## REVIEW

# The relationship between cancer and allergy

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## ABSTRACT

**Objective:** Review the literature on the relationship between cancer and allergy. **Method:** Study articles indexed in the databases of PubMed, Lilacs, Bireme and Scielo to verify whether there is a relationship among cancer, allergy, allergy skin tests and serum levels of immune markers. **Results:** Several studies have suggested an inverse association between allergy and cancer, while others have found no relationship between these entities, while still other authors have shown an increased risk of some cancers in allergic patients. The conflicting findings in previous studies are due in part to the method used, such as different definitions and measures for atopy, as well as variations in the control of confounding factors such as smoking and obesity. It is noteworthy that most of the studies were conducted in several countries and with different parameters. **Conclusion:** There is a lower incidence of allergy in patients with cancer, especially colorectal, pancreatic, and glioma.

Keywords: allergy and immunology, eosinophils, neoplasms, skin test.

#### **INTRODUCTION**

Cancer is a serious threat to public health worldwide and is currently the second leading cause of death in Brazil<sup>1</sup>. Researchers have described the role of several factors as the cause of this disease, including environmental, related to lifestyle and biological factors, including the immune system<sup>2</sup>.

The concept of immunosurveillance suggests that the immune system destroys neoplastic cells<sup>3</sup>. The predisposition of certain tumors in terms of primary or acquired immunosuppression, such as acquired immunodeficiency syndrome (AIDS) and after the use of immunosuppressors, is already well established<sup>4</sup>. Several studies suggest an inverse association between allergy and cancer,<sup>5-10</sup> while others find no relationship between them<sup>11-16</sup>.

The relationship of atopy with hyperreactivity of the immune system can be reinforced by the deviation of the response of T lymphocytes, T helper 1 (Th1) for the Th2 response in atopic patients. As a consequence, there is increased immune surveillance and increased cellular destruction, likely including malignant cells<sup>17,18</sup>. The cytokines produced by Th2 lymphocytes, such as interleukin 4

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Submitted: 17/04/2012. Aproved: 24/04/2012. (IL-4) and IL-10 possess antitumor properties<sup>19-22</sup>. A higher incidence of cancer has been demonstrated in chronic inflammatory conditions, and in frequent repetition, as is the case of atopic patients. In these cases, there is a continuous cycle of lesion and tissue repair, which can cause genetic disorders resulting in dysplasia and even cancer<sup>23-25</sup>.

For a better understanding of the relationship between allergy and cancer, there is a need for more research, including the addition of a more accurate diagnosis of atopy and the use of immune markers. It is noteworthy that most of the studies were conducted in other countries with different methods<sup>4,6-16,19,26-34</sup>.

### **METHODS**

A search was conducted of articles indexed in the databases of PubMed, Lilacs, Bireme and Scielo to assess the relationship among cancer, allergy, allergy skin tests and serum levels of immune markers. All articles in the literature were studied and their results compared.

### RESULTS

#### Epidemiological studies comparing cancer and allergy

The previous studies are mostly epidemiological and few have evaluated the association of immune markers among patients with cancer and allergies, and those who have, with contradictory results. A recent meta-analysis compared the association of atopy (considering only asthma and allergic rhinitis) with breast, prostate and colorectal cancers<sup>35</sup>. No relationship was found with breast cancer or colorectal cancer, but the association was positive for prostate cancer (relative risk (RR) 1.43, confidence interval of 95% (CI 95%) 1.08-1.91).

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Several studies have shown an inverse association between pancreatic cancer (RR 0.8, CI 95% 0.7-0.99) and glioma (odds ratio - (OR) 0.6, CI 95% 0.5-0.7) with allergy in general, while lung cancer was associated with asthma (OR 1.8, CI 95% 1.3-2.3)<sup>25,36-38</sup>.

The only study in this line of research in Brazil found fewer allergies in patients with cancer, comparing them with the general population  $(p < 0.001)^5$ .

The epidemiological studies were incomplete and were not controlled by factors such as smoking, drug use, alcoholism and obesity. Another point lacking of that study was the absence of a record of oligosymptomatic or previous allergies, generating false negatives<sup>39</sup>.

# Evaluation of the association among cancer, allergy and skin test

In order to reduce the bias inherent in epidemiological studies that use only data from questionnaires or interviews with patients, three prospective studies conducted diagnosis of atopy based on percutaneous skin tests (prick/puncture) for allergy in people previously without cancer<sup>16,33,40</sup>. An increased risk of prostate cancer was found among allergic patients (RR 2.9, CI 95% 1.26-6.68)<sup>33</sup> and absence of relationship with other tumors<sup>16,33,40</sup>. The limitation of those studies was the occurrence of cancer in a small percentage of patients. Skin testing for allergy in patients diagnosed with cancer is not described in the literature.

# Evaluation of the association among cancer, allergy and lgE

A biomarker of atopy was used to study the association with risk factors for cancer<sup>19,23,26,32,41</sup>. There was no relationship between IgE levels and cancers of breast, colorectal, lung and non-Hodgkin lymphoma<sup>19,23,32,41</sup>. There was a direct association with prostate cancer<sup>19</sup> and inversely with gliomas<sup>26</sup>.

# Evaluation of the association among cancer, allergy and eosinophils

Eosinophils may play a role in the onset of antitumor response<sup>42</sup> and their recruitment in the tumor may be related to Th2 and IL-4 response<sup>43</sup>. There is only one study that evaluated the association of blood eosinophil count with the risk of cancer and allergy<sup>44</sup>. In that prospective study conducted in the United States, the authors found reduced risk of colorectal cancer with elevated eosinophil count, but no correlation with lung cancer and breast cancer<sup>44</sup>.

### DISCUSSION

The relationship between cancer and allergy has been studied since the 1950s<sup>6,11,15</sup> and presents conflicting results. One possible cause for this lack of uniformity is the

diversity of study methods, with patient selection made for particular groups and uncontrolled for possible risk factors for cancer or allergy, such as sex, smoking, alcohol use, environment and associated diseases.

Allergy is a complex disease that involves immune factors dependent or not of IgE detected in the skin test and in serum measurements.

The controversial results between reports of allergy and skin tests reinforce the need for further studies to deepen the understanding of these diseases as to the immune system. There are few studies that assess serum IgE levels in cancer patients<sup>19,23,26,32,41</sup>. When inverse association between allergy and cancer is detected, those studies cite the theory of immunosurveillance<sup>5,19,20</sup>. Studies that found a direct relationship between cancer and allergy explained this association by lesion and defective tissue repair and its consequent genetic disorders<sup>3,8,20,36</sup>. Such physiopathological mechanisms stem from Th1 or Th2 response, but there are no measures of cytokines or other related biomarkers in studies of cancer and allergy, justifying the need for more research.

### CONCLUSIONS

In a review of the literature, there is a lower incidence of allergy in patients with cancer, especially pancreatic, colorectal and glioma.

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