STRIDER

It is a **harsh, high-pitched & mainly inspiratory sound** that results from obstruction of the **upper** airway. Generally, it can be differentiated from obstruction of the **middle** airway which produce monophonic wheeze and is inspiratory & expiratory, whereas obstruction of the **lower** airway produce polyphonic wheeze which is mainly expiratory.

Et. The most common causes of strider include:-

- **Infection of upper airway** e.g. Croup (acute or spasmodic), Acute epiglottitis, Bacterial tracheitis, Diphtheria.
- **Congenital malformation of Larynx** e.g. Laryngomalacia, Subglottic stenosis, Vocal cord paralysis, Laryngeal web/atresia/cleft, Subglottic hemangioma, Laryngocele or saccular cysts.
- **Acquired condition of larynx** e.g. Laryngeal papillomatosis & other laryngeal tumors, Foreign bodies, GERD, Anaphylaxis, Angioedema, Hypocalcemia, Hysterical strider.
- **Congenital malformation of Trachea** e.g. Tracheomalacia, Subglottic tracheal web or stenosis, Tumors, TEF.
- **Tracheal compression by external mass** e.g. Vascular ring or sling, Thyroid enlargement, Esophageal FB, Mediastinal masses.

Croup

Et. Mainly **viruses** e.g. **parainfluenza** (75%), influenza, adenovirus, RSV,measles, and rarely *Mycoplasma pneumoniae*.

Path. It is mainly due to **laryngotracheitis**, but **laryngotracheo-bronchitis** may occur in more severe cases.

Epid. Peak age **2 yr** with a range from 3 mo to 5 yr. It is higher in **male** &
mainly occurs in **winter** with positive **family hx** of croup or URTI in some cases.

C.M. It usually begin as **URTI** e.g. rhinorrhea, pharyngitis, mild cough, and low-grade fever for 1–3 days before croup which characterized by **barking cough, hoarseness of voice, & inspiratory strider**. Agitation and crying greatly aggravate the condition; the child may prefer to sit up in bed; it may be worse at night-

Inv. Croup is mainly a **clinical Dx.** After stabilization of the airway, **X-ray** of neck can be taken in A-P view which may show the ***"Steeple sign"*** due to laryngeal edema, although it is not specific.

Rx. ***Mild*** croup can be managed safely at **home** by cold night air or cool mist (unless patient has associated bronchospasm); whereas

moderate or severe croup should be managed at **hospital**, especially in the following situations: progressive strider, severe strider at rest, respiratory distress, hypoxia, cyanosis, depressed mental status, poor oral intake, or the need for reliable observation.
The child should be **calm** as much as possible & better managed in his parent's lap. Therapy may include:-
 Nebulized racemic epinephrine (or l-epinephrine) 1/2 ml+ 3 ml NS. It can be used every **20 min**, but the duration of activity is **<2 hr**. Therefore, observation should continue 2-3 hr after nebulization.
 Dexamethasone orally ≤ 0.6 mg/kg as **single dose** is effective as parenteral dexamethasone or nebulized budesonide.
 Heliox (helium+oxygen) may be effective in patient with severe croup that may need **intubation** or **tracheostomy**.
Pg. Excellent, but may **recur** with decreasing intensity for several days;however, it usually resolve completely within a week.

Spasmodic Croup

It is clinically **similar** to the ordinary croup, but **without** viral prodrome or fever. The attacks are usually less severe & have shorter duration. It may be due to viral, allergic or psychological causes. Rx is the same as above.

Bacterial Tracheitis

It usually **follow viral croup** after few days of apparent improvement.
Et. It mainly caused by ***Staph. aureus*** & less commonly by *Moraxella catarrhalis*, non-typable *Haemophilus influenza*, GABS, *&* anaerobes*.*
C.M. Patient usually has **high fever, toxic, respiratory distress & brassy cough**, as well as **purulent secretion** from the airway.
Inv.
 CXR show subglottic narrowing with patchy infiltration of lungs.
 Laryngoscope show a *"pseudo-membrane"* consist of copious, thick & purulent secretion (which should be suctioned).
Cx. Toxic-shock syndrome & Cardiorespiratory arrest can occur.
Rx. Oxygen with **IV antibiotics** e.g. vancomycin or clindamycin + 3rd generation cephalosporin. Intubation or tracheostomy may be needed in > half of cases.
Pg. Although it is a life-threatening infection, but prognosis is **excellent** with Rx.

Acute Epiglottitis (Supraglottitis)

It is a dramatic, **life-threatening** condition.
Et. It mainly caused by ***Haemophilus influenzae*** **type b** & less commonly by *Strep. pyogenes, Strep. pneumoni & Staph. aureus.*
C.M. Peak age ≈ **3 yr**. Onset usually **sudden** as fever & sore throat, then patient within hours become **toxic** with dyspnea, open mouth, muffled sound, tripod sitting, **dysphagia** & drooling of saliva; then become restless with increasing dyspnea, cyanosis & eventually develop coma.
Strider is a late finding and suggests near-complete airway obstruction.
Inv. Any **anxiety-provoking** interventions e.g. venepuncture or trying to see the epiglottis by tongue depressor may **aggravate** the condition, thus it should be **avoided until** airway is secured.
 X-ray of neck in lateral view with neck hyperextended may show the ***"Thumb sign"*** of epiglottis.
 Laryngoscope should only be done in the operating room which shows a large, *"cherry red"* epiglottis, aryepiglottic folds may also be involved.
 Culture of bacteria can be obtained from epiglottic surface, blood, or less from CSF.
Rx. Patient should be managed in the **ICU** with continuous oxygen, IV fluids & frequent monitoring. **ET intubation** or **tracheostomy** should be considered in **all** patients with epiglottitis for 2-3 days. Antibiotics should be given parenterally for 10 days e.g. **Ceftriaxone, Cefotaxime,** or **Ampicillin - Sulbactam.**

Laryngomalacia

It is the **most common** congenital anomaly of larynx and the most frequent cause of strider in infants and children that account **≈ 60%**.
C.M. Symptoms usually appear in the **first 2 wk** of life and increase in severity for up to **6 mo**, although **gradual improvement** can begin at any time.
Typically, **strider** is inspiratory, low pitched, and exacerbated by any **exertion (crying, agitation, feeding), supine position, or viral URTI**
Inv.
 Flexible laryngoscope shows collapse of supraglottic structures inward during inspiration.
 Bronchoscopy & CXR should be done if there is dyspnea or severe airway obstruction to exclude other airway anormalies.

Rx.

 Expectant observation is suitable for most infants because most symptoms resolve spontaneously. **Avoidance** of crying & agitation with sleeping in lateral position may be beneficial

 Patients with severe obstruction, life-threatening events (e.g. URTI), or Cxs e.g. cor-pulmonale, cyanosis, or FTT should be managed by endoscopic **supraglottoplasty** or **tracheotomy**.

FOREIGN BODIES IN THE AIRWAY

Infants and toddlers use their mouths to explore their surroundings; therefore, they are the most common victims. FBs are mainly lodged in the **right main bronchus**; peanuts are most commonly ingested.

C.M. Three stages of symptoms may result from aspiration of FB into the airway:-

1. ***Initial event;*** characterized by violent paroxysms of **coughing, choking & gagging** immediately after FB aspiration accompanied by **wheezing** (which is due to reflex bronchospasm); this is highly suggestive of FB in the airway.

- 2. ***Asymptomatic interval;*** the FB becomes lodged; **reflexes fatigue**, and immediate irritating symptoms **subside**, which may cause **delay** in Dx.

3. ***Complications;*** due to **obstruction, erosion, or infection** → fever, cough, hemoptysis, pneumonia, or atelectasis. These Cxs direct attention again to the presence of FB.

 CXR may be **normal** if taken in inappropriate way or the FB is radiolucent. Proper X-ray for suspected FB should be taken in both **A-P & lateral** views and during deep **expiration**.

Obstructive emphysema (air trapping) → shifting of mediastinum to the opposite side, in contrast to the atelectasis (which usually a late finding).

 Fluoroscopy, CT, & **MRI** are more diagnostic.

 Bronchoscopy is both diagnostic & theraputic.

Rx.

 Laryngeal FB can sometimes be dislodged by **upside-down** in infants, or ***Heimlich maneuver*** in children, otherwise should be removed by **direct Laryngoscope.**

 Tracheal & Bronchial FB should removed urgently by **rigid bronchoscope**

BRONCHIOLITIS

Path. Bronchiolitis is the **most common cause of wheezing in infants**
due to several mechanisms include:-
 The narrow airway caliber in infants results in ↑ resistance to airflow
 Chest wall of infants is very compliant; the inward pressure produced in expiration subjects the intrathoracic airways to collapse.
 Immunologic and molecular influences can also contribute to the infant's propensity to wheeze.
Et. RSV (**most common**), Human metapneumovirus (may cause co-infection with RSV), Parainfluenza, Adenovirus, Influenza, Rhinovirus, & infrequently *Mycoplasma pneumonia*.
Note: Bacteria have no role *in the etiology of bronchiolitis (although superinfection may rarely occur).*
Risk factors for bronchiolitis may include: male gender, bottle feeding, crowding, and family hx of minor RTI.
C.M. Acute bronchiolitis is usually preceded by **exposure** to an adult with minor respiratory syndrome within the previous wk. The infant 1st develops **mild URTI** e.g. sneezing, rhinorrhea, low-grade fever, & poor appetite. Gradually, **respiratory distress** ensues with paroxysmal wheezy cough, dyspnea, and irritability. **Apnea** may be more prominent than wheezing early in the course of disease especially in young (or former premature) infants.
Chest examination reveals **wheezing** as the most prominent feature with tachypnea, nasal flaring and retractions. Auscultation usually reveal overt wheezes with prolongation of expiratory phase +/_ fine crackles. **Diminished breath sounds** suggest very severe disease with nearly complete bronchiolar obstruction. Hyperinflation of the lungs may permit palpation of the liver.
Inv. Bronchiolitis is mainly a **Clinical Dx**, especially in previously healthy
infant presenting for the 1st time during community outbreak.
 CXR may show hyperinflation of lungs with patchy atelectasis.
 CBP is usually normal.
 Viral & other studies are used only to confirm Dx & to exclude other D.Dx
D.Dx. of wheezing in infant:-
 RTI by etiologies other than viruses.
 Asthma may be triggered by viral infection *(see later).*
 Aspiration e.g. FB, GERD.
 Mucociliary Clearance disorders e.g. CF, Bronchiectasis.

 Anatomic Abnormalities of airway
 Miscellaneous comditions e.g. Interstitial Lung diseases, HF.

Rx. Indications of admission to hospital include:
age <6 mo, severe respiratory distress, toxic appearance, requirement for supplemental oxygen, vomiting & dehydration, immunodeficiency, pre-existing pulmonary or cardiac disease, no response to home therapy, and non- compliant parents.
 Supportive therapy include: cool humidified **oxygen** (preferably by nasal cannula), good **hydration** (give fluids orally, or if not tolerated, by NG tube or IV), **suction** of secretions, & putting the infant in a **semi- sitting** position (with head & chest elevated at 30^0), and avoid sedation.
 Nebulization can be done with any of the following **5** agents:-
1. **β-agonists** e.g. salbutamol; it mainly effective when there is a component of bronchial hyper-reactivity (asthma). Otherwise, the response is unpredictable, therefore observe the response objectively.
2. **Epinephrin** may be more effective as bronchodilator than β-agonists.
3. **Anticholinergics** e.g. ipratropium bromide, it can be be used as an adjunct agent, but it mainly used in patient with tracheomalacia or bronchomalacia because β-agonists may worse these conditions.
4. **Steroid inhalation** e.g. budesonide may be indicated in moderate to severe wheezing, hx of atopy (food allergy, eczema
5. **Hypertonic Saline** nebulization & **Heliox** inhalation have also some benefit in bronchiolitis.
 Ribavirin by nebulization may be used for bronchiolitis due to RSV in infant who had other chronic lung or heart disease; whereas other antiviral agents (including palivizumab), as well as antibiotics have **no role** in Rx of bronchiolitis.

Pg. Infants with acute bronchiolitis may **deteriorate in the 1st 2-3 days** after illness & may remain so for up to **2 wk** & even may **die** during this critical period due to apnea, respiratory failure, or severe dehydration, although this is rare (<1%). A few proportion (10%) of infants may remain symptomatic for 3 wk.

Approximately **40%** of infants who wheeze will **wheeze again** with later viral RTI. These ***"Transient Wheezers"*** can be divided into 3 groups:-

✓ ***Early*** *wheezer;* wheezing in the **1st 3 yr** of life.
✓ ***Persistent*** *wheezer;* wheezing in the **1st 6 yr** of life.
✓ ***Late-onset*** *wheezer;* wheezing between **3 & 6 yr** of life.

Risk factors that predict which early wheezers will go on to have asthma in later life include: parental hx of asthma and allergies, maternal smoking, persistent rhinitis (apart from acute URTI), allergen sensitization, eczema at < 1 yr of age, peripheral eosinophilia (>4%), and frequent episodes of wheezing during infancy.

Pv.

 RSV-IVIG & Palivizumab may be given before and during RSV season for infants <2 yr with hx of prematurity, chronic lung disease, or some forms of CHD.

 Handwashing is the best measure to prevent nosocomial transmission

PNEUMONIA

Pneumonia is an inflammation of the lung parenchyma due to infectious or non-infectious causes. **Pneumonia & Diarrhea** are the most common cause of death in children worldwide.

Et. It can be divided according to the age of presentation as following:-

Age Group	**Frequent Pathogens (in order of frequency)**
Neonates (<3 wk)	Group B streptococcus,*E. coli,*other gram-negative bacilli, *Strep. pneumoniae, H. influenza*
3 wk-3 mo	RSV, other respiratory viruses (parainfluenza viruses, influenza viruses, adenovirus), S. pneumoniae, H. influenzae;if patient is afebrile, consider Chlamydia trachomatis
4 mo-4 yr	RSV, other respiratory viruses (as above), S. pneumoniae, H. influenzae, Mycoplasma pneumoniae, group A streptococcus
≥5 yr	M. pneumoniae, S. pneumoniae, Chlamydophila pneumoniae, H. influenzae, influenza viruses, adenovirus, other respiratory viruses, Legionella pneumophila

✓ ***Streptococcus pneumonia & Haemophilus influenzae*** are a common cause of pneumonia at **all ages.**

✓ **Viral agents** are important cause of pneumonia in the **1st 5 yr** of age (beyond the neonatal period), especially in winter months.

C.M. Respiratory distress manifested as dyspnea, tachypnea, grunting, nasal flaring, retractions of the supraclavicular, intercostal, and subcostal areas, cyanosis, and tachycardia. Fatigability, anorexia, vomiting, & diarrhea may also occur.
Chest examination may reveal diminished breath sounds with scattered rhonchi & crackles in early stages. In later stage, there may be consolidation with dullness on percussion and further diminished breath sounds. The **liver** may seem enlarged due to downward displacement of the diaphragm by hyperinflated lungs

Abdominal distention may be present due to paralytic ileus or air swallowing & **abdominal pain** is common in lower lobe pneumonia, whereas upper lobe pneumonia may produce **nuchal rigidity**.

Differentiation between:	***Bacterial***	***Viral pneumonia:-***
Prodrome of URTI:	***Brief***	Several days
Onset:	***Abrupt***	***Gradual***
Fever:	***Higher +/_ chills***	***usually Lower***
Prominent feature of Resp distress:	***Dyspnea & cough***	***Tachypnea +/_ wheezes***
Pleuritic chest pain:	***usually Yes***	***usually No***
CNS features:	***Anxiety, delirium***	***usually No***
CXR:	***usually Lober consolidation***	***Hyperinflation with bilateral interstitial infiltrates***
WBC:	***↑ (mainly granulocytes)***	***N or ↑ (mainly lymphocytes)***
Definitive Dx:	***Gram stain or culture of lung or pleural fluid***	***Isolation of the virus from respiratory secretion by PCR, culture, or by serology***

Note:
✓ **Sputum** is of little value in diagnosis of pneumonia in young children.

✓ **Blood cultures** is +ve in only 10% of pneumococcal pneumonia.
✓ **Portable U/S** is highly sensitive and specific in diagnosing pneumonia in children by determining lung consolidations and air bronchograms or effusions.
✓ **Staphylococcal pneumonia** is usually severe & may be associated with pneumatoceles, empyema +/_ bronchopulmonary fistulas, it is common between 1-5 yr of age.
✓ ***Mycoplasma pneumonia & Chlamydophila pneumonia*** cause **"Atypical Pneumonia syndrome"** which characterized by extrapulmonary manifestations, low-grade fever, patchy diffuse infiltrates on CXR, -ve Gram stain sputum, & poor response to penicillin antibiotics.
Cx. It results from either local or systemic spread of infection.
Local spread of bacteria within the thoracic cavity → pleural effusion, empyema, or pericarditis. It is mainly caused by *S. aureus, S. pneumonia, & S. pyogenes***Systemic spread** (bacteremia) is rare & mainly caused *S. pneumonia & H. influenzae* → meningitis, suppurative arthritis, or osteomyelitis.

Rx.
 Patient who is mildly ill, can be managed as outpatient with oral antibiotics e.g. **Amoxicillin**, 40-50 mg/kg/day, but higher doses (80-90 mg) if penicillin-resistant pneumococci is suspected.
Alternative agents include **Amoxicillin/clavulanate** or **Cefuroxime axetil**.
If *M. pneumoniae* or *C. pneumonia* is suspected, give **Azithromycin** or **Fluoroquinolone**.
 Indications of hospitalization include: age <6 mo, severe respiratory distress, toxic appearance, requirement for supplemental oxygen, vomiting & dehydration, multiple lobe involvement on CXR, SCA with acute chest syndrome, immunodeficiency, pre-existing pulmonary or cardiac disease, no response to home therapy with oral antibiotics, & noncompliant parents.
For hospitalized patient give **oxygen, hydration, & parenteral antibiotics** e.g. **Cefotaxime** or **Ceftriaxone**. If staphylococcal pneumonia is suspected, give **Vancomycin** or **Clindamycin**.
 Oral zinc, 10-20 mg/day reduces mortality among children with clinically defined severe pneumonia.
Note: *If* ***viral pneumonia*** *is suspected, it is reasonable to* ***withhold antibiotics*** *especially if the patient is mildly ill. However, because* ***up to 30%*** *of patients may have coexisting bacterial pathogens, therefore if deterioration in clinical status occurs, this should signal the possibility*

of superimposed bacterial infection and ***antibiotic Rx should be initiated.***

Pg. Patient with **uncomplicated** community-acquired bacterial pneumonia usually responds to therapy with **improvement in clinical symptoms within 2-3 days** after initiation of antibiotics, whereas **radiographic** improvement may lag up to **1 mo**.

❖ ***Slowly Resolving Pneumonia*** means persistence of symptoms or radiographic abnormalities beyond the expected time course. Causes include:-

1. **Bacterial resistance**.
2. **Complications** e.g. empyema.
3. **Non-bacterial etiologies** e.g. viruses.
4. **Bronchial obstruction** e.g. FB, endobronchial lesions, or mucous plug.
5. **Non-infectious causes** e.g. food aspiration, hypersensitivity pneumonitis, bronchiolitis obliterans, or eosinophilic pneumonia.
6. **Pre-existing diseases** e.g. immunodeficiencies, ciliary dyskinesia, cystic fibrosis, pulmonary sequestration, or cystic adenomatoid malformation.

In these situations, repeating CXR +/_ CT, MRI of chest or Bronchoscopy may help in determining the reason for delay in response to Rx. Empyema can be determined by US or CT scan.

❖ ***Recurrent Pneumonia*** is defined as **≥** 2 episodes/yr or **≥** 3 episodes ever, with radiographic clearing between them. Causes include:-

1. **Hereditary** disorders e.g. CF, SCA.
2. **Immunity** disorders e.g. cellular, humoral or phagocytic disorders.
3. **Ciliary** disorders e.g. Kartagener syndrome.
4. **Anatomical** disorders e.g. GERD, FB, TEF (H type), sequestration, lobar emphysema, bronchietasis...etc.

Pv. Vaccination against *Strep. pneumoniae, H. influenza*, & influenza virus
is highly recommended to ↓ the incidence of pneumonia.

ASTHMA IN CHILDREN

Asthma is a **chronic inflammatory condition** of the lung airways resulting in episodic airflow obstruction due to airways hyper-responsiveness to a provocative exosures (triggers).

It is a **common chronic disease** that causing considerable morbidity & once asthma has developed; ongoing exposures appear to worsen the condition.

Et. Unknown, but may be due to **multifactorial** inheritance, i.e. a combination of environmental exposures and inherent biological and genetic vulnerabilities.

Triggers of asthma include:

Exercise; crying, laughter, hyperventilation; Common viral infections of the respiratory tract; Aeroallergens in sensitized asthmatics (animal dander, indoor allergens, dust mites, cockroaches, molds) ; Seasonal aeroallergens e.g. Pollens (trees, grasses, weeds); Environmental tobacco smoke, air pollutants, dust, occupational exposures, strong or noxious odors or fumes, & cold dry air.

Note: *the last two triggers usually produce bronchoconstriction only (without inflammation).*

Path. Hyper-responsiveness of the airways consist of bronchoconstriction of smooth muscles, infiltration of inflammatory cells (especially eosinophils) with release of inflammatory mediators e.g. cytokines that result in airway edema, there is also basement membrane thickening, subepithelial collagen deposition, smooth muscle and mucous gland hypertrophy, and mucus hypersecretion. All these factors cause inflammation & airflow obstruction as well as the aberrant repair of injured airways tissues are contribute to the pathogenesis of asthma.

There are 2 types of childhood asthma:-

1. *Recurrent Wheezing* of early childhood that primarily triggered by common viralRTI; it usually **disappear by 6 yr** of age

2. *Chronic (Persistent) Asthma* that persist into later childhood and often adulthood. It usually associated with the following risk factors:-

- ✓ **Parental asthma**.
- ✓ **Allergy** e.g. atopic dermatitis, allergic rhinitis, food allergy, or inhalant allergen sensitization.
- ✓ **Severe lower RTI** e.g. Pneumonia or Bronchiolitis.
- ✓ **Other factors** e.g. male gender, hx of low birthweight, wheezing apart from colds, female who develop obesity (or early onset puberty), environmental tobacco smoke exposure, or eosinophilia **≥** 4%.

❖ The above risk factors can be divided into major & minor criteria that help in the prediction of asthma:-

✓ ***Major Criteria*** include: **Parent asthma, Atopic eczema, & Inhalant allergen sensitization.**

✓ ***Minor Criteria*** include: Allergic rhinitis, Wheezing apart from colds, Food allergen sensitization, & Eosinophils ≥ 4%.

1 major or **2 minor** criteria provide a high prediction for persistent asthma into later childhood, as well as, **asthma severity between 7 & 10 yr** of age is also predictive of asthma persistence into adulthood; however, milder disease is more likely to remit.

C.M.

Hx. Intermittent dry coughing +/_ expiratory wheezing are the most common chronic symptoms of asthma.

Respiratory symptoms usually worse at night, whereas daytime symptoms are often linked with physical activities or play. It also characterized by dramatic response to the bronchodilators & corticosteroids therapy.

Ex. Expiratory wheezing and prolonged expiratory phase +/_ diminished breath sounds in some ares of lungs, especially right lower posterior lobe (which indicate airway obstruction). **Crackles** may be due to excessive mucus production and inflammatory exudates.

More severe airway obstruction → inspiratory and expiratory wheezing or **silent** chest

D.Dx. Viral bronchiolitis; Bronchiolitis obliterans; FB aspiration; GERD;
TEF; Vocal cord dysfunction; Exercise-induced laryngeal obstruction; Immune deficiency; Bronchopulmonary mycoses; Interstitial lung diseases; Cystic fibrosis; Laryngotracheo-bronchomalacia; Congestive HF with pulmonary edema…etc.

Inv.

 CXR may be **normal** or may show **hyperinflation** (flattening of the diaphragms with ↑ chest diameter in the PA & lateral view) with peribronchial thickening.

It should be done in the **1st attack of asthma** to exclude other pathologies and often unnecessary thereafter, unless there is **suspicion of Cxs** e.g. atelectasis, pneumothorax or pneumomediastinum.

 Pulmonary Function Tests are objective methods in measuring the degree of airflow obstruction. It shows an obstructive pattern of lung disease (which is not specific for asthma).

✓ ***Spirometry;*** it can measure FEV_{1SEC}, FVC, & FEV_1/FVC compared with the predicted norms based on gender, height, & ethnicity. It is only suitable for children >6 yr after taking the highest reading of 3 attempts.

FEV_1 60%-80% of the predicted value indicates moderate airway obstruction, whereas <60% indicates severe obstruction.

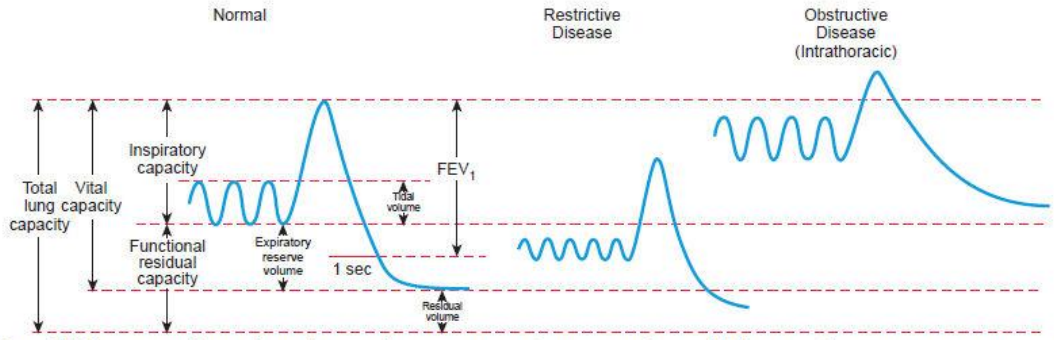

Figure 373-1 Spirogram showing lung volumes and capacities. FEV_1 is the maximum volume exhaled in 1 sec after maximum inspiration. Restrictive diseases are usually associated with decreased lung volumes and capacities. Intrathoracic airway obstruction is associated with air trapping and abnormally high functional residual capacity and residual volume. FEV_1 and vital capacity are decreased in both restrictive and obstructive diseases. The ratio of FEV_1 to vital capacity is normal in restrictive disease but decreased in obstructive disease. FEV, forced expiratory volume.

Bronchodilator response to an inhaled β-agonist is greater in asthmatics versus non-asthmatics with an improvement in FEV_1 ≥12%.

Note: *Bronchoprovocation challenges is rarely used nowadays.*

Exercise challenges (e.g. running for several min) can identify children with exercise-induced bronchospasm → worsening of FEV_1 >15%.

✓ ***Peak Expiratory Flow (PEF)*** monitoring devices provide a simple and inexpensive home use tool to measure airflow resistence; it can measure PEF variation during the day after comparison with the best personal (not the predicted) value, if >20% indicate significant obstruction. It is useful for those who are "poor perceivers" of their symptoms.

 Allergy Prick Skin Test is mainly used to assess sensitization to inhalant allergens which help in the prevention as well as prognosis of asthma. - 087 -

 Exhaled Nitric Oxide (FE_{NO}) measurement can be used as a marker of airway inflammation in asthma and also it help in titration of medications according to the degree of inflammation.

Rx. The following are **4 keys** for asthma management:-

1. **Asthma checkups;** follow-up of asthma should be every 2-4 wk until good control is achieved, then 2-4/yr to maintain good control.
2. **Control of factors contributing to asthma severity;** by control of asthma "triggers" & co-morbid conditions.
3. **Asthma pharmacotherapy;** it include long-term-control & quick-relief medications with step-up & step-down approach according to asthma severity.
4. **Patient education;** include a written material about daily medications (e.g. doses, SE, how to use inhalers) & the action plan for asthma exacerbations with teaching the patient how to use PEF device at home.

❖ ***Control of factors contributing to asthma severity:-***

 Eliminate or reduce problematic environmental exposures e.g. **allergens**, especially when Allergy Prick Skin Test is +ve; it also include avoidance of other airway **irritants** e.g. tobacco smoke; **annual influenza vaccination** is also necessary.

 Aspirin-exacerbated respiratory disease, or aspirin-induced asthma, is associated with chronic eosinophilic rhinitis and nasal polyposis. Inhibition of cyclooxygenase by aspirin and other NSAIS may → exacerbations of disease. Acetaminophen, a weak COX-1 inhibitor, is safe in low doses, but may produce symptoms in high doses. The incidence is rare in children <10 yr of age.

 Rx of co-morbid conditions e.g. **sinusitis & rhinitis** to ↓ exercise-induced bronchospasm because nasal breathing humidify and warm the inspired air with filtering out allergens and irritants.

Gastroesophageal reflux can worsen asthma by 2 mechanisms: 1st by aspiration of refluxed gastric contents & 2nd by "vagally-mediated" reflex bronchospasm. GERD should be suspected when asthma is difficult to control or aggravated by eating or sleeping. -088 -

❖ ***Long-Term Controller Medications:-***

 Inhaled Corticosteroids (ICS) e.g. Beclomethasone, Triamcinolone, Flunisolide, Fluticasone, Mometasone, & Budesonide. The last 3 drugs are considered "**2nd-generation**" due to ↑ anti-inflammatory potency and ↓ systemic bioavailability by extensive first-pass hepatic metabolism.

ICS can be delivered by 4 methods: **MDI** (Metered Dose Inhaler) which suitable for older children. **Spacer inhaler** is suitable for younger children because it does not need coordination. **DPI** (Dry Powder Inhaler) is breath-accuated. **Nebulizer** needs electricity. After ICS, mouth should be rinsed with water to ↓ SE e.g. & dysphonia.

Note: *ICS for children with persistent asthma does* ***not*** *alter the likelihood of outgrowing asthma in later childhood.*

 Long-acting Inhaled β-agonist (LABA) e.g. Salmeterol, it has prolonged onset of bronchodilator action (≈1 hr), whereas Formoterol has rapid onset (5–10 min); both have duration of action ≈12 hr, thus they used twice daily (usually in combination with ICS).

 Theophylline e.g. Aminophylline is also a bronchodilator with anti- inflammatory properties as a phosphodiesterase inhibitor, but it is no longer considered a first-line agent in young children because of its narrow therapeutic window, many drug interactions, & significant variability in the absorption and metabolism necessitating frequent dose monitoring; thus it is better used only for children >5 yr.
SE; Headache, vomiting, seizures, cardiac arrhythmias, & death!.

 NSAI agents e.g. Cromolyn and Nedocromil can inhibit exercise-induced bronchospasm, thus can replace SABA before exercise. These drugs have usually no SE, but should be used frequently (2-4 times/day).

 Leukotriene-modifying agents; e.g. Montelukast (approved for children ≥1 yr), Zafirlukast (≥5 yr) & Zileuton (≥12 yr). These drugs have broncho-dilator & targeted anti-inflammatory properties with very few SE.

 Anti-IgE (Omalizumab); it is a monoclonal antibody that binds IgE to prevent its binding to the high-affinity IgE receptor, thus blocking the IgE-mediated allergic responses and inflammation. It mainly used in patients >12 yr with moderate to severe allergic asthma as "add-on" - 089 -
therapy because it may cause severe anaphylaxis. Anti-Interleukine-5 (Mepolizumab) is monoclonal antibody recently added for Rx of asthma.

❖ ***Quick-Reliever (Rescue) Medications:-***

 Short-acting Inhaled β-agonists (SABA) e.g. Albuterol, Terbutaline, Pirbuterol, & Levalbuterol (which causes less tachycardia and tremor).
They have a rapid onset of action that last for 4–6 hr.

 Systemic Corticosteroids e.g. Prednisone, Prednisolone, or Methyl- prednisolone orally as short-course "burst" that mainly used for severe asthma exacerbations & sometimes for severe persistent asthma (because ICS are ineffective when there is severe airflow obstruction).
Their usual dose 1-2 mg/kg/day (max. 60 mg/day) orally as a single dose in the morning for 3-10 days, with tapering if administered for

>7 days. They usually absorbed rapidly and completely from the gut after 1- 2 hr.
Corticosteroids have many drug interactions e.g. Anticonvulsants & Rifampin ↓ their plasma concentration, whereas they ↑ with Macrolides & Ketoconazole.
Long-term use of systemic corticosteroids (or high-dose ICS) needs **monitoring of their SE** as in the following:-
CBP (neutrophilia & lymphopenia), **serum electrolytes** (hypokalemia & hypocalcemia), blood **sugar** (hyperglycemia), **BP** (hypertension), **weight** (gain), **height** (↓ especially in the 1st years after therapy), **bone age** by X- ray & DEXA (osteoporosis) & annual **eye** exam (cataract & glaucoma). Corticosteroids also can ↓ **immunity** & ↑ susceptibility to infectious diseases & **mask** the signs of inflammation.
Corticosteroids must never be stopped suddenly after long-term use because of the risk of **acute adrenal insufficiency** (which can be fatal). Double or triple the dose during physiologic stressors e.g. surgery, accident, or significant illness.
 Inhaled Anticholinergic agents e.g. Ipratropium bromide are mainly used in combination with SABA in acute severe asthma for children >12 yr; they have bronchodilator effect & ↓ mucus production. - 091 -

❖ ***Stepwise Approach in Asthma Management:-***

Step 1: **Mild Intermittent Asthma:** ≤2 day symp/wk or ≤2 night symp/mo. Rx. **Resque** medications only **without** daily controller Rx.
Step 2: **Mild Persistent Asthma:** >2 day symp/wk or >2 night symp/mo. Rx. Daily controller therapy by **only one** of following: low-dose ICS, NSAI agents, Leukotrine modifiers, or sustain-released Theophyllin.
Step 3: **Moderate Persistent Asthma:** daily symp or >1 night symp/wk.
Rx. Low-dose ICS + LABA (or Leukotrine modifiers or Theophyllin), or
Medium-dose ICS +/_ the above medications.
Step 4: **Severe Persistent Asthma:** continuous daily symp or frequent night symp. Rx. High-dose ICS + LABA +/_ Systemic corticosteroids.

Notes on the approach:-

 Quick-Reliever (Rescue) Medications can be used at any step when there is severe asthma exacerbations by: SABA (by inhalation or orally) +/_ Systemic corticosteroids (IV or orally). *See also Rx of severe asthma exacerbation.*

 There is recent classification of asthma management consist of 6 steps, but it has been disregarded because it is so complicated.
 Recently patients are classified according to their response to Rx into 3 groups: Well-controlled, Not well-controlled, & Very poorly controlled.
 The classification of asthma severity is depend on the most severe symptoms before Rx.
 In children >5 yr, asthma severity is also depend on FEV_1, PEF & PEF variability.
 Before step-up therapy, review patient medication technique, adherence, and environmental control.
 Step-down medications when there is a good control of asthma during the regular visits by ↓ the dose or frequency of medications. - 090 -

❖ ***Written action plan for home monitoring:-***

It should be used in all children with asthma for early recognition of asthma exacerbations to intensify Rx & prevent further deterioration; thus it can ↓ risk of asthma death by 70%.
Written Action Plan is divided into 3 zones according to the PEF (% of personal best) as follows:-
 Green zone: PEF >80% mean patient has a good control.
 Yellow zone: PEF 80-50% mean patient has a fair control but should use SABA (which can be repeated every 20 min), if no improvement, patient can take short course of oral corticosteroids or call his doctor.
 Red zone: PEF <50% mean patient has a poor control which necessitate immediate medical attention.

Note: *Patient who experiences a life-threatening asthma exacerbation, should have injectable epinephrine & portable oxygen at home.* - 092 -

SEVERE ASTHMA EXACERBATION (Status Asthmaticus)

❖ ***Risk factors*** for SAE include:-
 Biological e.g. Previous attacks, Severe airflow obstruction, Hx of rapidly occurring attacks, Increasing and large diurnal variation on PEF, Poor perception of dyspnea, Poor response to systemic corticosteroids, Male gender, & Low birthweight.
 Environmental e.g. Allergen exposure, Environmental tobacco smoke or air pollution exposure, & Urban environment.
 Economic & Psychosocial e.g. Poverty, Crowding, Young or uneducated mother, Inadequate or inaccessible medical care, & Family problems.

SAE can be **aborted by the quick-relief medications** (as mentioned in the yellow zone of action plan), but beware of frequent use of SABA when the airways are obstructed as this may → **vicious cycle**, because SABA may → ↑ pulmonary blood flow through obstructed unoxygenated areas of lung → more hypoxia → more bronchoconstriction → **ventilation- perfusion mismatch**.
Note: *Some patients who rely on the frequent use of SABAs as a "quick fix" without controller medications, i.e. consume >1 MDI/mo or >3 MDIs/yr; this indicate poor asthma control with ↑ risk of death.*
C.M. Dyspnea, tachypnea, retractions, use of accessory muscles, cyanosis, mental status changes, tripod sitting with inablility to talk, poor air exchange (or silent chest)**, tachycardia** (or bradycardia due to severe hypoxia)**, pulsus paradoxus** (may be absent due to respiratory muscle fatigue). **Dehydration** may occur due to poor oral intake & tachypnea → ↑ insensible water loss, although some patients may develop **SIADH**.
If the onset is **rapid**, it may dissolve rapidly with Rx, whereas if it progress **insidiously**, i.e. over days or weeks, it can cause resp muscle fatigue with respiratory failure which need mechanical ventilation.
PEF or FEV_1 in SAE usually **<50%** of personal best & oxymeter usually show severe **hypoxia** (<90%).
Inv.
- **CXR** may show Cxs e.g. atelectasis or air leak.
- **CBP** & serum electrolytes may be abnormal. - 093 -
- **BGA;** initially there may be **resp. alkalosis** (due to hyperventilation), then followed by **resp. acidosis** (due to hypoventilation by airway obstruction) +/_ **metabolic acidosis** (due to lactic acidosis by hypoxia).

Note: *Normal $PaCO_2$ at presentation is **ominous** sign of impending resp failure.*
Rx. Patient is better managed in the **ICU** with continuous cardiorespiratory monitoring with the following Rx:-
1. **Oxygen therapy** (maintain O_2 saturation >92%).
2. **Inhaled SABA** (can be repeated every 20 min).
3. **Systemic corticosteroids** as short-course (orally or parentrally).

If the above Rx fails to control the attack, consider the following:-
4. **Inhaled Ipratropium bromide** (usually mixed with SABA).
5. **Adrenalin** SC or IM (0.01 mg/kg).
6. **Terbutaline** infusion (with cardiorespiratory monitoring).
7. **Other medications** e.g. Aminophylline infusion, $MgSO_4$, or Heliox.

8. **Mechanical ventilation** for extreme cases with impending respiratory failure, especially when the patient develop ***Hopkins syndrome***, a rare synd due to idiopathic asthma-associated flaccid paralysis.

Note: *Chest physiotherapy & mucolytics are* ***not*** *recommended in SAE.*

Patient can safely **discharged** from hospital when there is a sustained improvement of symptoms, normal physical finding, PEF >70%, and O_2 saturation >92% (on room air for 4 hr).

Patient can be discharged on the same **rescue** medications, i.e. SABA & short-course oral corticosteroids. **Review** other controller medications & optimize them as needed and also advise on good home **monitoring**.

Pg. Recurrent coughing and wheezing occurs in **35% of pre-school age**

children; of these, **2/3 improve** on their own through the preteen years, whereas **1/3 continue** to have persistent asthma into later childhood.

Pv. Several **non-pharmaco-therapeutic measures** are supposed to prevent asthma e.g. avoidance of tobacco smoke (beginning prenatally!), prolonged breastfeeding (>4 mo), healthy diet, and active lifestyle.

Children who live in **rural** areas have low prevalence of asthma than those live in urban area, this has been attributed to the ***"Hygiene hypothesis"***.