Twin studies have revealed a positive evidence for environmental influences, where unshared environmental influences appeared to be important [6]. Most printed studies in this domain have ascertained that everywhere between 40% and 70% of asthma heredity is preferable to hereditary factors [7]. We stress that several studies on asthma genetics have been strengthen by diverse genome wide searches, that succeeded in establishing the linkage between asthma and genetic markers on 13 chromosome regions embodying chromosomes 5q31-33 (the gene cluster of good many interleukins), 6p21.3, 11q13 and 12q14.3-24.1 [6,8-15]. In this prospective study on 500 children we have appraised the asthma genetics, by estimating the FH of atopy of their respective family, including parents and brothers and/or sisters.

Materials and Methods

In order to investigate the genetic risk of a child with a family history (FH) of allergy, we have enlisted in this perspective study 250 children, 137 males and 113 females ethnically Italian, aged between...
The personal and FH of both parents and children Study children. We reckoned whether the babies were "at risk" of atopic disease because of a positive FH of atopy since one or both parents and/or their siblings suffered from asthma, or AD, or AR. The diagnosis of atopic diseases in the children was done according the following criteria: clinical history, physical examination and positive skin tests and/or RAST to the most common inhalant and/or food allergens. Two hundred and fifty healthy children, and their parents supplied during the same period from our outpatient clinic with no history of atopy of akin age, sex, and Italian origin were matched with the study group.

Informed consent was obtained from parents of each child. Skin prick test appropriate emergency equipment and medications were available on site. Antihistamine drugs and topical steroids were stopped at least 2 weeks before the application of the SPTs. Skin testing was done at baseline by the prick method on the volar surface of the forearm by a trained in allergy doctor with the cooperation of a qualified nurse. The skin was marked with a ballpoint pen for the allergens to be tested. The babies were then tested with: histamine hydrochloride (1 mg/ml) as a positive control and isotonic saline as a negative control. We continued with a battery of food and inhalant allergens, including whole CM protein, casein, lactalbumin, egg, fish, wheat, soy, Dermatophagoides pteronyssinus, Alternaria alternata, Lolium perenne, Olea europea and Parietaria officinalis (SARM, Roma, Italy). The diagnostic extract of each individual allergen was placed on the volar surface of the forearm as drops through which the skin was superficially pricked with a straight pin for one second. A new pin was used for each SPT and then discarded, and the drop of the extract was then wiped off about one minute after the prick [22]. SPTs were read 20 minutes after the test was finished 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 [16].

We took for positive only children with a +++ or ++++ reaction, that is a wheal ≥ 3 mm with an area about 7 mm² (cut-off), so we considered as positive only the children with a mean wheal diameter of ≥ 3 mm than the negative (saline) control. A positive (histamine) control was performed to ensure the absence of any antihistamine drug interference [23].

**Total IgE**

The determination of the total serum IgE level was done by paper radioimmunosorbent test (PRIST, Pharmacia Diagnostics AB, Sweden), and results were expressed in International Units per ml. Specific IgE antibodies and determination of specific IgE levels by radioligand test (Phadezym RAST, Pharmacia Diagnostics).

RAST results are expressed in «RAST Units» (PRU = Phadebas Rast Unit) as follows:

<table>
<thead>
<tr>
<th>Class</th>
<th>IgE Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st class</td>
<td>&lt; 0.35 IU/ml,</td>
</tr>
<tr>
<td>2nd class</td>
<td>&gt; 0.35 IU/ml and lesser than 0.7 IU/ml,</td>
</tr>
<tr>
<td>3rd class</td>
<td>between 0.7 IU/ml and 17 IU/ml,</td>
</tr>
<tr>
<td>4th class</td>
<td>&gt; 17 IU/ml.</td>
</tr>
</tbody>
</table>

Only RAST results > 0.35 IU/ml were considered as positive. The diagnosis of AD was made according to Hanifin and Rajka criteria [24]. The severity score of AD was evaluated according to the SCORAD index [25].

For the diagnosis of asthma, 3 episodes of wheezing without fever were required. Provocation tests with inhalant allergens were not feasible due to the young age of the children studied.

For the diagnosis of rhinitis, nasal discharge and/or blockage occurring continuously for at least 4 weeks plus the typical pale aspect of allergic mucosa on rhinoscopy, without any sign of infective rhinitis in other relatives was required.

The statistical calculations were performed using the X2 test.

**RESULTS** As demonstrated by FH, SPTs and RAST, 127 parents of the study children were affected with atopic disease (42.3%), in particular 51 fathers and 76 mothers, in addition to 25 brothers and/or sisters. These parents all tested positive for inhalant allergens (both SPTs and RAST), with the exception of 3 mothers positive to CM allergens and two children with allergic migraine. We stress that 90.2% of fathers, 81.6% of mothers and 91.7% of brothers/sisters suffered from respiratory allergy. In detail, 41.2% of fathers, 40.8% of mothers and 72.2% of brothers/sisters were asthmatic. In addition 49%, 40.8% and 19.4%, respectively, were affected with AR. Moreover 9.8% of fathers and 6.6% of mothers had urticaria, 2.9% of mothers and 10.5% of brothers/sisters had AD, and 4% of mothers had CMA (Table 1).

Twenty-five children were allergic, with a high proportion of cases of AD (52%), however the respiratory allergy affects 30.4% of these children (Table 2), who appear to have multiple sensitizations in 34.8% of cases (Table 3). Thirteen of these children had SPTs and RAST positive for food allergens (mostly CM and egg) and 10 for inhalant allergens.

In the control group 61 parents were allergic, and 40 were affected with respiratory allergy. In detail, 14.7% of fathers and mothers and 18.2% of brothers/sisters had asthma, 6.6%, 13.1% and 4.9%, respectively had AR and 6.6% of fathers and mothers ed 3.3% of brothers/sisters allergic ocularrhinitis. Further, 6.6% of fathers 13,1% of mothers and 1.6% of brothers had urticaria, 11,5% of mothers and...

<table>
<thead>
<tr>
<th>Atopic disease</th>
<th>No. (%)</th>
<th>F</th>
<th>M</th>
<th>(B/S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>52 (40.9)</td>
<td>21</td>
<td>31</td>
<td>6</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>57 (44.8)</td>
<td>25</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>2 (1.6)</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Urticaria</td>
<td>10 (7.8)</td>
<td>5</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Ocularrhinitis</td>
<td>3 (2.5)</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Food allergy</td>
<td>3 (2.5)</td>
<td>0</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>F</th>
<th>M</th>
<th>(B/S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>127</td>
<td>52</td>
<td>75</td>
<td>20</td>
</tr>
</tbody>
</table>

F = Fathers, M = mothers

**Table 1:** Parents of children affected with atopic disease.
1.6% of fathers and brothers AD, in addition to 3.3% of fathers, 11.5% of mothers and 8.2% of brothers/sisters with FA.

In the control group, 11 children were sensitized who in 15.5% of cases had respiratory allergy. Study children vs controls (p = 0.0161).

We have ascertained that a high number of parents of the study and control children were active smokers (Table 4). The statistical analysis revealed high statistically differences between fathers and mothers of the study group versus the parents of the controls, p = 0.0196 and p = 0.0387, respectively.

The statistical analysis has demonstrated highly significant differences between the two samples (p = 0.0001).

**Discussion**

The results do not allow us to confirm that a significant proportions of respiratory allergy is transmitted by mothers. We underline that 42.3% of parents are atopic, with a FH positive for respiratory allergy in 82-92% of cases. In the study sample 147 parents and brothers were affected with respiratory allergy (45.94%) versus 10.3% of controls who in 65.5% of cases had respiratory allergy. Therefore, asthma is a genetic disease, at least in 42.3% of cases. Respiratory allergy can have an autosomal dominant mode of inheritance, but by considering the whole atopic whole, the transmission can be polygenic. The high impact of the genetic factors in these children is stressed by the high proportion (85%) of asthmatic brothers/sisters. As regards the smoking parents it is very significant the number of couples smoking together. The low number of other relatives probably depends by the smaller apartments prevailing in Italy.

What our study evidently stresses is that a high number of parents, atopic parents, yet they themselves asthmatic, as we have ascertained, are smoking parents of asthmatic sons and daughters. Such data demonstrates in an unequivocal manner that cigarette smoke should be considered as a triggering factor of respiratory allergy. Therefore in babies at risk of atopy cigarette smoke should be regarded as an additional genetic factor, since asthma is more easily transmitted if an atopic parent smokes (even more if both parents smoke). However cigarette smoke is able to provoke asthma even in children of nonatopic parents, especially if the smokers are pregnant women: their children frequently suffer with Der p-induced asthma [16].

Allergic asthma and rhinitis, AD, urticaria and FA are genetic diseases of infants and children. Several investigators have provided evidence for a genetic localization for atopy. Babies of atopic parents are at high risk of developing atopic diseases, however the phenotypic expression of such disorders varies widely, being very mild in some infants and children, severe and frustrating in many, even lifethreatening in others, being also common, disabilitating, and chronic [17]. In particular we can now understand how strictly the genetic factors are linked with atopy: several cytokine genes are associated in the gene cluster of chromosome 5q32-q33, such as IL-3, IL-4, IL-5, IL-9, IL-12b, IL-13, and GM-CSF, together with the genes for the β2-adrenergic receptor [18]. It is likely that plural loci in the chromosome 5q31-q33 region are synergistically related to asthma susceptibility.

We have frequently spoken of respiratory allergy. However, a large number of cross-sectional studies have reported that asthma and AR commonly occur in children and adolescents [19-21]. Studies have demonstrated that AR occurs in 28-78% of older children and adolescents [19-21], versus approximately 5-20% of the general population [22]. Conversely, asthma has also been shown to affect up to 38% of AR patients [19-21], a data significantly higher than the 3-5% prevalence noted in the general population [22]. In an unpublished study on 411 children aged 7-13 years, asthma had an incidence of 31.5% and AR of 25.8%. Asthma and AR can have an early onset. The asthma affair is a little more intricate: the onset within the first year is certain in 34.5% [23-26], 56.2% [24,27], of babies, but a higher level (82.4%) is evident between the 4th and the 7th year [24,27-29]. That within the 8th year the asthma onset is manifest in 90% of children [28], is confirmed by the 92% proportion reached in patients less than 20 years of age [31]. As regards AR, the onset may be in the first year in 35% of children and in 59% of those aged 2-5 years [24], while in other studies are affected in 13-19% of cases [23,30].

Once atopy develops, it is now possible to prevent the clinical manifestations in a great proportion of cases (secondary prevention) by the use of pharmacological agents such as cromones and ketotifen [32]. In addition as demonstrated by the ETAC study we can prevent the onset of respiratory allergy in 50% of babies with AD following an 18-month administration of cetirizine [33]. Since the commitment to the Th2 phenotype in atopics appears to occur at any time between the ages of 2 and 5 years [34], the net implication is that within the first years of life there is a window open for immunoprophylaxis [35].

In conclusion, we have proven that asthma is a genetic disorder and that the transmission of allergy and asthma is fully genetic in children, mainly if asthmatic.
References


Copyright: © 2015 Cantani A. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.