بسم الله الرحمن الرحيم

TREATMENT OF ASTHMA

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- The treatment of asthma is straightforward, with the majority of patients now managed by internists and family doctors with effective and safe therapies.

TABLE 281-2 Aims of Asthma Therapy

- Minimal (ideally no) chronic symptoms, including nocturnal
- Minimal (infrequent) exacerbations
- No emergency visits
- Minimal (ideally no) use of a required β_2-agonist
- No limitations on activities, including exercise
- Peak expiratory flow circadian variation <20%
- (Near) normal PEF
- Minimal (or no) adverse effects from medicine

Abbreviation: PEF, peak expiratory flow.

- The main drugs for asthma:
- **bronchodilators**, which give rapid relief of symptoms mainly through relaxation of airway smooth muscle
- **controllers**, which inhibit the underlying inflammatory process.

BRONCHODILATOR THERAPIES

- Bronchodilators act primarily on airway smooth muscle to reverse the bronchoconstriction of asthma
- This gives rapid relief of symptoms but has little or no effect on the underlying inflammatory process. Thus, bronchodilators are not sufficient to control asthma in patients with persistent symptoms.
- There are three classes of bronchodilator in current use:
- B2-adrenergic agonists, anticholinergics, and theophylline; of these, B2-agonists are by far the most effective.

β2-Agonists

- β2-Agonists activate β2-adrenergic receptors, which are widely expressed in the airways.
- β2-Receptors are coupled through a stimulatory G protein to adenylyl cyclase, resulting in increased intracellular cyclic adenosine monophosphate (AMP), which relaxes smooth muscle cells and inhibits certain inflammatory cells, particularly mast cells.

◦ Mode of Action:

- The primary action of β2-agonists is to relax airway smooth-muscle cells of all airways, where they act as functional antagonists, reversing and preventing contraction of airway smooth-muscle cells by all known bronchoconstrictors. This generalized action is likely to account for their great efficacy as bronchodilators in asthma.
- There are also additional non-bronchodilator effects that may be clinically useful, including inhibition of mast cell mediator release, reduction in plasma exudation, and inhibition of sensory nerve activation.
- Inflammatory cells express small numbers of β2-receptors, but these are rapidly down-regulated with β2-agonist activation so that, in contrast to corticosteroids, there are no effects on inflammatory cells in the airways and there is no reduction in AHR.

- Clinical Use
- β2-Agonists are usually given by inhalation to reduce side effects.
- SABA, such as albuterol and terbutaline, have a duration of action of 3–6 h. They have a rapid onset of bronchodilatation and are, therefore, used as needed for symptom relief (relievers).
- Increased use of SABA indicates that asthma is not controlled.
- They are also useful in preventing EIA if taken prior to exercise.
- SABA are used in high doses by nebulizer or via a metered-dose inhaler (MDI) with a spacer.
- Long-acting β2-agonists (LABA) include salmeterol and formoterol, both of which have a duration of action over 12 h and are given twice daily by inhalation; and indacaterol, olodaterol, and vilanterol, which are given once daily.

- LABA have replaced the regular use of SABA
- **LABA should not be given in the absence of ICS therapy** as they do not control the underlying inflammation.
- They do, however, improve asthma control and reduce exacerbations when added to ICS, which allows asthma to be managed with lower doses of corticosteroids.
- This observation has led to the widespread use of fixed combination inhalers that contain a corticosteroid and a LABA, which have proved to be highly effective in the control of asthma and prevention of exacerbations.

- **Side Effects**
- Adverse effects are not usually a problem with β2- agonists when given by inhalation.
- The most common side effects are **muscle tremor** and **palpitations**, which are seen more commonly in **elderly** patients.
- There is a **small fall in plasma potassium** due to increased uptake by skeletal muscle cells, but this effect does not usually cause any clinical problem.

- ## Tolerance
- Tolerance is a potential problem with any agonist given chronically, but while there is down-regulation of β2-receptors, this does not reduce the bronchodilator response as there is a large receptor reserve in airway smooth-muscle cells.
- By contrast, mast cells become rapidly tolerant, but their tolerance may be prevented by concomitant administration of ICS.

- **Safety**
- The safety of β_2-agonists has been an important issue.
- There is an association between asthma mortality and the amount of SABA used, but careful analysis demonstrates that the increased use of rescue SABA reflects poor asthma control, which is a risk factor for asthma death.
- The slight excess in mortality that has been associated with the use of LABA is related to the lack of use of concomitant ICS, as the LABA therapy fails to suppress the underlying inflammation.
- This highlights the importance of always using an ICS when LABAs are given, which is most conveniently achieved by using a combination inhaler.
- Recent large safety studies have shown no adverse effects of LABA in adults or children.

Anticholinergics

- **Muscarinic receptor antagonists**, such as ipratropium bromide, prevent cholinergic nerve-induced bronchoconstriction and mucus secretion.
- They are less effective than β2-agonists in asthma therapy as they inhibit only the cholinergic reflex component of bronchoconstriction, whereas β2-agonists prevent all bronchoconstrictor mechanisms.
- **Long-acting muscarinic antagonists (LAMA),** including tiotropium bromide or glycopyrronium bromide, may be used as an additional bronchodilator in patients with asthma that is not controlled by maximal doses of ICS-LABA combinations, and improve lung function and further reduce exacerbations.

- High doses of short-acting anticholinergics may be given by nebulizer in treating acute severe asthma but **should only be given following β2-agonists**, as they have a slower onset of bronchodilation.
- **Side effects**
- are not usually a problem as there is little or no systemic absorption. The most common side effect is **dry mouth**; in elderly patients, **urinary retention** and **glaucoma** may also be observed.

Theophylline

- Theophylline was widely prescribed as an oral bronchodilator several years ago, especially as it was **inexpensive.**
- It has now fallen out of favor as **side effects are common**, and inhaled β2-agonists are much more effective as bronchodilators.
- The bronchodilator effect is due to **inhibition of phosphodiesterases in airway smooth-muscle cells**, which increases cyclic AMP, but doses required for bronchodilatation commonly cause side effects that are mediated mainly by phosphodiesterase inhibition.

- There is increasing evidence that theophylline at lower doses has anti-inflammatory effects, and these are likely to be mediated through different molecular mechanisms.
- Theophylline activates the key nuclear enzyme histone deacetylase-2 (HDAC2), which is a critical mechanism for switching off activated inflammatory genes and may therefore reduce corticosteroid insensitivity in severe asthma.

- Clinical Use
- Oral theophylline is usually given as a slow-release preparation once or twice daily as this gives more stable plasma concentrations than normal theophylline tablets.
- It may be used as an additional bronchodilator in patients with severe asthma when plasma concentrations of 10–20 mg/L are required, although these concentrations are often associated with side effects.
- Low doses of theophylline, giving plasma concentrations of 5–10 mg/L, have additive effects to ICS and are particularly useful in patients with severe asthma.
- Indeed, withdrawal of theophylline from these patients may result in marked deterioration in asthma control. At low doses, the drug is well tolerated.

- **IV aminophylline** (a soluble salt of theophylline) was used for the treatment of severe asthma but has now been largely replaced by high doses of inhaled SABA, which are more effective and have fewer side effects.
- Aminophylline is occasionally used (via slow IV infusion) in patients with severe exacerbations that are refractory to SABA.

- **Side Effects**
- Oral theophylline is well absorbed and is largely inactivated in the liver.
- Side effects are related to **plasma concentrations**; measurement of plasma theophylline may be useful in determining the correct dose.
- The most common side effects are **nausea, vomiting**, and **headaches** and are due to phosphodiesterase inhibition.
- **Diuresis** and **palpitations** may also occur, and at high concentrations **cardiac arrhythmias**, **epileptic seizures**, and **death** may occur due to adenosine A1-receptor antagonism.
- Theophylline side effects are related to plasma concentration and are rarely observed at plasma concentrations <10 mg/L.

- Theophylline is metabolized by CYP450 (CYP1A2) in the liver, and, thus, plasma concentrations may be elevated by drugs that block CYP450 such as **erythromycin** and **allopurinol**.
- Other drugs may also reduce clearance by other mechanisms leading to increased plasma concentrations

TABLE 281-3 Factors Affecting Clearance of Theophylline

Increased Clearance
• Enzyme induction (rifampicin, phenobarbitone, ethanol)
• Smoking (tobacco, marijuana)
• High-protein, low-carbohydrate diet
• Barbecued meat
• Childhood
Decreased Clearance
• Enzyme inhibition (cimetidine, erythromycin, ciprofloxacin, allopurinol, zafirlukast)
• Congestive heart failure
• Liver disease
• Pneumonia
• Viral infection and vaccination
• High carbohydrate diet
• Old age

CONTROLLER THERAPIES

Inhaled Corticosteroids

- ICS are by far the most effective controllers for asthma, and their early use has revolutionized asthma therapy.
- Mode of Action
- ICS are the most effective anti-inflammatory agents used in asthma therapy, **reducing inflammatory cell numbers and their activation** in the airways.
- ICS **reduce eosinophils** in the airways and sputum, and numbers of **activated T lymphocytes** and **surface mast cells** in the airway mucosa.
- These effects may account for the reduction in AHR that is seen with chronic ICS therapy.

- The molecular mechanism of action of corticosteroids involves several effects on the inflammatory process.
- The major effect of corticosteroids is to **switch off the transcription of multiple activated genes that encode inflammatory proteins** such as cytokines, chemokines, adhesion molecules, and inflammatory enzymes.
- Corticosteroids also activate anti-inflammatory genes such as mitogen-activated protein (MAP) kinase phosphatase-1, and **increase the expression of β2-receptors.**

- Clinical Use
- ICS are by far the **most effective controllers in the management of asthma** and are **beneficial in treating asthma of any severity and age**.
- ICS are usually given **twice daily,** but some may be effective **once daily in mildly symptomatic patients**.
- ICS rapidly **improve the symptoms of asthma**, and **lung function** improves over several days.
- They are effective in **preventing asthma symptoms**, such as **EIA and nocturnal exacerbations**, but also prevent severe exacerbations.

- ICS **reduce AHR**, but maximal improvement may take **several months of therapy**.
- **Early treatment** with ICS appears to **prevent irreversible changes in airway function** that occur with chronic asthma.
- Withdrawal of ICS results in slow deterioration of asthma control, indicating that they suppress inflammation and symptoms, but do not cure the underlying condition.
- ICS are now given as **first-line therapy for patients with persistent asthma**, but if they do not control symptoms at low doses, it is usual to add a LABA as the next step.

- Side Effects
- Local side effects include **hoarseness** (dysphonia) and **oral candid**iasis, which may be reduced with the use of a large volume spacer device.
- There has been concern about **systemic side effects** from lung absorption, but many studies have demonstrated that ICS have minimal systemic effects.
- At the highest recommended doses, there may be some **suppression of plasma and urinary cortisol concentrations**, but there is no convincing evidence that long-term treatment leads to impaired growth in children or to osteoporosis in adults.
- Indeed effective control of asthma with ICS reduces the number of courses of OCS that are needed and, thus, reduces systemic exposure to ICS.

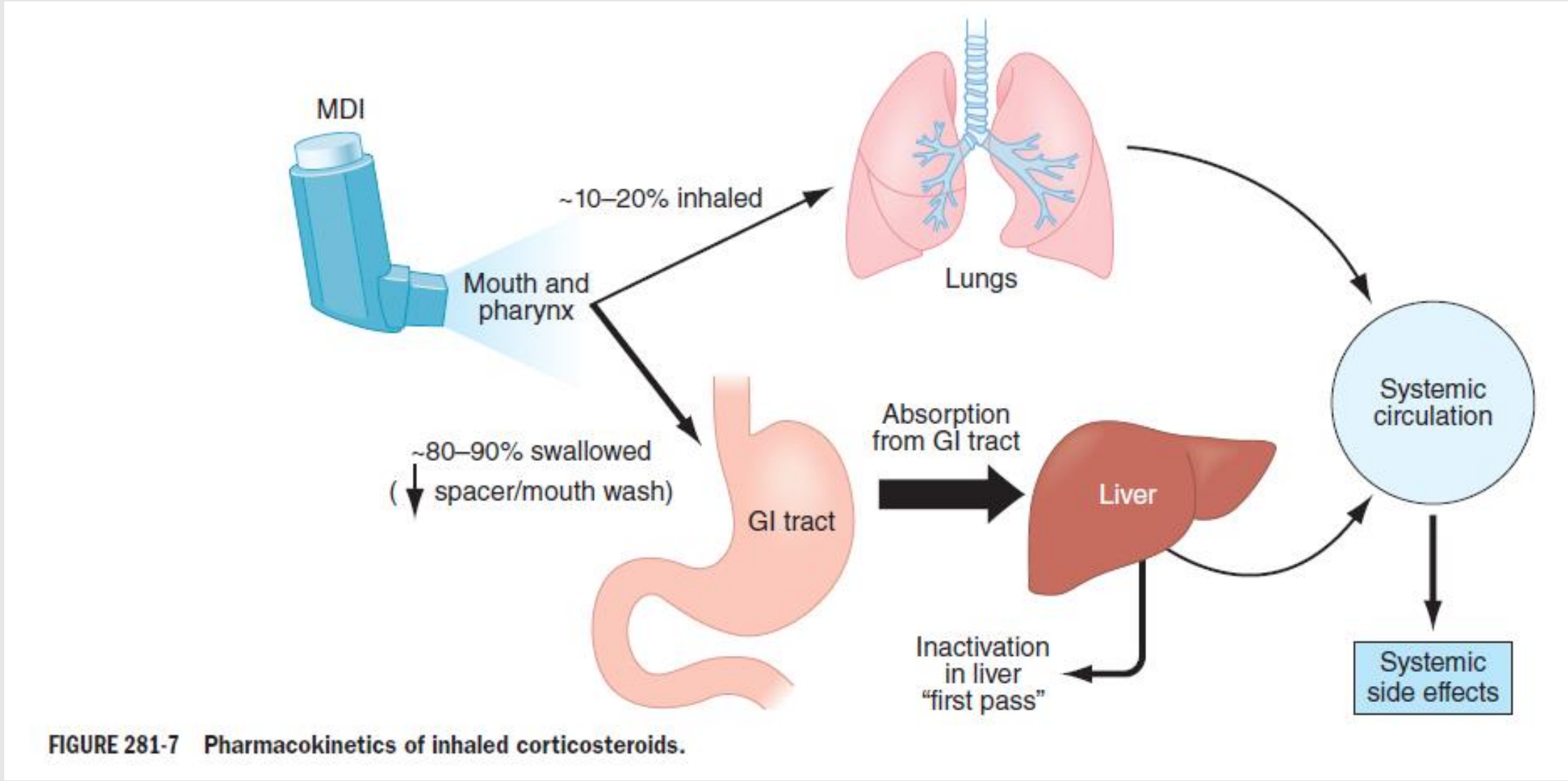

FIGURE 281-7 Pharmacokinetics of inhaled corticosteroids.

Systemic Corticosteroids

- Corticosteroids are used intravenously (hydrocortisone or methylprednisolone) for the treatment of acute severe asthma, although several studies now show that OCS are as effective and easier to administer.
- A course of OCS (usually prednisone or prednisolone 30–45 mg once daily for 5–10 days) is used to treat acute exacerbations of asthma; no tapering of the dose is needed.
- Approximately 1% of asthma patients may require maintenance treatment with OCS; the lowest dose necessary to maintain control needs to be determined.
- Systemic side effects, including truncal obesity, bruising, osteoporosis, diabetes, hypertension, gastric ulceration, proximal myopathy, depression, and cataracts, may be a major problem, and steroid-sparing therapies may be considered if side effects are a significant problem.

- If patients require maintenance treatment with OCS, it is important to **monitor bone density** so that **preventive treatment with bisphosphonates or estrogen in postmenopausal women** may be initiated if bone density is low.
- **Intramuscular triamcinolone** acetonide is a depot preparation that is occasionally used in noncompliant patients, but proximal myopathy is a major problem with this therapy.

Antileukotrienes

- Cysteinyl-leukotrienes are **potent bronchoconstrictors**; they cause **microvascular leakage** and **increase eosinophilic inflammation** through the activation of cys-LT1-receptors.
- These inflammatory mediators are produced predominantly by mast cells and, to a lesser extent, eosinophils in asthma.

- Antileukotrienes, such as **montelukast** and **zafirlukast**, block cys-LT1-receptors and provide **modest clinical benefit** in asthma.
- They **are less effective than ICS** in controlling asthma and have less effect on airway inflammation, but are **useful as an add-on therapy in some patients not controlled with low doses of ICS**, although less effective than a LABA.
- They are given **orally once or twice daily** and are well tolerated.
- Some patients show a better response than others to antileukotrienes, but this has not been convincingly linked to any genomic differences in the leukotriene pathway.

Cromones

- **Cromolyn sodium** and **nedocromil sodium** are asthma controller drugs that appear to **inhibit mast cell and sensory nerve activation**

➢ therefore, **effective in blocking trigger-induced asthma such as** EIA **and** allergen- and sulfur dioxide-induced symptoms.

- Cromones have relatively **little benefit in the long-term control of asthma** due to their **short duration of action** (at least **four times daily** by inhalation).
- They are **very safe** and were **popular in the treatment of childhood asthma**, although **now low doses of ICS are preferred** as they are far more effective and have a proven safety profile.

Steroid-Sparing Therapies

- Various immunomodulatory treatments have been used to reduce the requirement for OCS in patients with severe asthma, who have serious side effects with this therapy.
- Methotrexate, cyclosporin A, azathioprine, gold, and IV gamma globulin have all been used as steroid-sparing therapies, but ***none of these treatments has any long-term benefit*** and each is associated with a relatively high risk of side effects.

Anti-IgE

- Omalizumab is a blocking antibody that **neutralizes circulating IgE** without binding to cell-bound IgE and, thus, **inhibits IgE-mediated reactions**.
- This treatment has been shown to **reduce the number of exacerbations in patients with severe asthma** and may improve asthma control.
- However, the treatment is **very expensive** and is only suitable for highly selected patients who are **not controlled on maximal doses of inhaler therapy and have a circulating IgE within a specified range**.
- Patients should be given a **3- to 4-month** trial of therapy to show objective benefit.
- Omalizumab is usually given as a **subcutaneous injection every 2–4 weeks** and appears not to have significant side effects, although anaphylaxis is very occasionally seen.

Anti-IL-5

- Antibodies that block IL-5 (**mepolizumab, reslizumab**) or its receptor (**benralizumab**) markedly **reduce blood and tissue eosinophils** and **reduce exacerbations** in patients who have persistently increased sputum eosinophils despite maximal ICS therapy.

Immunotherapy

- Specific immunotherapy using injected **extracts of pollens or house dust mites** has **not been very effective in controlling asthma and may cause anaphylaxis**.
- Side effects may be reduced by sublingual dosing.
- **It is not recommended** in most asthma treatment guidelines because of lack of evidence of clinical efficacy and potential anaphylaxis.

Alternative Therapies

- Nonpharmacologic treatments, including hypnosis, acupuncture, chiropraxis, breathing control, yoga, and speleotherapy, may be popular with some patients.
- However, placebo-controlled studies have shown that each of these treatments lacks efficacy and cannot be recommended.
- However, they are not detrimental and may be used as long as conventional pharmacologic therapy is continued.

Bronchial Thermoplasty

- Bronchial thermoplasty is a bronchoscopic treatment using thermal energy to **ablate airway smooth muscle** in accessible bronchi.
- It may **reduce exacerbations** and **improve asthma control in highly selected patients not controlled on maximal inhaler therapy**, particularly when there is no increase in inflammation.

MANAGEMENT OF CHRONIC ASTHMA

- It is important to establish the diagnosis objectively using **spirometry or PEF measurements at home**.
- Triggers that worsen asthma control, such as **allergens** or **occupational agents**, should be avoided,
- Triggers, such as **exercise** and **fog**, which result in transient symptoms, provide an indication that more controller therapy is needed.
- It is important to assess asthma control, assessed by **symptoms**, **night awakening**, **need for reliever inhalers**, **limitation of activity** and **lung function**.
- Avoidance of side effects and expense of medications are also important.
- There are several validated questionnaires for quantifying asthma control, such as the Asthma Quality of Life Questionnaire (AQLQ) and Asthma Control Test (ACT).

TABLE 281-4 Asthma Control

CHARACTERISTIC	CONTROLLED (ALL OF FOLLOWING)	PARTLY CONTROLLED	UNCONTROLLED
Daytime symptoms	None (≤2/week)	>2/week	Three of more features of partly controlled
Limitation of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for reliever/ rescue treatment	None (≤2/week)	>2/week	
Lung function (PEF or FEV_1)	Normal	<80% predicted or personal best (if known)	

Stepwise Therapy

- For patients with mild, intermittent asthma, a SABA is all that is required
- Use of a reliever medication more than twice a week indicates the need for regular controller therapy.
- The treatment of choice for all patients is an ICS given twice daily. It is usual to start with an intermediate dose (e.g., 200 [µg] bid of [beclomethasone dipropionate] BDP) or equivalent and to decrease the dose if symptoms are controlled after three months.
- If symptoms are not controlled, a LABA should be added, which is most conveniently given by switching to a combination inhaler.
- The dose of controller should be adjusted accordingly, as judged by the need for a rescue inhaler.

- **Low doses of theophylline** or an **antileukotriene** may also be considered as an add-on therapy, but these are less effective than LABA.
- In patients with **severe asthma**, **low-dose oral theophylline** is also helpful
- when there is **irreversible airway narrowing, the long-acting anticholinergic** may be tried.
- If asthma is not controlled despite the maximal recommended dose of inhaled therapy, it is **important to check adherence and inhaler technique.**

- In these patients, maintenance treatment with an **OCS** may be needed and the **lowest dose that maintains control should be used**.
- Occasionally **omalizumab** and **anti-IL-5** may be tried in steroid-dependent asthmatics who are not well controlled.
- Once asthma is controlled, it is important to slowly decrease therapy in order to find the optimal dose to control symptoms.

Education

- Patients with asthma need to understand **how to use their medications** and the **difference between reliever and controller therapies.**
- Education may improve adherence, particularly with ICS.
- **All patients should be taught how to use their inhalers correctly**.
- In particular, they need to understand how to recognize worsening of asthma and how to step up therapy accordingly. Written action plans have been shown to reduce hospital admissions and morbidity rates in adults and children, and are recommended particularly in patients with unstable disease who have frequent exacerbations.

ACUTE SEVERE ASTHMA

- Exacerbations of asthma are feared by patients and may be life threatening.
- One of the main aims of controller therapy is to prevent exacerbations; in this respect, **ICS and combination inhalers are very effective.**

Clinical Features of ACUTE SEVERE ASTHMA

- Patients are aware of **increasing chest tightness, wheezing**, and **dyspnea** that are often not or poorly relieved by their usual reliever inhaler.
- In severe exacerbations patients may be so **breathless** that they are **unable to complete sentences** and may become **cyanotic**.
- Examination usually shows **increased ventilation, hyperinflation**, and **tachycardia**.
- **Pulsus paradoxus** may be present, but this is rarely a useful clinical sign.

- There is a **marked fall in spirometric values and PEF**.
- Arterial blood gases on air show **hypoxemia**, and **PCO2 is usually low** due to hyperventilation.
- **A normal or rising PCO2 is an indication of impending respiratory failure** and requires immediate monitoring and therapy.
- **A chest roentgenogram is not usually informative**, but may show pneumonia or pneumothorax.

TREATMENT of ACUTE SEVERE ASTHMA

- A high concentration of oxygen should be given by face mask to achieve oxygen saturation of >90%.
- The mainstay of treatment are high doses of SABA given either by nebulizer or via a MDI with a spacer.
- In severely ill patients with impending respiratory failure, IV β2-agonists may be given.
- A nebulized anticholinergic may be added if there is not a satisfactory response to β2-agonists alone, as there are additive effects.
- In patients who are refractory to inhaled therapies, a slow infusion of aminophylline may be effective, but it is important to monitor blood levels, especially if patients have already been treated with oral theophylline.

- **Magnesium sulfate** given **intravenously or by nebulizer** is effective when **added to inhaled β2-agonists**, and is relatively well tolerated but is **not routinely recommended**.
- **Prophylactic intubation** may be indicated for **impending respiratory failure**, **when the PCO2 is normal or rises.**
- For patients with respiratory failure, it is necessary to intubate and institute ventilation. **These patients may benefit from a general anesthetic**, such as halothane, if they have not responded to conventional bronchodilators.
- **Sedatives should never be given as they may depress ventilation**.
- **Antibiotics should not be used routinely** unless there are signs of pneumonia.

SPECIAL CONSIDERATIONS

- Refractory Asthma
- check adherence to therapy and inhaler technique.
- Some of these patients will require maintenance treatment with OCS
- investigate and correct any mechanisms that may be aggravating asthma

- There are two major patterns of difficult asthma:

1) some patients have **persistent symptoms and poor lung function**, despite appropriate therapy,
2) others may have normal or near normal lung function but **intermittent, severe (sometimes life-threatening) exacerbations.**

- MECHANISMS of Refractory Asthma
- The most common reason for poor control of asthma is poor adherence with medication, particularly ICS
- Adherence with ICS is difficult to monitor as there are no useful plasma measurements that can be made but measuring FENO may identify the problem.
- Compliance may be improved by giving the ICS as a combination with a LABA that gives symptom relief.

- There are several factors that may make asthma more difficult to control, including **exposure to high, ambient levels of allergens or unidentified occupational agents**.
- **Severe rhinosinusitis** may make asthma more difficult to control; upper airway disease should be vigorously treated.
- Drugs such as **beta adrenergic blockers**, **aspirin**, and **other cyclooxygenase (COX) inhibitors** may worsen asthma.
- Some women develop **severe premenstrual worsening of asthma**, which is unresponsive to corticosteroids and **requires treatment with progesterone or gonadotropin-releasing factors**.
- Few systemic diseases make asthma more difficult to control, but **hyper- and hypothyroidism** may increase asthma symptoms and should be investigated if suspected.

Corticosteroid-Resistant Asthma

- Complete resistance to corticosteroids is extremely uncommon and affects <1 in 1000 patients.
- It is defined by a failure to respond to a high dose of oral prednisone/prednisolone (40 mg once daily over 2 weeks), ideally with a 2-week run-in with matched placebo.
- More common is reduced responsiveness to corticosteroids where control of asthma requires OCS (corticosteroid-dependent asthma).

Brittle Asthma

- Some patients show chaotic variations in lung function despite taking appropriate therapy.
- Some show a persistent pattern of variability and may require OCS or, at times, continuous infusion of β2-agonists (type I brittle asthma),
- others have generally normal or near-normal lung function but precipitous, unpredictable falls in lung function that may result in death (type 2 brittle asthma).

➢ These latter patients are difficult to manage as they **do not respond well to corticosteroids**, and the **worsening of asthma does not reverse well with inhaled bronchodilators**.

➢ The most effective therapy is **subcutaneous epinephrine**, which suggests that the worsening is likely to be a localized airway anaphylactic reaction with edema.

➢ In some of these patients, there may be allergy to specific foods.

TREATMENT of Refractory Asthma

- It is important to check adherence and the correct use of inhalers and to identify and eliminate any underlying triggers.
- **Low doses of theophylline** may be helpful in some patients, and theophylline withdrawal has been found to worsen in many patients.
- Many of these patients will require **maintenance treatment with OCS**, and the minimal dose that achieves satisfactory control should be determined by careful dose titration.
- Steroid-sparing therapies are rarely effective.
- In some patients with **allergic asthma, omalizumab** is effective, particularly when there are frequent exacerbations.

Aspirin-Sensitive Asthma

- A small proportion (1–5%) of asthmatics become worse with **aspirin and other COX inhibitors**, although this is much more commonly seen in severe cases and in those patients with frequent hospital admission.
- Aspirin-sensitive asthma is a well defined phenotype of asthma that is usually preceded by **perennial rhinitis** and **nasal polyps** in **nonatopic** patients with a **late onset of the disease**.
- Aspirin, even in small doses, characteristically provokes **rhinorrhea, conjunctival injection, facial flushing, and wheezing.**
- **Selective COX2 inhibitors** are safe to use when an anti-inflammatory analgesic is needed.
- Aspirin-sensitive asthma **responds to usual therapy with ICS.**
- **antileukotrienes** should be effective in these patients

Pregnancy

- Approximately one-third of asthmatic patients who are pregnant improve during the course of a pregnancy, one-third deteriorate, and one-third are unchanged.
- poor control may have **adverse effects on fetal development**.
- The drugs that have been used for many years in asthma therapy have now been shown to be safe and without teratogenic potential.
- These drugs include **SABA**, **ICS,** and **theophylline**
- there is less safety information about newer classes of drugs such as **LABA**, **antileukotrienes**, and **anti-IgE.**

- If an OCS is needed, it is better to use **prednisone rather than prednisolone** as it cannot be converted to the active prednisolone by the fetal liver, thus protecting the fetus from systemic effects of the corticosteroid.
- There is no contraindication to breast-feeding when patients are using these drugs.

Cigarette Smoking

- Smoking asthmatics have more severe disease, more frequent hospital admissions, a faster decline in lung function, and a higher risk of death from asthma than nonsmoking asthmatics.

Surgery

- If asthma is well controlled, there is no contraindication to general anesthesia and intubation.
- Patients who are treated with OCS will have adrenal suppression and should be treated with an increased dose of OCS immediately prior to surgery.
- Patients with FEV1 <80% of their normal levels should also be given a boost of OCS prior to surgery.
- High maintenance doses of corticosteroids may be a contraindication to surgery because of increased risks of infection and delayed wound healing.