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EFFECTIVENESS OF DIFFERENT METHODS OF SPECIFIC DESENSITIZATION BY MICROBIAL ALLERGENS

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U. S. BOARD ON GEOGRAPHIC NAMES TRANSLITERATION SYSTEM

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

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

FOLLOWING ARE THE CORRESPONDING RUSSIAN AND ENGLISH

DESIGNATIONS OF THE 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}
rot	curl
lg	log

EFFECTIVENESS OF DIFFERENT METHODS OF SPECIFIC DESENSITIZATION BY MICROBIAL ALLERGENS

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The method of specific desensitization by microbial allergens received dissemination in our country in recent years. The leading significance of microbial allergy with bronchial asthma is recognized by many researchers (A. D. Ado; P. K. Bulatov; Hajos). At present, microbial allergens are employed which differ in the procedure for preparation (A. Ye. Vershigora; Ye. I. Gudkov; Malota and co-authors; Holman and Swineford) and in their nature (auto- and heterovaccines, phagolysates, etc.); different ways of their introduction in the organism of the patient are utilized (subcutaneously, intracutaneously, per os). In spite of the fact that each of the methods being applied has supporters, a comparative estimate of their effectiveness is not given thus far.

We set a goal to examine several most widely accepted methods for specific desensitization by microbial antigens. The latter were prepared in the microbiology laboratory of the Kiev Scientific

Research Institute of Otolaringology (A. Ye. Vershigora) and they were employed by a single scheme of systematic continuous medical treatment in gradually increasing doses, beginning with subthreshold concentrations at gradually increasing intervals. Periods of observation were from 6 months to 5 years.

We employed the following types of microbial antigens: "soluble", which are a supernatant liquid of microbial suspension not containing microbial cells; "full" antigens which also include microbial cells, and the products of their metabolism without the admixture of the nutrient medium prepared from specially selected strains with the most explicit allergen properties (virdescent and β-hemolytic streptococci, white and golden staphylococci, pneumococci, the Saccharomyces candida albicans, Sarcina tetragenus, Bacillus coli and the micrococcus Neisser). The "full" antigens were represented by autovaccines (of all autostrains isolated from sputum), heterovaccines, which are a mixture of antigens on which positive skin reactions were detected on the patient, and also by a combined vaccine, which is a standard mixture of all 9 forms of microorganisms, most frequently sown from the sputum of patients with bronchial asthma. The quantity of microbial bodies of each antigen in the initial combined vaccine is taken in such a way that its subsequent cultures corresponded to the working concentrations of its component parts when using them isolatedly (Table 1).

Treatment was carried out subcutaneously and intracutaneously.

Treatment by "soluble" or noncellular allergens was received by 40 patients. In the preliminary examination a limited spectrum of positive skin reactions was observed which were detected on 1 of the 9 tested allergens among 5 patients, on 2 - of 28, on 3 - of 6, on 4 - of 1 patient. Most frequently the positive reactions were caused by the white and golden staphylococcus, and also by Bacillus coli from which therapeutic vaccines were

Table 1. Composition and concentration of the initial combined vaccine and its subsequent cultures.

Antigen	Quantity (in mℓ)	Quantity of microbe bodies in 1 mℓ			
		Initial	In titre 1:10	In titre 1:100	In titre 1:1000
Strept. α	1	1 billion	100 million	10 million	1 million
Strept. β	1	1 billion	100 million	10 million	1 million
Staph. alb.....	1	100 million	10 million	1 million	100 thousand
Staph. aur.....	1	100 million	10 million	1 million	100 thousand
Pneumoc.....	1	1 bil.ion	100 million	10 million	1 million
Cand. albic.....	1	1 billion	100 million	10 million	1 million
Sarcina tetr.....	1	100 million	10 million	1 million	100 thousand
B. coli.....	1	10 million	1 million	100 thousand	10 thousand
Neiss. cathar.....	1	10 million	1 million	100 thousand	10 thousand
Altogether.....	9	4320 million	432 million	43 million 200 thousand	4 million 320 thousand
In 1 mℓ		480 million	48 million	4 million 800 thousand	480 thousand
In 0.1 mℓ		48 million	4 million 800 thousand	480 thousand	48 thousand

also composed. A positive effect was obtained only on 10 patients. Of the indicated number of patients, on 8 treatment was subsequently continued by the "full" antigen with the previous effect. In 3 patients with a negative result, the subsequent treatment by the "full" antigen led to a considerable improvement in the condition.

Treatment with the autovaccine was conducted on 31 patients. First skin samples were placed with each autostrain. In the absence of a positive reaction the appropriate antigens were not introduced in the vaccine. A positive result of treatment was achieved in 16 patients. Of them, in 12 treatment subsequently continued with heterogeneous antigens, whereupon in not one case did the need to return to an autovaccine arise. With 4 patients after the unsuccessful use of a heterogeneous vaccine an autovaccine was used, but the result did not change.

Treatment with a heterovaccine was obtained by 190 patients. Upon preliminary inspection, as a rule, sensitization to several microbe antigens was discovered; therefore, the therapeutic vaccines contained from 2 to 7 (more frequently 3-5) allergens. Positive results of treatment were achieved in 93 patients. The combined vaccine was applied to 51 patients. A preliminary examination of a patient entailed the determination of a therapeutic culture, for which skin samples with the 1st, 2nd and 3rd cultures of the vaccine were set up. A positive result in treatment was achieved in 28 patients. Statistical processing of the reduced data of the methods of alternative variation established the authenticity of the difference between "soluble" and "full" allergens ($P<0.001$) and its absence between auto-, and heterovaccines and the combined vaccine (Table 2).

We conducted the comparison of the effectiveness of the intracutaneous and subcutaneous methods of treatment in 2 groups of patients: those treated subcutaneously (156 patients) and

Table 2. Effectiveness of the medical treatment of patients with bronchial asthma by different microbial allergens.

Antigens	Number of patients	Results of treatment		
		positive	negative	doubtful
"Full" (heterovaccine)	190	93 (49%)	82 (43.2%)	15 (7.8%)
"Soluble"	40	10	27	3
Autovaccine.....	31	16	14	1
Combined vaccine.....	51	28	19	4

intracutaneously (85). In the first group, the effectiveness of therapy was noted in 48% of the patients, in the second - in 54.1% of the patients (Table 3). No statistically reliable distinction between them was established.

Table 3. Results of the treatment of patients with bronchial asthma by the subcutaneous and intracutaneous introduction of microbial allergens.

Method of treatment	Number of patients	Result of treatment		
		positive	negative	doubtful
Subcutaneous	156	75 (48%)	70 (46%)	11 (6%)
Intracutaneous	85	46	31	8

Malota and co-authors and Spielman use for the desensitizing therapy microbial antigens which do not contain microbial cells. However not only toxins, ferments, and other products of the metabolism of a microbial cell, but also the latter itself possess antigenic properties. Therefore, it can be assumed that the corpuscular antigens should exert both a more powerful sensitizing and desensitizing action on the organism. Clinical approval confirmed the obvious advantage of "full" antigens which is

determined already with the diagnostic examination of the patient. The lower antigen quality of the "soluble" antigens does not permit disclosing the hypersensitivity which the patient has in so wide a range as is accomplished when using full antigens. Although it was established that inherent to those sick with "microbial" bronchial asthma is a polyallergy - increased sensitivity simultaneously to several microbial allergens (A. Ye. Vershigora and Ye. N. Sidorenko; Findeisen and Wemmer), noncellular antigens usually do not disclose it. Hence, their low therapeutic effectiveness. Bergquist, Hajos, and other authors consider, that most suitable for desensitizing therapy are autovaccines; Baird and Cornet, on the contrary, recognize considerably greater effectiveness with heterogeneous antigens.

According to our observations, auto- and the heterovaccines (both individual and combined) gave positive therapeutic results in approximately the identical percentage of the cases. However, each of the indicated forms of antigens has its own features which must be considered in their selection. Thus, apparently, the use of an autovaccine is expedient in those cases where the sensitization is caused and is supported by the effect of autoflora. However, literature data testify to the dynamicity of the species composition of the microflora of the sputum of patients with bronchial asthma (Kortekangas; A. Ye. Vershigora). This circumstance makes difficult or even doubtful the possibility of the production of an autovaccine precisely from the strain which causes sensitization. The negative skin samples for antigens from autostrains reinforce these doubts. In connection with the renewal of the microflora of the patient's sputum the need appears for changing the autovaccine in the course of treatment. Meanwhile, the production of an autovaccine is an extremely laborious and prolonged process which requires the constant communication of clinicians with the highly skilled microbiological laboratories. Taking into account this circumstance, and also the absence of a substantial advantage of an autovaccine for its

effectiveness over a heterovaccine, in cases of mass use in practice we should give preference to the latter. Special attention is deserved by the combined vaccine whose high effectiveness is determined, apparently, by its broad antigenic spectrum. In the opinion of Oehling, best would be a vaccine consisting of the largest possible number of microbial strains which populate the respiratory tracts. The practical advantages of the combined vaccine consist of simplicity of examination, which is connected with the absence of the need for setting up diagnostic samples. Instead of the minimum 18 injections usually necessary for the development of the specific antigens, in the composition of individual heterovaccines it is necessary to make only 3-4 injections to determine the initial therapeutic concentration; in this case an 8 times smaller quantity of microbial bodies is introduced in the patient than when setting up skin samples by each allergen in an isolated manner. The treatment with a standard mixture creates a tremendous savings of time both during the composition of the vaccine and during the mass examination and treatment of the patients. With this method a considerably lesser quantity of vaccine is consumed and, therefore, a considerably lesser quantity of antigen is introduced in the patient.

With subcutaneous and intracutaneous methods, the same scheme of treatment was utilized: the quantity of introduced antigen of each concentration was successively increased from 0.1 to 1 ml; any dose was inserted at one time. Unlike subcutaneous introduction, with intracutaneous introduction, for the very same dose of antigen the local reaction appears repeatedly. Since in this case the subsequent doses are increased, the increase in them occurs many times slower than with the subcutaneous method. This is the advantage of intracutaneous treatment, since during the same period of it and, therefore, with an equal number of injections the patient receives a total considerably lesser quantity of antigen. Thus with the use of a heterovaccine during a year 1,450,926,000 microbial bodies were introduced

subcutaneously and with intracutaneous treatment 159,173,000. In this case, the risk of an overdose of antigen and, accordingly, the number of general reactions is considerably decreased; if with the subcutaneous method the latter were observed in 3.3% of the cases, then with the intracutaneous method they were observed in 2.5%.

Conclusions

1. The "soluble" noncellular microbial allergens possess low therapeutic effectiveness considerably inferior to "full" antigens.

2. The effectiveness of autovaccines, heterovaccines, and a combined vaccine is approximately identical.

3. The somewhat greater effectiveness, and the main thing, a considerably lesser quantity of microbial antigens introduced in the organism make it possible to give preference to the intracutaneous method of treatment.

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