}

Our study had several limitations. Although the low rate of MRSA found in our sample is reassuring, establishing true prevalence data would require a much larger sample. We designed a new AD score that we thought would give a much better longitudinal assessment of disease severity based on direct (frequency of topical application) and indirect (admissions to hospital) indicators and patient and family perspectives than the existent AD scores. The lack of previous validation may have interfered with the accuracy of our severity data. In addition,

our data cannot be generalized to other Canadian provinces or to primary care settings.

The results of this study confirmed a high rate of colonization by *S. aureus* in pediatric AD patients, which was associated with more severe AD and older age. Consequently, we anticipate that the infants in our study, who had less severe manifestations of the disease but were colonized by *S. aureus*, will exhibit a progression of disease severity throughout childhood. The management implication for infants with AD is that *S. aureus* colonization should be determined and eradication attempted whenever possible. The reassuringly low MRSA rate found in this study requires further proof from larger prospective studies conducted in multiple settings.

Acknowledgment

We are grateful for the assistance of Noorulain Malik, research assistant, to physician trainees in our clinic who helped with patient recruitment.

References

- Williams HC. Epidemiology of atopic dermatitis. *Clin Exp Dermatol* 2000; **25**: 522–529.
- Barbeau M, Bpharm HL. Burden of atopic dermatitis in Canada. *Int J Dermatol* 2006; **45**: 31–36.
- Horii KA, Simon SD, Liu DY, Sharma V. Atopic dermatitis in children in the United States, 1997–2004: visit trends, patient and provider characteristics, and prescribing patterns. *Pediatrics* 2007; **120**: 527–534.
- Eichenfield LF, Hanifin JM, Luger TA, et al. Consensus conference on pediatric atopic dermatitis. *J Am Acad Dermatol* 2003; **49**: 1088–1095.
- Leung AK, Hon KL, Robson WL. Atopic dermatitis. *Adv Pediatr* 2007; **54**: 241–273.
- Hanifin JM, Cooper KD, Ho VC, et al. Guidelines of care for atopic dermatitis, developed in accordance with the American Academy of Dermatology (AAD)/American Academy of Dermatology Association “Administrative Regulations for Evidence-Based Clinical Practice Guidelines”. *J Am Acad Dermatol* 2004; **50**: 391–404.
- Suh L, Coffin S, Leckerman KH, et al. Methicillin-resistant *Staphylococcus aureus* colonization in children with atopic dermatitis. *Pediatr Dermatol* 2008; **25**: 528–534.
- Koreen L, Ramaswamy SV, Graviss EA, et al. Spa typing method for discriminating among *Staphylococcus aureus* isolates: implications for use of a single marker to detect genetic micro- and macrovariation. *J Clin Microbiol* 2004; **42**: 792–799.
- Holtfreter S, Grumann D, Schmutde M, et al. Clonal distribution of superantigen genes in clinical *Staphylococcus aureus* isolates. *J Clin Microbiol* 2007; **45**: 2669–2680.
- Rijnders MI, Deurenberg RH, Boumans ML, et al. Population structure of *Staphylococcus aureus* strains isolated from intensive care unit patients in the Netherlands over an 11-year period (1996 to 2006). *J Clin Microbiol* 2009; **47**: 4090–4095.
- Breuer K, Haussler S, Kapp A, Werfel T. *Staphylococcus aureus*: colonizing features and influence of an antibacterial treatment in adults with atopic dermatitis. *Br J Dermatol* 2002; **147**: 55–61.
- Nakamura MM, Rohling KL, Shashaty M, et al. Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage in the community pediatric population. *Pediatr Infect Dis J* 2002; **21**: 917–922.
- Baker BS. The role of microorganisms in atopic dermatitis. *Clin Exp Immunol* 2006; **144**: 1–9.
- Leyden JJ, Marples RR, Kligman AM. *Staphylococcus aureus* in the lesions of atopic dermatitis. *Br J Dermatol* 1974; **90**: 525–530.
- Machura E, Karczewska K, Findysz-Wylag B, et al. Influence of *Staphylococcus aureus* skin colonization on degree of sensitization in atopic dermatitis children. *Pol Merkur Lekarski* 2008; **25**: 51–56.
- Chiu LS, Ho MS, Hsu LY, Tang MB. Prevalence and molecular characteristics of *Staphylococcus aureus* isolates colonizing patients with atopic dermatitis and their close contacts in Singapore. *Br J Dermatol* 2009; **160**: 965–971.
- Bonness S, Bieber T. Molecular basis of atopic dermatitis. *Curr Opin Allergy Clin Immunol* 2007; **7**: 382–386.
- Gong JQ, Lin L, Lin T, et al. Skin colonization by *Staphylococcus aureus* in patients with eczema and atopic dermatitis and relevant combined topical therapy: a double-blind multicentre randomized controlled trial. *Br J Dermatol* 2006; **155**: 680–687.
- Breuer K, Kapp A, Werfel T. Bacterial infections and atopic dermatitis. *Allergy* 2001; **56**: 1034–1041.
- Hon KL, Lam MC, Leung TF, et al. Clinical features associated with nasal *Staphylococcus aureus* colonization in Chinese children with moderate-to-severe atopic dermatitis. *Ann Acad Med Singapore* 2005; **34**: 602–605.
- Farajzadeh S, Rahnema ZZ, Kamyabi Z, Ghavidel B. Bacterial colonization and antibiotic resistance in children with atopic dermatitis. *Dermatol Online J* 2008; **14**: 21.
- Gelmetti C, Colonna C. The value of SCORAD and beyond. Towards a standardized evaluation of severity?. *Allergy* 2004; **59**: 61–65.
- Lebon A, Labout JA, Verbrugh HA, et al. Role of *Staphylococcus aureus* nasal colonization in atopic dermatitis in infants: the Generation R Study. *Arch Pediatr Adolesc Med* 2009; **163**: 745–749.
- Low DE, Garcia M, Callery S et al. Methicillin-resistant *Staphylococcus aureus*-Ontario. *Can Dis Wkly Rep* 1981; **7**: 249–50.
- Simor AE, Ofner-Agostini M, Bryce E, et al. Laboratory characterization of methicillin-resistant *Staphylococcus aureus* in Canadian hospitals: results of 5 years of

- National Surveillance, 1995–1999. *J Infect Dis* 2002; 186: 652–660.
- 26 Atkinson C, Waters V, Ford-Jones EL, Richardson SE, eds. Methicillin-resistant *Staphylococcus aureus* (MRSA) at the Hospital for Sick Children (HSC), Toronto: 1996–2005. 107th General Meeting of the American Society for Microbiology, May 21–25, 2007, Toronto, ON.
 - 27 Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 2003; 290: 2976–2984.
 - 28 Cohen PR. Community-acquired methicillin-resistant *Staphylococcus aureus* skin infections: a review of epidemiology, clinical features, management, and prevention. *Int J Dermatol* 2007; 46: 1–11.
 - 29 Cohen PR. Community-acquired methicillin-resistant *Staphylococcus aureus* skin infections: implications for patients and practitioners. *Am J Clin Dermatol* 2007; 8: 259–270.
 - 30 Cohen PR. The skin in the gym: a comprehensive review of the cutaneous manifestations of community-acquired methicillin-resistant *Staphylococcus aureus* infection in athletes. *Clin Dermatol* 2008; 26: 16–26.
 - 31 Daum RS. Clinical practice. Skin and soft-tissue infections caused by methicillin-resistant *Staphylococcus aureus*. *N Engl J Med* 2007; 357: 380–390.
 - 32 Suh LM, Honig PJ, Yan AC. Methicillin-resistant *Staphylococcus aureus* skin abscesses in a pediatric patient with atopic dermatitis: a case report. *Cutis* 2006; 78: 113–116.
 - 33 Roesch A, Linde HJ, Landthaler M, Vogt T. Elimination of a community-acquired methicillin-resistant *Staphylococcus aureus* infection in a nurse with atopic dermatitis. *Arch Dermatol* 2005; 141: 1520–1522.
 - 34 Mulvey MR, MacDougall L, Cholin B, et al. Community-associated methicillin-resistant *Staphylococcus aureus*, Canada. *Emerg Infect Dis* 2005; 11: 844–850.
 - 35 Moran GJ, Krishnasadan A, Gorwitz RJ, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med* 2006; 355: 666–674.
 - 36 Frazee BW, Lynn J, Charlebois ED, et al. High prevalence of methicillin-resistant *Staphylococcus aureus* in emergency department skin and soft tissue infections. *Ann Emerg Med* 2005; 45: 311–320.
 - 37 Chung HJ, Jeon HS, Sung H, et al. Epidemiological characteristics of methicillin-resistant *Staphylococcus aureus* isolates from children with eczematous atopic dermatitis lesions. *J Clin Microbiol* 2008; 46: 991–995.
 - 38 Zhang K, McClure JA, Elsayed S, et al. Coexistence of Pantón–Valentine leukocidin-positive and -negative community-associated methicillin-resistant *Staphylococcus aureus* USA400 sibling strains in a large Canadian health care region. *J Infect Dis* 2008; 197: 195–204.
 - 39 Feil EJ, Enright MC. Analyses of clonality and the evolution of bacterial pathogens. *Curr Opin Microbiol* 2004; 7: 308–313.
 - 40 Ko KS, Lee JY, Baek JY, et al. Characterization of *Staphylococcus aureus* nasal carriage from children attending an outpatient clinic in Seoul, Korea. *Microb Drug Resist* 2008; 14: 37–44.
 - 41 Oliveira DC, Tomasz A, de Lencastre H. The evolution of pandemic clones of methicillin-resistant *Staphylococcus aureus*: identification of two ancestral genetic backgrounds and the associated mec elements. *Microb Drug Resist* 2001; 7: 349–361.
 - 42 Oliveira DC, Tomasz A, de Lencastre H. Secrets of success of a human pathogen: molecular evolution of pandemic clones of methicillin-resistant *Staphylococcus aureus*. *Lancet Infect Dis* 2002; 2: 180–189.
 - 43 Kim DW, Park JY, Park KD, et al. Are there predominant strains and toxins of *Staphylococcus aureus* in atopic dermatitis patients? Genotypic characterization and toxin determination of *S. aureus* isolated in adolescent and adult patients with atopic dermatitis. *J Dermatol* 2009; 36: 75–81.
 - 44 Smyth DS, Feil EJ, Meaney WJ, et al. Molecular genetic typing reveals further insights into the diversity of animal-associated *Staphylococcus aureus*. *J Med Microbiol* 2009; 58: 1343–1353.
 - 45 Battisti A, Franco A, Merialdi G, et al. Heterogeneity among methicillin-resistant *Staphylococcus aureus* from Italian pig finishing holdings. *Vet Microbiol* 2010; 142: 361–366.
 - 46 Sung JM, Lloyd DH, Lindsay JA. *Staphylococcus aureus* host specificity: comparative genomics of human versus animal isolates by multi-strain microarray. *Microbiology* 2008; 154: 1949–1959.
 - 47 Ellington MJ, Yearwood L, Ganner M, et al. Distribution of the ACME-arcA gene among methicillin-resistant *Staphylococcus aureus* from England and Wales. *J Antimicrob Chemother* 2008; 61: 73–77.
 - 48 Schuenck RP, Nouer SA, Winter Cde O, et al. Polyclonal presence of non-multiresistant methicillin-resistant *Staphylococcus aureus* isolates carrying SCCmec IV in health care-associated infections in a hospital in Rio de Janeiro, Brazil. *Diagn Microbiol Infect Dis* 2009; 64: 434–441.
 - 49 Feil EJ, Cooper JE, Grundmann H, et al. How clonal is *Staphylococcus aureus*? *J Bacteriol* 2003; 185: 3307–3316.
 - 50 Fowler VG Jr, Nelson CL, McIntyre LM, et al. Potential associations between hematogenous complications and bacterial genotype in *Staphylococcus aureus* infection. *J Infect Dis* 2007; 196: 738–747.