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Case Report: Severe Persistent Asthma with Acute Exacerbation

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ABSTRACT

Asthma is a chronic inflammatory disease of the airways characterized by airway hyperresponsiveness to various stimuli, leading to recurrent symptoms such as wheezing, shortness of breath, chest tightness, and coughing, especially at night or in the early morning. While asthma management guidelines exist, the clinical presentation of severe persistent asthma with acute exacerbation requires detailed documentation to improve diagnostic accuracy and treatment outcomes. The research aims to present a comprehensive analysis of severe persistent asthma with acute exacerbation in an adult patient, demonstrating diagnostic approach and management strategies. The research presents a 55-year-old male patient who arrived with worsening shortness of breath that had begun five hours before admission. Clinical evaluation included detailed history taking, physical examination, laboratory investigations, spirometry, and chest radiography. The patient reported being unable to take deep breaths, described a heavy feeling in the chest, and produced audible wheezing. The dyspnea was accompanied by a productive cough with yellowish sputum that worsened at night. He could not speak fluently—only in short phrases—felt more comfortable sitting upright and appeared anxious. Spirometry showed an FVC of 48% predicted and an FEV_1 of 41% predicted, confirming severe airway obstruction. Treatment included combination therapy with ipratropium bromide and salbutamol inhalation, budesonide inhalation, and oral salbutamol. This case demonstrates the importance of comprehensive clinical assessment and spirometric evaluation in diagnosing severe asthma exacerbations, emphasizing the need for prompt recognition and appropriate stepped therapy to prevent life-threatening complications.

Keywords: *Asthma, Acute Exacerbation, Spirometry, Case Report*

INTRODUCTION

Asthma is a chronic inflammatory disease of the airways characterized by hyperresponsiveness to various stimuli, causing recurrent symptoms such as wheezing shortness of breath, chest heaviness, and coughing, especially at night or early in the morning. These symptoms are associated with variable and reversible airway obstruction, both spontaneously and after therapy (GINA, 2024).

A definite diagnosis of asthma requires consistent respiratory symptoms as well as evidence of variable expiratory airflow obstruction, demonstrated by spirometry examination. Early recognition and intervention of asthma exacerbations are essential to prevent progression to a severe, life-threatening stage (Goldin, Hashmi, and Cataletto, 2024).

Data from the 2018 Basic Health Research (Riskesdas) show that the prevalence of asthma is 2.4% of the population. This prevalence has increased compared to the 2013 Riskesdas, which was only 2.1%, indicating an upward trend. In children, asthma is more common in males up to the age of 20, after which the prevalence becomes equal between males and females. This difference may be caused by atopy or by smaller airway size in boys than in girls (Sinyor and Concepcion Perez, 2023).

Previous research on asthma case reports has predominantly focused on pediatric populations or specific phenotypes such as allergic asthma, with limited comprehensive documentation of adult-onset severe persistent asthma with acute exacerbation in the Indonesian healthcare context. Studies by Castro-Rodriguez et al. (2016) have explored risk factors in childhood asthma, while research by Louis et al. (2022) has provided European

guidelines for adult asthma diagnosis. However, there remains a gap in detailed case presentations demonstrating the practical application of diagnostic criteria and treatment protocols in emergency clinical scenarios. International literature has shown varying approaches to asthma phenotyping and endotyping, but Indonesian-specific clinical presentations have been underrepresented in the medical literature (Boulet et al., 2019; Carr et al., 2018).

Recognition and intervention of asthma exacerbations are essential to prevent progression to a severe, life-threatening stage. Asthma deaths often reflect a lack of recognition of disease severity and delays in therapy escalation, emphasizing the importance of symptom control assessment (Levy et al., 2024). The research problem addressed centers on the need for comprehensive documentation of severe persistent asthma with acute exacerbation presentations in clinical practice (Heaney et al., 2021). While asthma management guidelines provide theoretical frameworks, real-world clinical cases demonstrate the complexity of diagnostic decision-making and treatment implementation, particularly in emergency settings where rapid assessment and intervention are critical (Papi et al., 2020).

The urgency of documenting such cases stems from the significant morbidity and mortality associated with severe asthma exacerbations. According to global statistics, asthma affects over 260 million people worldwide and causes approximately 450,000 deaths annually, many of which are preventable through proper recognition and management of exacerbations. In Indonesia, the rising prevalence from 2.1% in 2013 to 2.4% in 2018 indicates an increasing healthcare burden that demands improved clinical awareness and management strategies (Dharmage et al., 2019).

The research gap specifically lies in the limited availability of comprehensive case reports demonstrating the integration of clinical presentation, diagnostic testing, and management approaches for severe asthma exacerbations in adult patients within the Indonesian healthcare system. While guidelines exist, their practical implementation in real clinical scenarios requires detailed documentation to improve healthcare provider education and patient outcomes.

The novelty of this Case Report: Severe Persistent Asthma with Acute Exacerbation lies in its comprehensive documentation of the diagnostic and therapeutic approach to severe persistent asthma with acute exacerbation, integrating current GINA 2024 guidelines with practical clinical application. This case provides detailed spirometric data, complete laboratory investigations, and step-by-step management decisions that can serve as an educational tool for healthcare providers managing similar presentations.

The specific objectives of this Case Report: Severe Persistent Asthma with Acute Exacerbation are: (1) to present a detailed clinical presentation of severe persistent asthma with acute exacerbation in an adult patient; (2) to demonstrate the diagnostic approach using spirometry and supportive investigations; (3) to illustrate the application of current asthma management guidelines in clinical practice; (4) to analyze treatment response and clinical outcomes; and (5) to provide educational insights for healthcare providers managing similar cases.

The benefits of this research include enhancing clinical education for healthcare providers managing asthma exacerbations, providing practical examples of guideline implementation in real clinical scenarios, contributing to the Indonesian medical literature on

adult asthma management, and serving as a reference for emergency department protocols. The implications extend to improving diagnostic accuracy, optimizing treatment protocols, and potentially reducing asthma-related morbidity and mortality through better clinical recognition and management strategies.

METHOD

This case report utilized a comprehensive clinical case study methodology, following standard medical case reporting guidelines. The approach included systematic documentation of patient presentation, clinical evaluation, diagnostic investigations, and treatment outcomes. A 55-year-old male patient came to the emergency room of Pasar Rebo Hospital with complaints of shortness of breath that worsened since 5 hours before entering the hospital (SMRS). The patient feels unable to breathe deeply, the chest feels heavy, and his breathing is sound. Tightness is accompanied by a yellowish cough with phlegm and gets heavier at night, so the patient cannot sleep well. The patient also cannot speak fluently, can only speak in fragments, feels more comfortable in an upright sitting position, and appears restless. Other symptoms such as cold sweats and weight loss are denied.

The patient admitted that he had a history of shortness of breath since the age of 15 and had a history of allergy to dust and cold temperatures. A similar history is admitted to be in his grandfather. The patient also has a smoking habit.

On physical examination, the patient appeared to be moderately ill with composing consciousness. Vital signs were blood pressure of 130/85 mmHg, pulse rate of 122 times per minute, respiratory rate 34 times per minute, temperature of 37.2 °C, and oxygen saturation of 93 % of the water room. Nutritional status is classified as excessive, with a body weight of 75 kg and a body weight of 170 cm. In lung auscultation, wheezing was found in both lung fields.

In routine hematology support examinations, hemoglobin was 15.3 g/dL; hematocrit 50 %; erythrocytes 5.7 million/µL; leukocytes 11.36 10^3/µL; platelets 201 thousand/µL; MCV 87 fL; MCH 27 pg/mL, MCHC 31 g/dL; basophil 0%; eosinophil 1%; neutrophils of the rod 0 %; segmental neutrophils 81 %; lymphocytes 9%; monocytes 9%; and absolute lymphocytes 1022 /µL. Clinical chemistry obtained SGOT (AST) 20 U/L; SGPT (ALT) 22 U/L; blood urea 26 mg/dL; blood creatinine 1.14 mg/dL; eGFR 76 mL/min/1.73 m^2; and blood glucose at 133 mg/dL. Electrolytes obtained sodium (Na) 138 mmol/L; potassium (K) 3.6 mmol/L; and chloride (Cl) 103 mmol/L. Blood gas analysis obtained a pH of 7.50; pCO_2 24 mmHg; HCO_3^- 18.9 mmol/L; BE -4.4 mmol/L; and Saturation of O_2 97.4%.

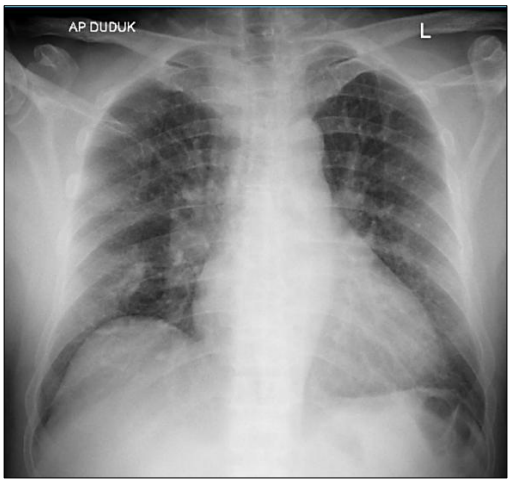

Figure 1. Thoracic Photo Overview

The results of the spirometry examination showed FVC of 48% and FEV1 of 41%. Thoracic photographs show infiltrates in the bilateral middle lung field and right lower lung field. The patient was then administered in the form of a combination of inhalation of ipratropium bromide and salbutamol every 6 hours, inhalation of budesonide every 12 hours, and salbutamol tablets 2 mg three times a day.

RESULTS AND DISCUSSION

A 55-year-old man came to the emergency room of Pasar Rebo Hospital with complaints of worsening shortness of breath since 5 hours before admission, accompanied by cough with yellowish phlegm, wheezing, and sleep disturbances at night. The patient appeared restless, could only speak intermittently, felt comfortable in an upright sitting position, and on auscultation wheezing was found in both lung chambers.

Routine hematological support examinations found erythrocytes (5.7 million/µL), hemoglobin (15.3 g/dL), hematocrit (50%), and platelets (201 thousand/µL) in the normal range; there is leukocytosis (11.36 × 10^3/µL) with a predominance of segmental neutrophils (81 %) as well as lymphopenia (9 %); Erythrocyte index (MCV 87 fL, MCH 27 pg) is normal, but MCHC is slightly low (31 g/dL). Clinical chemistry examination found good liver function (AST 20 U/L, ALT 22 U/L); urea (26 mg/dL) and creatinine (1.14 mg/dL) were still normal; eGFR (76 mL/min/1.73 m^2) showed a decrease in mild renal filtration; and blood sugar when (133 mg/dL) is within normal limits. The results of the electrolyte examination showed sodium 138 mmol/L; potassium 3.6 mmol/L; and 103 mmol/L chloride within normal limits.

Blood gas analysis examination obtained a pH of 7.50; pCO_2 24 mmHg; HCO_3^- 18.9 mmol/L). Spirometry results with FVC 48% and FEV1 41%, as well as thoracic infiltrate photographs in the middle and lower lungs. The diagnosis in patients is established based on more objective spirometry results leading to acute exacerbation severe persistent asthma.

Asthma is a chronic inflammatory disease of the airways characterized by hyperresponsiveness of the airway to various stimuli, which causes recurrent symptoms such as wheezing (wheezing), shortness of breath, chest heaviness, and coughing, especially at night or early in the morning. This symptom is associated with varied and reversible airway obstruction, both spontaneously and after therapy (GINA, 2024). This chronic inflammation involves a variety of cells (such as eosinophils, T lymphocytes, macrophages, mastocytes, and

neutrophils), as well as inflammatory mediators that contribute to airway remodeling and bronchial sensitivity to various stimuli (Kumar, V., Abbas, A.K., Aster, J.C., 2020).

Asthma is one of the most common chronic diseases worldwide. Its prevalence is estimated to reach more than 260 million people globally and causes about 450,000 deaths per year, mostly in low- and middle-income countries (GINA, 2024). Data from the 2018 Basic Health Research (Riskesdas) shows that the prevalence of asthma based on the diagnosis of health workers in Indonesia is 2.4% of the population. This prevalence increased compared to the 2013 Riskesdas which was only 2.1%, indicating an upward trend.

The EVE (Ethnic Variation in Asthma) consortium identified a locus of susceptibility for TSLP (thymic stromal lymphopoietin), a cytokine from epithelial cells that plays a role in initiating asthma-related inflammation. TSLP expression is higher in asthmatic patients than in healthy individuals (Parnes et al., 2022). Preterm birth (<36 weeks) increases the risk of asthma in childhood to adulthood (Leps, Carson and Quigley, 2018). Exposure to secondhand smoke during pregnancy lowers the baby's lung function and increases the likelihood of asthma (Castro-Rodriguez et al., 2016). Pregnant women's diet, especially vitamin D deficiency, is associated with wheezing and asthma early in life (Wolsk et al., 2017).

The classification of asthma by severity is based on the frequency of symptoms, the degree of impaired lung function, the frequency of exacerbations, and the need for therapy before optimal treatment is given. Traditionally, the NAEPP/GINA guidelines have divided asthma into four main categories which can be seen in table 1.

Table 1. Classification of Asthma by Severity

Level	Symptom	Night Symptoms	FEV1 or PEF	Variability
Ringan Intermiten	<2×/week	<2×/month	≥80 % prediction	<20%
Mild Persistent	>2×/week, not every day	≥2×/month	≥80 % prediction	20-30 %
Medium Persistent	Daily	>1×/week	60-80 % prediction	>30%
Persistent Weight	Continuous	Often	<60 % prediction	>30%

The latest approach in asthma management emphasizes more on the level of control than the classification of static severity. Control criteria according to GINA were evaluated in the last 4 weeks, including frequency of daytime symptoms, nighttime symptoms, activity limitations, need for sedatives, and pulmonary function. This classification is described in table 2.

Table 2. Classification of Asthma Based on Symptom Control Level

Characteristics	Controlled	Partially Controlled	Uncontrolled
Symptom	None (less than twice a week)	More than twice a week	Three or more symptoms in the category of partially controlled asthma appear at any time of the week
Activity Restrictions	None	Any time of the week	
Nocturnal *Symptoms*	None	Any time of the week	
The Need for a Reliever	None (twice or less in a week)	More than twice a week	
Lung Function	Usual	Less than 80 % (approximate or from the best condition when measured)	
Exacerbations	None	Once or more in a year	Once a week

The latest medical literature emphasizes approaches to the clinical phenotype and molecular endotype of asthma. Phenotype refers to apparent clinical characteristics, while endotype refers to the underlying biological/immunological mechanisms.

Table 3. Classification of Asthma Based on Phenotype and Endotype

Characteristics	T2-High Asthma (Type 2 High)	Asma T2-Low (Non-T2)
Clinical Phenotype	Allergic, eosinophilic, child/young adult onset	Non-allergic, neutrophilic or pauci-granulocytic, adult onset
Immunological endotype	*Th2-mediated (IL-4, IL-5, IL-13)*	*Th1/Th17-mediated (IL-8, IL-17, TNF-α)*
Clinical Characteristics	*Atopic*, history of allergies (rhinitis, eczema), high IgE, high FeNO	*Non-atopic*, often obese, smoking, symptom control difficult
Biomarker	Eosinophils blood/sputum ↑, IgE ↑, FeNO ↑	Eosinophils & IgE normal/low, FeNO normal
Response to ICS	Good (high response to inhaled corticosteroids)	Less (steroids are less effective against neutrophils)

Spirometry is the main test to establish the diagnosis. Airway obstruction was found with FEV1/FVC < 0.75 indicating limited airflow. The diagnosis is established if there is reversibility with an increase in FEV1 ⩾ 12 % and ⩾ 200 mL afterbronchodilators (Louis et al., 2022; GINA, 2023). PEF (Peak Expiratory Flow) can be used when spirometry is not available. The diagnosis was supported by a daily PEF variability of >10% or a difference of >20% between morning and night for 1-2 weeks (GINA, 2023).

FeNO (Fractional Exhaled Nitric Oxide) reflects eosinophilic inflammation. Values of ⩾50 ppb support the diagnosis of T2-high type asthma and predict a good response to ICS (Midhun et al., 2025; GINA, 2023). Blood eosinophil levels of ⩾300 cells/μL supporteosinophilic asthma, associated with a higher risk of exacerbations, but not a major diagnostic criterion (Louis et al., 2022; Midhun et al., 2025). Total/specific IgE is elevated in allergic asthma, but not specific. Useful for immunological profiles and consideration of biologic (anti-IgE) therapies (Louis et al., 2022).

The management of asthma according to the Global Initiative for Asthma (GINA) 2024 is based on a stepwise approach and retrospectively classification of asthma severity based on the level of therapy needed to achieve control. GINA 2024 recommends 5 steps of therapy (Steps 1-5) according to the severity and control of asthma.

1. Mild Asthma

Table 4. Management of Mild Asthma

Mild Asthma	
Definition	Controlled with low-intensity therapy.
GINA Therapy Steps	Step 1-2 (beginning of therapy).
Primary Control Therapy	Low-dose ICS (e.g., low-dose combination ICS-formoterol) is used as needed *(PRN)* without a routine daily dose. Alternative: Daily low-dose ICS.
Relief Therapy	ICS-formoterol *PRN* (as an anti-inflammatory reliever).
	Alternative *Track* 2: SABA *PRN* + ICS inhalation per use of SABA.
Additional Therapy	No need for control; avoid SABA monotherapy due to the risk of exacerbation.

2. Moderate Asthma

Table 5. Moderate Asthma Management

Moderate Asthma	
Definition	Controlled with Step 3 or 4 therapy (low to moderate dose ICS-LABA).

GINA Therapy Steps	Step 3-4 (escalation therapy).
Primary Control Therapy	Low- or medium-dose ICS-PROFIT daily (e.g., low-moderate dose budesonide-formoterol on *MART).* The dosage is adjusted to achieve control.
Relief Therapy	ICS-formoterol *PRN* remains as a reliever (part of *the MART* regimen).
	Alternative: SABA *PRN* if using a separate ICS-LABA regimen/*Track* 2.
Additional Therapy	Tiotropium (LAMA) can be considered as *an add-on* in Step 4 if the control is still suboptimal. Other routine additional therapies are generally not necessary at this stage.

3. Severe Asthma

Table 6. Severe Asthma Management

	Severe Asthma
Definition	It remains uncontrolled even after high-dose optimal therapy (requires high doses of ICS-LABA to be controlled).
GINA Therapy Steps	Step 5 (highest).
Primary Control Therapy	ICS-LABA high doses daily (e.g., combination high doses of inhalation). It is usually referred to a specialist center for therapy optimization.
Relief Therapy	ICS-formoterol *PRN* (if using *Track* 1/MART, stay as a reliever).
	Alternative *Track* 2: SABA *PRN,* but the risk of exacerbation is higher.
Additional Therapy	Biological Therapy (according to phenotype): examples of anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP for eligible type-2 asthma.

Description: ICS = inhaled corticosteroid (inhaled corticosteroid); PROFIT = long-acting; MART = maintenance and reliever therapy (maintenance therapy + relievers with ICS-formoterol); OCS = oral corticosteroid.

Overall, the goal of asthma management is to achieve good symptom control and prevent exacerbations with the lowest effective dose of medication. After asthma has been controlled for at least 3 months, GINA recommends a step-down to find a minimum dose that still maintains control.

CONCLUSION

Asthma is a chronic inflammatory airway disease characterized by reversible bronchial hyperresponsiveness leading to episodic symptoms such as wheezing, shortness of breath, coughing, and chest heaviness. Diagnosis relies primarily on spirometry, with an FEV1/FVC ratio less than 0.75 and significant bronchodilator response, or alternatively peak expiratory flow variability when spirometry is unavailable. Management follows the stepwise approach outlined in GINA 2024 guidelines, aiming to control symptoms and prevent exacerbations using the lowest effective medication dose. A reported case of a 55-year-old man presenting with severe persistent asthma exacerbation highlights the clinical features, spirometric confirmation (FVC 48%, FEV1 41%), and a combined therapeutic regimen of inhaled bronchodilators and corticosteroids. Clinical recommendations emphasize maintaining high suspicion for severe exacerbations, utilizing spirometry whenever possible, employing comprehensive pharmacologic treatment, educating patients on triggers and inhaler use, ensuring regular follow-up, and strengthening healthcare systems' capacity for appropriate diagnostic and therapeutic resources. Future research should focus on evaluating real-world implementation of guideline-directed asthma management in diverse clinical settings, particularly in resource-limited environments, to identify barriers and optimize outcomes for patients with severe persistent asthma exacerbations.

REFERENCES

Boulet, L. P., Reddel, H. K., Bateman, E., Pedersen, S., FitzGerald, J. M., & O'Byrne, P. M. (2019). Phenotypes and endotypes of adult asthma: Moving toward precision medicine. Journal of Allergy and Clinical Immunology, 144(1), 1-17. https://doi.org/10.1016/j.jaci.2019.05.031

Carr, T. F., Altisheh, R., & Zitt, M. (2018). Asthma exacerbations: Pathogenesis, prevention, and treatment. Journal of Allergy and Clinical Immunology: In Practice, 6(4), 1144-1155. https://doi.org/10.1016/j.jaip.2018.05.022

Castro-Rodriguez, J. A., Forno, E., Rodriguez-Martinez, C. E., & Celedón, J. C. (2016). Risk and protective factors for childhood asthma: What is the evidence? Journal of Allergy and Clinical Immunology: In Practice, 4(6), 1111-1122.

Dharmage, S. C., Perret, J. L., & Custovic, A. (2019). Epidemiology of asthma in children and adults. Frontiers in Pediatrics, 7, 246. https://doi.org/10.3389/fped.2019.00246

Global Initiative for Asthma (GINA). (2023). Global strategy for asthma management and prevention. Available at: https://ginasthma.org

Global Initiative for Asthma (GINA). (2024). Global strategy for asthma management and prevention. https://ginasthma.org

Goldin, J., Hashmi, M. F., & Cataletto, M. E. (2024). Asthma. In StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. [updated 3 May 2024; cited 2025 Jul]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430901/

Heaney, L. G., Busby, J., Bradding, P., Chaudhuri, R., Mansur, A. H., Niven, R., Pavord, I. D., Brightling, C. E., & Costello, R. W. (2021). Management of asthma exacerbation in the emergency departments. World Allergy Organization Journal, 14(7), 100556. https://doi.org/10.1016/j.waojou.2021.100556

Kumar, V., Abbas, A. K., & Aster, J. C. (2020). Robbins and Cotran pathologic basis of disease (10th ed., pp. 689-692). Philadelphia: Elsevier.

Leps, C., Carson, C., & Quigley, M. A. (2018). Gestational age at birth and wheezing trajectories at 3-11 years. Archives of Disease in Childhood, 103(12), 1138-1144.

Levy, M. L., Bacharier, L. B., Bateman, E. D., Boulet, L. P., Brightling, C. E., Buhl, R., Brusselle, G., Castro, M., Chung, K. F., Davin, E., Fabbri, L. M., Israel, E., Humbert, M., Jackson, D. J., Korn, S., Maurer, M., O'Byrne, P. M., Paggiaro, P., Park, H. S., ... FitzGerald, J. M. (2024). Phenotyping of severe asthma in the era of broad-acting anti-asthma biologics. The Journal of Allergy and Clinical Immunology: In Practice, 12(5), 1214-1227. https://doi.org/10.1016/j.jaip.2024.01.040

Louis, R., Satia, I., Ojanguren, I., et al. (2022). European Respiratory Society guidelines for the diagnosis of asthma in adults. European Respiratory Journal, 60(3), 2101585.

Midhun, J., Nair, K. V., Shameem, N., et al. (2025). Correlation between serum IgE, absolute eosinophil count and spirometry with FeNO in asthma patients. Egyptian Journal of Bronchology, 19, 74.

Ministry of Health Republic of Indonesia. (2018). Riset Kesehatan Dasar (2018). Jakarta: Badan Penelitian dan Pengembangan Kesehatan, Kemenkes RI.

National Asthma Education and Prevention Program (NAEPP). (2020). Expert panel report 4: Guidelines for the diagnosis and management of asthma. National Heart, Lung, and Blood Institute (NHLBI), NIH.

Papi, A., Blasi, F., Canonica, G. W., Morandi, L., Richeldi, L., & Rossi, A. (2020). Treatment strategies for asthma: Reshaping the concept of asthma management. Allergy, Asthma & Clinical Immunology, 16, 75. https://doi.org/10.1186/s13223-020-00472-8

Parnes, J. R., Molfino, N. A., Colice, G., Martin, U., Corren, J., & Menzies-Gow, A. (2022). Targeting TSLP in asthma. Journal of Asthma and Allergy, 15, 749-765.

Sinyor, B., & Concepcion Perez, L. (2023). Pathophysiology of asthma. In StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. [updated 24 Jun 2023; cited 2025 Jul]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551579/

Wolsk, H. M., Chawes, B. L., Litonjua, A. A., Hollis, B. W., Waage, J., Stokholm, J., Bønnelykke, K., Bisgaard, H., & Weiss, S. T. (2017). Prenatal vitamin D supplementation reduces risk of asthma/recurrent wheeze in early childhood: A combined analysis of two randomized controlled trials. PLOS ONE, 12(10), e0186657.