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## ROLE OF GENOTYPES OF STAPHYLOCOCCUS SPP. IN THE CLINICAL COURSE OF ALLERGIC DERMATOSES

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### Abstract

The article provides data from molecular genetic studies to identify genotypes of staphylococci in patients with allergic skin diseases. Examined 312 patients with allergic dermatoses at the age from 7 to 67 years. Clinical-microbiological and molecular-genetic studies have shown that in patients with allergic skin diseases, genotypes of staphylococci are isolated in 44.5% of cases. Among them, methicillin-resistant staphylococcus aureus (MRSA) was detected in 58 out of 142 DNA samples, which accounted for 40.8% of cases. Whereas the genotypes of methicillin-sensitive staphylococcus

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(MSSA) were detected in 61 (42.9%) patients, and methicillin-resistant coagulonegative *Staphylococcus* spp (MRCoNS) - in 23, which amounted to 16.2% of cases, respectively.

**Keywords:** allergic dermatoses, atopic dermatitis, allergodermatitis, clinical picture, severity, staphylococcus, staphylococcus genotypes, methicillin-resistant staphylococcus.

### 摘要

这篇文章提供了分子遗传学研究的数据，以确定过敏性皮肤病患者的葡萄球菌基因型。检查了312名年龄在7至67岁之间的过敏性皮肤病患者。临床微生物学和分子遗传学研究表明，在过敏性皮肤病患者中，44.5%的病例分离出葡萄球菌基因型。其中，142份DNA样本中有58份检出耐甲氧西林金黄色葡萄球菌（MRSA），占病例数的40.8%。而在61名（42.9%）患者中检测到甲氧西林敏感葡萄球菌（MSSA）的基因型，在23名患者中检测到耐甲氧西林凝固阴性葡萄球菌（MRCoNS），分别占病例的16.2%。

**关键词：**过敏性皮肤病，特应性皮炎，过敏性皮炎，临床表现，严重程度，葡萄球菌，葡萄球菌基因型，耐甲氧西林葡萄球菌。

### Introduction

Many human diseases are accompanied by violations of symbiotic interactions within the microbial community, as well as the relationship between the macroorganism and its microbiota. [1, 2, 3, 4, 5, 6]

For most staphylococci, the natural habitat is the surface of the human skin, mucous membranes, where they persist without harming the host's body. [7, 8, 9, 10] In chronic dermatoses, changes occur in the microbiocenoses of the skin, in particular, the degree of contamination of the skin by representatives of the genus *Staphylococcus*, especially *st. aureus*. In this regard, the question arises about the etiopathogenetic role of these bacteria in the development of skin pathologies. [11, 12, 13, 14]

One of the key roles in the mechanisms of the development of the disease is assigned to *Staphylococcus aureus* - *s. aureus*. [15, 16, 17] Studies have established that the development of exacerbations of ALD and their severe course in some cases is explained by colonization of *s. aureus*, secreting toxins - superantigens that cause polyclonal activation of T-lymphocytes and macrophages that produce pro-inflammatory cytokines and modulate the development of the immune response. [18, 19]

Purpose of the study. To assess the detectability of staphylococcal genotypes in patients with allergic skin diseases, taking into account the clinical course.

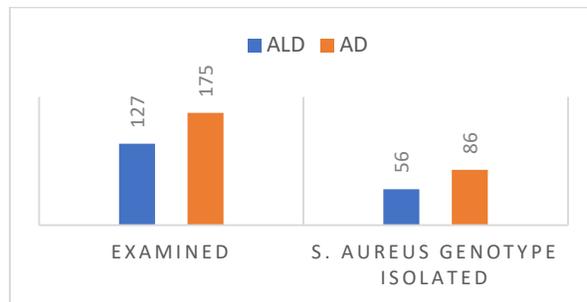
### Materials And Methods

We examined 312 patients with allergic skin diseases at the age from 7 to 67 years. All patients underwent clinical, microbiological, molecular genetic and statistical studies. Clinical studies consisted of assessing the severity according to the SCORAD index. To detect and quantify the DNA of methicillin-sensitive and methicillin-resistant *s.aureus*, methicillin-resistant coagulone-negative *Staphylococcus* spp. in biological material - skin scales of lesions in 312 patients with allergic skin diseases were determined by the method of polymerase chain reaction (PCR) with hybridization-fluorescence detection "AmpliSense \* MRSA-screen-titer - FL". The analysis of the results was carried out using the software of the used PCR device in the "real time" mode.

## Results

The results of microbiological and genetic studies showed that among 312 patients with allergic dermatoses (137 - ALD and 175 - AD), 142 patients were found to have genotypes of *staphylococcus* spp., which amounted to 45.5%. According to the clinical form, among 127 patients with allergic dermatitis, 56 (44.1%) patients were found to have the *s.aureus* genotype, while among 175 patients with AD, 86, which amounted to 49.1%, respectively. (Fig. 1) The presence of the marker gene *st.aureus* in 100% (142 cultures) of cases was also confirmed by the PCR method.

**Fig. 1. Indicator of detectability of *s.aureus* genotypes in the studied groups of patients with allergic dermatoses (abs)**



**Table 1. Indicators of *st.aureus* genotypes isolated from biosubstrates in patients with allergic dermatoses.**

St.aureus culture	MRSA	MSSA	MRCoNS
Total culture N=142	58	61	23
%	40,8	42,9	16,2

As can be seen from the table, methicillin-resistant *staphylococcus* (MRSA) was detected in 58 out of 142 DNA samples, which accounted for 40.8% of cases. Whereas the genotypes of methicillin-sensitive *staphylococcus* (MSSA) were detected in 61 (42.9%) patients, and methicillin-resistant coagulonegative *Staphylococcus* spp (MRCoNS) - in 23, which amounted to 16.2% of cases, respectively.

Taking into account the sexual aspect, genotypes of *staphylococci* in 52.1% (74 out of 142) cases were detected in males and in females - 47.8% (68), respectively.

**Table 2. Characteristics of detection of genotypes of *staphylococci*, depending on the sex of patients. (abs,%)**

	MRSA	MSSA	MRCoNS
<b>Males</b> N=74	31 (41,9%)	28 (37,8%)	15 (20,3%)
<b>Females</b> N=68	27 (39,7%)	33 (48,5%)	8 (11,7%)

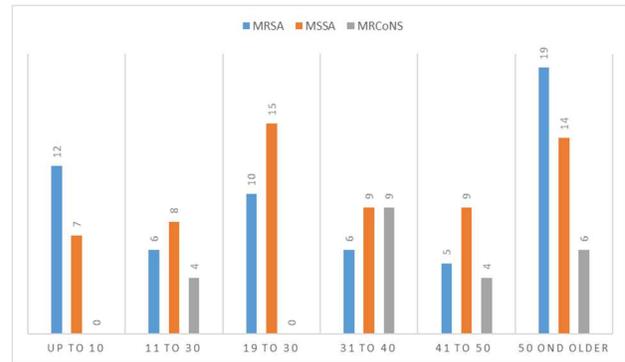
As can be seen from the table, depending on the type of genotypes, methicillin-resistant *S. aureus* (MRSA) was most often isolated in males - 41.9% (31 of 74), methicillin-sensitive staphylococcus (MSSA) - in 37.8% (28) and methicillin-resistant coagulone-negative *Staphylococcus* spp (MRCoNS) - in 20.3% (15), respectively. Whereas in females in our cases, MSSA was most often detected - 48.5% (33 out of 68), MRSA - in 39.7% (27) and MRCoNS - in 11.7% (8) cases.

Analysis of the results of molecular genetic studies of staphylococcus genotypes, depending on the age of patients, showed that in children under 10 years old - in 19 years (13.4%), 11-18 years - 17 (11.9%), 19-30 years - 25 (17.6%), 31-40 years old - in 24 (16.9%), 41-50 years old - in 18 (12.7%) and over 50 years old - in 39, which amounted to 27.5% cases respectively.

Taking into account the type of genotypes of staphylococci, MRSA was most often detected in children under 10 years of age - 20.7% (12 out of 58), in a young - active age - 17.2% (10) and over 50 years old - 32.7% (19) respectively. Whereas MSSA was most often detected at a young - active age - 24.6% (15 out of 61) and over 50 years - 22.9% (14), respectively. And MRCoNS was most often identified in the active-

working age of 31-40 years - 39.1% (9 out of 23) of cases. (Fig. 2.)

**Fig. 2. Characteristics of the detection of genotypes of staphylococci, taking into account the age of patients (abs)**



Thus, the analysis of the results obtained shows that the genotypes of staphylococci are most often isolated in males in 52.1%, while in females it was 47.8% of cases. Depending on the type of genotypes, *S. aureus* MRSA was most often isolated in males - 41.9%, MSSA - in 37.8% and MRCoNS - in 20.3% of cases, respectively. Whereas in females, MSSA was most often detected - 48.5%, MRSA - in 39.7% and MRCoNS - in 11.7%, respectively.

The clinical course of patients with allergic dermatoses with identified methicillin-resistant *S. aureus* (MRSA) disease had a chronic, often recurrent course, resistance to basic therapy, especially to external treatments - topical corticosteroid drugs. Subjectively, patients were often bothered by intense itching.

It should be noted that in patients with AD with isolated *S. aureus* MRSA, the skin-pathological process was more often characterized by lichenoid, pruriginous eruptions against the background of hyperemia and skin infiltration. Basically, in 78.4% of cases, patients

noted the absence of seasonality of the disease [20, 21, 22].

Whereas in the group of patients with allergic dermatitis with isolated MRSA, the skin-pathological process was characterized by erythematous rashes, which are widespread, accompanied by periodic severe itching and resistance to external therapy.

It should be noted that the patients used external steroid preparations for a long time without the supervision of doctors - dermatologists, which the patients took at home without permission. Also, the literature data indicate that one of the factors in the detection of genotypes is the lack of phagocytosis, which requires further study.

Among 142 patients in 23, coagulase-negative (coagulase-negative) staphylococci MRCoNS - non aureus were isolated. In this case, *Staphylococcus saprophyticus* was mainly isolated - 11 out of 23, *S. haemolyticus* - 7, and *Staphylococcus epidermidis* - 5, respectively.

The results of molecular genetic studies analyzed taking into account the clinical form of dermatoses revealed the following indicators. (table 2.)

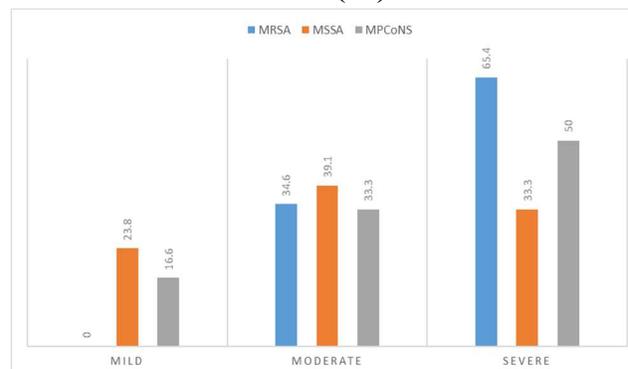
**Table 2. Indicators of detection of *S. aureus* genotypes in patients with allergic dermatoses, taking into account the clinical form.**

Nosology	MRSA	MSSA	MRCoNS
AD N= 86	41 (47,7%)	28 (33,5%)	17 (19,7%)
ALD N=56	17(30,4%) )	33(58,9%) )	6 (10,7%)

As follows from the table, taking into account the clinical form in patients with atopic dermatitis, MRSA was isolated in 41 (47.7%), MSSA - in 28 (33.5%) and MRCoNS - in 17, which amounted to 19.7% of cases. Whereas in the group of patients with allergic dermatitis, the largest number was genotypes of methicillin-sensitive staphylococcus (MSSA) - 33 (58.9%), MRSA - in 30.4% (17) and MRCoNS - in 6, which amounted to 10.7% of cases, respectively.

The results obtained were also analyzed depending on the severity of allergic dermatoses. (fig. 4.)

**Fig. 4. Detection rate of *s.aureus* genotypes depending on the severity of the SCORAD index (%)**

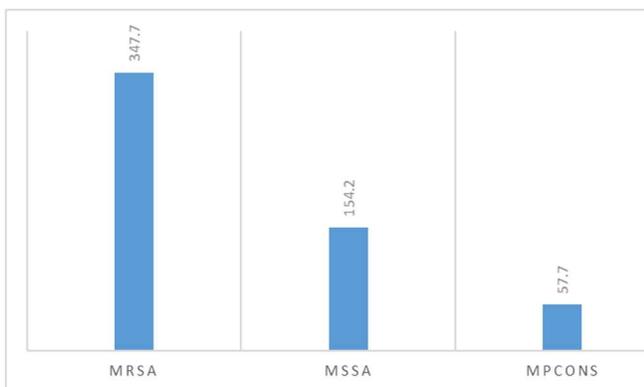


As follows from the figure, methicillin-resistant staphylococcus (MRSA) was most often isolated in patients with moderate and severe severity - 34.6% and 65.4%, respectively, while methicillin-susceptible staphylococcus (MSSA) - with moderate severity - 39.1% , and coagulase-negative (coagulase-negative) staphylococci (MRCoNS) - in severe - 50% and moderate - 33.3% of cases, respectively.

Analysis of the degree of colonization taking into account the genotypes of *s.aureus*

and staphylococcus spp. revealed the following features: for example, the level of contamination of methicillin-resistant staphylococcus (MRSA) averaged  $347.7 \pm 12.3$  CFU, while MSSA -  $154.2 \pm 9.7$  CFU and MRCoNS -  $57.7 \pm 2.6$  CFU, respectively. (fig. 5.)

**Fig. 5. Indicator of the degree of colonization of genotypes *s.aureus* and staphylococcus spp. (abs)**



The data obtained have revealed a new clinical course - methicillin-resistant forms of allergic dermatoses.

A thorough analysis of the clinical course of methicillin-resistant forms of allergic dermatoses, taking into account the isolated strains of *S. Aureus*, showed that in the group of AD patients with MRSA, the clinical picture of the skin-pathological process was characteristic of an erythematous-squamous process with lichenification and pruriginous forms of AD. Then, in ALD patients, the MRSA genotype was more often detected in erythematous rashes. The clinical course had a moderate to severe course, accompanied by intense itching and resistance to basic therapy.

In patients with MSSA and MRCoNS, the skin-pathological process was also characterized by erythematous-squamous, pruriginous eruptions with lichenification. Whereas in the group of patients with allergic dermatitis, the skin-pathological process was characterized by small papular rashes against the background of hyperemia. Subjectively, patients were worried about periodic itching.

The anamnestic data of patients with ALD with identified genotypes contributed to the establishment of provoking factors for the emergence of invasive forms of bacterial colonization on the skin in patients. Long-term use of steroid drugs for external use (elocom, momethox, betamethasone propionate) - 72.6%, antibacterial drugs (tetracycline, gentamicin series) - 47.8%, topical immunosuppressants (protopics) - 37.9%.

In our opinion, the data obtained are important as factors contributing to the persistence of opportunistic microorganisms on the skin in patients with allergic skin diseases.

Study of indicators of sensitivity to antibacterial drugs of genotypes of staphylococcus spp. et *s.aureus* revealed the following features: the MRSA genotype is most sensitive to fluoroquinolone antibiotics - 78.1% of cases, to cephalosporin antibiotics - in 37.1% of cases. Whereas the MSSA genotype was the most sensitive to antibiotics of the cephalosporin series - 56.8% and aminoglycosides - 39.2%, respectively. Coagulase-negative (coagulase-negative) staphylococci were most sensitive to antibiotics of the tetracycline series - 69.4%.

Thus, clinical, microbiological and molecular genetic studies have shown that in patients with allergic skin diseases, genotypes of staphylococci are isolated in 44.5% of cases. Among them, methicillin-resistant staphylococcus aureus (MRSA) was detected in 58 out of 142 DNA samples, which accounted for 40.8% of cases. Whereas the genotypes of methicillin-sensitive staphylococcus (MSSA) were detected in 61 (42.9%) patients, and methicillin-resistant coagulonegative Staphylococcus spp (MRCoNS) - in 23, which amounted to 16.2% of cases, respectively.

The results obtained indicate the development of methicilline-resistant allergic forms of dermatoses, which requires new optimal methods of external therapy.

## Conclusion

1. The results of microbiological studies of the skin of the lesions showed that among 432 patients, 312 were seeded gram + chemoorganotropic facultative anaerobic bacteria from the Mycrococeae family - Staphylococcus spp., Which accounted for 72.2% of cases. Among 312 patients, ALD was 82 (26.3%) and AD - 230, which was 73.7%.

2. Molecular genetic studies have established that in patients with allergic skin diseases in 44.5% of cases, genotypes of staphylococci are isolated. Among them, methicillin-resistant staphylococcus aureus (MRSA) was detected in 58 out of 142 DNA samples, which accounted for 40.8% of cases. Whereas the genotypes of methicillin-sensitive staphylococcus (MSSA) were detected in 61 (42.9%) patients, and methicillin-resistant coagulonegative Staphylococcus spp (MRCoNS)

- in 23, which amounted to 16.2% of cases, respectively.

3. The analysis of the results obtained shows that the genotypes of staphylococci are most often isolated in males in 52.1%, while in females it was 47.8% of cases. Depending on the type of genotypes, S. aureus MRSA was most often isolated in males - 41.9%, MSSA - in 37.8% and MRCoNS - in 20.3% of cases, respectively. Whereas in females, MSSA was most often detected - 48.5%, MRSA - in 39.7% and MRCoNS - in 11.7%, respectively.

4. Taking into account the clinical form, MRSA was most often isolated in patients with atopic dermatitis - in 47.7%, and MSSA - in 33.5% and MRCoNS - in 19.7% of cases. Whereas in patients with allergic dermatitis, the largest number was MSSA genotypes - 58.9%, and MRSA - 30.4% and MRCoNS - 10.7% of cases, respectively, which indicates the development of methicillene-resistant forms of allergic dermatoses, which requires new methods of treatment, especially with external therapy.

## References:

1. Bayazitova L.T. Virulent properties of staphylococcal skin microflora in atopic dermatitis: author. dis. Cand. honey. Sciences: 14.01.09 / Bayazitova Lira Tabrisovna. - Ufa, 2009.-- 22 p.
2. Belousova T.A., Goryachkina M.A., Katranova A.G. Features of skin microbiocenosis in patients with allergic dermatoses: the problem of choosing external therapy. // Clinical Dermatology and Venereology. - No. 3. - 2013 - S. 13-19.

3. Gostev V.V., Sidorenko S.V. Bacterial biofilms and infections // *Journal of Infectology*. 2010. Vol. 2, No. 3. P. 4–15.
4. Elisyutina O.G., Fedenko E.S. The role of *Staphylococcus aureus* in the pathogenesis of atopic dermatitis
5. Kalyuzhka E.A. "Genetic risk factors for the development of allergic diseases in children" 2016 - vip. 1, volume 2 (127), pp. 16-20.
6. Kozlova N.S., Barantsevich N.E., Barantsevich E.P. Antibiotic resistance of causative agents of purulent septic infections in a multidisciplinary hospital // *Problems of medical mycology*. 2018. T 20. N 1. S. 40-48.
7. Mavlyanova Sh.Z. Atopic dermatitis. // *Monograph*. - Toshkent - 2014. –S. 163.
8. Methicillin-resistant *Staphylococcus aureus*: the problem of distribution in the world and in Russia. [www.fesmu.ru](http://www.fesmu.ru).
9. Murashkin N.N., Gluzmin M.I., Bakulev A.L. The role of methicillin-resistant strains of *Staphylococcus aureus* in the pathogenesis of severe forms of atopic dermatitis in children // *Bulletin of Dermatol. and venerol*. 2012. Vol. 1. P. 68–76.
10. Mokronosova M.A., Maksimova A.E., Baturo A.P. et al. Influence of various methods of external therapy on the colonization of the skin by *Staphylococcus aureus* and the course of atopic dermatitis // *Russian Allergological Journal*. 2004. - No. 12. - S. 58-61.
11. Olisova O.Yu. Therapeutic skin care for atopic dermatitis. // *Wedge. dermatology and venereology*. - 2009. - No. 1. S. 54-57.
12. Tyurin Yu.A. The role of pathogenicity factors of *Staphylococcus aureus* in the development of atopic dermatitis / Yu. A. Tyurin, DA Dolbin // *Zh. microbiol*. 2008. - No. 4. - S. 105-110.
13. Hamaganova IV Pustular diseases, skin. Attending physician: 2006, No. 9, pp. 5-12.
14. Alsterholm M., Flytstrom I., Bergbrant I. M., Faergemann J. Fusidic acid-resistant *Staphylococcus aureus* in impetigo contagiosa and second infected atopic dermatitis. *Acta Derm Venereol* 2010; 90: 1: P. 52-57.
15. Baker B.S. The role of microorganisms in atopic dermatitis // *ClinExp Immunol.*, 2006. - Vol. 144. - P. 1-9.
16. Biber, T. Atopic dermatitis: from the genes the skin lesions / T. Biber, A. Wollenberg // *Allergy*. 2000. - Vol. 55. - P. 205-213.
17. Brodská P, Panzner P, Pizinger K, Schmid-Grendelmeier P. IgE-mediated sensitization to malassezia in atopic dermatitis: more common in male patients and in head and neck type. *Dermatitis*. 2014; 25 (3): P. 120-126.
18. Clarke S.R. A of *Staphylococcus aureus* is a broad spectrum, iron-regulated adhesin / S. R. Clarke, M. D. Wiltshire, S. J. Foster // *Molecular Microbiology*. 2004. - Vol. 51, No. 5. - P. 1509-1519.
19. Salgado C.D. Community-acquired methicillin-resistant *Staphylococcus aureus*: A

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meta-analysis of prevalence and risk factors / C. D. Salgado, B. M. Farr, D. R. Galfee // Clin. Infect. Dis. 2003. - Vol. 36. - P. 131-139.

20. Spaulding A.R., Lin Y.C., Merriman J.A. et al. Immunity to Staphylococcus aureus secreted proteins protects rabbits from serious illnesses. Vaccine. 2012, 30 (34): 5099-5109.

21. Stevens DL, Herr D, Lampiris H et al; the Linezolid MRSA Study Group. Linezolid versus

vancomycin for the treatment of methicillin-resistant Staphylococcus aureus infections. Clin Infect Dis 2002; 34: 1481-1490.

22. Zollner T. M., Wichelhaus T. A., Hartung A. et al. Colonization with superantigen producing Staphylococcus aureus associated with increased severity of atopic dermatitis // Clin. Exp. Allergy. 2000. - Vol. 30: - No. 7. - P. 994-1000.