Clinical Research Report

Role of Th17-cell related cytokines in geriatric asthma

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Abstract
Objective: This study aimed to investigate the pathogenesis of geriatric asthma through immunoglobulin E (IgE), interleukin-17A (IL-17A), IL-17F, and glucocorticoid receptor-β (GR-β) expression.

Methods: We studied 51 geriatric male patients with asthma and 50 young male patients with asthma. We also included 21 normal geriatric males and 21 normal young males. All geriatric and young patients were divided into groups according to pulmonary function. Levels of cytokines, such as IgE, IL-17A, IL-17F, and GR-β, were measured. Pulmonary function was assessed. The results from patients were compared with those from the 42 healthy subjects.

Results: Serum IgE, IL-17A, IL-17F, and GR-β levels in geriatric patients with moderate or severe asthma were significantly higher than those in young patients with moderate asthma and in the normal population. Geriatric patients with asthma had higher asthma control test scores than did young patients with asthma.

Conclusion: Hormone resistance in geriatric male patients with asthma is more serious than that in young male patients with asthma. Airway inflammation and airway remodeling in geriatric male patients with asthma may be more serious than those in young male patients with asthma, even when there is similar pulmonary function.

Keywords
Geriatric asthma, immunoglobulin E (IgE), interleukin, glucocorticoid receptor-β (GR-β), inflammation, airway remodeling

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Background
Asthma is characterized by bronchoconstriction, airway hyper-reactivity, inflammation, mucus hypersecretion, and
remodeling. These processes are coordinate-
ed by a complex cytokine network. Active
asthma is common in patients older than
65 years and can be severe and disabling,
with marked ventilatory impairment\(^1\) and
a negative effect on quality of life.\(^2\)
Importantly, this age group has the highest
rate of death from asthma and asthma-
related physician office visits, and the
second highest rate of asthma
hospitalizations.\(^3\)

There are no specific questionnaires or
cytokine markers for diagnosis and moni-
toring of geriatric asthma.\(^4\) There is limited
knowledge on the best pharmacological
management strategies for asthma medica-
tion in older adults, largely owing to their
exclusion from clinical trials.\(^4\) Current
guidelines for patients with asthma are
derived from studies on younger patients
because older patients are frequently
excluded from clinical trials.\(^5\)

Aging is associated with low-grade,
chronic, systemic inflammation, character-
ized by increased levels of interleukin-6
(IL-6) and tumor necrosis factor-\(\alpha\).\(^6\) The
effects of immunosenescence and inflam-
maging on airway inflammation in older
individuals with asthma are not well estab-
lished. However, some studies have provid-
ed insights. Older patients with asthma
have increased sputum neutrophils com-
pared with younger patients.\(^7\) Airway neu-
trophilia in older patients with asthma is
associated with increased levels of sputum
neutrophil mediators, and airway cytokine
expression is associated with Th17 cells.\(^8\)
This could contribute to increased airway
neutrophilia. Determining the type of
underlying airway inflammation in older
adults with asthma is important because
neutrophilic asthma is often less responsive
to corticosteroid treatment.\(^9,10\) Th17 cells
may play an important role in the patho-
genesis of geriatric asthma. IL-17A was ini-
tially recognized for its similarity to a
sequence belonging to the open reading
frame 13 of Herpesvirus saimiri.\(^11\)
Moreover, five additional members,
IL-17B, IL-17C, IL-17D, IL-17E, and
IL-17F, were discovered between 2000 and
2002.\(^12–18\) Th17 cells, but not Th2 cells,
mediate steroid-resistant airway inflamma-
tion and airway hyper-reactivity in a mouse
model of asthma.\(^19,20\)

Glucocorticoids (GCs) are routinely used
as anti-inflammatory drugs in the treatment
of asthma. When overexpressed by trans-
fection, glucocorticoid receptor (GR)-\(\beta\)
may function as a dominant negative mod-
lator of GR-\(\alpha\). People with asthma who
are GC-resistant express higher amounts
of GR-\(\beta\) and develop a weaker reaction to
tuberculin compared with people with
asthma who are GC-sensitive.\(^21\) GR-\(\beta\) is
more abundant than GR-\(\alpha\). GR-\(\beta\) functions
as a dominant negative inhibitor of GR-
\(\alpha\)-mediated transactivation.\(^22,23\)

How cytokines play a role in the patho-
genesis of geriatric patients with asthma is
unclear. Therefore, this study aimed to
examine the pathogenesis of geriatric
asthma.

**Methods**

**Ethics approval and consent to
participate**

The study was approved by the Qingdao
Municipal Hospital Research Ethics
Committee. All patients were fully
informed about the purpose and procedures
of the study, and the patients provided writ-
ten consent to participate.

**Geriatric patients with asthma**

We studied 51 older patients who were
recently diagnosed with bronchial asthma
from the Qingdao Municipal Hospital
Group Emergency Department and the
Respiratory Medicine Department. Selection
criteria for the patients included
the following: aged 65 years or older and men; diagnosed with bronchial asthma according to Global Initiative for Asthma guidelines (2014 version); not using inhaled corticosteroid treatment; had good compliance; and volunteered to participate in the study and signed informed consent. Exclusion criteria included the following: comorbidity with other serious organ diseases (except for other lung diseases such as chronic obstructive pulmonary disease and neoplastic diseases); comorbidity with pleural effusion, acute myocardial infarction, or severe ventricular reshaping (cardiac ultrasonography with more than a 12-mm interval) disease, had 6 months of lung rehabilitation training or could not tolerate or cooperate with pulmonary function testing; and poor compliance.

**Healthy control group**

We included participants from a health examination population from the Qingdao Municipal Hospital Group Emergency Department and Respiratory Medicine Department. Participants were excluded for the following reasons: if they had chronic lung disease, allergic rhinitis, atopic dermatitis, or other diseases (excluding peripheral venous blood eosinophilia); if they had a family history of asthma; no acute upper respiratory tract infection or pulmonary infection in the last 4 weeks; and they had been using GCs or immunosuppressive agents.

**Young patients with asthma**

We included approximately 50 patients who were recently diagnosed with bronchial asthma from the Qingdao Municipal Hospital Group Emergency Department and the Respiratory Medicine Department. Inclusion criteria for these patients included the following: approximately 50 years old and men; diagnosed with bronchial asthma according to Global Initiative for Asthma guidelines (2014 version); not using inhaled corticosteroid treatment; had good compliance; and volunteered to participate in the study and signed informed consent. Exclusion criteria included the following: comorbidity with other serious organ diseases (except for other lung diseases such as chronic obstructive pulmonary disease and neoplastic diseases); comorbidity with pleural effusion, acute myocardial infarction, or severe ventricular reshaping (cardiac ultrasonography with more than a 12-mm interval) disease, had 6 months of lung rehabilitation training, or could not tolerate or cooperate with pulmonary function testing; and poor compliance.

**Pulmonary function tests**

All patients with stable bronchial asthma had a lung function test at approximately 9 am to determine forced expired volume in 1 s/forced vital capacity (FEV1/FVC), percentage of forced expired volume in 1 s (FEV1%), and vital capacity.

**Blood collection and observation indices**

Hospitalized patients were provided standardized treatment. When the patient’s condition had improved, blood was collected at 7 am (i.e., on an empty stomach) 1 day before discharge. All patients with stable bronchial asthma had an empty stomach at 7 am on the days before discharge. Patients in the control group had blood taken on an empty stomach at 7 pm. Serum levels of IL-17A, IL-17F, GR-β, and IgE were determined using enzyme-linked immunosorbent assays. Body mass index (BMI) was based on Criteria Of Weight for Adults issued by the National Health and Family Planning Commission of China in 2013.
**Grouping of patients with asthma**

Patients with moderate asthma were classified into the following groups: group A1, older asthma group (n = 24): FEV1/FVC < 80%, FEV1 > 60%; and group B1, young asthma group (n = 26): FEV1/FVC < 80%, FEV1 > 60%. Patients with severe asthma were classified into the following groups: group A2, older asthma group (n = 27): FEV1/FVC < 80%, FEV1 < 50%; group B2: youth asthma group (n = 24): FEV1/FVC < 80%, FEV1 < 50%. Normal older people were classified into group C1 (n = 21) and normal young people into group D1 (n = 21).

The five-item asthma control test (ACT) questionnaire was used to assess the level of asthma control. Factors affecting the course of asthma and the degree of control in patients were assessed with our own questionnaire and the ACT.

**Statistical analysis**

SPSS for Windows, Version 16.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis of the data. Data are expressed as the mean ± standard deviation for data with a normal distribution. The t-test was used for comparing the results from two groups of participants. Correlation coefficients between IL-17A, IL-17F, and GR-β, and measures of pulmonary function in patients at different stages of asthma were calculated. The test level was α = 0.05.

**Results**

**Patients with moderate asthma**

The mean age in group B1 was significantly younger than that in group A1 (P < 0.05, Table 1). The mean age in group D1 was significantly younger than that in group C1 (P < 0.05). There were no significant differences in pulmonary function indices between groups A1 and B1. The mean ACT score in group B1 was significantly lower than that in group A1 (P < 0.05). There were no significant differences in arterial blood gases between groups A1 and B1, and between groups C1 and D1. There was no significant difference in BMI

| Characteristic | Group A1 | Group B1 | Group C1 | Group D1 |
|----------------|---------|---------|---------|---------|
| Age (years)    | 71.1 ± 4.7 | 47.2 ± 5.6<sup>○</sup> | 67.8 ± 4.9 | 48.1 ± 5.7<sup>★</sup> |
| Pulmonary function |        |         |         |         |
| FEV1/FVC (%)    | 71.1 ± 6.7 | 72.5 ± 7.1 | 85.7 ± 4.2<sup>★</sup> | 86.7 ± 4.8<sup>★</sup> |
| FEV1%           | 66.7 ± 4.8 | 67.1 ± 5.7 | 87.2 ± 4.7<sup>★</sup> | 88.2 ± 5.1<sup>★</sup> |
| Arterial blood gases |        |         |         |         |
| pH              | 7.41 ± 0.05 | 7.42 ± 0.06 | 7.39 ± 0.03 | 7.38 ± 0.02 |
| PO2 (mmHg)      | 87.1 ± 5.1 | 88.4 ± 6.2 | 90.1 ± 5.7 | 87.2 ± 4.5 |
| PCO2 (mmHg)     | 37.7 ± 4.7 | 38.2 ± 4.6 | 39.1 ± 4.2 | 40.3 ± 3.9 |
| ACT score       | 11.2 ± 2.3 | 15.1 ± 3.4<sup>○</sup> | –        | –        |
| BMI (kg/m²)     | 25.1 ± 2.1 | 24.8 ± 2.3 | 25.2 ± 1.8 | 24.9 ± 2.1 |

Values are mean ± standard deviation. <sup>○</sup>P < 0.05, compared with group A1; <sup>★</sup>P < 0.05, compared with group B1; <sup>★</sup>P < 0.05, compared with group C1. FEV1/FVC: forced expired volume in 1 s/forced vital capacity; FEV1%: percentage of forced expired volume in 1 s; PO2: partial pressure of oxygen; PCO2: partial pressure of carbon dioxide; ACT: asthma control test; BMI: body mass index.
between groups A1 and B1, and between groups C1 and D1.

IL-17A levels were significantly lower in group B1 than in group A1 (P < 0.05, Table 2). IL-17A levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all P < 0.05). There was no significant difference in IL-17A levels between groups C1 and D1. IL-17F levels were significantly lower in group B1 than in group A1 (P < 0.05). IL-17F levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all P < 0.05). There was no significant difference in IL-17F levels between groups C1 and D1. GR-β levels were significantly lower in group B1 than in group A1 (P < 0.05). GR-β levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all P < 0.05). There was no significant difference in GR-β levels between groups C1 and D1. IgE levels were significantly lower in group B1 than in group A1 (P < 0.05). IgE levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all P < 0.05). There was no significant difference in IgE levels between groups C1 and D1.

There were significant correlations between FEV1% and serum IL-17A levels (all P < 0.05), with correlation coefficients of 0.336 (group A1), 0.134 (group B1), 0.135 (group C1), and 0.131 (group D1) (Table 3). FEV1/FVC was significantly correlated with serum IL-17F levels and pulmonary function in the different groups.

Table 2. Th17-related cytokines in patients with moderate asthma and normal people.

| Cytokines | Group       | Group A1       | Group B1       | Group C1       | Group D1       |
|-----------|-------------|----------------|----------------|----------------|----------------|
| IL-17A (ng/L) | 5.76 ± 0.45 | 4.52 ± 0.47<sup>△</sup> | 3.61 ± 0.35<sup>*,△</sup> | 3.48 ± 0.37<sup>*,△</sup> |
| IL-17F (ng/L) | 4.12 ± 0.37 | 3.74 ± 0.41<sup>△</sup> | 2.78 ± 0.32<sup>*,△</sup> | 2.67 ± 0.31<sup>*,△</sup> |
| GR-β (nmol/L) | 15.2 ± 1.23 | 11.3 ± 1.01<sup>△</sup> | 5.31 ± 0.46<sup>*,△</sup> | 5.29 ± 0.45<sup>*,△</sup> |
| IgE (ng/mL) | 313 ± 27.1 | 291 ± 23.5<sup>△</sup> | 71.3 ± 6.4<sup>*,△</sup> | 69.3 ± 5.9<sup>*,△</sup> |

Values are mean ± standard deviation. <sup>△</sup>P < 0.05, compared with group A1; <sup>*,△</sup>P < 0.05, compared with Group B1. IL-17A: interleukin-17A; IL-17F: interleukin-17F; GR-β: glucocorticoid receptor-β; IgE: immunoglobulin E.
levels in group A1 (r = 0.322) and group B1 (r = 0.256) (both $P < 0.05$).

**Patients with severe asthma**

The mean age in group B2 was significantly younger than that in group A2 ($P < 0.05$, Table 5). The mean age in group D1 was younger than that in group C1 ($P < 0.05$). There was no significant difference in pulmonary function between groups A2 and B2. The mean ACT score in group B2 was significantly lower than that in group A2 ($P < 0.05$). There were no significant differences in arterial blood gases and BMI between any of the groups.

IL-17A levels were significantly lower in group B2 than in group A2 ($P < 0.05$, Table 6). IL-17A levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all $P < 0.05$). There was no significant difference in IL-17A levels between groups C1 and D1. IL-17F levels were significantly lower in group B2 than in group A2 ($P < 0.05$). IL-17F levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all $P < 0.05$). There was no significant difference in IL-17F levels between groups C1 and D1. GR-β levels were significantly lower in group B2 than in group A2 ($P < 0.05$). GR-β levels in groups C1 and D1 were significantly lower than those in groups B1 and A1 (all $P < 0.05$). There was no significant difference in GR-β levels between groups C1 and D1. IgE levels were significantly lower in group B2 than in group A2 ($P < 0.05$).

| Table 5. Clinical features of patients with severe asthma and normal people. |
|------------------------------------------|---------|---------|---------|---------|
| **Characteristics**                    | **Group A2** | **Group B2** | **Group C1** | **Group D1** |
| Age (years)                             | 72.3 ± 4.5 | 48.4 ± 5.1 | 67.8 ± 4.9 | 48.1 ± 5.7 |
| Pulmonary function                      |          |          |          |          |
| FEV1/FVC (%)                            | 71.1 ± 6.7 | 72.5 ± 7.1 | 85.7 ± 4.2 | 86.7 ± 4.8 |
| FEV1%                                   | 45.1 ± 3.8 | 44.1 ± 4.7 | 87.2 ± 4.7 | 88.2 ± 5.1 |
| Arterial blood gases                    |          |          |          |          |
| pH                                      | 7.39 ± 0.04 | 7.42 ± 0.06 | 7.39 ± 0.03 | 7.38 ± 0.02 |
| PO2 (mmHg)                              | 84.1 ± 6.2 | 88.4 ± 6.2 | 90.1 ± 5.7 | 87.2 ± 4.5 |
| PCO2 (mmHg)                             | 35.7 ± 3.9 | 38.2 ± 4.6 | 39.1 ± 4.2 | 40.3 ± 3.9 |
| BMI (kg/m²)                             | 22.1 ± 2.1 | 22.5 ± 2.3 | 25.2 ± 1.8 | 24.9 ± 2.1 |

Values are mean ± standard deviation. $\circ P < 0.05$, compared with group A2; $\bullet P < 0.05$, compared with group B2; $\circ P < 0.05$, compared with group C1. FEV1/FVC: forced expired volume in 1 s/forced vital capacity; FEV1%; percentage of forced expired volume in 1 s; PO2: partial pressure of oxygen; PCO2: partial pressure of carbon dioxide; ACT: asthma control test; BMI: body mass index.

| Table 6. Th17-related cytokines in patients with severe asthma and normal people. |
|------------------------------------------|---------|---------|---------|---------|
| **Cytokines**                           | **Group A2** | **Group B2** | **Group C1** | **Group D1** |
| IL-17A (ng/L)                           | 7.23 ± 0.31 | 5.97 ± 0.34 | 3.61 ± 0.35 | 3.48 ± 0.37 |
| IL-17F (ng/L)                           | 5.78 ± 0.41 | 4.12 ± 0.36 | 2.78 ± 0.32 | 2.67 ± 0.31 |
| GR-β (nmol/L)                           | 17.3 ± 1.52 | 14.3 ± 1.31 | 5.31 ± 0.46 | 5.29 ± 0.45 |
| IgE (ng/mL)                             | 378 ± 35.1 | 312 ± 27.9 | 71.3 ± 6.4 | 69.3 ± 5.9 |

Values are mean ± standard deviation. $\circ P < 0.05$, compared with group A1; $\bullet P < 0.05$, compared with Group B1. IL-17A: interleukin-17A; IL-17F: interleukin-17F; GR-β: glucocorticoid receptor-β; IgE: immunoglobulin E.
groups C1 and D1 were significantly lower than those in groups B1 and A1 (all $P < 0.05$). There was no significant difference in IgE levels between groups C1 and D1.

There were significant correlations between FEV$_1$% and serum IL-17A levels (all $P < 0.05$), with correlation coefficients of 0.381 (group A2), 0.264 (group B2), 0.135 (group C1), and 0.131 (group D1) (Table 7). FEV$_1$/FVC was significantly correlated with serum IL-17A levels in group A2 ($r = 0.281$) and in group B2 ($r = 0.134$) (both $P < 0.05$). There were significant correlations between FEV$_1$% and serum IL-17F levels (all $P < 0.05$), with correlation coefficients of 0.672 (group A2), 0.234 (group B2), 0.135 (group C1), and 0.131 (group D1) (Table 8). FEV$_1$/FVC was significantly correlated with serum IL-17F levels 0.359 in group A2 ($r = 0.359$) and in group B2 ($r = 0.198$) (both $P < 0.05$).

**Discussion**

Asthma is characterized by chronic airway inflammation caused by abnormal T cell responses. Inflammation is finely modulated by CD4$^+$ T lymphocytes, including Th1, Th2, and Th17 cells. Infiltration of inflammatory cells and release of inflammatory factors leads to increased bronchial contractions, and asthmatic symptoms, such as wheezing and shortness of breath.

Several different inflammatory signatures have been identified with asthma phenotypes. IL-17A is a newly described proinflammatory cytokine that is secreted by a subtype of T helper lymphocytes (i.e., Th17 cells). Increased IL-17A expression is associated with many chronic inflammatory diseases in humans, such as asthma.

Some older patients with asthma appear to have IL-17A-mediated airway inflammation and increased airway neutrophils. In our study, serum IL-17A levels in geriatric patients with moderate or severe asthma were significantly higher than those in young patients with moderate asthma and in the normal population. These results suggest that the level of airway inflammation in geriatric patients with asthma is higher than that in young patients with asthma. Milovanovic et al. suggested that IL-17A enhances IgE production. In a small subset of allergic patients compared with normal controls, these authors showed higher numbers of IL-17A-producing CD4$^+$ T cells (Th17) after polyclonal activation of whole blood.

Recent research has shown a predominant Th2-mediated allergic inflammation with increased eosinophils in bronchoalveolar lavage fluid, increased IgE hyperssecretion, and increased CD4$^+$ Th2 cytokine.

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**Table 7.** Correlations between serum IL-17A levels and pulmonary function in the different groups.

| IL-17A | Groups | FEV$_1$% | FEV$_1$/FVC |
|--------|--------|---------|-------------|
|        | Group A2 | 0.381* | 0.281*     |
|        | Group B2 | 0.264* | 0.134*     |
|        | Group C1 | 0.167* | –          |
|        | Group D1 | 0.189* | –          |

*P < 0.05; *P > 0.05. IL-17A: interleukin-17A; FEV$_1$/FVC: forced expired volume in 1 s/forced vital capacity; FEV$_1$%: percentage of forced expired volume in 1 s.

**Table 8.** Correlations between serum IL-17F levels and pulmonary function in the different groups.

| IL-17F | Groups | FEV$_1$% | FEV$_1$/FVC |
|--------|--------|---------|-------------|
|        | Group A2 | 0.672* | 0.359*     |
|        | Group B2 | 0.234* | 0.198*     |
|        | Group C1 | 0.135* | –          |
|        | Group D1 | 0.131* | –          |

*P < 0.05; *P > 0.05. IL-17F: interleukin-17F; FEV$_1$/FVC: forced expired volume in 1 s/forced vital capacity; FEV$_1$%: percentage of forced expired volume in 1 s.
secretion of IL-5 and IL-13. In our study, IgE levels in geriatric patients with asthma were significantly higher than those in young patients with asthma, even in cases with no differences in lung function. Our results indicated that IgE levels were significantly higher in geriatric patients with asthma mediated by IL-17A than in younger patients. Sex is a critical determinant of IgE levels, where males have a stronger tendency towards higher total IgE levels than females. Therefore, we chose male patients as research subjects to ensure homogeneity of our study.

Kawaguchi et al. suggested that the IL-17F protein stimulates the production and release of neutrophil cytokines in human bronchial epithelial cells and that IL-17F levels have a close relationship with airway remodeling. These authors also showed that a local allergen challenge increased the signal for IL-17F mRNA among bronchoalveolar lavage cells in patients with allergic asthma. Al-Ramli et al. reported an increase in subepithelial immunoreactivity for IL-17F protein in patients with verified asthma. This increase in IL-17F protein followed the severity of disease, as did the corresponding mRNA levels. Interestingly, Al-Ramli et al. showed IL-17F protein in the epithelial layer and even within epithelial cells in the same patients who expressed IL-17A in the submucosa. Therefore, IL-17F and IL-17A may be expressed simultaneously. In our study, IL-17F levels in geriatric patients with asthma were significantly higher than those in young patients with asthma, with no differences in lung function. These results indicated that airway remodeling was significantly more serious in geriatric patients with asthma than in young patients with asthma.

Increased serum IL-17A levels are associated with hormone resistance and severity of asthma. IL-17A has been proposed to affect global corticosteroid responsiveness through effects on the GR. These cells may promote the release of neutrophil chemotactic factors and induce expression of GR-β, which is responsible for corticosteroid hyporesponsiveness in immune cells. In our study, GR-β levels in geriatric patients with asthma were significantly higher than those in young patients with asthma, with no differences in lung function.

ACT questionnaires are suitable for measuring asthma control in patients with asthma. An ACT score below 20 indicates poor asthma control and has a close relationship with corticosteroid responsiveness. Our results that geriatric patients with asthma had higher ACT scores than young patients with asthma suggest hormone receptor resistance.

Severe asthma is associated with increased airway remodeling, characterized by increased mucous cell metaplasia and increased airway smooth muscle mass. IL-17A increases airway mucous expression in human airway epithelial cells and mouse models of airway inflammation. In primary differentiated human airway epithelial cells, IL-17A and IL-1β increased mucin 5AC gene expression and protein production through a nuclear factor-κB-dependent pathway. The current literature suggests that lower IL-17A levels are sensitive to corticosteroid therapy in a condition that is typically corticosteroid resistant. In our study, the correlations between IL-17A levels and pulmonary function were significantly weaker than those between IL-17F and pulmonary function. Furthermore, the correlations between IL-17A and IL-17F levels and pulmonary function in geriatric patients with asthma were stronger than those between IL-17A and IL-17F and pulmonary function in young patients.

This study has two main limitations. First, only male geriatric patients with...
asthma were included. Additionally, the sample size was relatively small.

We conclude that hormone resistance in geriatric male patients with asthma is more serious than that in young male patients with asthma. Airway inflammation and airway remodeling play an important role in promoting development of geriatric asthma. Airway inflammation and airway remodeling in geriatric male patients with asthma may be more serious than that in young male patients with asthma with similar pulmonary function. Modulation of this cytokine network could contribute to understanding of the pathogenesis of patients with asthma and development of new therapeutic strategies.

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Availability of data and materials
Anonymized data from the current study are available from the corresponding author on reasonable request.

Authors' contributions
Zhang Quan-san and Sun Zhaojia contributed to hypothesis generation, data acquisition, and analysis and interpretation of the data for this work. Xu Xiaohong and Li Ying provided statistical support and assistance in interpretation of the results. All authors approved the final version and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of conflicting interest
The authors declare that there is no conflict of interest.

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