

# Anaphylaxis + Acute Asthma

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# Definition

Severe  
life threatening  
generalised  
hypersensitivity reaction

(Milder cases are also sometimes termed anaphylaxis)

# Definition

## **ANAPHYLACTIC**

**IgE** Ab mediated - Type I hypersensitivity

-IgE mediated de-granulation of MAST cells

*Parenteral penicillin, hymenopteran stings, food*

## **ANAPHYLACTOID**

**Non- IgE** Ab mediated trigger release

*Radiocontrast media, aspirin and other NSAIDs*

**The clinical syndrome produced is similar**

# Actions of Mediators

## **VASODILATATION AND OEDEMA**

Histamine, PAF, Tryptase, Bradykinin

## **BRONCHOCONSTRICTION, MUCOSAL OEDEMA, MUCUS PRODUCTION**

Histamine, Prostaglandin D<sub>2</sub>, LTC<sub>4</sub>, LTD<sub>4</sub>

## **CHEMO-ATTRACTANTS**

Neut chemotactic factor, ECF, LTB<sub>4</sub>

# Clinical

- A disease of the well
  - Rarely described in very unwell or shocked
- Life-threatening reactions within minutes
  - most symptoms within 30 min
  - Some may not occur for up to 3 days post exposure
- The faster a reaction- the more severe it is likely to be.

# CAUSES

## **DRUGS**

- IV contrast - 1/40,000 fatalities
- Antibiotics- 85% of all fatalities due to IV penicillin
- Anti-venom
- Streptokinase
- Aspirin and NSAIDS

## **ENVIRONMENTAL**

- Bites and stings
- Foods
- Pollen
- Heat/cold
- Exercise

## **OCCUPATIONAL**

- latex

# CAUSES

## DRUGS

- IV contrast - 1/40,000 fatalities
  - 1-2% of all patients receiving will have some kind of reaction
- Antibiotics- 85% of all fatalities due to IV penicillin
- Anti-venom
- Streptokinase
- Aspirin and NSAIDS

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# IV contrast

- Anaphylactoid reaction - Not related to prior exposure
- Shellfish or iodine allergy not a contraindication
  - Rare to have iodine allergy
  - More likely 'betadine' reaction
- Reactions tend to occur in hyperosmolar IV contrast
  - LMW contrast decreases the reaction to approximately 0.5%
  - Reactions usually rare- fatality is ~0.9/100,000 cases
- Pretreatment with antihistamines and steroids:
  - Where prior reactions
  - Atopic or asthmatic patients

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# Antibiotics

- Penicillin
  - 1 in 5000 exposures to parenteral penicillin
  - Only 20% with allergy have a positive skin test for IgE
  - Cross reactivity:
    - 1st gen cephalosporins ~ 5%
    - 3rd gen cephalosporins - rare
- High Risk Groups
  - EBV -to amoxicillin
  - HIV ->20% to sulphur
  - Cystic Fibrosis
    - » 30% allergic to: piperacillin, ceftazidime, ticarcillin

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# Aspirin and NSAID's

- Commonly implicated
- Bronchospasm
- X-reactivity between various NSAID's

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# BEE STINGS

- More reactions to this than all other
- 
- 2-4% of population susceptible
- 25% of adults react to the second sting
  - Generalised urticaria is risk factor for future anaphylaxis
  - Localised reactions are not.

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## **ENVIRONMENTAL**

- Bites and stings
- **Foods**
- Pollen
- Heat/cold
- Exercise

## OCCUPATIONAL

- latex

# FOOD ALLERGY

- Affects 2% of overall population -Usually mild and limited to GIT
- Affects 6% of children- 85% usually resolve by age 5
  - Eggs / Cows milk
  - Associations
    - Non-breast fed
    - Early solid food
- Cross reactivity between foods
  - 5% legumes
  - 50% peanuts with almonds, walnuts
  - 50% with fish / 75% with shellfish
  - 90% with cow's and sheep's and goat's milk

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# LATEX ALLERGY

- Results in Type I hypersensitivity
  - Irritant dermatitis
    - Erythema, dryness, scaling, cracking
- Type IV allergic Contact dermatitis
  - Eczematous rash
  - Vesicle formation

# Clinical

Diagnosis is clinical

## CUTANEOUS REACTIONS

- Erythema
- Urticaria
- Pruritis
- Angioedema
- Conjunctivitis
- Rhinitis

# Clinical

## **RESPIRATORY**

Tight throat

Cough

Stridor

Wheeze

## **CVS**

Syncope

Dizziness

Tachycardia

Hypotension

Arrhythmias

Confusion

Coma

## **GIT**

Cramps

Nausea, vomiting

Diarrhoea

## **OTHER**

Lacrimation

Headache

Generalised oedema

APO

Vaginal discharge

DIC

# Clinical

<b>RESPIRATORY</b>	<b>CVS</b>	<b>GIT</b>	<b>OTHER</b>
Tight throat	Syncope	Cramps	Lacrimation
Cough	Dizziness	Nausea, vomiting	Headache
Stridor	Tachycardia	Diarrhoea	Generalised oedema
Wheeze	Hypotension		APO
	Arrhythmias		Vaginal discharge
	Confusion		DIC
	Coma		

# Clinical

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# Investigations

- Not really necessary
- ECG and monitoring for severe
- Mast Cell tryptase assay
  - Highly sensitive indicator of anaphylaxis
  - Elevated 1-6 hours
  - Used in post mortems
  - Unclear in terms of current use

# MANAGEMENT

1st LINE

# Sensitivity Testing

- May need to test if reaction unknown
  - Especially for cephalosporins when penicillin allergy known
  - Many protocols
  - No real standard
    - 0.001mg - 0.005 - 0.01 - 0.05 - 0.1 - etc

# First Line Treatment

Depends on severity of the reaction and previous reactions

**A - secure airway** - may be surgical

**B- Breathing** - BVM + oxygen

**C- Circulation** - IV access

**ADRENALINE**

**FLUIDS**

# First Line Treatment

MONITOR

ECG

NIBP

LIE FLAT

# ADRENALINE

## **Alpha adrenergic stimulation**

- increases PVR
- Improves BP
- Improves coronary artery perfusion
- Reverses peripheral dilatation
- Decreases angioedema

## **Beta adrenergic stimulation**

- Beta 1
  - +ve inotrope
  - +ve chronotrope
- Beta 2
  - Bronchodilator

Beta adrenergic stimulation also INCREASES cAMP

-inhibits further MAST cell and BASOPHIL mediator release

# ADRENALINE

## Nebulised Adrenaline

- Put it on FIRST
- 1-4ml of 1:1000

EARLY MILD/SLOW PROGRESSIVE  
NO MONITORING AVAILABLE

1:1000 adrenaline  
0.3-0.5mg IM  
Repeat every 5-10 minutes

SHOCK / SEVERE DYSPNOEA  
MONITOR

0.75-1.5mcg/kg  
1:100,000 IV  
Give 10-20mcg/min  
In arrest give 1mg

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# FLUIDS

- Plasma loss of up to 50% of circulating volume
- Bolus 10-20ml/kg of ?

# Second Line Treatment

ANTIHISTAMINES

STEROIDS

GLUCAGON

AMINOPHYLLINE

# ANTI-HISTAMINES

For cutaneous symptoms

- H1 Receptor Blocker
  - eg promethazine 25mg IV
  
- H2 Receptor Blocker
  - eg Ranitidine 50mg IV

# Second Line Treatment

ANTIHISTAMINES

**STEROIDS**

GLUCAGON

AMINOPHYLLINE

# STEROIDS

- For severe Bronchospasm
  - Hydrocortisone 5mg/kg IV to max of 250mg
  - Dexamethasone 8mg IV

# Second Line Treatment

ANTIHISTAMINES

STEROIDS

GLUCAGON

AMINOPHYLLINE

# OTHERS

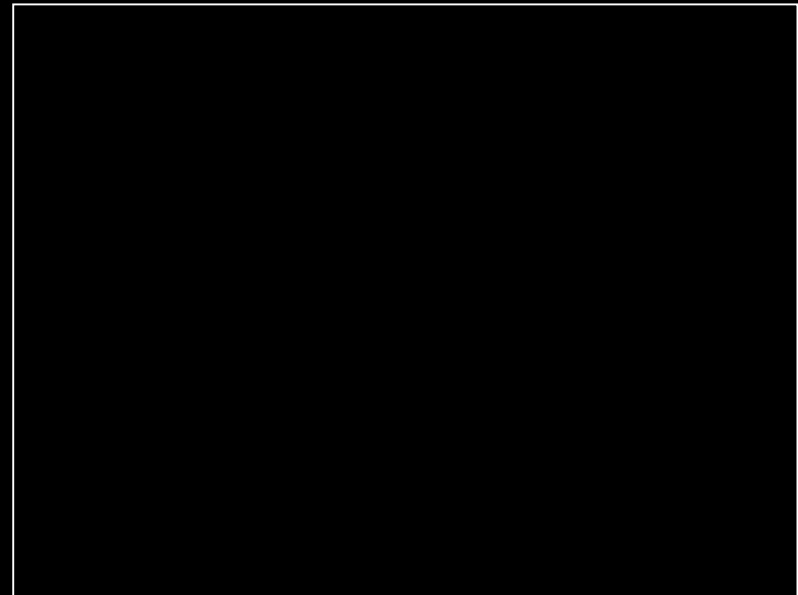
- Glucagon
  - 1mg every 5 min
  - For hypotension in patients on beta blockers as may not respond to adrenaline for hypotension
- Aminophylline
  - 5mg/kg IV over 30min loading, then infusion 0.5mg/kg/hr
- MgSO<sub>4</sub>
  - 10mmol slow IV

# DISPOSITION

- All patients receiving adrenaline need monitoring
  - Stable patient need ~ 6-8hrs as up to 5% chance of biphasic anaphylaxis
- Continue meds for 3 days
  - H1 + H2 + steroids
- Reassess precipitants
- Allergy Testing
- EPI pen
- Immunotherapy

# Epi Pen

- Not recommended for children <10kg
- 150mcg for 10-20kg children
- 300mcg for >20kg
  
- Auto-injector
- To be used at onset of symptoms
- Lateral thigh injection
- Store at <25°C



# Immunotherapy

- De-sensitization
- Increasing doses of allergen
- Long term maintenance therapy

# The 'Hygiene' Theory

- Atopic Diseases- IgE mediated
  - Increased prevalence in
    - Western Europe
    - USA
    - Australia
  - Good evidence that environment plays a role
    - Western Society immune system is deprived of microbial antigens that are needed to stimulate T-helper cells

# Reunification of Germany

- Asthma and atopy had lower incidence in East Germany before reunification
- Controversial as high rate of asthma and atopy in poor blacks in USA

# Acute Asthma

# Asthma

- Our concept of asthma mechanisms has changed
- It is a result of:
  - Genetic factors- atopy
  - Environmental factors
    - Viruses
    - Allergens
    - Occupational exposures
- Most important recent advances are that IgE antibody mediated responses in the lung are now recognised.

# Epidemiology

- Increasing incidence
  - 2% of ED presentations overall
  - 10% of urban presentations
- Decreased death rates
- Majority of cases are children
  - Incidence of up to 20% in Austr, NZ, UK

# Definition

Episodic, Reversible, Bronchoconstriction

- The development of more refractory inflammation results in:
  - Bronchial oedema
  - secretions
- Implication of no underlying airway destruction

# Epidemiology

- In some countries a disease of urbanisation and affluence, in others associated with lower socio-economic status.
- In <10yo            M:F    2:1
- 18-54yo            M:F    1:2
- Childhood asthma persists into adulthood in ~50%

# Pathophysiology

## **EXTRINSIC ASTHMA**

TYPE I hypersensitivity

IgE mediated

## **INTRINSIC ASTHMA**

Non-immune initiation

infections

drugs

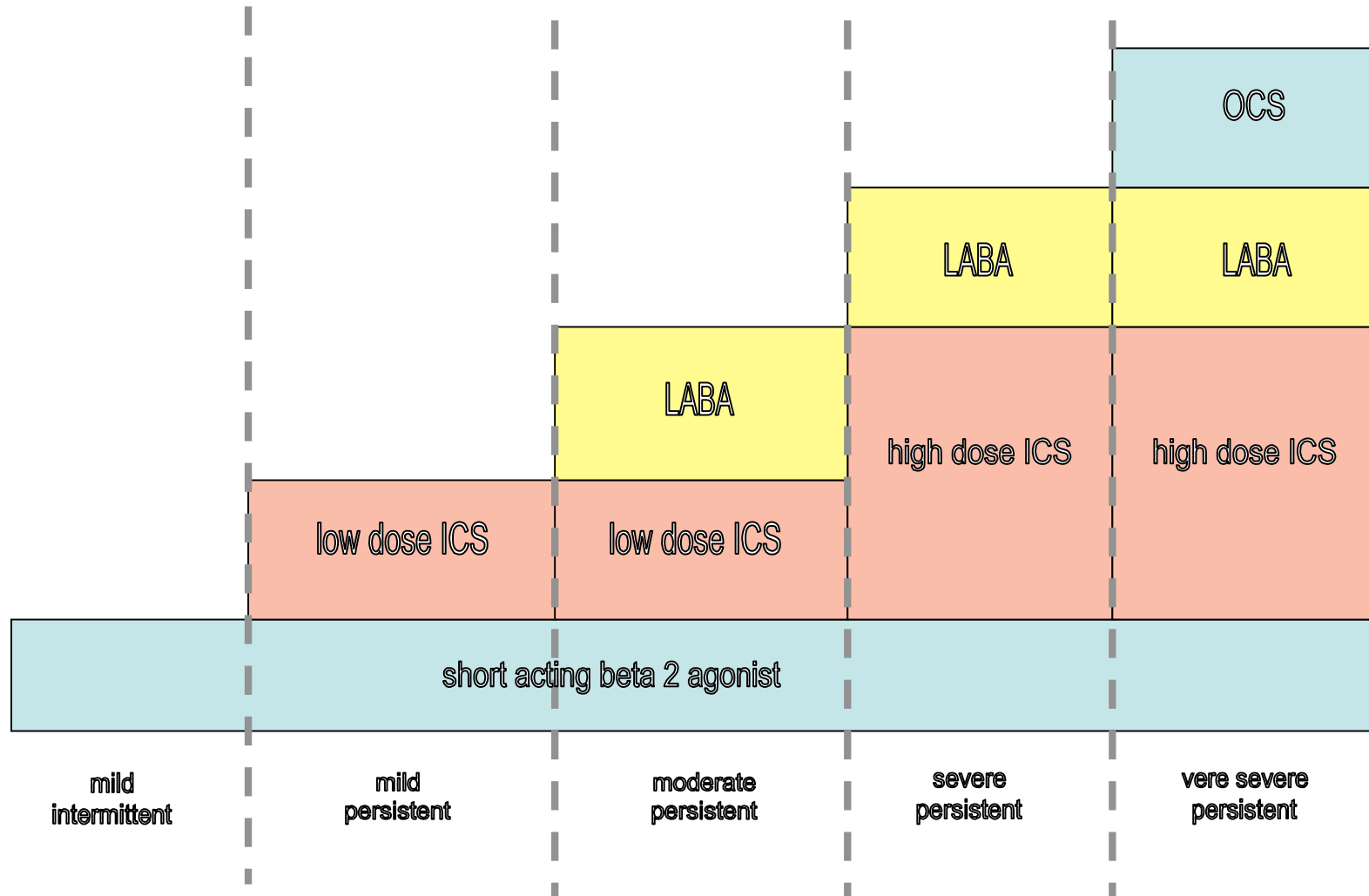
pollutants

exercise

# ACUTE ASTHMA

- The acute exacerbation is different to the chronic patient
- Rapidity of onset is important
  - Slow grumbling vs Rapid onset

# Who are we talking about?



# History in Acute Asthma

- Previous life-threatening episodes
- ICU admissions
- Intubation
- Oral steroids within the previous 6 months
- Do they take 'drugs'- any type, not just inhaled
  - Doubles risk of mortality

# CLINICAL SEVERITY

- **MILD**
  - Able to speak normally
  - PEFR >300L/min(>60%predicted/best)
- **MODERATE**
  - Dyspnoea at rest
  - Speaking in short sentences
  - Wheeze and chest tightness
  - Short-lived relief from usual therapy
  - PEFR 200-300L/min(40-60% predicted/best)
- **SEVERE**
  - Sweating, restless
  - Laboured breathing
  - Words or short phrases
  - Tachycardic
  - O2 sats<90% on RA
  - PEFR<200L/min(<40% or cant do)
- **RESUSCITATION**
  - Exhausted, cyanotic, can't speak
  - O2 sats<90% despite high flow oxygen
  - PEFR- what are you thinking?

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# Paediatric Severity

SIGNS	MILD	MODERATE	SEVERE	LIFE THREATENING
<b>EXAMINATION</b>				
Talks in	sentences	phrases	words	words
Accessory muscle use	no	minimal	moderate	severe
Physical exhaustion	no	no	yes	yes
Wheeze on auscultation	variable	moderate	quiet	quiet
<b>VITALS</b>				
pulse	<100	tachy	Tachy+	Tachy ++
oximetry	>94%	90-94%	<90%	<90%
spirometry	>60%	40-60%	?	?
Pulsus paradoxus	no	perhaps	yes	yes

# Associated Symptoms

- Fever
  - Chest infection
- Chest Pain
  - PE
  - Pneumothorax
  - CCF(cardiac asthma)

# Investigations

## LABS

### FBE

- Leukocytosis

### EUC

- Mild hypokalaemia

### ABG's

- Not routine

## IMAGING

### CXR

- If suspect pneumothorax and pneumonia.

# Management

## **GOALS OF MANAGEMENT**

- Management appropriate to clinical severity
- Ensure adequate oxygenation
- Reverse bronchospasm
- Minimise inflammatory response

# Management

## MILD

- $\beta$ -adrenergic agonist
  - Salbutamol
    - Metered dose inhaler
    - Spacer
- Commence ICS if patient not already on them
- Education and follow-up

## MODERATE

- Oxygen
  - Sats >92%
- $\beta$ -adrenergic agonist
  - Nebuliser
    - 5mg
  - MDI
  - How much?
- Systemic corticosteroids
  - 50mg prednisolone or
  - 250mg hydrocortisone

# Management

## MILD

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## MODERATE

- Oxygen
  - Sats >92%
- $\beta$ -adrenergic agonist
  - Nebuliser
    - 5mg
  - MDI
  - How much?
    - 3 doses over an hour
- Systemic corticosteroids
  - 50mg prednisolone or
  - 250mg hydrocortisone

# Management

## **SEVERE**

- Monitoring
  - cardiac, NIBP, pulse oxymetry
- Oxygen
- Salbutamol-(neb/IV) + corticosteroids + ipratropium  $\pm$  magnesium  $\pm$  adrenaline  $\pm$  ventilation

# Management

INITIAL SEVERITY	MILD	MODERATE	SEVERE	LIFE THREATENING
INITIAL TREATMENT	Salbutamol(inh) <20kg 4-6 puffs >20kg 8-12 puffs steroids	Salbutamol(inh) 20minutely x3 Steroids(po)	Salb cont.(neb) Steroids Ipratropium	Salb cont.(neb) +IV Steroids IV Ipratropium
REVIEW	60 min Improving?	60 min Improving?	30 min Improving?	Improving?
ONGOING TREATMENT	If improving taper to q1-3hrs	Taper to 3hrs	Taper to 1 hour?	Reduce salbutamol?
DISPOSITION	Salbutamol q4hrs steroids	Salbutamol q4hrs steroids	Ward admit	ICU

# Salbutamol $\beta$ -adrenergic agonist

## First line of treatment

- Relax bronchial smooth muscle
- Also have non-bronchodilatory effects
  - inhibit MAST cell mediator release
  - Reduce plasma exudation
  - Inhibit sensory nerve activation
- Continuous dosing- (No upper limit of dosing)
  - Mask-escapes - Spacer-use equipotent dose
- Racemic Salbutamol
  - R and L isomers- Right is therapeutic
    - Levalbuterol- more potent, fewer side effects
- Parenteral salbutamol
  - 5mcg/kg bolus then infusion 1-20mcg/min
  - High dose 2000mcg bolus then large doses up to 10mg
    - No published evidence for this approach
    - Evidence in animal models of cardiac toxicity

# Salbutamol Controversy

- Association between increased asthma mortality and SABA and LABA
- Reality is;
  - It is a reflection of worsening asthma
  - It reflects a lack of use of ICS

# Ipratropium

- Muscarinic Receptor Antagonist
  - Prevents cholinergic nerve induced bronchoconstriction
- Used with  $\beta$ -adrenergic agonist
- There may be benefit in **severe** asthma
- Some evidence that stat significant improvement in FEV1- but no clinical significance
- Can give it continuously (500mcg q 20min)
  - Non-selective
  - Not absorbed
  - 3-30min speed of onset
  - 1/2 of effect in the first 3 min

# Steroids

- 40mg prednisolone is minimum dose
  - Not efficacious below this
- 250mcg IV hydrocortisone
- Taper not needed unless on for ~1 month

# Adrenaline

- Subcut/IM has similar effect to neb salbutamol
  - Small studies
  - Include all spectrum of severity
- IV -no real evidence head to head that better than selective agents.

# Aminophylline

- No evidence for use in adults in acute setting
  - Cardiac arrhythmias
  - Some use in ICU literature(may decrease ventilation time)
- Some evidence for use in children
  - Controversial
    - Some studies show improved spirometry and lower intubation rates
    - Others show no greater benefit if adequate doses of bronchodilators

# Magnesium

- Smooth muscle relaxant
  - Impedes calcium uptake into smooth muscle
- In mild to moderate asthma
  - No benefit
- In severe asthma
  - Significant increases in FEV1
  - Reduced admission rates
  - 2g over 20 minutes

# HELIOX

- HELIUM : OXYGEN mixture at 70:30 or 80:20
  - Flow mechanics
  - No conclusive evidence
    - Small trials
    - Inadequate doses of Beta agonists

# KETAMINE

- Sympathomimetic effects
  - Direct relaxant effects on bronchial smooth muscle
- Histamine antagonism
- No benefit conferred
- Standard of care in intubation in children
  - Bronchodilator
  - Supports blood pressure

# Leukotriene Inhibitors

Montelukast Zafirlukast

- Produced by MAST cells
- Leukotrienes exhibit activity that mimics that of asthma.
- Found in increased amounts in acute exacerbations
- May be some role in chronic
  - Less effective than ICS and LABA
- No acute role?
  - Some studies showing rapid FEV1 increase in acute-but correlation with clinical improvement?

# Cromones

nedocromil sodium, cromolyn sodium

- Inhibit MAST cells
- Good for trigger induced asthma
- Short duration of action- little long term benefit
- Safe
- BUT low dose ICS more effective

# Anti IgE

Omalizumab

- Blocks antibody-binds to circulating IgE
- Reduces numbers of exacerbation of severe asthma
- Very expensive
- Selective patient population
  - Not controlled by max ICS
- No acute role

# Immunodilatory treatment

- Used to reduce oral steroid treatment in patient with side effects
- Associated with serious side effects
  - Methotrexate
  - Cyclosporine
  - Azathioprine
- None have long term benefits

# Antibiotics

- No evidence for use in extrinsic acute asthma

# CPAP and BIPAP

- Reduce airways resistance
- Bronchodilate
- Counter atelectasis
- Reduce work of respiration
- May reduce need for intubation in severe asthma
  - Small studies.

# What if we have to intubate?

- Up to 10% of asthma presentations go to ICU
  - Some for intubation, some for monitoring
- Intubation carries up to 5% mortality
  - Complications include
    - Barotrauma
    - Pneumothorax
    - Pneumomediastinum
    - Hypotension 2° to auto PEEP
- Need to:
  - Maximise oxygenation
  - Maximise expiratory time(I:E ratios)
  - Allow permissive hypercapnea

# Who needs admission?

- The only difficult group are the moderate group
- Admission needed if:
  - Pre-treatment PEFr or FEV1 is <25% predicted
  - Post-treatment is <40% predicted
  - Previous serious asthma
  - Poor compliance
  - Poor social conditions
  - Limited access
- If PEFr is 40-60% - watch for few hours.