BRONCHIAL ASTHMA IN CHILDREN (treatment)

Plan of the lecture

- 1. INDICATIONS for HOSPITALIZATION
- 2. Exacerbation treatment
- 3. MEDICATIONS for basic therapy of BA
- 4. Step therapy of BA
- 5. Inhalation technology by MDPI
- 6. Allergen specific immune therapy

INDICATIONS for HOSPITALIZATION

- Severe attack
- Poor efficacy for 2-6 hours of treatment
- Children with high mortality risk from BA:
  - Intubation or arteficial breathing supply in anamnesis;
  - Exacerbations for the last year that demand hospitalization
  - Children with oral GCS treatment or those who stop it.
  - Children with frequent usage of β-agonists (more than 1 inhalator per mo)
  - Psycho-social family problems or poor compliance.

Exacerbation treatment at ambulatory stage

- Inhaling short-acting β2-agonist every 20 min during the hour through matured inhalator or spacer.

Fine response	Incomplete response	Bad response
FEV1 more than 80%, effect of β2-agonist is preserved for 3-4 hours, continue β-agonist every 3-4 hours for 24 hours	FEV1 60-80%, continue β-agonist for 1-2 hours, add oral GCS0,5-1 mg/kg (after prednisone) add inhalative cholinolytic	FEV1 less than 60%, continue β-agonist with interval less than an hour add oral GCS 0,5-1 mg/kg Add inhalative cholinolytic, Hospitalization with emergency
Attend the doctor for recommendations	**Immediately call the doctor for recommendations**	**Emergency hospitalization**

Asthma exacerbation treatment algorithm in hospital

Symptoms evaluation (BA severity criteria)

Taking history, physical examining, lab data.

Initial therapy

1. O_2 inhalation until saturation by O_2 will be more than 95%;
2. Inhalation short-acting β-agonist: 2 inhalations of salbutamol through matured device or 2,5 ml of salbutamol through nebulizer every 20 min for 1 hour.;
3. If response is absent or patient has previously take systemic GCS or attack is severe : prednisone 1-2 mg/kg/day, max 20 mg for children of lessthan 2 years old and 30 mg of 2-5 years old.;
4. Sedative therapy is contraindicated during the exacerbation period.

Repeat evaluation of patients condition severity an hour later

FEV1, O_2 saturation, another tests if necessary.

Attack of moderate severity	Severe attack
FEV1 60-80%; Symptoms of moderate severity, accessory muscle involvement into respiration act; **Therapy** Inhalation β-gonist or cholinolytic every 60 min; Oral GCS; Usage of methylxantines; If treatment efficiant continue for 1-3 hours.	Evaluate anamnesis : patient from the list of high risk; FEV1 less than 60%, Symptoms are severe, retractions of subclavicular pits; Efficacy of previous therapy is absent **THERAPY** Oxygen therapy Inhalation β-agonist or cholinolytic; Systemic GCS; It can be used IV injection of methylxantines

Efficacy evaluation 1-2 hours later		
Nice response	**Incomplete response**	**Bad response**
▪Condition improvement is preserved 1 hour after last medication intake ▪Physical examining is normal ; ▪FEV1 is ore than 70%; ▪Distress is absent; ▪Sat O_2 more than 95%	▪Evaluate anamnesis: patient of high risk; ▪Physical examining: symptoms are ranged from slight to moderate; ▪FEV1 is less than 60%; ▪Sat O_2 isn't improve;	▪ Evaluate anamnesis: patient of high risk; ▪Physical examining: symptoms are severe, dizziness, conscience confusion; ▪FEV1 less than 30% ▪$PaCO_2$ 45 mmHg; ▪PaO_2 60 mm Hg;
Discharging home	**Continue treatment in hospital**	**Transfer patient to rhehanimation**
▪ FEV1 more than 60%, ▪Inhalation β-agonist ▪Oral GCS 3-5 дней ▪Patient tuition of correct medication intake,review of treatment plan, physician observation.	▪Oxygen therapy; ▪ Inhalation β-agonist, cholinolytic; ▪Oral or IV GCS 1-2mg/kg every 6 hours 1 day, later every 12 hours, later once per day for 3 days . ▪FEV1, Sat O_2, pulse monitoring	▪Oxygen therapy; ▪ Inhalation β-agonist, cholinolytic; ▪IV GCS; ▪Possible IV injection of β-agonist; ▪Possible IV injection of methylxantines; ▪Possible intubation and artificial ventilatory therapy (AVT);

MEDICATIONS for basic therapy of BA

- Membrane stabilizers of mast cells: derivates of chromolicate acid - (intal, chromohexal, chromogen), **SODIUM NEDOCROMYL** (tiled, tiled-mint);
- Glucocorticosteroids
  - **Systemic** (**hydrocortizone, dexamethazone, methylprednisolone, prednisolone, polcortolone**),
  - **Inhalation**
    - **Beclamethasone (becodisk, becotid, aldecin)**
    - **Fluticasone propionat (seretid, flixotid)**
    - **Budesonid (Pulmicort)**
    - **Flunisolid (Ingacort)**

)
- β-agonists long-acting
  - **Salmaterol (Serevent, Serevent rotadisk)**
  - **Klenbuterol (Spiropent)**
  - **Formoterol (Formoteroloxis, Foradil)**
- Leukotrien receptors antagonists **(Acolad (Zafirlucast), Singular (Montelukast)).**

Treatment approach based on control level

Control level		Therapeutic activity
Controlled BA		Minimal basic therapy to provide BA control
Partially controlled BA		Increase therapy (“step up”)
Uncontrolled BA		Increase therapy until complete control will be achieved
BA exacerbation		Treat as an exacerbation

decrease

increase

Обострение Б

Short acting bronchodilators

+ SCS + urgent allergologist consulting/ hospitalization

Urgent hospitalization!

Criteria	**Mild**	**Moderate**	**Severe**	**Threatening of asphyxia**
Dyspnea	While moving	While speaking	In rest	
Position	Can lay	Prefer to sit	Orthopnoe (sitting in banding forward position with fixing by hands)	
Speech	Normal	Interrupted, by interrupted sentences	By separate words	
Conscience	Irritation is possible	Usually agitation	Usually agitation	Somnolence, sopor
RR	Increased	Increased	Frequently >30/min	
Accessory musculature invovement	Usually NO	Usually	Usually	Paradoxical diaphragm movement

Адаптировано из: GINA 2010: www.ginasthma.org

Clinic recommendations of children allergology and immunology 2010 (Ukraine)based on GINA (2009)

Step 1	Step 2	CStep 3	Step 4	Step 5
Therapy increasing				
Patient tuition				
Elimination measure				
	Short acting β_2 – agonists per need			
NO	Choose one of the options	Prescribe one of the options	Prescribe moderate or high dosages of IGCS	ADD one or more options to step 4
	Low dosages of IGCS	Low dosage of IGCS+ β_2–agonist long acting (LABA) (preferable) or	Add one or more options	Minimal oral GCS Or/and
	or Antileikotriens (ALT)	Moderate or high dosages of IGCS or	LABA Or/and	Anti- IgE
		Low doasges of IGCSC + ALT or	ALT Or/and	
		Low dosages of IGCS + teophylline long released	Theophylline long released	

Step therapy of BA

- Step 1, including reliever medication usage per need, is assigned only for patients without support therapy. In the cases of more frequent symptoms or episodic exacerbations constant support therapy is necessary (Step 2 or more) as addition to reliever medications.

- Steps 2-5 **include reliever medications combination per need together with support therapy. IGCS is recommended as initial support therapy in patients with BA of any age at step 2.**

Step therapy of BA

- At step 3 is recommended **combination of IGCS in low dosage together with LABA in fixed combination Thanks to additive effect of combined therapy low dosages are quite sufficient. Increasing of IGCS dosage is necessary for patients who hasn't get control of BA after 3-4 mo of therapy.**

Step therapy of BA

- Monotherapy of BA without GCS is prohibited because it increases significantly mortality risk for patients

- If control of BA is gained on the basic therapy by combination of IGCS and LABA and is sustained more than 3 mo long it's possible to decrease steadily the dosages of medications.
- In severe BA and long non adequate previous therapy this period may be more long – 6-12 months.

- Termination of support therapy is possible if complete control of BA is present on minimal dosages of anti-inflammatory drug and absence of symptoms recurrence during one year.

How to perform basic therapy in children with BA?

- To define control level of disease
- To choose medications
- To choose the type of inhalator device
- To define the date of next visit for monitoring treatment efficiency

Sustaining treatment of BA: Chromons

Sodium chromoglycate, Sodium nedocromil

- ***Activity mechanism***: suppress inflammatory mediator releasing from mast cells; influence on inflammatory process in respiratory tract during prolong therapy hasn't been proved
- ***Significance in BA treatment isn't established***
  - It has been proved that Sodium nedocromil decrease relapsing of BA exacerbations, but influence to another condition parameters in BA doesn't differ from placebo influences. .
  - *Side effects:* irritability of pharynx and unpleasant taste.

Адаптировано из: GINA 2007: www.ginasthma.org; Клинические рекомендации по детской аллергологии и иммунологии 2008

Sustaining treatment of BA: Leikotriens antagonists

- *Zafirlukast, Montelukast*
  Антагонисты лейкотриенов
- ***Activity mechanism***: Leukotriens receptors blockage in respiratory tract or blockage of 5-lipoxygenase – prevention of leukotrien effects.

- ***Significance of BA therapy:***
  - Has weak variable bronchodilator effect
  - Provide partial defending of bronchospasm after physical loading
  - Decrease symptoms severity including cough
  - Improve respiratory function,
  - Decrease inflammatory activity in respiratory tract,
  - Usually less effective than low dosages of IGCS

- ***Side effects:*** good tolerance. Can't be completely excluded inducing of Chardge-Stross syndrome. .

GINA 2007: www.ginasthma.org

Sustaining therapy of BA: IGCS

Beclomethasone dipropionate, Budesonide, Fluticasone propionate

Activity mechanism: **inflammatory process suppression in respiratory tract**

They are the most effective medications that suppress inflammatory process in BA

They are recommended children of any age

- Effectively decrease symptoms of BA,
- Improve life quality and respiratory tract functioning,
- Decrease bronchial hyperreactivity,
- Inhibit inflammation in respiratory tract,
- Decrease frequency and severity of exacerbations, frequency of hospitalizations
- Decrease mortality rate in asthma

Dosing

- Main effect of IGCS can be gained in dosage of 200 mcg/day in Budesonide
- Dosage increasing provide non significant efficiency raising but increase side effects risk
- To get disease control adding of second medication for sustaining therapy is preferable comparatively to IGCS dosage increasing

Адаптировано из GINA 2009: www.ginasthma.org

Equipotent day IGCS dosages

Medication	Low daily dosages (mcg)	Moderate daily dosages (mcg)	High daily dosages (mcg)
Doses for children less than 12 years old			
Beclomethasone dipropionate	**100-200**	**>200-400**	**>400**
Budesonide	**100-200**	**>200-400**	**>400**
Flutikazone	**100-200**	**>200-500**	**>500**
Dosages for adolescencts			
Beclomethasone dipropionate	**200-500**	**>500-1000**	**>1000-2000**
Budesonide	**200-400**	**>400-800**	**>800-1600**
Flutikazone	**100-250**	**>250-500**	**>500-1000**

Эквивалентность (эквипотентность) препаратов определяли на основе их сравнительной эффективности.

Адаптировано из: GINA 2007: www.ginasthma.org

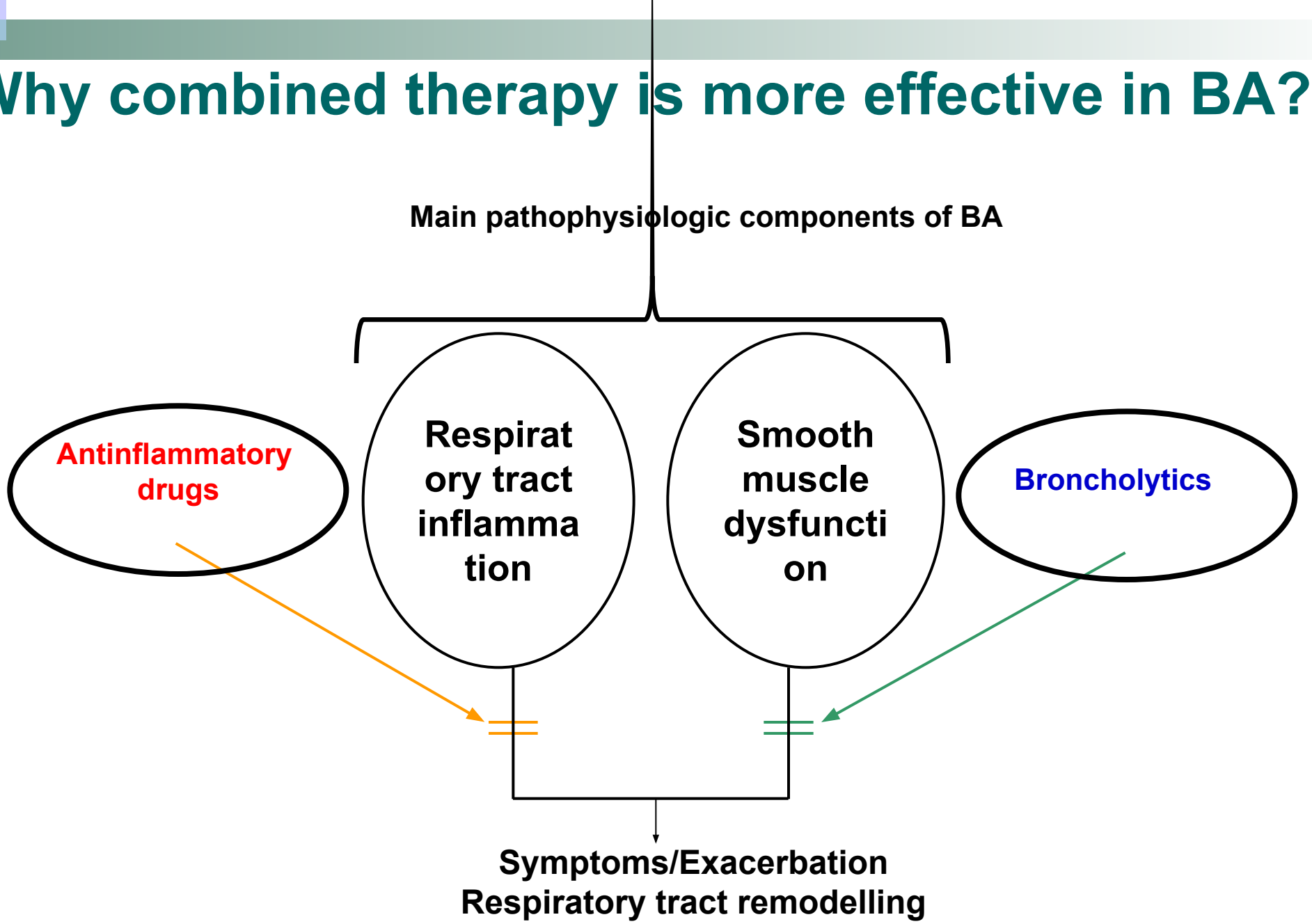
Sustaining therapy of BA: Long-acting *β2-agonists (LABA)*

SALMETEROL, FORMOTEROL

- ***Activity mechanism***: produce bronchial smooth muscle relaxation ,decrease vessel permeability, improve muco-cilliary clearance
- ***Its role in BA treatment***:
  - Can't be used as monotherapy of BA as there are no evidence of their antiinflammatory activity
  - LABA must be used only in combination with adequate dosage with IGCS, preferably in the fixed combination.
  - They are effective concerning the symptoms, respiratory functioning, exacerbations.
  - Provide control of BA in majority of patients more promptly with lower dosages comparatively to monotherapy by IGCS.

Адаптировано из: GINA 2007: www.ginasthma.org

Why combined therapy is more effective in BA?



Sustaining therapy of BA:

Fixed combinations of IGCS +LABA

- **Fluticasone propionate + Salmeterol (Seretide) from 4 years old**
- **Budesonide + Formoterol (Simbicort) from 6 years old**

Usage of fixed combinations:

- Of the same efficiency as separate inhalators usage
- More suitable for patients
- Improves performance of doctor's prescriptions by patient (compliance)
- Garantees usage not only the bronchodilator but antinflammatory drug as well

GINA 2007: www.ginasthma.org

Place of antileukotrien (AL) medications in therapy of BA

GINA recommendations

Toddlers
Controlled BA
Partially controlled BA (GCS or AL medication)
Noncontrolled BA (GCS+ AL medication)

Children older than 5 years old
1 degree
2degree (GCS or AL medication)
3 degree (GCS + AL medication)
4 degree (GCS +AL medication)
5 degree

AL medications (Montelukast, Zafirlukast, Pranlukast)

PRACTALL consensus

IGCS

AL

Insufficient control

или

Increase IGCS dosage

Add AL

Insufficient control

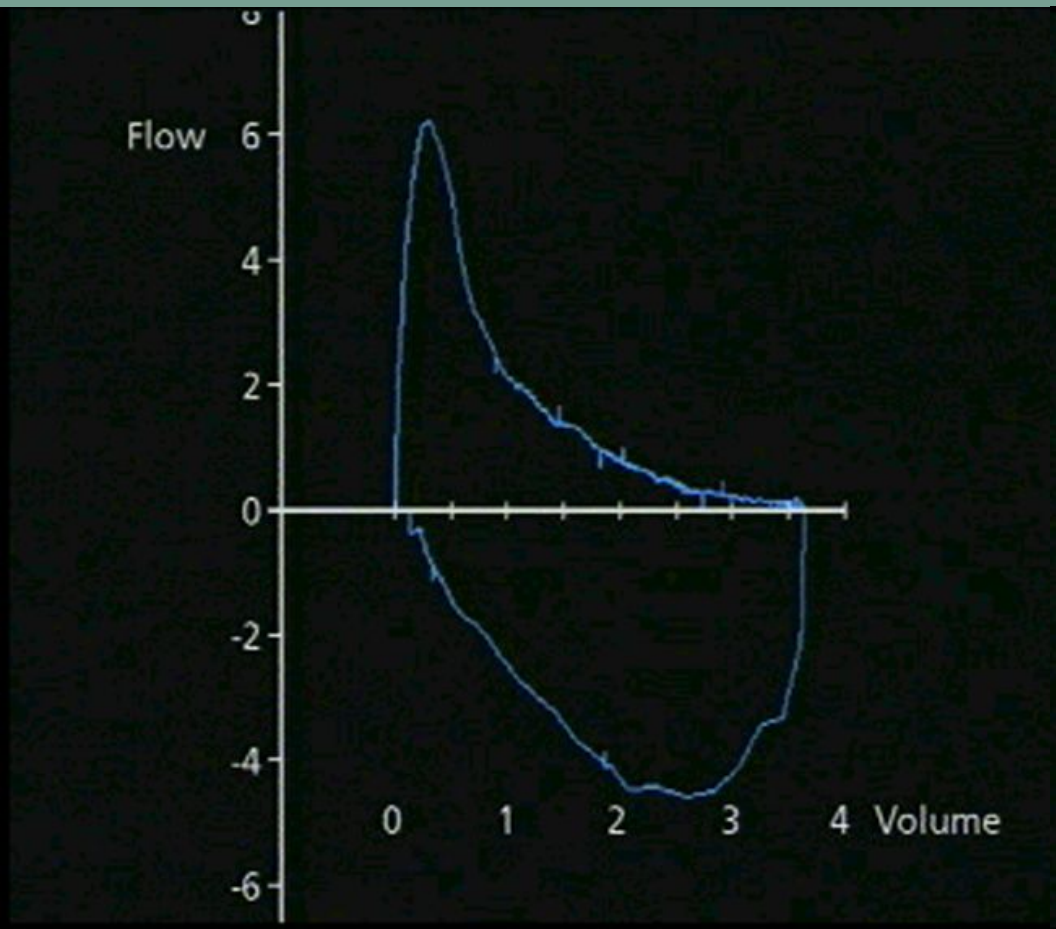
1. Increase IGCS dosage,
2. Or add AL,
3. Or add LABA

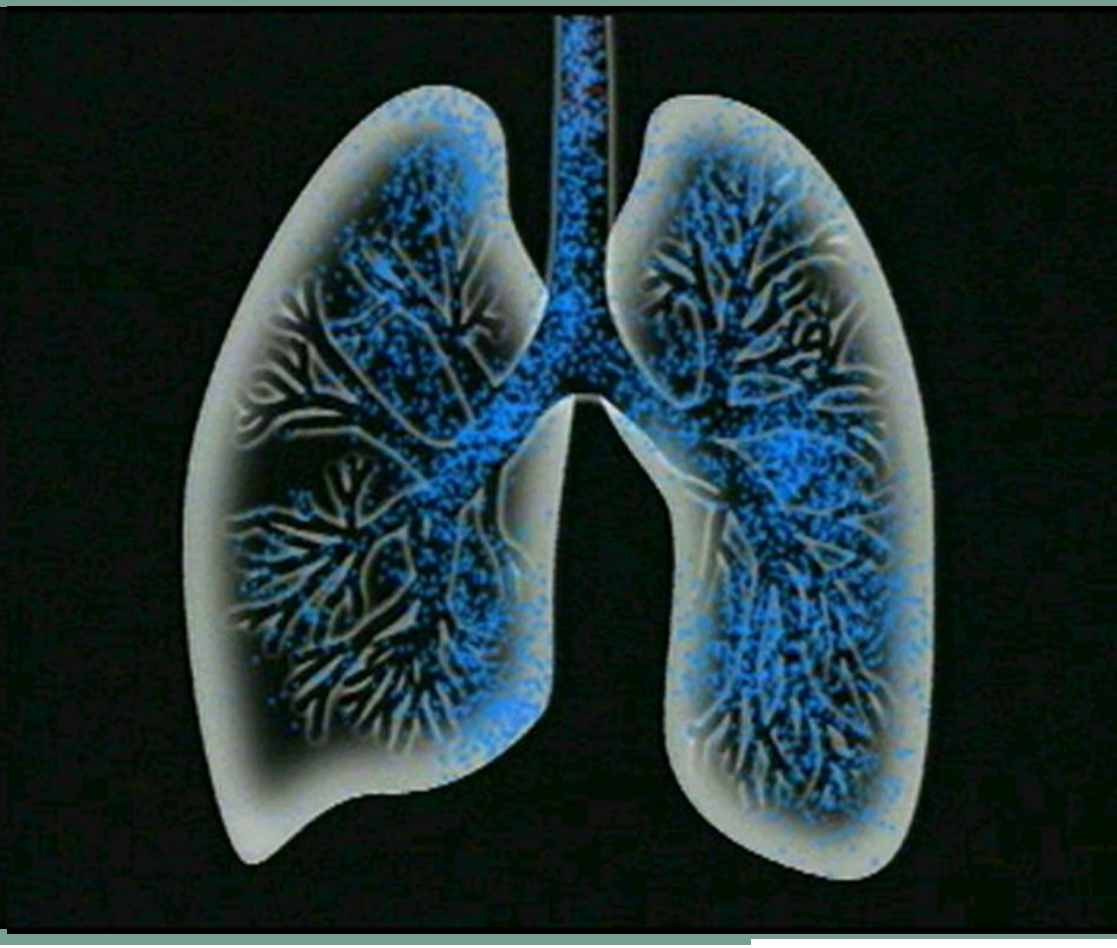
Insufficient control

Theophyllines
Oral GCS

Variability of inspiratory flow can provide inaquality of medication distribution

Normal variability of inspiratory flow





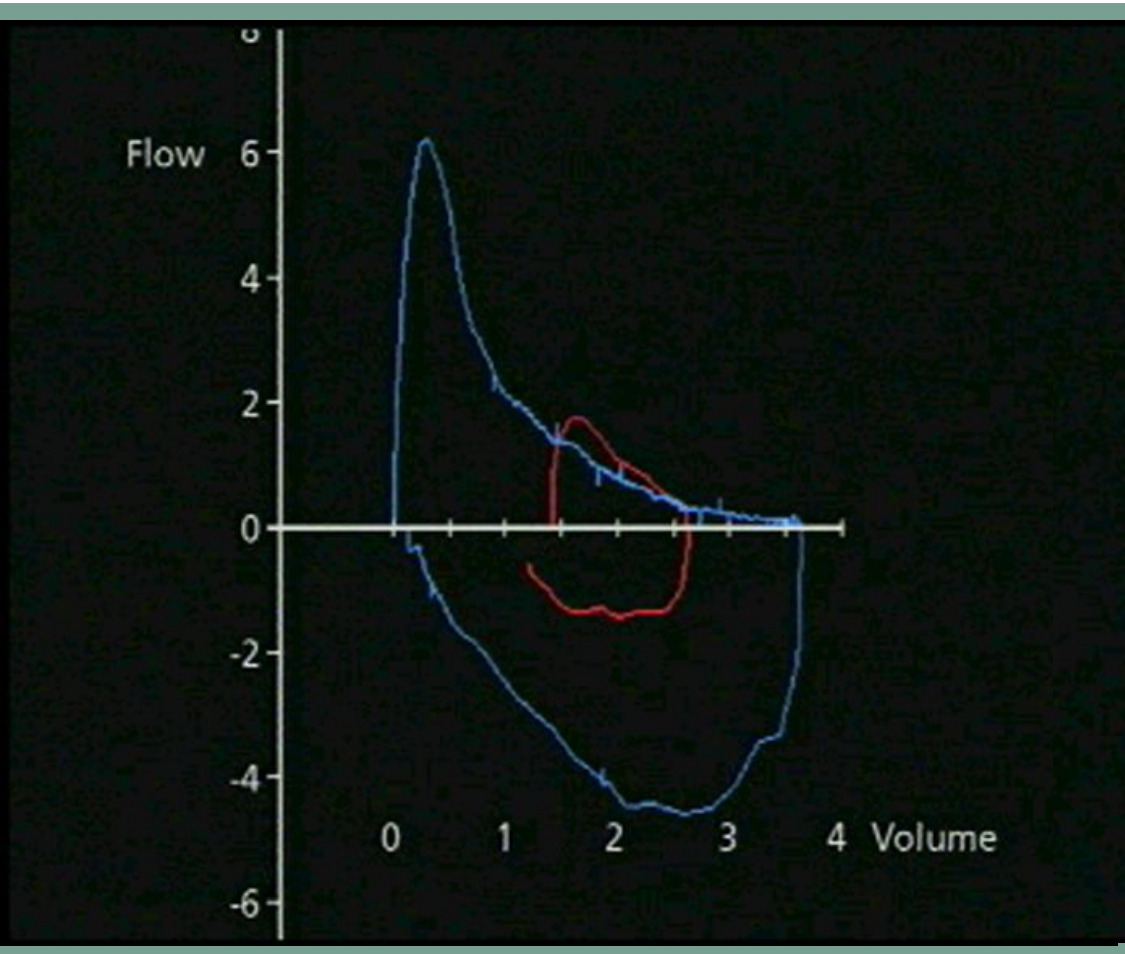
Spirometric curves in patients with BA

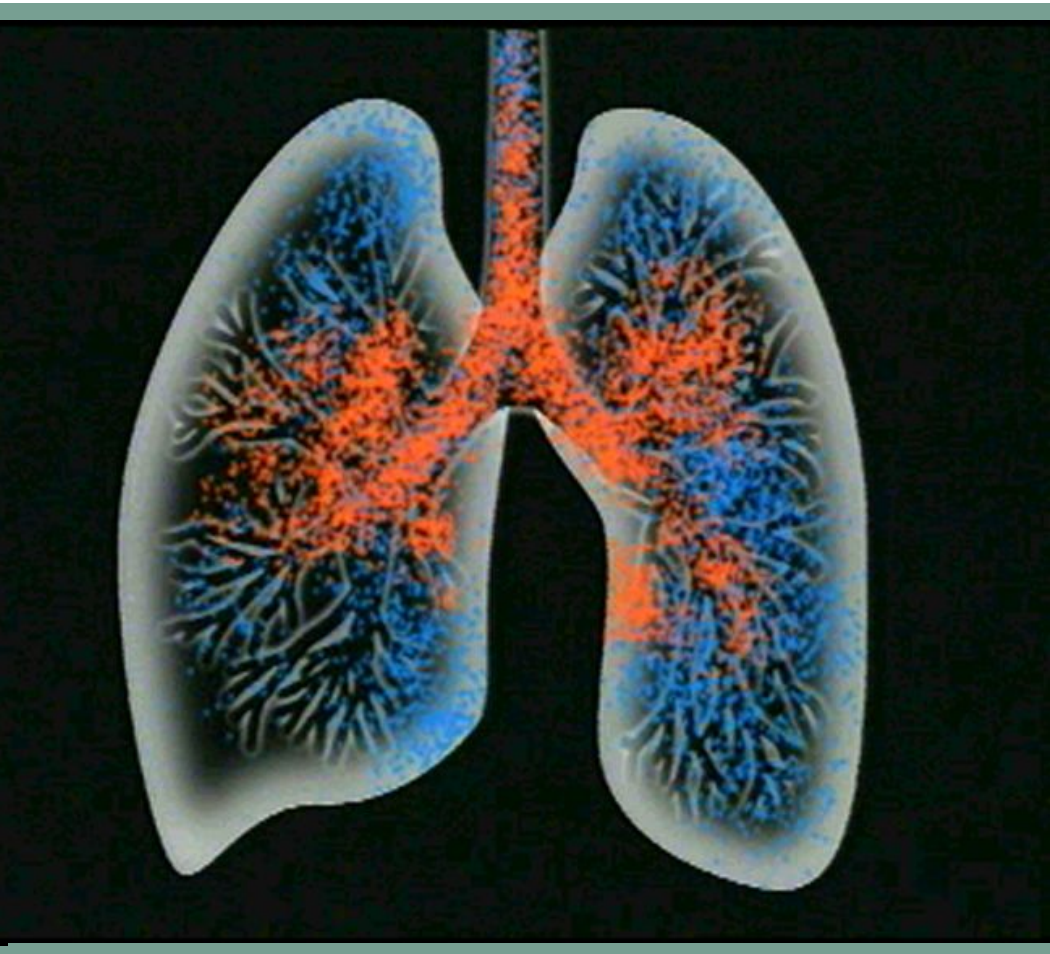
Scheme of medication distribution

Deep inhale – medication deposition in peripheral lungs

Normal variability of inspiratory flow

Variability of inspiratory flow can provide irregularity of medication distribution





Flowmetric curves in BA patient in repeating respiratory attempts

Scheme of medication distribution

Superficial respiration –deposition of drugs in central lung parts

Devices for inhalation of medications

- Metered dosed aerosol inhaler (MDAI)
- Meterd aerosol inhaler with spacer (MDAI+ spacer)
- Meterd powder inhaler (MPI)
- Nebulizers

Technology of inhalation with MDAI

- Stand up to increase mobility of diaphragm
- Take off cap from inhaler
- Shake up inhaler*
- Exhale through tightly closed lips to release lungs from air
- Hold inhaler vertically tightly embrace it by lips and simultaneously press MDAI and inhale
- Close lips and hold respiration for 10 sec
- Exhale by nose

After inhalation of IGCS obligatory rinse mouth by water!

*При использовании новых, бесфреоновых ингаляторов необходимость во встряхивании баллончика отсутствует.

MDAI (metered dosed aerosol inhaler)

If you can’t synchronize MDAI inhaling use it together with spacer

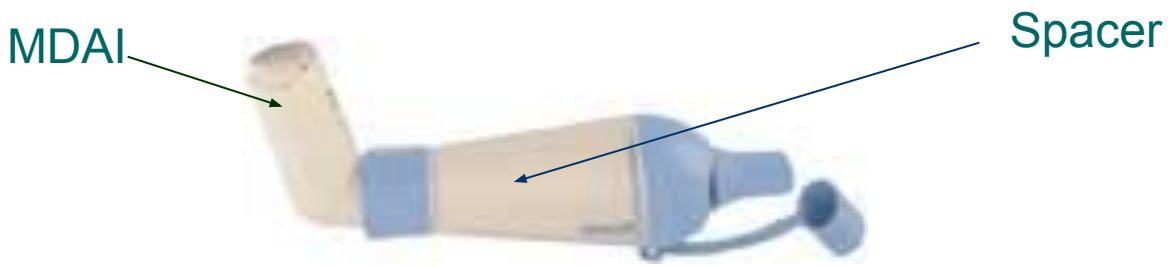
- Spacer usage considerably decrease medication deposition in oral cavity and pharynx , improve its delivery to lungs, decrease topical and systemic side effects due to IGCS

- Spacer usage is recommended to patients, who can’t coordinate inhaling with inhaler activation

1. *Адаптировано из: GINA 2007:* www.ginasthma.org 2. Клинические рекомендации. Педиатрия. Бронхиальная астма. А.А. Баранов (ред.) Гэотар-Медиа. 2005.

Technology of inhalation through spacer

MDAI combination with spacer



Optimal technology of aerosol inhalation through spacer is deep slow inhale or two calm deep inhales (4-5 inhales for children) after releasing of one dosage into the chamber or calm usual breathing for children.

Inhalation technology through spacer in infants and toddlers *Babyhalers*

- Special spacers are babyhalers
- They are supplied by the one side valve, that prevent loosing of aerosol during inhalation and holding aerosol particles during exhalation.
- These spacers are used with special masks, selected to mouth sizes and tightly adjacent
- to face.It can be used in infants and toddlers.

Клинические рекомендации. Педиатрия. Бронхиальная астма. А.А.Баранов (ред.) Гэотар-Медиа. 2005.

MDPI (metered dosed powder inhaler)

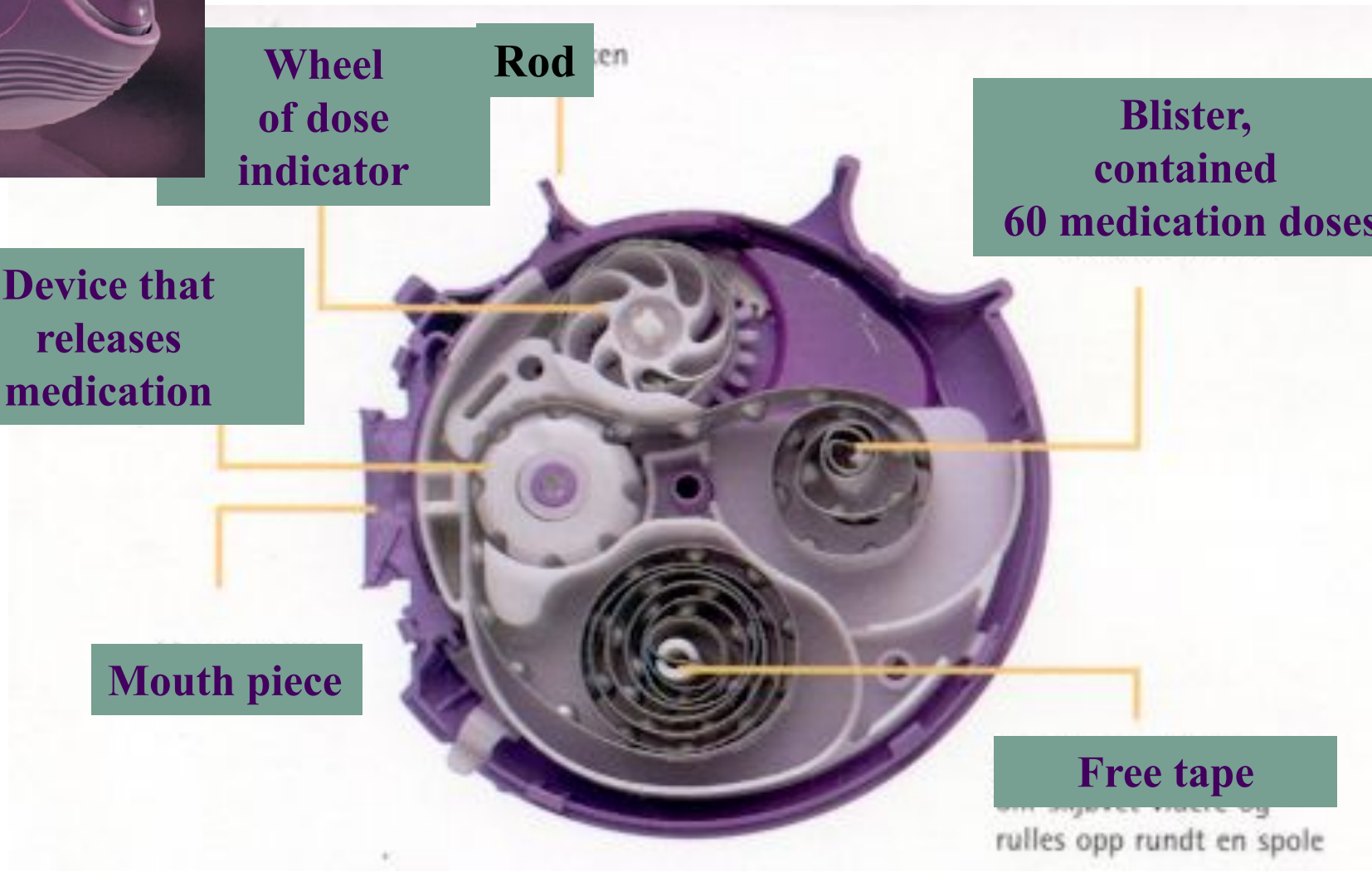
- Usage of MDPI doesn’t demand synchronizing of inhaling with inhaler activation.
- Clinic effect of medications inhalation through MDI and MDPI is the same as well in exacerbation and remission stage.
- Topical side effects are more rare in IGCS through MDPI.
- Nowadays there are such types of MDPI:
  - Multidisk,
  - Turbuhaler,
  - Diskhaler,
  - Aeroliser.

Клинические рекомендации. Педиатрия. Бронхиальная астма. А.А.Баранов (ред.) Гэотар-Медиа. 2005.

Inhalation technology by MDPI

- Prepare inhaler according instruction
- Perform exhalation
- Tightly cope mouth piece by lips
- Make prompt and deep inhalation

Multidisk (Diskus, Accuhaler)

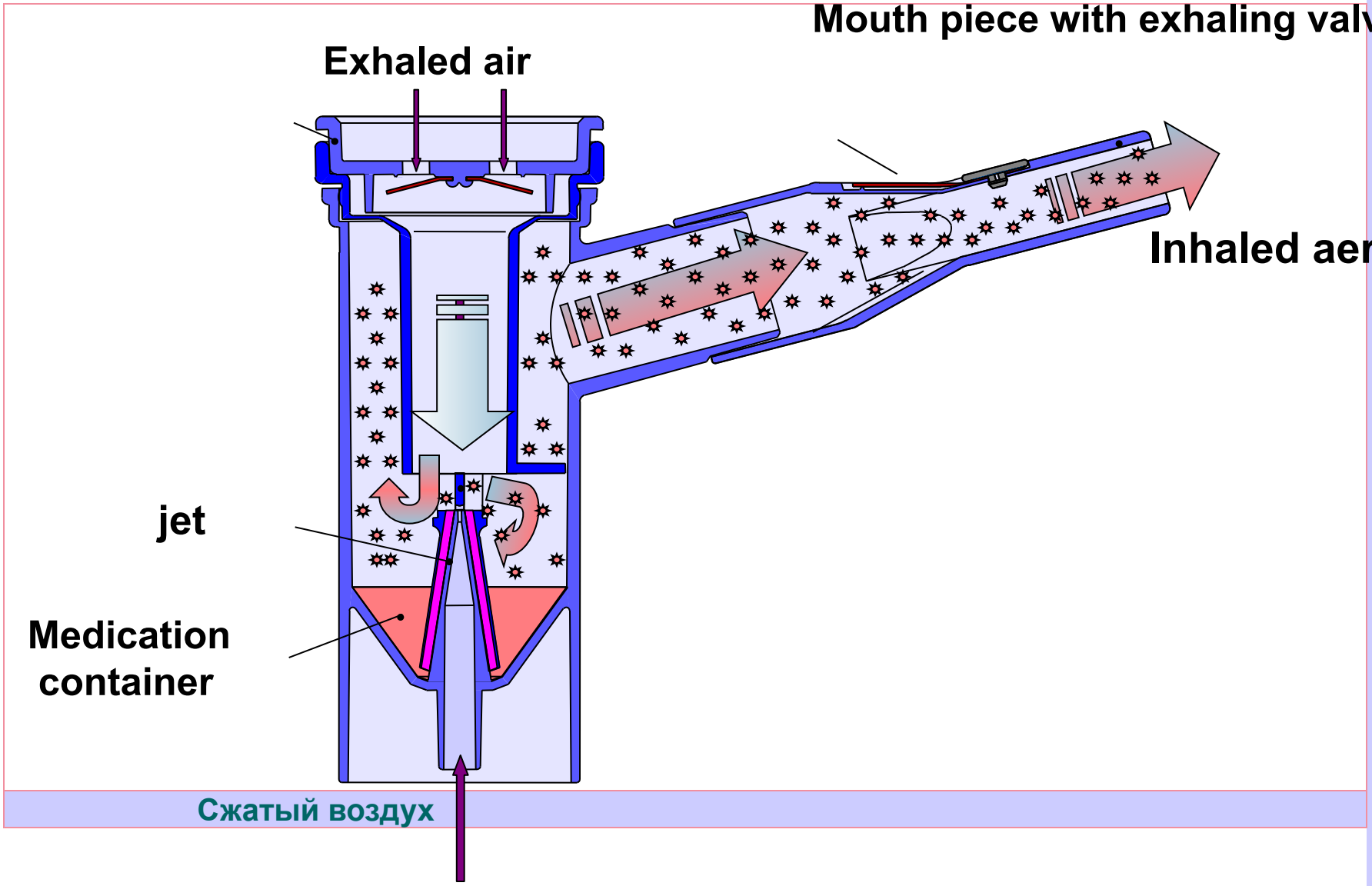


Nebuliser

- Types of nebulisers:
  - compressor
  - ultrasound
- Medication inhalation by nebulizer is performed for 5 min. Elongation of inhalation to 10 min provides non-significant additional effect.
- Nebuliser is used predominantly during severe BA exacerbation

Клинические рекомендации. Педиатрия. Бронхиальная астма.
А.А.Баранов (ред.) Гэотар-Медиа. 2005.

Nebuliser working scheme



Choice of inhaling device for children

Age	Preferable device	Alternative device
Less than 4 years old	MDI + spacer with facial mask	Nebulizer with facial mask
4–6 years old	MDI + spacer with mouth peace	Nebulizer with facial mask
Older than 6 years old	MDPI or MDI with spacer and mouth piece	Nebulizer with facial mask or mouth peace

1. *GINA 2007:* www.ginasthma.org 2. Клинические рекомендации. Педиатрия. Бронхиальная астма. А.А.Баранов (ред.) Гэотар-Медиа.2005.

Medications for nebulizer therapy

- **Ventolin (in nebula 2,5 ml/2,5 mg in undiluted form)**
- **Berodual (solution for inhalations 20 ml in flaconis)**
- **In mild attack 0,1 – 0,02 ml/kg once**
- **In moderate BA attack 0,15 – 0,03 ml/kg**
- **In severe BA attack 0,15 ml every 20 min 3 times, later 0,15 – 0, 3 ml/kg every 3-4 hour.**
- **Prolong therapy 24 – 48 hours, 0,25 every 4-6 hours.**

Asthma control is the main physician task

Адаптировано из: GINA 2007: www.ginasthma.org

Allergen specific immune therapy

- **Nowadays is the only effective treatment method that provides changing of natural course of allergic diseases and prevent BA development in patients with allergic rhinitis.**
- **Standard allergen vaccines are used.**
- **Under the influence of allergen specific immune therapy there is tendency to bronchial reactivity decreasing . It permit to get full control of BA.**

Control questions

- Treatment in depending on a diagnosis.
- Check-up of patients with pathology of respiratory system.
- Physical therapy methods of treatment.
- Sanatorium-and-spa treatment of children with pathology of sanatorium-and-spa treatment ways.
- Methods of prevention. Genetic aspects of diseases of asthma.
- The educational programs are in treatment of asthma.