

## Modern schemes of RAS treatment in children: development, application, effect

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### Summary

The variant and often unclear etiology of RAS in children, the general treatment of the condition must necessarily be complex, while the local treatment applied must inevitably be symptomatic.

The purpose of this article is to lay out and describe the various schemes of treatment of RAS in children. Objective clinical parameters will be studied so that the different schemes of treatment can be compared in terms of efficiency. A set of general principles concerning the treatment of children with RAS will also be deduced.

Material and method. Sixty children with RAS - diagnosed as having "idiopathic recurrent aphthae" - were included in the group for treatment. A number of different aphthous ulcerations in the mucous membrane - characteristic of some general illnesses, deficiencies and conditions due to compromised immunity - were excluded from the study.

The treatment of children with RAS includes general and local treatment. Results and conclusion. During the treatment the recurrences become less frequent, the discomfort and the pain in the mouth cavity are alleviated, the period needed for the healing of aphthae gets shorter as well and the number of recurring aphthae decreases.

Keywords: recurrent aphthous stomatitis (RAS), food diet, style of life, adhesive bases, immunomodulators.

### Introduction

The recurrent aphthous stomatitis (RAS) in the childhood is characterized by oral lesions of the "aphthae minor" type, according to the World Health Organization classification of recurrent aphthae and aphthosis [1,2,3,4]. Many exogenous and endogenous factors participate in the etiology of the recurrent aphthae and aphthosis. The different factors interact, and, as is the case of many other diseases, some are of primary importance while others comprise something of a background against which the disease develops. The immune system is an

important factor here, because of the mouth cavity being the feeding factor for many immunopathogenic factors of bacterial or medicinal origin, organic or inorganic character, etc. [5,6,7] Again, both the secretive local immunity and the general humoral and cellular immunity simultaneously manifest themselves in the mouth cavity. The mouth cavity provides the necessary conditions for the development of both allergic processes and autoimmunity. It can also condition the emergence of immunodeficiency. The pathogenic mechanisms of RAS usually remain hypothetical, though. [8,9,10]

Because of the variant and often unclear

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etiology of RAS in children, the general treatment of the condition must necessarily be a complex one, while the local treatment applied must inevitably be a symptomatic one [11,12,13]. Many different medicines and methods of general and local treatment have been proposed in the relevant literature. Because of the varying etiopathogenesis of RAS, the individual approach - taking into account the specific risk of recurrence of the condition, and providing specific treatment for each individual patient - has been establishing itself as the most adequate one. Hence, the necessity of developing a set of general principles and schemes concerning the complex treatment of RAS. These are essential if adequate treatment is to be dispensed to patients on an individual basis [14,15,16,17].

It is the purpose of this article to lay out and describe the various schemes of treatment of RAS in children. Objective clinical parameters will be studied so that the different schemes of treatment can be compared in terms of efficiency. A set of general principles concerning the treatment of children with RAS will also be deduced.

## Material and methods

Sixty children with RAS - diagnosed as having "idiopathic recurrent aphthae" - were included in the group for treatment. A number of different aphthous ulcerations in the mucous membrane - characteristic of some general illnesses, deficiencies and conditions due to compromised immunity - were excluded from the study.

The treatment of children with RAS comprised: general and local treatment.

### 1. General treatment

#### 1.1. Food diet

A regimen was worked out, excluding a wide variety of food items - known from the relevant literature and from our own experi-

ence to be strongly allergenic or capable of disturbing the local oral tolerance of the mucous membrane. These are: cow milk, tomatoes, veal, yolk, walnuts, carrots and peas.

The so-called "abrasive foods", such as potato crisps, kernels and other kinds of hard food were added to the group of food items to be avoided. These are foods that can easily harm the mucous membrane of the mouth cavity. It was also recommended that the consumption of hot foods and strong condiments be reduced.

The consumption of sour drinks such as lemon juice, orange juice, etc., as well as the consumption of chocolate, strawberries, seafood and citrus was put under control too.

The food was supposed to be wholesome and up to the requirements of a salutary diet.

#### 1.2. Food additives

It has been acknowledged recently - as a number of reported studies in the relevant literature have - that the risk of RAS increases with the occurrence of a deficit of: tiamin (vitamin B1), riboflavin (vitamin B2), pyridoxine (vitamin B6) and iron. The following foods are recommended so that the supply of these substances is restored:

- for vit. B1: whole-grain bread, white rice, haricot beans, tender pork;
- for vit. B6: tuna fish, bananas, liver, spinach;
- for vit. B12: eggs, milk, sea food, poultry; measures must also be taken so that favorable conditions are created for the absorption of the vitamin in the stomach and intestines;
- fruit and vegetables rich in vit. C and vit. A;
- probiotic - the Bulgarian medication Entirosan was made use of for the purpose. It is a food additive containing active cells of lactobacilli and bifidobacteria. The medication also contains vitamins and microele-

ments - in a form that makes absorption by the organism easier, as well as organic acids and amino acids.

### 1.3. Style of life

The following recommendations were made concerning the way of life of children with RAS:

⌘ Reducing stress to a minimum. Since different forms of regimen and different ways of imposing a regimen are suitable for the parents of different children in stress, the expert professional advice of a psychologist was recommended.

⌘ Keeping an optimum oral hygiene, requiring the observation of the following rules:

- Excluding all toothpastes containing sodium lauryl sulphate. The detergent is considered to be the reason for erosion of oral mucous membrane, which in children with RAS leads to the emergence and recurrence of aphthae. For example, such detergents are: Oral-B and ControlRx (produced by the "Oral-B" company, USA). Taking care that vulnerable places in the mouth cavity predisposed to produce aphthae - the free mucous membrane in the area of the transitory vestibular fold and the cheeks - are not brushed and thus injured.

⌘ Creating in children the habit of regularly gargling their mouth with anti-microbial waters, as prescribed by a stomatologist.

⌘ Creating the habit and skill of treating the aphthae at the onset of their emergence - in the prodromal phase, accompanied by a feeling the patient is familiar with.

⌘ Sanitizing the mouth cavity and the teeth so that bad obturations and sharp edges of teeth with caries do not create conditions for irritation of the mucous membrane.

⌘ Informing the child and his parents on the important issues concerning the emergence and treatment of the recurrent aphthae

- the active participation of the patient in the process of treatment is essential for the final recovery from the condition.

## 2. Local treatment of recurrent aphthae

A couple of different therapeutic methods were employed in the local treatment so that we could alternate and combine them. Different combinations of methods can be applied so that the most efficient combination is arrived at. It is also possible to alternate the different combinations of methods possible so that the organism does not get accustomed to a medication, thus lessening the therapeutic effect.

Basic methods in local treatment

⌘ Application of antiseptic and anti-inflammatory solutions for gargling of the

mouth: chlorhexidine medications: Hexoral, Peridex;

- medications with benzidamine hydrochloride: Tantum Verde;

- propolis medications: Propodent.

The medications have been selected in accordance with the age of the child and applied for gargling three times a day, after brushing the teeth.

⌘ Local treatment of the aphthae with Adhesive bases - These are polymeric medications containing different active components with an anesthetic effect and the capacity to cover the aphtha with a film. They release their active component for about 20-30 minutes, thus protecting the lesion from mechanical irritation. The following medications were used in the study:

- Solcoseryl<sup>1</sup> - Adhesive paste with an active component stimulating epitalisation.

- Adhesive base<sup>1</sup> -NK: with sodium chromoglycate as an active component; the sodium chromoglycate has an anti-histamine effect achieved by suppressing the degranulation of the mastocytes.

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<sup>1</sup> "Adhesive base" is a polymeric medication for the local treatment of oral lesions. It has been developed in Bulgaria and is registered as an invention. Adhesive base exists in two versions: Adhesive base-NK and Adhesive base D.

- Adhesive base D: with dexametazone as an active component; dexametazone has a non-specific anti-inflammatory effect.

Each aphtha that emerged during the period of controlled treatment had to be treated three times a day right from the start of the prodromal period.

⌘ Application of polybacterial immunomodulators for the improvement of the local immunity in the mouth.

- Dentavax<sup>2</sup> - lysate made out of five species of killed bacterial cells from the oral microflora (*Streptococcus aureus*, *Streptococcus pyogenes*, *Klebsiella Pneumoniae*, *Candida Albicans* and *Lactobacillus acidophilus*) - was made use of for that purpose.
- Imudon - a medication with similar composition, produced in France, was made use of too.

The immunomodulators were applied in accordance with the patients' age. From 4 to 6 tablets for sucking per day were given to the patients for a period of 14-20 days, the treatment starting with the beginning of the three-month period for medical supervision.

⌘ Application of probiotics - Enterosan<sup>3</sup> - a medication with high concentration of live active cells of different species of *Lactobacillus* and *Bifidobacteria* - half a tablet two times a day for a period of ten days.

Schemes applied for the local treatment of children with RAS

Four combinations of medications for local treatment of patients with RAS were worked out.

First combination:

- solutions for gargling of the mouth;
- polybacterial immunomodulators;

Second

- combination bases;
- polybacterial immunomodulators;

Third combination:

- solutions for gargling of the mouth;
- polybacterial immunomodulators;
- local treatment of the aphthae with

Adhesive bases;

Fourth combination:

- solutions for gargling of the mouth;
- local treatment of the aphthae with

Adhesive bases.

The 60 children treated were divided into four groups of 15 children. The scheme of the general treatment was the same, while the local treatment was conducted in four different combinations.

In accordance with their concomitant illnesses, the children with RAS were treated by means of different therapeutical methods, as follows:

- In children with allergies, medications for local treatment with an antihistamine effect were used, namely Adhesive base-NK and Adhesive base-D, combined with polybacterial immunomodulators for strengthening the local immunity.
- In children with frequent anginas, medications with a local anti-inflammatory and antiseptic effect were recommended, combined with polybacterial immunomodulators for strengthening the local immunity.
- For a part of the children with indigestion, Enterosan was also used in the treatment scheme so that the local immunity, both in the mouth and the stomach and intestines, could be positively influenced.

The age of the children was taken into

<sup>2</sup> Bulgarian polybacterial immunomodulator, developed by the National Centre for Contagious and Parasitic diseases.

<sup>3</sup> A Bulgarian probiotic

consideration in determining both the dosage and the choice of medications.

The distribution of children according to the medications administered is illustrated by *Table 1*.

The oral lesion, called "aphtha", was the unit of observation in the children treated.

The effect from the treatment was studied for a period of three months, during which the children were asked to keep a diary describing five basic parameters that gave us the clinic picture of the treatment.

Patients were studied two times a month. The data were registered by means of a questionnaire developed by us for the purpose of studying children with RAS.

#### Parameters of RAS evaluation

The following parameters were registered:

1. Number of recurrences during the whole study;
2. Number of aphthae per recurrence;
3. Size of the biggest aptha per recurrence - determined by the patient with the help of a scale that we developed for the purpose:

Small aphthae - code 1	0.3 cm
Medium aphthae - code 2	0.3-0.8 cm
Big aphthae - code 3	0.8-1.0 cm
- code 4	< 1.0 cm

4. Feeling of oral discomfort. The evaluation was made with the help of a scale for self-evaluation developed by us and including the following degrees:

- 0 - lack of discomfort;
- First degree - small discomfort;
- Second degree - medium pain;
- Third degree - strong pain.

5. Duration of the recurrences. The duration of the recurrences is counted in days.

**Statistical processing:** The data were processed with adequate statistical methods involving variation and alternative analysis.

#### Results

The generalized results from the study - conducted with the treatment schemes developed by us - are presented in five tables.

**Table 1.** Distribution of children treated from Recurrent Aphthae according to the local treatment schemes applied

	Types	Children with first combination	Children with second combination	Children with third combination	Children with fourth combination
Antiseptics and anti-inflammatory medications for gargling	Hexoral Peridex	4	-	5	2
	Tantum Verde	5	-	5	6
	Propodent	6	-	5	7
Polybacterial immunomodulator	Imudon	7	8	8	-
	Dentavax	8	7	7	-
Adhesive bases for local treatment of aphthae	Solcoseryl	-	6	5	4
	Adhesive base NK	-	5	5	6
	Adhesive base D	-	4	5	5

Five parameters have been selected by us to present the dynamics of the condition. It was in terms of these five parameters that the effect from the different treatment schemes was compared.

First parameter: Number of recurrences during the time of controlled treatment

The results from the comparative study of the number of recurrences per child according to the different treatment schemes are presented in *Table 2*.

Comparing the number of recurrences according to the four different treatment schemes, the best results are shown in the case of the fourth treatment scheme, treatment schemes two and three ranking next in efficiency. The corresponding values of 2 prove statistically that in treatment schemes four, two and three the children have approximately two recurrences for the study

period, while in treatment scheme one the average is three recurrences.

Second parameter: Average number of aphthae per recurrence during the period of controlled treatment

The generalized results from the comparative study of the average number of aphthae per recurrence are shown in *Table 3*.

The comparison between the average number of aphthae occurring in the case of the different treatment schemes for the three months during which the treatment was dispensed, shows that the first and the second treatment schemes evince the greatest degree of difference in results from one another. The greatest number of aphthae can be observed in case of the first scheme, while the smallest average number of aphthae can be observed in the case of the second scheme.

**Table 2.** Number of recurrences in accordance with the different treatment schemes

Parameters	First treatment scheme 1	Second treatment scheme 2	Third treatment scheme 3	Fourth treatment scheme 4	2. P
Children with 2 recurrences	0	9	8	10	$\chi^2_{1,2} = 12.87$ $P < 0.001$ $\chi^2_{1,4} = 30$ $P < 0.001$
Children with 3 recurrences	15	6	7	5	$\chi^2_{1,3} = 10.9$ $P < 0.01$

**Table 3.** Average number of aphthae per recurrence in the different treatment schemes during the time of the study

Parameters	First recurrence			Second recurrence			Third recurrence			Total	
	Children		Aphthae	Children		Aphthae	Children		Aphthae		
	n	$\chi$	Sp	n	$\chi$	Sp	N	$\chi$	Sp	$\chi$	Sp
First scheme 1	15	3.53	1.2	15	3.2	0.9	15	3.13	0.8	3.28	1.0
Second scheme 2	15	3.2	0.83	15	2.46	0.71	6	2.5	0.5	2.77	0.82
Third scheme 3	15	3.06	0.57	15	3.0	0.51	7	3.0	0	3.02	0.49
Fourth scheme 4	15	3.06	0.57	15	3.06	0.77	5	3.0	0.89	3.05	0.89
TP	$\chi^2_{1,2} = 2.55$ $P < 0.05$			$\chi^2_{1,3} = 3.34$ $P < 0.05$			$\chi^2_{2,4} = 2.3$ $P < 0.01$				

Third parameter: Size of the biggest aphtha per recurrence during the time of controlled treatment

Fourth parameter: Degree of oral discomfort during the recurrences

The comparative data concerning the size of the aphthae during the period of controlled treatment are shown in *Table 4*.

The results from the study of the degree of discomfort during the treatment administered are shown in *Table 5*.

The size of the aphthae reached code 2 (0.3-0.8 cm) and code 3 (0.8-1.0 cm).  $\chi^2$  was estimated by comparing the different - in terms of the treatment applied - groups of patients. The biggest aphthae were observed in the first treatment scheme (code 3: 0.8-1.0 cm). In the other groups, the sizes of the aphthae were similar, with a slight predominance of code 2, i.e. a size of 0.3-0.8 cm.

Comparing the mouth discomfort in the different treatment schemes, it is worth mentioning that within the application of the first treatment scheme most of the recurrences (60%) evince the third degree of discomfort. The application of the fourth treatment scheme evinces the highest frequency of recurrences with the smallest degree of discomfort.

**Table 4.** Size of the biggest aphthae per recurrence in the different treatment schemes for the time of the study

Aphthae - size in cm	Code 1 (0.3 cm)	Code 2 (0.3-0.8?m)	Code 3 (0.8-1.0 cm)	Code 4 (< 1.0 cm)	$\chi^2$ P
First scheme 1	0	19	26	0	$\chi^2_{1,4} = 13.18$ P < 0.01
Second scheme 2	4	24	8	0	
Third scheme 3	0	26	11	0	$\chi^2_{1,2} = 8.14$ P < 0.01
Fourth scheme 4	4	26	5	0	

**Table 5.** The degree of oral discomfort during a recurrence in the different treatment schemes

Oral discomfort	First degree		Second degree		Third degree		Total	
	n	%	n	%	n	%	n	%
First treatment scheme	1	2%	17	38%	27	60%	45	100%
Second treatment scheme	6	17%	26	72%	4	11%	36	100%
Third treatment scheme	10	27%	27	73%	0	0%	37	100%
Fourth treatment scheme	11	31%	24	69%	0	0%	35	100%
TP	$T_{1,4} = 3.59$ P < 0.001 $T_{1,3} = 3.29$ P < 0.001 $T_{1,2} = 2.27$ P < 0.05		$T_{1/2} = 3.25$ P < 0.01		$T_{1,2} = 2.83$ P < 0.05			

Fifth parameter: Duration of the recurrences during the period of controlled treatment

The duration of the recurrences is shown in *Table 6*.

Comparing the duration of the recurrences in the different treatment schemes, the same regularity can be observed. In the case of application of the first treatment scheme, there are no recurrences that would last less than 9 days. The number of relapses lasting up to 12 days here is equal to the number of relapses lasting up to 15 days. Clearly, it is within the first treatment scheme that the recurrences have the longest duration.

The application of the second treatment scheme shortens considerably the duration of the recurrences. Next in efficiency are the fourth and the third treatment schemes.

## Discussion

It becomes perfectly clear from the study conducted that the first treatment scheme is the most efficient one in terms of all five criteria studied. The substitution of the locally applied - with "Adhesive bases" - covering of the aphthae with medications for gargling had no positive therapeutic effect.

As far as the other treatment schemes are concerned, the second treatment must be recommended. Treatment schemes three and

four can be applied too. The usage in the three treatment schemes - by contrast with the first treatment scheme - of "Adhesive bases" - for local treatment of the aphthae - can be considered as a precondition for the efficient symptomatic treatment of recurrent aphthae in children.

The regulative diet aimed at excluding the most frequent food allergens directly responsible for the recurrence of the aphthae is a new palliative method of treatment of the condition. It can be part of the complex treatment of RAS in children and was applied as such in the treatment of our patients.

It was found out in the comparative study of the application of the different treatment schemes that the best therapeutic effect in children with recurrent aphthae is achieved by locally applied Adhesive bases - Solcoseryl, as well as by the Bulgarian medication "Adhesive base NK" and "Adhesive base D" developed in two versions: with sodium chromoglycate as an active component and with dexametazone as an active component. The symptomatic anti-inflammatory, desensitizing, anaesthetizing and epithelizing effect of "Adhesive base NK", as well as its excellent adhesion on the wet mucous membrane of the mouth makes it very appropriate as medication for RAS.

In the second version, namely "Adhesive base D", dexametazone is a mod-

**Table 6.** Duration of recurrences in the different treatment schemes during the period of controlled treatment

Duration	8-10 days	10-12 days	13-15 days	2 P
	Number of recurrences	Number of recurrences	Number of recurrences	
First treatment scheme 1	0	25	20	$\chi^2_{1,2} = 8.08$ $P < 0.001$
Second treatment scheme 2	8	24	4	$\chi^2_{1,3} = 1.11$ $P < 0.001$
Third treatment scheme 3	3	23	11	$\chi^2_{1,4} = 9.77$ $P < 0.01$
Fourth treatment scheme 4	1	30	4	$\chi^2_{2,4} = 6.52$ $P < 0.01$

ern corticoid with wide application for local treatment of recurrent aphthae, well described in modern literature [16,17].

The existent wide range of solutions for gargling with antiseptic and anti-inflammatory effect is a suitable means for the prevention of secondary bacterial infections in the case of the different oral lesions as well as in the case of RAS. These solutions cannot be a substitute for the "Adhesive bases" in the treatment of RAS, though.

The inclusion in the treatment schemes of polybacterial immunomodulators (Dentavax and Imudon) for regulating the local immunity and the oral tolerance, as well as the employment of the probiotic Enterosan - a food additive with active cells of Lactobacillus and Bifidobacteria - is evaluated by us as very promising modern method of regulating the oral ecosystem.

Our controlled study took three months. The period was sufficient and the study comprehensive enough for us to be able to recommend now the treatment schemes we developed. The keeping to a food regimen for a long period of time, as well as the children with recurrent aphthae following the recommended new life style, is a recipe for success.

The recurrences becoming less frequent, the discomfort and pains in the mouth cavity being alleviated, as well as the period needed for the healing of the aphthae becoming shorter and the number of the aphthae recurring decreasing, are part of the later results observed.

## Conclusion

The generalized results from the diagnostics and treatment of the most common cases of

recurrent aphthae in children lead us to the following basic principles of treatment of children with RAS that we recommend when a choice of a treatment method is made:

Basic principles of treatment of children with RAS:

1. The treatment must be dependent on the special characteristics of each individual child, especially on the concomitant chronic illnesses, the general health status and the immunity status.

2. The treatment must necessarily include a suitable food diet, teaching the child new feeding habits and the imposition of an altogether new way of life due to which the recurrence of the condition becomes rarer and the discomfort in the mouth is alleviated.

3. The treatment must include vitamins and food additives that have a positive effect on the general condition of the organism and can compensate some deficiencies in the organism (vit. B, Fe, folic acid, other vitamins, enzymes, etc.), in case there are such deficiencies.

4. Local treatment must involve the application of medications that alleviate oral discomfort and prevent the development of a secondary infection in the mouth.

5. The stomatologist must teach the patient the ability to evaluate the condition of his or her mouth so that an optimum treatment can be arrived at.

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