A home-made meat-based formula for feeding atopic babies: a study in 51 children

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Abstract. – Background. Several elimination diets have been suggested based on results of skin prick tests (SPTs) or IgE antibodies to foods, thus allowing the identification of the most common offending food(s), including CM (cow’s milk), egg, peanut and wheat. But unbalanced, inappropriate dietary manipulation in infants with food allergy (FA) can have critically deleterious consequences. We have investigated the effectiveness of a home-made meat-based formula (HMMBF) (Rezza’s diet) in babies with food-induced atopic dermatitis (AD), a common, disabling, chronic disease of infancy.

Patients and Methods. Rezza’s diet was given for two months to 25 infants (median age 6.9 months) affected with AD and FA and the differences of body weight and AD severity score were recorded before and after the diet period. Data were analysed using the T and c2 tests.

Results. There was a significant improvement in both the evaluated parameters, whereas in 26 control atopic babies they remained unchanged.

Conclusion. The results of our study indicate that the HMMBF, also based on the experience of several authors, is a useful oligoantigenic diet for the treatment of food-induced AD, and the prevention of the atopic march.

Key Words:
Atopic children with food allergy, Home-made meat-based diet, Nutritional value, Atopic march.

Introduction

For centuries human milk (HM) has been the only way of feeding human neonates, thus CM allergy (CMA) was virtually unknown in infants. Since the start of this century CM formulas became an always more common HM substitute when HM was unavailable, and other formulas have been developed in order to reduce the antigen load and therefore the risk of sensitization. As a consequence, paediatricians and paediatric allergists are now bombarded with a large variety of information of new special formulas and are confronted with a difficult choice regarding the nutritional adequacy, the immunogenicity and allergenicity of the available CM substitutes of HM. Such formulas are necessary for feeding babies with CMA and, according to recent data, they can be also useful for “high risk” babies, when HM is not available, for the prevention of atopic diseases. Among these formulas, Rezza’s diet is also a useful oligoantigenic diet for the diagnosis of FA. Several groups have used with good results and infants’ compliance this diet, that we employ as suggested by Rezza et al for babies with CMA.

Studies on HMMBFs in Atopic Children

The management of CMA is by exclusion of CM antigens from the diet. Recent studies on elimination diets in CMA children have changed previous attitudes completely, since they appear to reverse the alterations in cell-mediated and humoral immunity decreasing the levels of antigen-specific IgE concentrations, improve the capacity of T-cell regulation and decrease the peripheral blood mononuclear cells response to allergen stimulation. However, there is no consensus (as there was) as to select dietary manipulations in order to insure the complete avoidance of offending foods, which in addition is an important mean of identifying a FA. Our research has not surely ascertained who decided to employ a meat-based diet in the treatment of allergy children. Possibly Trousseau, a French clinician was the first, a century ago, to suggest a diet based on the meat of birds. An elimination diet with meat was used ap-
parently for the first time in 1926-1928 by Rowe who suggested oligoantigenic foods with the strict restriction of the offending ones\(^9\). In particular, his diet No. 3 allows 4 types of meat, that is lamb, beef, chicken and bacon\(^9\). This diet is very difficult to follow unless the parents are given exact instruction about which foods must be avoided\(^10\). Rowe also mentioned homogenised lamb, beef, and beef liver, and suggested their use in such formulas\(^9\). However, Glaser preferred lamb as the meat base rather than beef, since beef was shown to be sensitising\(^11\). An additional impetus for such investigation has been the landmark diagnostic study by Goldman et al\(^12\), the first to scientifically and nutritionally tailor in 1963 for children a food list for CM-free diet, including lamb, pork and bacon. A nother team fed babies with CMA aged 2,4-9 months a base-line formula, made up by lamb, corn oil, carbohydrates and water\(^13\). A further cohort of children aged 2 weeks to 2,4 years with chronic diarrhoea were successfully treated with Lambase, a lamb-substituted formula\(^14\). Moreover, babies aged 0,1-12 months\(^15\) or 30-136 days\(^16\) with protracted intractable diarrhoea related to CM intolerance were treated with a chicken-based feeding regimen that was found to be a highly effective form of dietary treatment. In children with severe AD and FA, after a full clinical assessment, staged diagnostic and curative diets were introduced. Stage 3 included lamb or rabbit, vegetables, etc.: all in all, this approach led to the improvement of the children studied\(^17\). More recent studies have shown that H M M B F is more easily accepted than CM hydrolysate formulas\(^8\), and can be prescribed even to children aged 8-9 years, almost always with a good compliance\(^2\).

The formula is prepared as follows: fresh or frozen lean lamb’s meat (free of fat and tendons) is cut into small pieces, boiled and minced, then mixed with the other diet components. Once clinical improvement is achieved, wheat and saccharose are reintroduced into the diet, then various foods in sequence, with the exception of CM and dairy products\(^2\). This diet provides 740 calories per litre and is very nutritive in infants with FA. In general it is well-accepted even by very young babies with diarrhoea caused by CMA, and it is very palatable and therefore well accepted\(^1,4,19\). We have calculated the nutritional value of Rezza’s diet\(^18\), confronting it with the ESPGAN Guidelines\(^20\) (Table III).

One of the major advantages is that this diet can be tailored to the individual patient, that is vegetables, other types of fruit and meat, wheat flour and other nutrients can be added to the diet according to the age and weight of the child, and the physician careful control (Table IV)\(^19\). The parents should receive detailed instructions for H M M B F preparation\(^4\). In children even 13.3-year-old white potatoes, lettuce, cooked carrots, cabbage, zucchini, cauliflower, Brussels sprouts, pears, and rabbit or pork meat, other types of

<table>
<thead>
<tr>
<th>Clinical data</th>
<th>Time (median)</th>
<th>No of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea subsided</td>
<td>7 days</td>
<td>41/41</td>
</tr>
<tr>
<td>Growth resumption</td>
<td>15 days</td>
<td>41/41</td>
</tr>
<tr>
<td>Tolerance to CM</td>
<td>24 mos</td>
<td>25/37</td>
</tr>
<tr>
<td>Intolerance to CM</td>
<td>6 yrs</td>
<td>12/37</td>
</tr>
<tr>
<td>Other sensitivities</td>
<td>6 yrs</td>
<td>27/37</td>
</tr>
</tbody>
</table>

Data from reference 1.
fruit and wheat flour can be added to the diet with good compliance. Thus the Rezza’s diet can be tailored to the suspected sensitivities of the individual patient, with an ultimate objective, to personalise it as soon as possible, introducing additional foods with the prick+prick method, one at a time, every 5-7 days, always with prudence, for example citrus fruit, tomatoes, other greens, legumes, parsley. However, the addition to HMMBF of additional foods may require a challenge test. The continuing supervision of a dietician and/or a doctor, and laboratory tests may be useful adjuncts.

In our experience, instead of lamb’s meat, chicken, pork, or rabbit meat may be given, excluding chicken and turkey if the child is egg-allergic. Bovine meat should be avoided since it may have antigens cross-reacting with CM proteins, in addition, bovine serum albumin is present both in CM and in bovine meat, thus sensitising ≥ 10% of children.

### Table II. Composition of Rezza’s Diet (HMMBF) (per liter).

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamb meat</td>
<td>g 100</td>
</tr>
<tr>
<td>Olive oil</td>
<td>g 40</td>
</tr>
<tr>
<td>Rice flour</td>
<td>g 70</td>
</tr>
<tr>
<td>Table salt</td>
<td>g 2</td>
</tr>
<tr>
<td>Water until to</td>
<td>1 liter</td>
</tr>
<tr>
<td>Calcium</td>
<td>mg 500</td>
</tr>
<tr>
<td>Vitamins</td>
<td>as needed</td>
</tr>
</tbody>
</table>

From reference 4.

A number of studies have shown that babies aged 2 weeks–2 months have been fed the Rezza’s diet, therefore HMMBF can be used in genetically predisposed babies for primary prevention of atopy.

The introduction of the Rezza’s diet led to the dramatic decline of the number of infants classified as having the so-called “early intractable diarrhoea”, since it was understood that the majority of cases of this condition were due to CMA. Rezza et al put also an end to the invasive practice of parenteral nutrition, which was previously necessary in several of these babies. Indeed the parenteral nutrition included also Ca caseinate, which obviously perpetuated the diarrhoea in CMA infants.

### Patients and Methods

We have studied 51 children (33 males and 18 females) aged 4 to 19 months (median 6.9) referred to the Division of Allergy and Immunology of the Rome University “La Sapienza” because they were affected by severe AD and suspected CMA on the basis of personal history and strong positive SPTs to CM and egg.

The diagnosis of AD was made according to Hanifin and Rajka criteria. After an elimination diet of 4-6 weeks, 25 children were fed for two months the Rezza’s diet as previously specified, to which a Ca supplement (500 mg/day) was added according to Table II. Patients body weights were assessed at the beginning of and two months following the HMMBF feeding, about at the same hour, and using the same balance. The severity score of AD was recorded with body diagrams according to the SCORAD index.

### Skin Prick Test

Skin testing was done at baseline by the prick method on the volar surface of the fore-
The babies were tested with: histamine hydrochloride (1 mg/ml) as a positive control and isotonic saline as a negative control, and with a battery of food and inhalant allergens, such as: whole CM protein, casein, lactalbumin, egg, fish, wheat, and soy (SARM, Rome, Italy). They were placed on the volar surface of the forearm as drops through which the skin was superficially pricked with a straight pin. A new pin was used for each prick test.

SPTs were read at 20 minutes and considered positive as follows:

+ when the wheal was the half of the histamine wheal;
++ when the wheal was equal to the histamine wheal;
+++ when the wheal was two-fold the histamine wheal;
++++ when the wheal was more than two-fold the histamine wheal.

We took for positive only children with a +++ or ++++ reaction, that is a wheal \( \geq 3 \text{ mm} \) with an area \( = 7 \text{ mm}^2 \) (cut-off). We considered as positive only the children with a mean wheal diameter of 3 mm or larger than the negative (saline) control. A positive (histamine 1:1000) control was performed to ensure the absence of any antihistamine drug interference.

**Challenge Test**

At the end of the 4-6 week period, open challenge tests (OCTs), due to the very young age of the babies, were performed in the hospital under observation in a unit staffed to undertake emergency equipment. CM or egg was administered as follows, while for wheat we prepared a mixture of flour and boiled water (2:1-1.25): a drop of CM (or of emulsioned raw egg, or of wheat mixture) was put upon the inner border of the lower lip, and a further 5 ml of CM (or 1 ml of emulsioned raw egg, or of wheat mixture) were given after 5 minutes. One hundred ml of CM or half-boiled egg, or of wheat mixture were given after 30 minutes. The reactions were defined as immediate if the first symptoms occurred within minutes-two hours of ingesting the food antigen, and delayed if the first symptoms occurred after four hours. If any symptoms secondary to the challenge test were observed, the challenge test in the hospital was terminated. After the last administration of the tested food the children were watched for at least 4 hours and then discharged.

**Control Department**

The remaining 26 children served as controls, and were subjected to the same diagnostic tests as the study children. During a two-month period they were fed the usual elimination diets prescribed to such babies.

**Informed Consent**

Informed consent was obtained from parents of each study and control child.

**Statistical Analysis**

Data were statistically analysed using the Student t and the \( \chi^2 \) tests.

**Results**

At the first visit, before the prescription of Rezza's diet the body weight of the 51 babies was between 6500 and 12,200 grams (mean 7950), according to Italian standards, and at the end between 7600 and 13,500 grams (mean 9000) in the study group, with a high statistically significant difference \( (p = 0.0001) \), whereas in the control babies the body weight remained practically unchanged \( (p = 0.0001) \). Before the diet the 25 study babies had a SCORAD index of 66 (mean 23-71) and after the Rezza's diet of 11 (mean 10-13) \( (p = 0.0001) \), whereas in the controls the SCORAD index remained practically unchanged \( (p = 0.0001) \).

OCTs done at the beginning of the study period with CM, egg and wheat yielded the following results: in the study group, 13 babies tested positive for CM, 6 for egg, 3 for wheat, 2 for CM and egg, and 2 for CM and wheat, while among the controls 11 babies tested positive for CM, 7 for egg, 2 for wheat, 5 for CM and egg (NS).

No child refused the diet, and the compliance was good during the whole study period.

**Discussion**

The results of the present study show that two-month feeding HMMBF induced, com-
pared to controls, a significant increase in weight gain ($p = 0.0001$), as well as a parallel significant reduction ($p = 0.0001$) of the severity score of skin lesion, thus confirming the HMMBF hypoallergenicity and its effectiveness as diagnostic tool in food-induced AD. These data confirm that the Rezza’s diet used by us is nutritionally adequate.

What is the rationale for considering HMMBF among hypoallergenic formulas for infant nutrition? Several formulas have been suggested for infant nutrition. A’s regards lamb, which was selected as a source of meat, only one study found a 5% of SPT positivity, while for pork meat there were a 5% 29 and a 10% SPT positivity. However Sampson demonstrated that high SPT positivity were reduced to almost 0 with double-blind, placebo-controlled food challenge (DBPCFC). Moreover, 4 out of 40 children reacted to lamb at home according to parents’ “diagnoses” (?), and lamb was changed to rabbit.

Rice was preferred as source of carbohydrate. In Western countries 5 anaphylactoid reactions to rice have been reported in the last 20 years (vomiting, diarrhoea and shock) in infants aged 3-10 months. Only in two cases the challenge test was positive, and in one baby lesion similar to enterocolitis were seen. However, at least in Italy, rice allergy in babies with CMA is nearly unknown.

Olive oil was and is chosen for its high nutritional value, whereas peanut oil has provoked allergic symptoms in 18,6% of children, and sunflower oil even anaphylaxis in an infant. Peanut oil can be found also in vitamin D preparations in children aged 4-35 months, those receiving drops in which was present peanut oil had SPTs positive for peanut.

Rezza’s diet is also a useful oligoantigenic diet to be used in several cases of CMA and for the diagnosis and treatment of FA (Table V), allowing other nutrients to be given. We stress its pleasant taste, the adaptability to individual needs, and the low cost of its constituents. Accordingly, FA can be excluded or confirmed in the growing number of children referred with the suspected diagnosis of multiple food intolerances. In children allergic to one or two food proteins is seems more practical the elimination of these foods based on clinical history and SPTs, however we have found the highest value of Rezza’s diet when the foods to be eliminated are more than two. Additional formulas include soy protein and hydrolysate formulas about which we have published, or submitted extensive studies.

Which is then the rationale for using Rezza’s diet? A consistent issue regards the drawbacks of elimination diets. During the last decades, hazards of elimination diets for children with FA have been stressed. Elimination diets may be constructed in several ways and can be adapted to the suspected sensitivities of the individual patient, so they are more easily tolerated than the more general elimination diets, and patients’ compliance is improved. In other cases, the diet may be restricted to a few foods, such as those of Rezza’s diet that are rarely implicated in FA. Unsupervised, unbalanced and inappropriate dietary alterations in infants with FA may be commonplace, a sign of potentially serious health problems. In this sense > 50% of 73, 5.1 year-old children with mild AD were started on diets based on sources coming from media, books, magazines, or radio and/or TV programs (51%), friends (32%), general practitioners (27%) district nurses or health visitors (18%), personal observations (7%) psychologists, homeopaths, teachers and herbalists (8%). Harmful practices included the use of goat milk (64%) or of particularly dangerous diets (6%). There was no growth retardation, but only 10% of children claimed benefit from such diets. Low intakes of nutrients have been shown in children during an elimination diet. Severe consequences such as malnutrition, Kwashiorkor and failure to thrive have been reported following a restricted diet in children with FA.
Finally, goat milk proteins share antigenic cross-reactivity with CM proteins, in up to 100% of CMA children. However, a few food oligoantigenic diagnostic elimination diet is crucial in order to avoid the most common offending foods in children with AD and multiple food hypersensitivity: the use of lamb as the meat base obviates any debate regarding this issue, mainly in view of the present results (Table VI).

### Conclusion

FA is disease of many infants and toddlers, though the proportion of children in whom it is severe is unclear. Diagnosis and management depend on dietary manipulation carried out in a rational way with dietetic help. HMMBFs are very well accepted by infants and parents. In addition to its hypoallergenicity, first established 20 years ago, this diet has several advantages compared with other special formulas (Table IV). In 20 years of paediatric allergy practice, we have proved the very good results of this diet in several hundreds of babies with CMA, whose parents never reported side effects, other than a scarce compliance for the salt taste, which was always resolved substituting the salt with sugar or saccharose. Therefore, a few food hypoallergenic, oligoantigenic elimination diet is critical to avoid the most common offending foods in children with CMA and for diagnostic objectives. Institutions devoted to the control of foods for children should ensure careful control in order to avoid immunogenic and allergenic products, since non-appropriate use and/or abuse of such products can have negative effects on children health.

One final word about the hypoallergenicity of lamb meat. We have never read a paper reporting a case of lamb meat allergy. If the allergenicity of a given protein is related not only to its molecular weight, but also to the sequences of the aminoacids, we deem that the aminoacids sequences in lamb meat are not suitable to form reactive epitopes.

### Table VI. Prerequisites of an ideal CM substitute.

<table>
<thead>
<tr>
<th></th>
<th>Soy proteins</th>
<th>Hydrolisates</th>
<th>Elementary diet</th>
<th>Rezza’s diet</th>
<th>Goat’s milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunogenicity</td>
<td>±</td>
<td>+</td>
<td>+</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Allergenicity</td>
<td>±</td>
<td>+</td>
<td>+++</td>
<td>±</td>
<td>±</td>
</tr>
<tr>
<td>CM proteins (βLG)</td>
<td>No</td>
<td>+</td>
<td>++</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Nutritional adequacy</td>
<td>Yes</td>
<td>?</td>
<td>?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pleasant taste</td>
<td>±</td>
<td>No</td>
<td>±</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Low cost@</td>
<td>Yes</td>
<td>No</td>
<td>±</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Easy availability</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>?</td>
<td>Yes</td>
</tr>
</tbody>
</table>

H = highly, P = partially, βLG = β-lactoglobulin, * = high crossreactivity.

### References

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28) AAS K, BACKMAN A, BELIN L, WEEKE B. Standardization of allergen extracts with appropriate methods. The combined use of skin prick testing and radioallergosorbent test. Allergy 1978; 33: 130-137.


