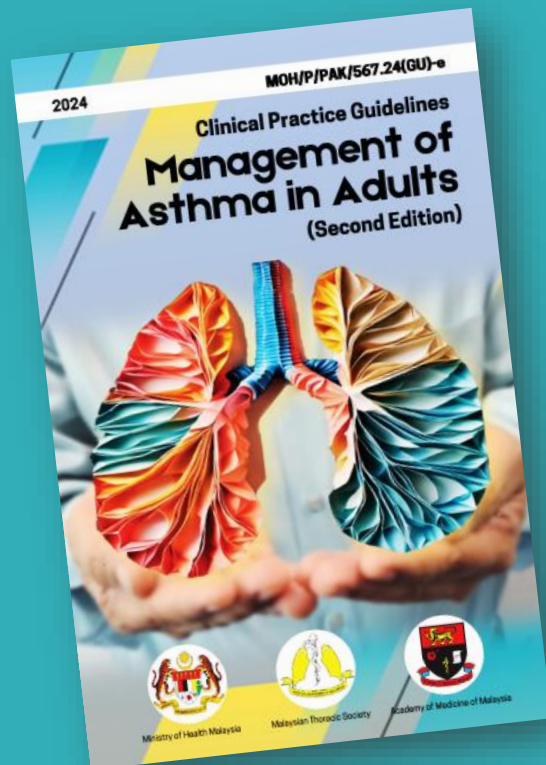


TRAINING OF CORE TRAINERS ON CPG

MANAGEMENT OF ASTHMA IN ADULTS (SECOND EDITION)



LECTURE 1 RISK FACTORS & DIAGNOSIS

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Learning Objectives



To learn on:

- Risk factors of asthma in adults
- Definition of asthma
- Diagnosis of asthma

A. Recent asthma symptom control (but also ask the patient/caregiver about the whole period since last review#)

In the past 4 weeks, has the patient had:

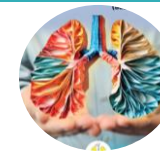
		Well controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms more than twice/week?	Yes <input type="checkbox"/> No <input type="checkbox"/>	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• SABA* reliever for symptoms more than twice/week?	Yes <input type="checkbox"/> No <input type="checkbox"/>			
• Any activity limitation due to asthma?	Yes <input type="checkbox"/> No <input type="checkbox"/>			

B. Risk factors for poor asthma outcomes

Assess risk factors at diagnosis and periodically, particularly for patients experiencing exacerbations.

Measure FEV₁ at start of treatment, after 3–6 months of ICS-containing treatment to record the patient's personal best lung function, then periodically for ongoing risk assessment.**a. Risk factors for exacerbations****Uncontrolled asthma symptoms:** Having uncontrolled symptoms is an important risk factor for exacerbations.⁸⁵

Factors that increase the risk of exacerbations even if the patient has few asthma symptoms†

SABA over-use: High SABA use (≥3 x 200-dose canisters/year associated with increased risk of exacerbations, increased mortality particularly if ≥1 canister per month)^{86–89}**Inadequate ICS:** not prescribed ICS, poor adherence,⁹⁰ or incorrect inhaler technique⁹¹**Other medical conditions:** Obesity,^{92,93} chronic rhinosinusitis,⁹³ GERD,⁹³ confirmed food allergy,⁹⁴ pregnancy⁹⁵**Exposures:** Smoking,⁹⁶ e-cigarettes,⁹⁷ allergen exposure if sensitized,^{96,98} air pollution^{99–102}**Psychosocial:** Major psychological or socioeconomic problems^{103,104}**Lung function:** Low FEV₁ (especially <60% predicted),^{96,105} high bronchodilator responsiveness^{93,106,107}**Type 2 inflammatory markers:** Higher blood eosinophils,^{93,108,109} high FeNO (adults with allergic asthma on ICS)¹¹⁰**Exacerbation history:** Ever intubated or in intensive care unit for asthma;¹¹¹ ≥1 severe exacerbation in last year^{112,113}**b. Risk factors for developing persistent airflow limitation****History:** Preterm birth, low birth weight and greater infant weight gain,¹¹⁴ chronic mucus hypersecretion^{115,116}**Medications:** Lack of ICS treatment in patient with history of severe exacerbation¹¹⁷**Exposures:** Tobacco smoke,¹¹⁵ noxious chemicals; occupational or domestic exposures⁶²**Investigation findings:** Low initial FEV₁,¹¹⁶ sputum or blood eosinophilia¹¹⁶**c. Risk factors for medication side-effects****Systemic** Frequent OCS, long-term, high-dose and/or potent ICS, P450 inhibitors¹¹⁸**Local:** High-dose or potent ICS,^{118,119} poor inhaler technique¹²⁰

Definition

Risk Factors For?

1. Poor Asthma Outcome
2. Exacerbations
3. Developing Persistent Airflow Limitations
4. Medication Side Effects

Definition: Risk Factors For Developing Asthma



2. RISK FACTORS

- Asthma is a multifaceted respiratory disease resulting from interactions between various risk factors.
- Understanding these risk factors is crucial for effective prevention and treatment of asthma.

Refer to **Table 1** on risk factors for developing asthma.

Table 1: Risk Factors for Developing Asthma

Category	Risk Factors
Host/Genetic	<ul style="list-style-type: none"> • Female • Atopy • Bronchial hyperresponsiveness • Parental asthma
Environmental	<ul style="list-style-type: none"> • Exposure to allergens (e.g. house-dust mite, pollen, cockroach) • Tobacco smoke • Air pollution • Occupational irritants (e.g. nitrogen dioxide, carbon monoxide, sulphur dioxide, fine particulate matter)
Perinatal/Childhood	<ul style="list-style-type: none"> • Younger maternal age • Maternal pre-eclampsia • Maternal tobacco consumption during pregnancy • Born via caesarean section • History of not receiving breastmilk • Lower pulmonary function of neonates
Co-morbidities	<ul style="list-style-type: none"> • Obesity • Allergic rhinitis • Chronic rhinosinusitis • Gastroesophageal reflux disease
Socioeconomic	<ul style="list-style-type: none"> • Limited access to education and/or health care

Source:

1. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2024. Updated May 2024 (Available at: www.ginasthma.org)
2. Plaza Moral V, Alobid I, Álvarez Rodríguez C, et al. GEMA 5.3. Spanish Guideline on the Management of Asthma. Open Respir Arch. 2023;5(4):100277.
3. Scottish Intercollegiate Guidelines Network & British Thoracic Society. British Guideline on the Management of Asthma. SIGN-BTS;2019



Risk Factors For Developing Asthma

Table 1



Risk Factors: Host/Genetic

- **Female:** more prevalent in females than males from 13–14 years onwards. The same change is seen with asthma attacks, with the risk of an asthma admission
- **Atopy:** atopic dermatitis/atopic rhinitis [OR=3.5, 95% CI 2.3 to 5.3]
- **Bronchial hyperresponsiveness** [OR=4.2, 95% CI 1.92 to 9.23]
- **Parental asthma:**
Asthma predictive index – Major criteria: Medical diagnosis of asthma in one of the parents.



Risk Factors: Host/Genetic-2

WHY FEMALE:

- Sex hormone (estrogen & progesterone) - affects airway immune response and inflammatory pathway.
- Estrogen enhances Th2-mediated immune response promoting allergic inflammation (IL-4, IL-5, IL-13), IgE production, and eosinophilic activity.
- Progesterone – increases airway hyperresponsiveness and modulates β -receptor function.
- Airway anatomy – smaller airways & lung volumes
- Neuropsychological & stress factors – higher levels of anxiety
- Asthma phenotypes: adult-onset asthma, obesity related



Risk Factors: Environmental

Exposure to allergens: e.g. house-dust mite, pollen, cockroach (aeroallergen)

Tobacco smoke: RR=3.9, 95% CI 1.7 to 8.5
HR=1.43, 95% CI 1.15 to 1.77

Air pollution : OR=1.34, 95% CI 1.17 to 1.54

Occupational irritants: e.g. nitrogen dioxide, carbon monoxide, sulphur dioxide, fine particulate matter

Risk Factors: Perinatal/Childhood



- Younger maternal age
- Maternal pre-eclampsia
- Maternal tobacco consumption during pregnancy
- Born via caesarean section
- History of not receiving breastmilk
- Lower pulmonary function of neonates



Risk Factors: Co-morbidities

- **Obesity:** [RR=1.50, 95% CI 1.22 to 1.83]
- **Allergic rhinitis:**
10-40% patients with allergy rhinitis have asthma.
[OR=4.16, 95% CI 3.57 to 4.86]
- **Chronic rhinosinusitis:**
with and without nasal polyps – associated with more severe asthma, especially with nasal polyps.
[RR=3.53, 95% CI 2.11 to 5.91]
- **Gastroesophageal reflux disease**



Other Risk Factors

- **Socio-economic:** Limited access to education and/or health care
- **Pre-menstrual asthma:**
Refers to worsening of asthma symptoms in females in days leading up to their menstrual period.
 - increasing age (SMD=0.42, 95% CI 0.03 to 0.82) and
 - longer duration of asthma (SMD=0.81, 95% CI 0.41 to 1.20)



Definition: Asthma Diagnosis

3. DIAGNOSIS

Asthma is a heterogeneous disease with distinct inflammatory patterns. In Type 2 (T2)-high asthma, inflammation is driven by T2 cytokines [interleukin (IL)-4, IL-5 and IL-13], leading to eosinophilic inflammation, elevated IgE and increased fractionated exhaled nitric oxide (FeNO) levels. This phenotype is typically responsive to inhaled corticosteroids (ICS) and biologics targeting T2 pathways. In contrast, neutrophilic asthma is associated with low or absent T2 inflammation and may involve IL-17 and other non-T2 cytokines, with neutrophilic inflammation and steroid resistance often observed.



Definition: Asthma Diagnosis-2

- Asthma is a **heterogeneous disease** with **distinct inflammatory patterns**.
- In **Type 2 (Th2)-high asthma**, inflammation is driven by **T2 cytokines [interleukin (IL)-4, IL-5 and IL-13]**, leading to **eosinophilic inflammation, elevated IgE** and **increased** fractionated exhaled nitric oxide (**FeNO**) levels. This phenotype is typically responsive to inhaled corticosteroids (ICS) and biologics targeting T2 pathways.
- In contrast, **neutrophilic asthma** is associated with **low or absent T2** inflammation and may involve IL-17 and other non-T2 cytokines, with **neutrophilic inflammation** and **steroid resistance** often observed.

Asthma: Genetic Susceptibility

T2-High Asthma



- ↑ Eosinophils
- ↑ Cytokines (IL-33, IL-25, TSLP, IL-13, IL-5)

Often found in allergic asthma
Causes inflammation, airway hyper responsiveness

T2-Low Asthma



- ↑ Neutrophils
- ↑ Cytokines (IL-17, TNF-alpha, IL-1B, NLRP3)
- Cause inflammation in lungs less likely to respond to steroids

Genes Linked to Asthma

Th2

IL-33
TSLP
IL-4

Histamine

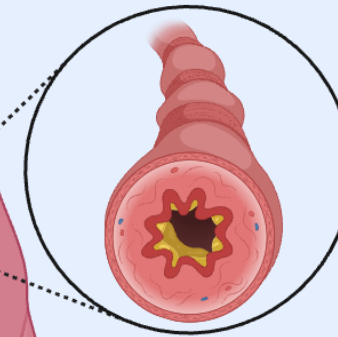
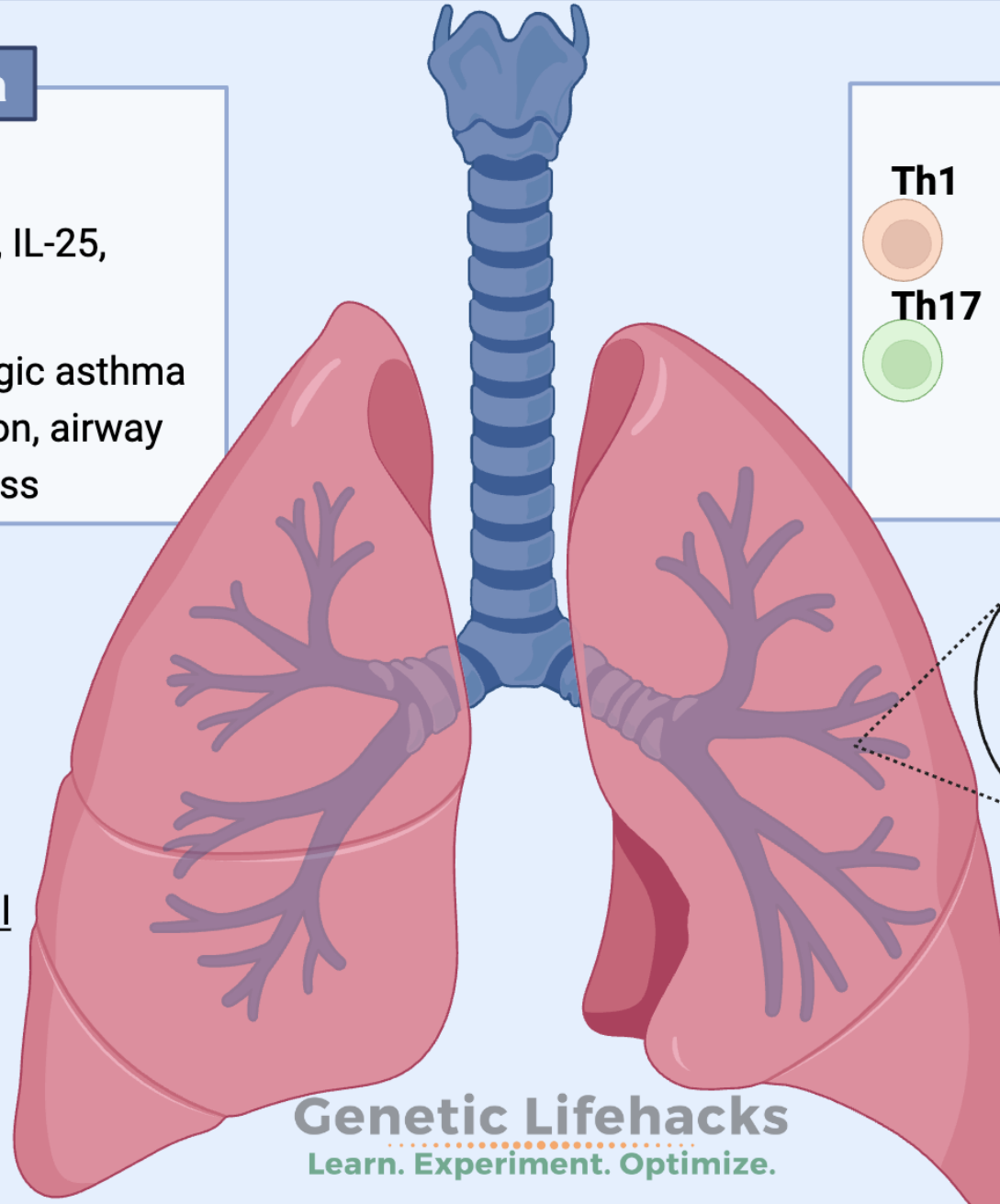
IL-13
HNMT
HRH1

Th1, Th17

TBX2
IL17A
TNF
IL1R1

Environmental

GSTA1
GSTP1
GSMB
SOD2



Other Asthma Phenotypes:

Asprin-induced asthma
Smoking-induced asthma
Asthma in the elderly
Obesity-induced asthma
Combined T2-high/T2-low



Genetic Lifehacks
Learn. Experiment. Optimize.



Definition: Asthma Diagnosis-3

- There is no gold standard test in diagnosing asthma. The diagnosis is based on a combination of clinical history, physical examination findings and lung function test with evidence of variable and reversible airway obstruction.

A thorough history taking to identify asthma symptoms is important for accurate diagnosis. Physical examination may appear normal particularly when the patient is not experiencing an asthma exacerbation. Physical examination is important to rule out other conditions with similar symptoms. Typical clinical signs of asthma include tachypnoea, rhonchi, prolonged expiratory phase and decreased breath sounds.

Table 2: Clinical Features Suggestive of Asthma

Table 2. Clinical Features Suggestive of Asthma

Clinical History and Symptoms	
Common symptoms	Wheeze Cough Chest tightness Shortness of breath
Symptoms variability	Episodic symptoms Diurnal symptoms Symptoms after/during exercise
Triggers	Common colds (viral infection) Allergen e.g house dust mites, pets Cold weather Irritants: <ul style="list-style-type: none"> • smoke • haze • strong smell i.e. perfumes, cleaning solutions • exhaust fumes
History of atopy	Allergic rhinitis Eczema
Family history of atopy	Asthma Allergic rhinitis Eczema
Physical Examination	
Respiratory examination	Use of accessory muscles Audible wheeze Rhonchi on auscultation

Physical Examination

Table 2

- General examination.
- Anthropometry: BMI ≥ 27.5 kg/m² (Obesity).
- Vital signs: Temp, PR, BP, RR, SpO₂ (normal, uncontrolled vs acute exacerbation)
- Auscultation



Physical Examination	
Respiratory examination	Use of accessory muscles Audible wheeze Rhonchi on auscultation

Table 3: Investigations for Asthma

Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction	
Spirometry	A $FEV_1/FVC < 0.7$ or $<$ lower limit normal (LLN)
Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment
	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml from baseline after four weeks on ICS
Peak Expiratory Flow Rate (PEFR)	A $\geq 20\%$ improvement in PEFR following bronchodilator treatment
	A $\geq 20\%$ improvement in PEFR from baseline after four weeks on ICS
	Diurnal Variation <ul style="list-style-type: none"> • PEFR measured and recorded at least twice daily (morning and evening) over two weeks. • PEFR variability of $\geq 20\%$ is suggestive of asthma. Refer to Appendix 3 on Peak Expiratory Flow Rate Variability and Appendix 4 on Peak Expiratory Flow Normogram .
Bronchoprovocation Test*	Methacholine challenge test <ul style="list-style-type: none"> • A PC20 value of ≤ 8 mg/ml is a positive test
	Mannitol challenge test <ul style="list-style-type: none"> • Decrease in FEV_1 of $\geq 15\%$ from baseline at cumulative dose of ≤ 635 mg is a positive test
	Exercise challenge test <ul style="list-style-type: none"> • Decrease in FEV_1 of $\geq 10\%$ from baseline
Detection of T2-high inflammation	
Blood eosinophils	Threshold for blood eosinophils is ≥ 150 cells/ μ L or $>4\%$
IgE**	Total serum IgE >100 kU/L
	Any allergen-specific IgE >0.35 kU/L
FeNO**	Elevated FeNO level (≥ 50 ppb)

*Not routinely performed in clinical practice

**To be performed when resources are available





Investigations For Asthma

- **Spirometry should be used** to diagnose asthma whenever possible.
- Forced expiratory volume in one second (**FEV1**) and forced vital capacity (**FVC**) are parameters obtained from spirometry. These parameters are used to show evidence of obstructive lung disease and reversibility (refer to **Table 3**).



Investigations For Asthma₂

(Page 6)

Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction	
Spirometry	A $FEV_1/FVC < 0.7$ or $<$ lower limit normal (LLN)
Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment
	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml from baseline after four weeks on ICS



Investigations For Asthma⁻³

(Page 6)

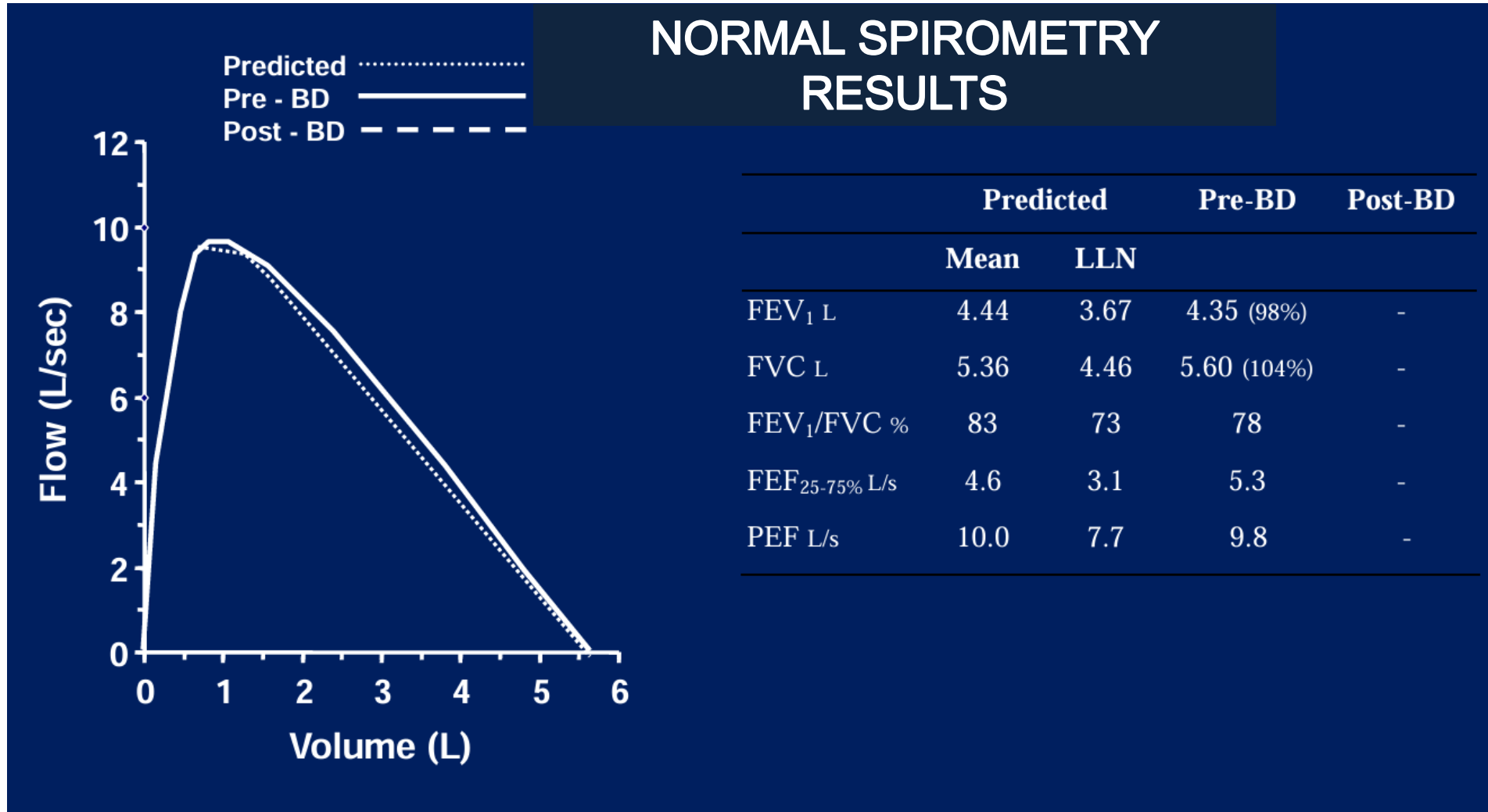
Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction	
Spirometry	A $FEV_1/FVC < 0.7$ or $<$ lower limit normal (LLN)
Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment
	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml from baseline after four weeks on ICS



Investigations For Asthma-4

Example of spirometry results

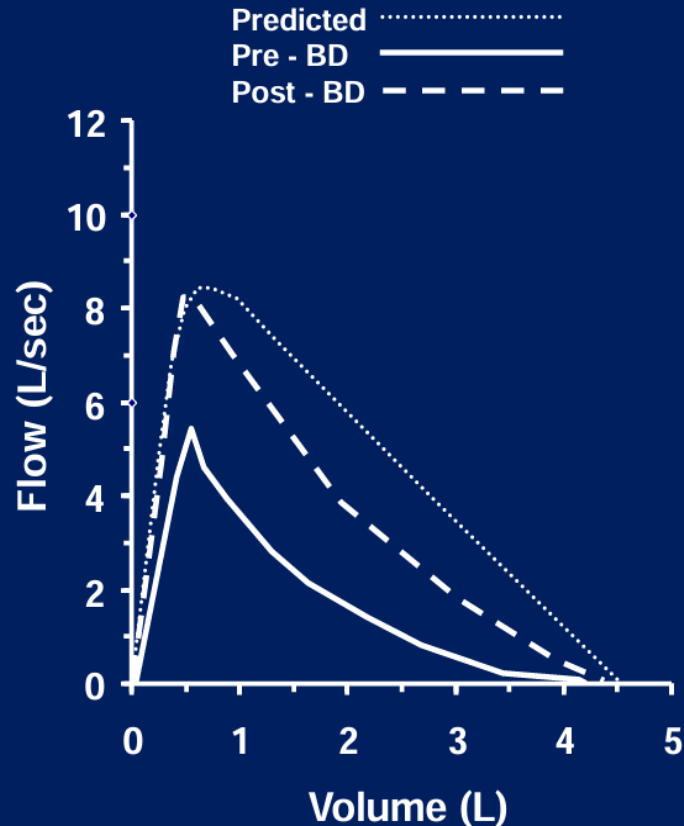




Investigations For Asthma-5

Example of spirometry results

ASTHMA SPIROMETRY RESULTS



	Predicted		Pre-BD	Post-BD
	Mean	LLN		
FEV ₁ L	4.30	3.58	2.31 (54%)	3.36 (78%)
FVC L	5.1	4.25	4.65 (91%)	4.90 (96%)
FEV ₁ /FVC %	84	74	50	69
FEF _{25-75%} L/s	4.7	3.2	2.1	3.9
PEF L/s	9.4	7.3	5.5	8.3



Investigations For Asthma-6

Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment

Interpretation: Asthma

- The **concavity/scoop** in the expiratory flow volume curve.
- **Low FEV1/FVC ratio = 50% (< 70%)** indicates an obstructive pattern
- Pre-bronchodilator FEV1 is 54% predicted, indicating a moderate obstructive pattern
- **FEV1** from 54% (pre-bron) rise to 78% (post-bron) = **24% increment**
- **FEV1** (pre-bron) 2.31L rise to 3.36L (post-bron) = **1.05 L (1050ml) increment** with the FEV1/FVC ratio increasing from 50% to 69%
- **FVC** from 4.65 L rise to 4.90 liter = 0.25L = **250ml (which >200ml from baseline)**
- These results are highly suggestive of asthma



Investigations For Asthma.7

(Page 6)

Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction	
Spirometry	A $FEV_1/FVC < 0.7$ or $<$ lower limit normal (LLN)
Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment
	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml from baseline after four weeks on ICS



Investigations For Asthma-8

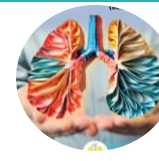
- When **SPIROMETRY IS NOT AVAILABLE**, peak expiratory flow meter (**PEFR**) may be used instead.
- These tests (**spirometry & PEFR**) should be performed:
 - i. before treatment,
 - ii. at 3 – 6 months after treatment and
 - iii. periodically (1 – 2-yearly) to establish patient's personal best FEV1 and monitor for lung function decline.
- A low FEV1 indicates underlying untreated airway inflammation and is a risk factor for future exacerbation.



Investigations For Asthma⁹

Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Peak Expiratory Flow Rate (PEFR)	A $\geq 20\%$ improvement in PEFR following bronchodilator treatment
	A $\geq 20\%$ improvement in PEFR from baseline after four weeks on ICS
	<p>Diurnal Variation</p> <ul style="list-style-type: none">• PEFR measured and recorded at least twice daily (morning and evening) over two weeks.• PEFR variability of $\geq 20\%$ is suggestive of asthma. <p>Refer to Appendix 3 on Peak Expiratory Flow Rate Variability and Appendix 4 on Peak Expiratory Flow Normogram.</p>



Investigations For Asthma⁻¹⁰

- Peak expiratory flow rate (**PEFR**) can be measured **using both peak flow meter and spirometry** machine.
- **Peak flow meter** is used primarily for **home monitoring**.
- Whereas, **spirometry** is performed in a clinical setting under **supervision of a healthcare provider**.
- Whenever possible, **PEFR should be recorded before treatment** is initiated. It should be monitored **at 1-hour post-treatment** and **regular intervals** until a **clear response** has occurred **or a plateau** is reached.

Peak Expiratory Flow Rate Variability



- Peak expiratory flow (PEF) rate variability is an alternative way to diagnose patients with asthma.
- Firstly, patients need to be **educated on the use of the PEF meter at home**.
- Preferably, the **correct technique and reading** are being done in the **clinic** before asking the patient to do **(record) it at home**.
- Patient is asked to use the **same PEF meter (to reduce bias)** to record his peak expiratory flow in the **morning and evening**, preferably at the **same time of the day**.
- They need to be advised to do PEF **reading three times** and record the **highest** reading in a given table.

Investigations For Asthma - PEFR



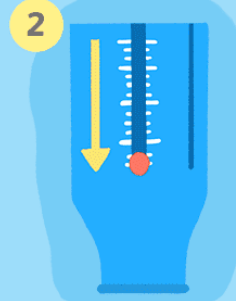
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(Second Edition)



How to Take a Peak Flow Measurement



1
Purchase a peak
flow meter
(from \$10)



2
Place marker at 0
(or lowest number)



3
Stand up.
Inhale deeply



4
While holding breath,
place mouthpiece between
teeth with lips sealed



5
Blow out as hard and
fast as possible



6
Write down number
shown on meter



7
Repeat twice

Investigations For Asthma – PEF_R-2



Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Peak Expiratory Flow Rate (PEFR)	<p>Diurnal Variation</p> <ul style="list-style-type: none">• PEFR measured and recorded at least twice daily (morning and evening) over two weeks.• PEFR variability of $\geq 20\%$ is suggestive of asthma. <p>Refer to Appendix 3 on Peak Expiratory Flow Rate Variability and Appendix 4 on Peak Expiratory Flow Normogram.</p>

Appendix 3: Peak Expiratory Flow Rate Variability

Diurnal PEF variability is calculated from twice daily readings as below:

Trainers on CPG
hma in Adults

$$\frac{\text{Day's highest} - \text{Day's lowest}}{(\text{Mean of day's highest and lowest})} \times 100$$

Then the average of each day is calculated over 1 to 2 weeks.

Example:

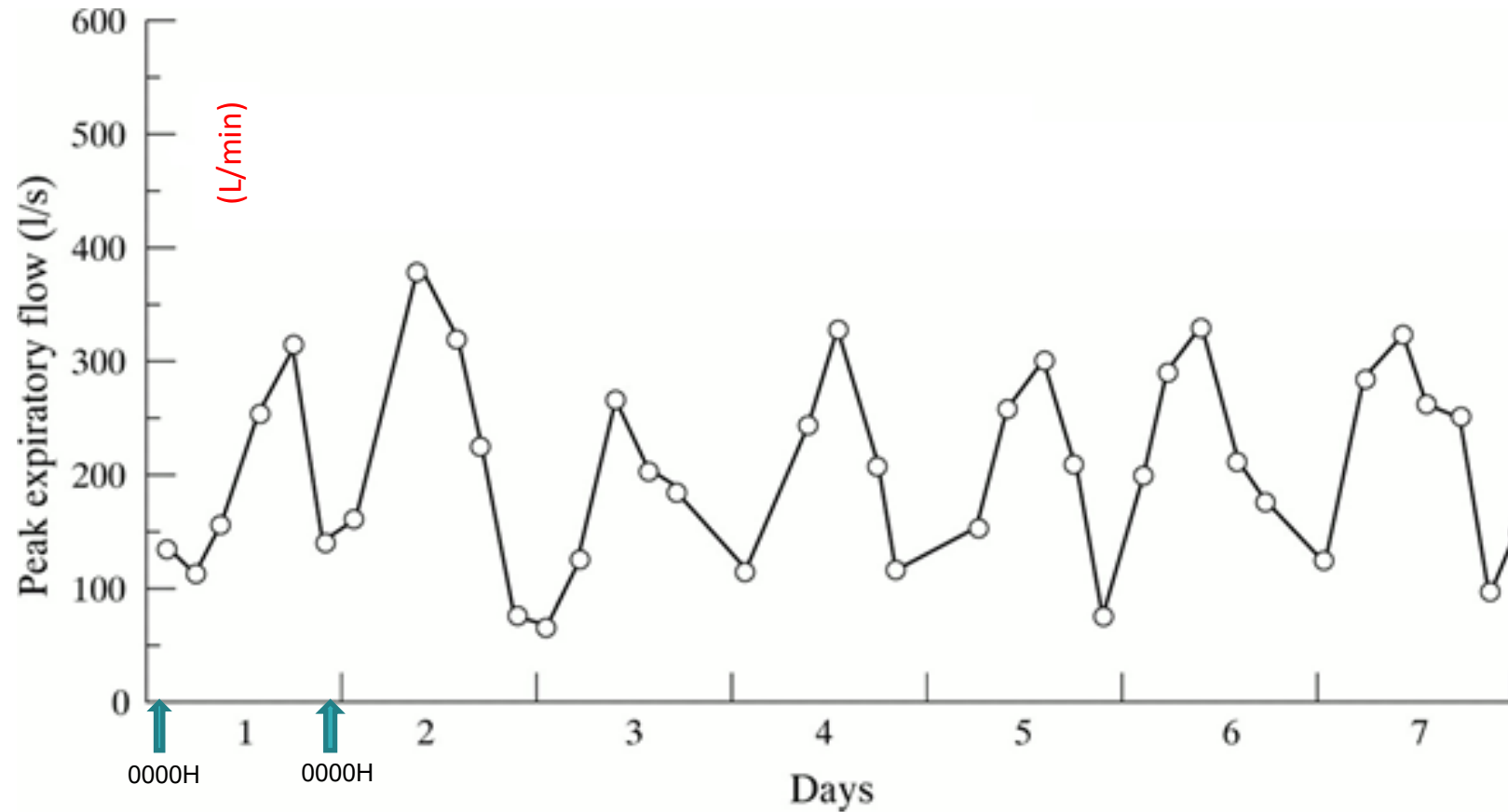
Date	Morning PEFR	Evening PEFR	Mean of day's highest and lowest	Calculation	Diurnal PEF variability
8/4/2024	500	560	$(500 + 560) \div 2 = 530$	$(560 - 500)/530 \times 100\%$	11.3 %
9/4/2024	460	580	520	$120/520 \times 100\%$	23.0 %
10/4/2024	440	570	505	$130/505 \times 100\%$	25.7 %
11/4/2024	480	600	540	$120/540 \times 100\%$	22.2 %
12/4/2024	460	580	520	$120/520 \times 100\%$	23.0 %
13/4/2024	460	560	510	$100/510 \times 100\%$	19.6 %
14/4/2024	490	590	540	$100/540 \times 100\%$	18.5 %

Total diurnal PEF Variability = $(11.3 + 23.0 + 25.7 + 22.2 + 23.0 + 19.6 + 18.5) = 143.3\%$

Mean Diurnal PEF Variability = $143.3 \% \div 7 \text{ days} = 20.47 \%$

Diurnal PEF Variability is significant if the reading is $\geq 20\%$ in adults

Scenario 2 – Peak Flow Chart



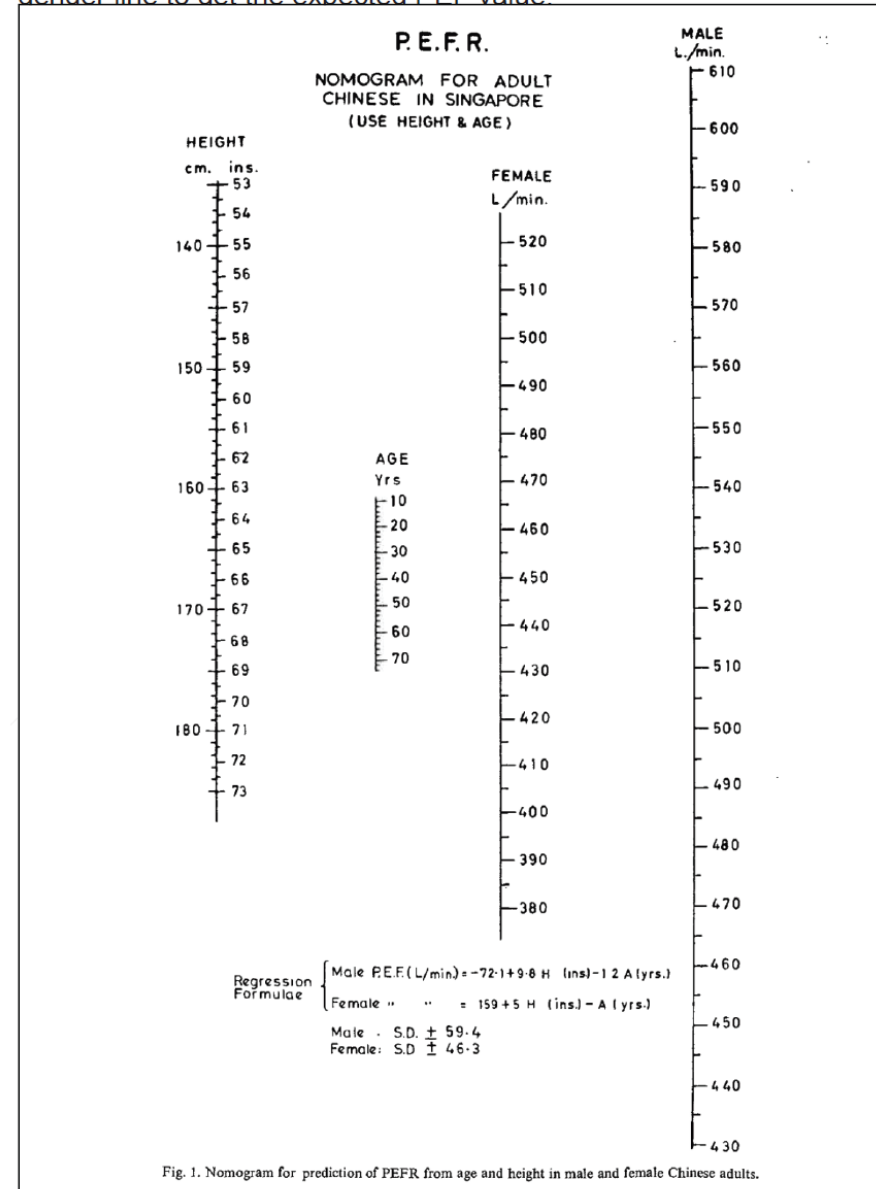
- Is the peak flow rate of 400 L/min at presentation normal for him?
- Interpret his peak flow chart.

Appendix 3: Peak Expiratory Flow Rate Variability



PEAK EXPIRATORY FLOW NOMOGRAM

Mark the patient's height and age on the respective lines. Draw a straight line connecting the two points and extend this line to the corresponding gender line to get the expected PEF value.



Example

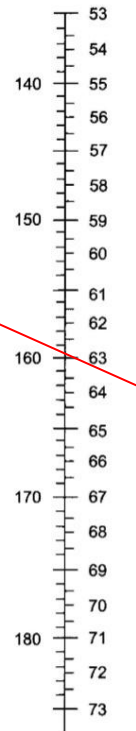
- Is the peak flow rate of 400 L/min at presentation normal for him?
- 40, male, ht 161 cm
- Predicted PEFR 500 L/min

$$\frac{400}{500} \times 100 = 80\%$$

Appendix

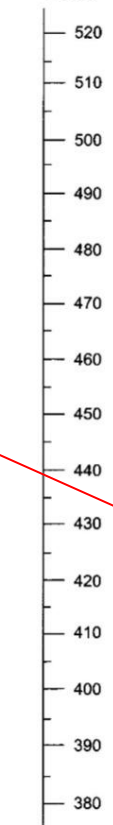
PEF normogram

HEIGHT
CM INS

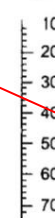


P.E.F.R. NOMOGRAM FOR ADULT CHINESE IN SINGAPORE (USE HEIGHT & AGE)

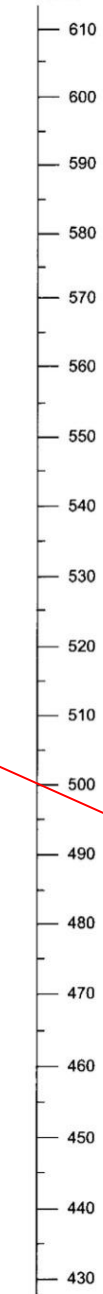
FEMALE
L/min



Age



MALE
L/min



Regression
Formula

$$\begin{aligned} & \text{Male PEF(L/min)} = 72.1 + 9.8 \text{ H (ins)} - 12 \text{ A (yrs)} \\ & \text{Female PEF(L/min)} = 159 + 5 \text{ H (ins)} - \text{A (yrs)} \\ & \text{Male SD} \pm 59.4 \\ & \text{Female SD} \pm 46.3 \end{aligned}$$

Investigations For Asthma – Bronchoprovocation Test



Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Bronchoprovocation Test*	Methacholine challenge test <ul style="list-style-type: none">• A PC20 value of ≤ 8 mg/ml is a positive test
	Mannitol challenge test <ul style="list-style-type: none">• Decrease in FEV₁ of $\geq 15\%$ from baseline at cumulative dose of ≤ 635 mg is a positive test
	Exercise challenge test <ul style="list-style-type: none">• Decrease in FEV₁ of $\geq 10\%$ from baseline

*Not routinely performed in clinical practice

Investigations For Asthma – Bronchoprovocation Test-2



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The tests are indeed **similar to spirometry pre- and post-bronchodilator**, but instead of giving a bronchodilator to improve lung function, **methacholine/mannitol/exercise is given to provoke bronchoconstriction, detect airway hyperreactivity**. Avoid bronchodilators, strenuous exercise and caffeine 2 days prior.

Methacholine challenge test

- A PC (provocative concentration), PC 20 value of ≤ 8 mg/ml is a positive test.

Mannitol challenge test

- Decrease in FEV1 of $\geq 15\%$ from baseline at cumulative dose of ≤ 635 mg is a positive test

Exercise challenge test [Target heart rate 85%: $220 - \text{age (yrs)} \times 85\%$]

- Decrease in FEV1 of $\geq 10\%$ from baseline.

Investigations For Asthma – Blood Eosinophils



Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Detection of T2-high inflammation	
Blood eosinophils	Threshold for blood eosinophils is ≥ 150 cells/ μ L or $>4\%$
IgE**	Total serum IgE >100 kU/L
	Any allergen-specific IgE >0.35 kU/L
FeNO**	Elevated FeNO level (≥ 50 ppb)

Investigations For Asthma – Blood Eosinophils-2



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WHOLE BLOOD

* Erythrocyte Sedimentation Rate (ESR)	36	mm/hr	H	1 - 15	IR detection vertical tube predilution
White Blood Cell	7.32	$\times 10^9/L$		4.00 - 10.00	Fluorescent Flow Cytometry
Red Blood Cell	5.39	$\times 10^{12}/L$		4.50 - 5.50	DC Detection
Haemoglobin	15.4	g/dL		13.0 - 17.0	SLS-Haemoglobin method
Haematocrit	45.9	%		40.0 - 50.0	Calculated
Mean Cell Volume	85.2	fL		83.0 - 101.0	Calculated
Mean Cell Haemoglobin	28.6	pg		27.0 - 32.0	Calculated
Mean Cell Haemoglobin Concentration	33.6	g/dL		31.5 - 34.5	Calculated
Red Cell Distribution Width CV	13.0	%		11.6 - 14.0	Analysis of RBC
Platelet	296	$\times 10^9/L$		150 - 410	DC Detection
Neutrophil %	49.2	%		40.0 - 80.0	Flow Cytometry
Lymphocyte %	34.8	%		20.0 - 40.0	Flow Cytometry
Monocyte %	6.3	%		2.0 - 10.0	Flow Cytometry
Eosinophil %	9.3	%	H	1.0 - 6.0	Flow Cytometry
Basophil %	0.4	%		0.0 - 2.0	Flow Cytometry
Absolute Neutrophil Count	3.60	$\times 10^9/L$		2.00 - 7.00	Calculated
Absolute Lymphocytes Count	2.55	$\times 10^9/L$		1.00 - 3.00	Calculated
Absolute Monocyte Count	0.46	$\times 10^9/L$		0.20 - 1.00	Calculated
Absolute Eosinophil Count	0.68	$\times 10^9/L$	H	0.00 - 0.50	Calculated
Absolute Basophil Count	0.03	$\times 10^9/L$		0.00 - 0.10	Calculated

Investigations For Asthma – Blood Eosinophils-3



Eosinophil %	9.3	%	H	1.0 - 6.0
Absolute Eosinophil Count	0.68	$\times 10^9/L$	H	0.00 - 0.50

✓ Definition:

$$1 \mu\text{L} = 10^{-6} \text{ liter}$$

That means a microliter is:

- One-millionth of a liter
- 0.000001 L
- 1/1,000,000 of a liter

How do you convert eosinophils results of $0.68 \times 10^9/L$ into cells/ μL ?

To convert eosinophils from $\times 10^9/L$ to cells/ μL , follow this simple conversion:

✓ Conversion Formula:

$$1 \times 10^9/L = 1000 \text{ cells}/\mu\text{L}$$

So, to convert:

$$0.68 \times 10^9/L = 0.68 \times 1000 = \boxed{680 \text{ cells}/\mu\text{L}}$$

✎ Final Answer:

$$0.68 \times 10^9/L = 680 \text{ cells}/\mu\text{L}$$

Investigations For Asthma – IgE



Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Detection of T2-high inflammation	
Blood eosinophils	Threshold for blood eosinophils is ≥ 150 cells/ μ L or $>4\%$
IgE**	Total serum IgE >100 kU/L
	Any allergen-specific IgE >0.35 kU/L
FeNO**	Elevated FeNO level (≥ 50 ppb)

**To be performed when resources are available

Investigations For Asthma – IgE₂



Training of Core Trainers on CPG
Management of Asthma in Adults
(Second Edition)

DR MAZAPUSPAVINA

Hospital Universiti Teknologi Mara (Puncak Alam)

Hospital UiTM (Puncak Alam), Jabatan Makmal Diagnostik Klinikal

Kuala Selangor

Selangor



Patient Name :

Ward / Clinic :

Age :

IC No. :

DOB : 04/12/1985

Lab No. : 0122021752

Date Received : 27/06/2022 16:35

Date Reported : 28/06/2022 10:30

Report Status : Final

*** Immunoglobulin E (IgE)

Result

Unit

Reference range

>2500.0 IU/mL

< 100

INTERPRETATION OF TOTAL Ig E RESULT:

< 25 IU/mL: Atopic allergy unlikely but can not be excluded.

25 -100 IU/mL: Atopic allergy possible around 50% probability the higher of the IgE, the higher the probability.

> 100 IU/mL: Atopic allergy highly probable.

Validated by Low Hwei Jean, Clinical Lab Scientist (Serology) LablinkHQ 28/06/22 10:30:29 AM

✓ Conversion Relationship:

1 IU/mL = 1 kU/L

Why?

Because:

1 IU/mL = 1000 IU/L = 1 kU/L

🔄 Now Convert:

2500 IU/mL = 2500 kU/L

🖋️ Final Answer:

2500 IU/mL = 2500 kU/L

Investigations For Asthma - FeNO



Table 3: Investigations for Asthma

Investigation	Description
Demonstration of airway obstruction variability or reversibility	
Detection of T2-high inflammation	
Blood eosinophils	Threshold for blood eosinophils is ≥ 150 cells/ μ L or $>4\%$
IgE**	Total serum IgE >100 kU/L
	Any allergen-specific IgE >0.35 kU/L
FeNO**	Elevated FeNO level (≥ 50 ppb)

**To be performed when resources are available

Investigations For Asthma – FeNO₂



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- FeNO stands for Fractional exhaled Nitric Oxide
- It is a **non-invasive test** that measures the **amount of nitric oxide (NO) in your breath.**
- Nitric oxide (NO) is a gas naturally produced by the **lining of the airways.** In asthma, especially **eosinophilic or allergic asthma, inflammation causes** the airway cells to produce **more nitric oxide.**
- So, FeNO acts as a **marker of airway inflammation.**

Investigations For Asthma – FeNO₂



- **FeNO is not a definitive test for diagnosing asthma.** Although it tends to be high in asthma with T2 airway inflammation, it can also be **elevated in non-asthmatic conditions** e.g. eosinophilic bronchitis, allergic rhinitis and eczema.
- In patients with suspected asthma, a **high FeNO level of >50 ppb** predicts **better response to ICS therapy** than low level.
- However, **a low FeNO level** should **not be used** as a reason to **withhold ICS treatment** as in non-T2 inflammation asthma, FeNO levels are not typically elevated.

Investigations for Asthma– FeNO



How Does FeNO Testing Work?

Fractional exhaled Nitric Oxide (FeNO) testing, measures the level of Nitric Oxide (NO) in your breath - a marker of airway inflammation often found in asthma.¹

Taking a FeNO Test



FeNO levels are measured in parts per billion (ppb).

ATS/ERS Clinical Guidelines Summary for Interpreting FeNO Levels^{2,3}



These reflect the ATS and ERS guidelines. Please note that there are additional guidelines available.

Why is FeNO Testing Useful¹?

- Non-invasive.
- Quick and easy to do.
- Aids in asthma diagnosis.
- Guides inhaled steroid use.

MANAGEMENT OF PATIENTS WITH ONGOING OR RECENT ASTHMA-LIKE SYMPTOMS, NOT TREATED WITH ICS OR COMBINATION THERAPY			
	Low	Intermediate	High
FeNO value (ppb), patients ≥12 years of age	<25	25-50	>50
FeNO value (ppb), patients <12 years of age	<20	20-35	>35
In the case of a >40% increase from previously stable levels, interpret as high FeNO.			
Consider as response to ICS	Increase >10 ppb from last measurement		Increase ≥20% from last measurement
Interpretation with respect to steroid response*	Unlikely to respond to corticosteroids		Highly likely to respond to corticosteroids
Possible Alternate Diagnoses	Other causes to consider		
	<ul style="list-style-type: none">• Anxiety/hyperventilation• Cardiac disease• COPD• GERD• Noneosinophilic asthma• Rhinosinusitis• Vocal cord dysfunction• Cystic fibrosis• Primary ciliary dyskinesia (FeNO <5 ppb)		<ul style="list-style-type: none">• Atopic asthma• High levels of allergen exposure• Infection as a reason for worsening symptoms• COPD with mixed inflammatory phenotype• Eosinophilic bronchitis

Investigations for Asthma– FeNO



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Machine price:
MYR 5K-15K



Uncover Airway Inflammation: Assess with FeNO Test

A FeNO test measures airway inflammation. It is commonly used as an inflammation marker for asthma management and assessment.

RM**210***
per session

> FeNO test is suitable for individuals with:



Asthma

Benefits of FeNO Test

- > Easy-to-perform test with high level of accuracy
- > Ideal for investigating young asthmatic children

FeNO testing can help diagnose asthma



HEALTH TECHNOLOGY ASSESSMENT REPORT

MOH/P/PAK178.09/(TR)



MINISTRY OF HEALTH MALAYSIA

EXHALED NITRIC OXIDE MEASUREMENT USING NIOX OR NIOX MINO

Health Technology Assessment Section (MaHTAS)
Medical Development Division, Ministry of Health Malaysia
Level 4, Block E1, Parcel E, Government Offices Complex,
62590 Putrajaya, MALAYSIA

Table 3: Investigations for Asthma



Table 3: Investigations For Asthma

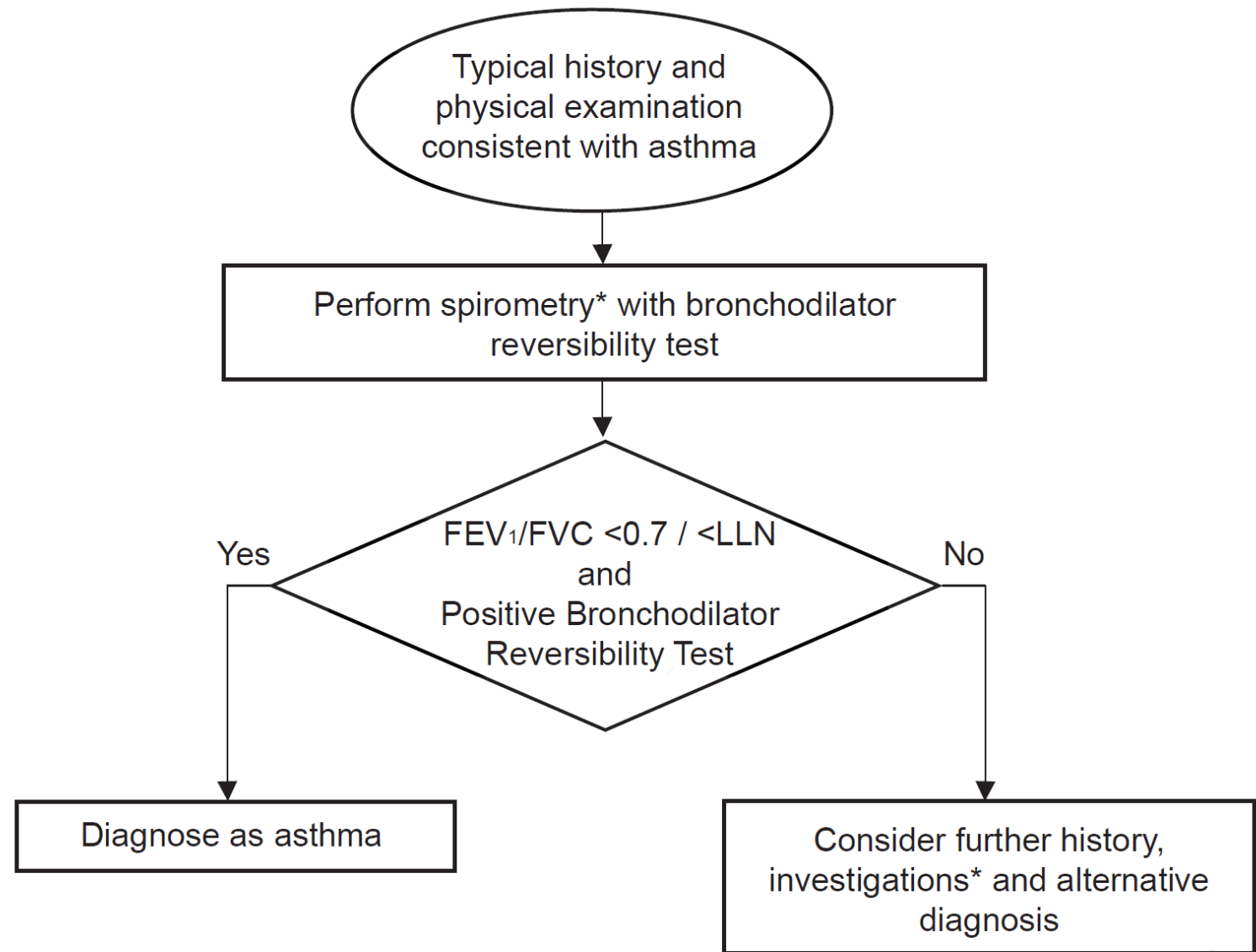
Investigation	Description
Demonstration of airway obstruction	
Spirometry	A $FEV_1/FVC < 0.7$ or $<$ lower limit normal (LLN)
Demonstration of airway obstruction variability or reversibility	
Spirometry	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml following bronchodilator treatment
	An improvement in FEV_1 or FVC $\geq 12\%$ AND ≥ 200 ml from baseline after four weeks on ICS
Peak Expiratory Flow Rate (PEFR)	A $\geq 20\%$ improvement in PEFR following bronchodilator treatment
	A $\geq 20\%$ improvement in PEFR from baseline after four weeks on ICS
	Diurnal Variation <ul style="list-style-type: none"> PEFR measured and recorded at least twice daily (morning and evening) over two weeks. PEFR variability of $\geq 20\%$ is suggestive of asthma. Refer to Appendix 3 on Peak Expiratory Flow Rate Variability and Appendix 4 on Peak Expiratory Flow Normogram .
Bronchoprovocation Test*	Methacholine challenge test <ul style="list-style-type: none"> A PC20 value of ≤ 8 mg/ml is a positive test
	Mannitol challenge test <ul style="list-style-type: none"> Decrease in FEV_1 of $\geq 15\%$ from baseline at cumulative dose of ≤ 635 mg is a positive test
	Exercise challenge test <ul style="list-style-type: none"> Decrease in FEV_1 of $\geq 10\%$ from baseline
Detection of T2-high inflammation	
Blood eosinophils	Threshold for blood eosinophils is ≥ 150 cells/ μ L or $> 4\%$
IgE**	Total serum IgE > 100 kU/L
	Any allergen-specific IgE > 0.35 kU/L
FeNO**	Elevated FeNO level (≥ 50 ppb)

*Not routinely performed in clinical practice

**To be performed when resources are available

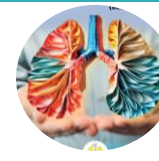
RECAP

**Figure 1:
Diagnosis of
Asthma
(page 7)**



*Refer to **Table 3**.

Figure 1: Diagnosis of Asthma in Treatment Naïve Patients



Diagnosis of Asthma

- For patients who are on ICS treatment, improvement of symptoms supports an asthma diagnosis.
- For patients on treatment who **do not show airflow variability**, consider **repeating spirometry** after withholding bronchodilator:
 - four hours for short-acting β 2-agonists (SABA)
 - 24 – 48 hours for long-acting β 2-agonists (LABA)]
 - or during symptoms.

TAKE HOME MESSAGES



Recommendation 1

- Diagnosis of asthma should be made based on typical clinical history, physical examination and evidence of airway obstruction variability.
 - Spirometry is the preferred tool to demonstrate airway obstruction variability or reversibility.



- Any questions?

Thank You!!



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