AD/A-002 892

LABORATORY DIAGNOSTIC METHODS AND SPECIFIC DESENSITIZING THERAPY FOR INFECTIOUS-ALLERGIC DISEASES

A. E. Vershigora

Foreign Technology Division
Wright-Patterson Air Force Base, Ohio

19 November 1974

FTD-MT-24-2484-74

FOREIGN TECHNOLOGY DIVISION

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A. Ye. Vershigora

UNCLASSIFIED
Security Classification

AD1002 552

DOCUMENT CONTROL DATA - R & C

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1 ORIGINATING ACTIVITY (Corporate author) Foreign Technology Division Air Force Systems Command U. S. Air Force	2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED 2b. GROUP

3 REPORT TITLE

LABORATORY DIAGNOSTIC METHODS AND SPECIFIC DESENSITIZING THERAPY FOR INFECTIOUS-ALLERGIC DISEASES

4 DESCRIPTIVE NOTES (Type of report and inclusive dates)

Translation

5 AUTHOR(S) (First name, middle initial, last name)

A. Ye. Vershigora

6 REPORT DATE 1972	7a. TOTAL NO. OF PAGES 9	7b. NO OF REFS 0
8a. CONTRACT OR GRANT NO. b. PROJECT NO c. d.	9a. ORIGINATOR'S REPORT NUMBER(S) FTD-MT-24-2484-74 9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)	

10 DISTRIBUTION STATEMENT

Approved for public release; distribution unlimited.

11 SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY Foreign Technology Division Wright-Patterson AFB, Ohio

13 ABSTRACT

06

(15)

DD FORM 1 NOV 68 1473

UNCLASSIFIED
Security Classification

EDITED MACHINE TRANSLATION

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By: A. Ye. Vershigora

English pages: 9

Source: Sovremennyye Problemy Otorinilaringolii, Respublikanskiy Mezhvedomstvennyy Sbornik, Izd vo Zdorov'ya, Kiev, No. 3, 1972, pp. 3-8

Country of Origin: USSR
Requester: FTD/PDTR
This document is a SYSTRAN machine aided translation, post-edited for technical accuracy by: Joseph E. Pearson
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Block	Italic	Transliteration	Block	Italic	Transliteration
А а	*А а*	A, a	Р р	*Р р*	R, r
Б б	*Б б*	B, b	С с	*С с*	S, s
В в	*В в*	V, v	Т т	*Т т*	T, t
Г г	*Г г*	G, g	У у	*У у*	U, u
Д д	*Д д*	D, d	Ф ф	*Ф ф*	F, f
Е е	*Е е*	Ye, ye; E, e*	Х х	*Х х*	Kh, kh
Ж ж	*Ж ж*	Zh, zh	Ц ц	*Ц ц*	Ts, ts
З з	*З з*	Z, z	Ч ч	*Ч ч*	Ch, ch
И и	*И и*	I, i	Ш ш	*Ш ш*	Sh, sh
Й й	*Й й*	Y, y	Щ щ	*Щ щ*	Shch, shch
К к	*К к*	K, k	Ъ ъ	*Ъ ъ*	"
Л л	*Л л*	L, l	Ы ы	*Ы ы*	Y, y
М м	*М м*	M, m	Ь ь	*Ь ь*	'
Н н	*Н н*	N, n	Э э	*Э э*	E, e
О о	*О о*	O, o	Ю ю	*Ю ю*	Yu, yu
П п	*П п*	P, p	Я я	*Я я*	Ya, ya

*ye initially, after vowels, and after ъ, ь; e elsewhere. When written as ë in Russian, transliterate as yë or ë. The use of diacritical marks is preferred, but such marks may be omitted when expediency dictates.

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GRAPHICS DISCLAIMER

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RUSSIAN AND ENGLISH TRIGONOMETRIC FUNCTIONS

Russian	English
sin	sin
cos	cos
tg	tan
ctg	cot
sec	sec
cosec	csc
sh	sinh
ch	cosh
th	tanh
cth	coth
sch	sech
csch	csch
arc sin	$\sin^{-1}$
arc cos	$\cos^{-1}$
arc tg	$\tan^{-1}$
arc ctg	$\cot^{-1}$
arc sec	$\sec^{-1}$
arc cosec	$\csc^{-1}$
arc sh	$\sinh^{-1}$
arc ch	$\cosh^{-1}$
arc th	$\tanh^{-1}$
arc cth	$\coth^{-1}$
arc sch	sech^{-1}
arc csch	csch^{-1}

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rot	curl
lg	log

GREEK ALPHABET

Alpha	A	α			Nu	N	ν	
Beta	B	β			Xi	Ξ	ξ	
Gamma	Γ	γ			Omicron	O	o	
Delta	Δ	δ			Pi	Π	π	
Epsilon	E	ε			Rho	P	ρ	
Zeta	Z	ζ			Sigma	Σ	σ	ς
Eta	H	η			Tau	T	τ	
Theta	Θ	θ			Upsilon	T	υ	
Iota	I	ι			Phi	Φ	φ	ϕ
Kappa	K	κ			Chi	X	χ	
Lambda	Λ	λ			Psi	Ψ	ψ	
Mu	M	μ			Omega	Ω	ω	

LABORATORY DIAGNOSTIC METHODS AND SPECIFIC DESENSITIZING THERAPY FOR INFECTIOUS-ALLERGIC DISEASES

A. Ye. Vershigora
Kiev

The laboratory of microbiology and immunology of the Kiev scientific and research institute of otolaryngology in collaboration with certain clinical departments of the Kiev institute for the improvement of physicians and the Kiev medical institute over a period of a number of years carried out investigations on the methods of preparing microbial allergens, the diagnostics of infectious allergy and desensitization in the case of infectious-allergic otorhinolaryngological diseases and bronchial asthma in adults and children.

Microflora. In the case of infectious-allergic diseases sensitization to microbial antigens is usually detected. The question of its role in the etiology of rhinosinusopathy, chronic tonsillitis and bronchial asthma remains debatable. Thus, for instance, Miescher, et al, (1956), and Zavazal (1965) consider that the establishment of allergization to microbial allergens can be important for explaining the etiology of diseases, and Blumstein (1957) and Bourdial (1963) assume that in establishing etiology

allergy to microbes is a secondary criterion and sensitization to exogenous allergens - is the primary criterion.

Investigations were carried out on the microflora detected on the mucous membrane of the upper respiratory tract in patients with infectious-allergic otorhinolaryngological diseases and bronchial asthma, as compared with the changes in mucous membrane in the case of sensitization to homologous antigens and with the changes in a number of indicators of specific and nonspecific immunity.

L. K. Grinevich (1968) and E. V. Gorshevikova (1970) established that staphylococcus is most frequently detected on the nasal mucous membrane of rhinosinusopathic patients. In certain cases staphylococcus was isolated in a pure culture or the flora completely eluded detection. In a parallel microbiological investigation of the nasal and pharyngeal mucus in one and the same patient the pharyngeal flora was more diverse with regard to species. β-hemolytic streptococcus and also Staphylococcus aureus were considerably more frequently detected in the pharynx than in the nose. In the patients with chronic tonsillitis β-hemolytic streptococcus was cultured from the tonsils in 21.9% of the cases, and staphylococcus - in 48.5% of the cases (Ye. T. Sviridenko and M. V. Tarasyuk, 1969). In winter micrococci Neisseria frequently infect patients with chronic tonsillitis (Ye. T. Sviridenki, et al., 1970).

The microflora in the sputum of patients with bronchial asthma was of various species, was dynamic (motile), and Streptococcus viridans was most frequently detected. In a twofold investigation Streptococcus viridans, Neisseria micrococcus and Candida albicans were detected in the majority of the patients. Somewhat more rarely detected were β-hemolytic streptococcus, virulent staphylococcus, enterococcus, pneumococcus and other forms of microbes.

Taking into account the detected dynamicity (motility) of the species composition of the microbes, it is possible to assume that all the enumerated species of microbes upon repeated investigation of the materials can be periodically encountered in all patients with bronchial asthma. Sometimes β-hemolytic streptococcus, Streptococcus viridans, staphylococcus and Candida albicans were grown in pure cultures (A. Ye. Vershigora, 1969). Candida albicans was frequently detected in material extracted from the ears of patients with chronic suppurative otitis, especially during the prolonged application of antibiotics for medical treatment (T. P. Danil'chuk, 1968).

The findings make it possible to advance the assumption that the sources of the infection of the nasal and bronchial mucous membrane are the pharynx and the tonsils, and they confirm the opinion of other researchers concerning the fact that staphylococcus possesses a tropism towards the nasal mucous membrane. It is possible also to assume that a considerable mass of antigens of a specific species of microbe at the time of a predominance of the monoflora can have a sensitizing effect on the organism. Staphylococcus can be this type of microbe for the nasal mucous membrane, while for other sections of the mucous membrane of the upper respiratory tract primarily β-hemolytic streptococcus, Candida albicans and Neisseria micrococcus can have this affinity.

Allergens. Until recently insufficient attention has been given to the special selection of the strains employed for the preparation of allergens. It was established in our investigations (A. Ye. Vershigora, 1969) that different strains of one and the same species of microbes were not identical in their allergenic properties. Thus, antigens of one of eight strains of β-hemolytic streptococcus caused positive reactions in 20 patients, and of another - in only 5. Allergens of only two strains caused immediate reactions and +++ and ++++ reactions. Analogous results were also obtained in studying the allergenic properties of staphylococcus,

enterococcus, Candida albicans and Neisseria micrococcus. The differences in the biological activity of the strains were not correlated with their allergenic activity. These data served as the basis for selecting highly allergenic strains of the different species of microbes employed by us for the preparation of allergens. In this case we proceeded from the assumption that highly allergenic strains more frequently cause sensitization and that their antigens will be more specific in skin reactions and more effective in carrying out specific desensitizing therapy.

The selecting of the strains was carried out by studying skin reactions in patients to the antigens of several strains of just one species of microbes.

For the purpose of diagnosis and desensitization, we prepared complete microbial antigens of the microbes most frequently detected in the upper respiratory tract - a mixture of microbial cells with the products of their metabolism without a nutrient medium admixture (A. Ye. Vershigora, 1966).

In selecting the nature of the antigens we proceeded on the basis of the data of literature concerning the fact that corpuscular and soluble microbial antigens can have a sensitizing effect on the organism.

Sensitization to microbial antigens. The investigations of T. I. Begunova (1968), L. A. Bezrukov (1968), A. Ye. Vershigora (1968), L. V. Vizirenko (1968), Ye. N. Sidorenko (1970) established that in patients with rhinosinusopathy and bronchial asthma in the event of severe skin reactions to the intradermal administration of complete microbial antigens eosinophilia was detected in the blood and sputum from the bronchi. In this case vacuoles were frequently detected in the cytoplasm of the eosinophils (T. I. Begunova, 1970) and the histaminopexic index of the blood serum is reduced. (V. V. Baeva, 1967; G. F. Glukhovskaya, Ye. N. Sidorenko, 1969). These

data attest to the fact that allergization to microbial antigens can be accompanied by the sensitization of the entire organism.

The neutrophil damaging reaction has been broadly employed for a number of years as a specific indicator of allergy. It was established in the investigations of L. A. Bezrukov (1968), L. V. Vizirenko (1968), of I. P. Myagkaya and Ye. N. Sidorenko (1968), L. D. Karpenko (1969) that the neutrophil damaging reaction under the effect of complete microbial antigens correlated with skin reactions to the intradermal administration of a homologous antigen or with indicators of nonspecific sensitization of the organism. However, no sharp differences were detected as compared with these indices in persons of the control group. Variations in the data on this test can depend on subjectivistic elements in taking into account the results of this reaction. Difficulties also arise in interpretation, since blood neutrophils do not have a direct relationship to the mechanisms of the development of hypersensitivity. The neutrophil damage occurs more rapidly during an inflammatory reaction.

As an indicator of specific sensitization in a number of works (L. A. Bezrukov, 1968; T. I. Begunova, 1968; A. Ye. Vershigora, 1965-1970; L. V. Vizirenko, 1968; Ye. N. Sidorenko, 1970; E. V. Gorshevikova, 1968) skin reactions to microbial antigens were studied. It was shown that in patients with bronchial asthma and rhinosinusopathy skin reactions to the intradermal administration of complete microbial antigens correlated with the indicators of general allergization of the organism; however, the dependence of skin reactions on a homologous species of microbes in the investigated material from patients was not noted. Threshold doses of antigen were employed for skin tests. A threshold dose was taken to be that quantity of antigen amplified by 10 times with respect to that which causes a reaction with an intensity of + in half of the patients examined. Since skin reactions to microbial antigens

are detected not only in sick people, but also in healthy persons, the selection of the antigen doses has paramount importance in evaluating their doses. Very large antigen doses will cause a high percent of falsely positive, and very small doses - falsely negative reactions.

Skin reactions were not an absolute indicator of specific sensitization, since in some patients they were positive in the absence of other indicators of allergy and negative in their presence. It is possible that in the first case Jones-Mout type [Translator's Note. This reaction was not found in the available sources.] reactions were noted, and in the second their absence could be due to an insufficient set of allergens, which were employed for the skin tests. In spite of this, the findings make it possible to draw a conclusion about the fact that intense skin reactions to complete microbial antigens are specific. It should also be noted that in patients with bronchial asthma and rhinosinusopathy allergization to exogenous allergens is relatively rarely detected (Ye. N. Sidorenko, 1970). This indicates the independent importance of allergy to microbial antigens.

There are bases to assume that the specificity of reactions to microbial antigens can be increased by employing individual chemical fractions from the complete or corpuscular microbial antigen. It was revealed in I. I. Tsmokalyuk's investigation (1970) that the protein, nucleoprotein and polysaccharide fractions of a complete staphylococcal antigen cause skin reactions in patients with rhinosinusopathy and chronic tonsillitis. Most allergenic was the protein fraction, which frequently caused delayed skin reactions in healthy persons and immediate skin reactions in sick people.

In comparison with healthy persons, people who were suffering from infectious-allergic otorhinolaryngological diseases manifested a greater number of immediate reactions to all fractions of the

antigen and intense skin reactions to polysaccharide manifested themselves, which were absent in healthy persons.

In persons suffering with chronic tonsillitis intense skin reactions were more frequently caused by the nucleoprotein fraction of the corpuscular antigen of β-hemolytic streptococcus of group A, than by the protein and polysaccharide fractions (L. K. Chulaevskaya, 1970).

The results of the investigations attest to the fact that the employment of individual chemical fractions is more valuable for diagnosis, than the employment of complete allergens; thus, it is expedient to carry out further investigations in this direction.

Specific and nonspecific immunity. The data in literature concerning the interconnection of the indices of allergy and immunity do not give sufficient justification for final judgments on this question.

The results of our investigations on this aspect are the following. In the case of a large inoculation of the nasal mucous membrane with staphylococcus in rhinosinusopathic patients smaller titers of staphylococcal antitoxin were detected in the blood serum and more intense skin reactions to staphylococcal antigen were found (E. V. Gorshevikova, 1970). Patients with sharply expressed sensitization to microbial antigens contained titers of staphylococcal agglutinins and larger titers of lysozyme in their blood serum (A. Ye. Vershigora, 1969; E. V. Gorshevikova, 1969). There was no success in detecting autoantibodies to the antigen from the tonsil tissue in patients with chronic tonsillitis and to the antigen from polyps in rhinosinusopathic patients in Boyden's reaction. The detected titers of autoantibodies in the patients did not exceed the titers in the persons of the control group (T. I. Begunova, 1970; G. M. Leshchenko, 1970). In the blood serum of

the majority of patients with chronic tonsillitis in carrying out Dan'ye's reaction autoantibodies to the tissue antigen from tonsils were detected (G. M. Leschenko, 1970).

Staphylococcal antigen also causes blasttransformation reactions in a culture of lymphocyte cells sensitized with a homologous antigen of experimental animals and lymphocytes of rhinosinusopathic patients (E. V. Gorshevikova, T. I. Begunova, 1970).

The results of conducted investigations make it possible to assume that the degree of sensitization to staphylococcal antigen in infectious-allergic diseases is in direct dependence on the titers of antibodies in the blood serum to the soluble antigens and in inverse dependence on the titers of antibodies to corpuscular antigens.

Desensitizing medical treatment. The purpose of the investigations in this direction is to explain the advisability of employing specific desensitization with microbe antigens in clinic, to approve the various antigens, methods and ways of administering them to the organism. The method of specific desensitization with complete microbial antigens is effective in bronchial asthma in adults in 50% of the cases (Ye. N. Siderenko, 1970), in children - in 67% of the cases (I. M. Rudnev and coll., 1970) and in 29-72% of the cases - in patients with rhinosinusopathy (L. V. Vizirenko, 1967; T. I. Begunova, 1968).

The employment of complete allergens is more effective than soluble allergens. The method of intradermal administration of antigens is more preferable than subcutaneous administration. The advantage of autovaccines over heterogeneous antigens has not been established. The results of medical treatment are better in patients with sufficient indications for the carrying out of desensitization with microbial antigens and with medical treatment with a continuous course over a long period of time.

During desensitization a change in some indicators of non-specific immunity occurs in the patients - the titer of lysozyme drops off and the titer of complement in the blood serum is raised.

The continuous administration of microbial allergens to patients with bronchial asthma and rhinosinusopathy over a period of a number of years does not cause pathological changes in the blood and urine (Ye. N. Sidorenko, 1970).

The results of long-term investigations in our laboratory make it possible to recommend the implementation into practice of specific desensitization with complete microbial antigens according to the methods of preparing and employing microbial allergens developed and tested in our investigations.