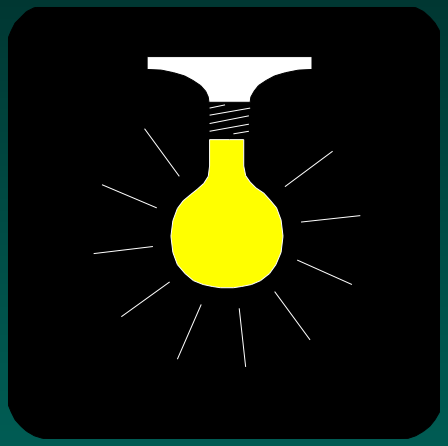
Anesthetizing the Pediatric Patient with Asthma



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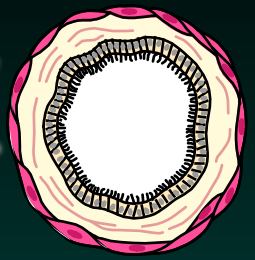
Disclosure Statement

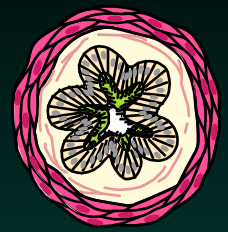
- Nothing to disclose

Learning Objectives

- Discuss the pathophysiology of pediatric patients with asthma
- Describe the current medical management of this disease state
- Describe an approach to the anesthetic management for pediatric patients with this co-existing disease

Asthma





- Greek word - difficulty breathing
- 4 - 9% of children in U.S.
- Onset
  - 50% by age 3
  - 80% by age 5

Asthma

- Most common chronic childhood disease repeated attacks of airway obstruction and airway responsiveness to trigger factors- exercise, allergens and viral
- Most prevalent with family history of atopy
- Triggers- viral, indoor and outdoor allergens, exercise, tobacco smoke and poor air quality
- Infants and preschool age may wheeze and cough with LRTI
- Evidence based – sparse <5 years of age

Clinical Signs of Asthma

- Dyspnea
- Wheezing
- Cough
- Chest tightness

Pathological Signs of Asthma

- Airway inflammation
- Smooth muscle hypertrophy
- Edema
- Mucous plugging
- Plasma exudation
  - Shedding of epithelium and cilia

Difference in Adult and Children- Lung Physiology

- Children 50% of total airway resistance is in peripheral airways - adults 20%- small changes in peripheral airway resistance increase total airway resistance
- Larger closing volume due to increased chest wall compliance and decreased lung compliance
- Decreased lung volumes- early airway closure, CV > FRC, V/P mismatch, intrapulmonary shunting, hypoxemia
- Air trapping - increased lung volume and reduced compliance -increased work of breathing
- Accessory muscles and diaphragm fatigue - infants

Patterns of Wheezing

1. Transient wheezing – wheeze 1st 2-3 years of life but do not wheeze after age 3
2. Non atopic wheezing – triggered by viral infections- remits later in life
3. Persistent asthma – wheezing associated with the following
   - Clinical manifestations of atopy (eczema, allergic rhinitis, conjunctivitis, food allergy) blood eosinophilia and/or elevated total IgE
   - Specific IgE mediated sensitization to foods in infancy and early childhood and susceptibility to common inhaled allergens
   - Inhaled allergen sensitization prior to 3 years of age especially with sensitization and high levels of exposure to perennial allergens in the home
   - A parental history of asthma

PRACTALL consensus report Allergy 2008;63:5-34

Determinants - 1

- Genetic factors – first degree relatives
- Environment and lifestyle as disease modifier triggers

-Allergens – food allergies, indoor allergies (pets, dust mites, mold) and outdoor allergens – (pollens or molds)

- Infection – viral respiratory infection – single most frequent asthma trigger – rhinovirus, RSV in infants – hyper-responsiveness and damage after infection

-Tobacco smoke – strongest – domestic and environmental risk for recurrent coughing/wheezing or asthma at any age in childhood

PRACTALL consensus report Allergy 2008;63:5-34

Determinants - 2

- Pollutants – air pollution
- Nutrition – breast feeding protects development of atopic disease, particularly in atopic heredity
- Irritants – perfume, dust, chlorine
- Exercise – triggers wheezing in most asthmatics – unique asthma phenotype
- Weather – extreme temperatures and high humidity
- Stress – increased with parental stress levels

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Phenotype – Age One of the Strongest Determinants

- Infants (0-2 years old) – major indicator of severity
- Preschool children (3-5 years old) – viral or exercise induced, allergies
- School children (6-12 years old) – atopy seasonality, allergies
- Adolescents – atopic and nonatopic, smoking

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Immunologic Abnormalities

- T cell immunity – imbalance between Th1 and Th2 cytokines
- Atopy – IgE antibodies – allergen sensitization and aberrant response to viral infections – frequent in infancy – increasingly apparent in preschool and school age children

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Structure – Function Interactions - 1

- Airway remodeling – (smooth M hypertrophy, angiogenesis, increased vascularity, chronic inflammatory cell infiltration, goblet cell hyperplasia, collagen disposition, thickening of basement membrane and decreased elasticity of airway wall) – changes persist in absence of symptoms for 6 years
- Bronchial inflammation – airway hyper-responsiveness
- Nasal inflammation

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Structure – Function Interactions - 2

- Inflammatory cells – eosinophil, neutrophils, and cells infiltrate epithelium and cause inflammation
- Airway obstruction - edema, mucus, hyper-secretion and smooth M contraction
- Airway hyper-responsiveness and neural control – cholinergic excitation and adrenergic inhibitors

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Asthmatic Patients

Group I — Patients have a history of asthma but have been asymptomatic and are on no routine medications.

Group II — Patients who have recurrent attacks of asthma and are on prophylactic medications but are not actively symptomatic.

Group III — Patients who are symptomatic or who are deteriorated from their normal condition.

$Beta_2$ Adrenergic Agonists

- Acute or chronic therapy
- Inhaled β_2 adrenergic - faster, fewer side effects
  - Albuterol, terbutaline, fenoterol, pirbuterol, and salmeterol
- Smooth muscle relaxation and increased mucociliary clearance via adenyl cyclase increasing cAMP, decreased histamine release
- May also be given by MDI, oral or IV routes

Corticosteroids

- Anti-inflammatory- used earlier in treatment
- Potentiate beta adrenergic system, inhibit release of mediators of inflammation and edema
- Inhaled agents - control symptoms, preserves lung function, reduces airway inflammation, decreases total airway reactivity, minimizes the risk of systemic toxicity
- IV agents- may be useful for emergency surgery in patients that are wheezing

Inhaled Corticosteriods

- Growth can be affected – dry powder inhalers worse than MDI's, less effective if taken in morning
- Hypothalamic pituitary axis supression – may occur with beclomethasone > 800 ug or equivalent
- Bone – no effect on bone density
- Ocular – posterior subcapsular cataracts, ocular hypertension, glaucoma
- LABA should not be used without an appropriate concurrent ICS dose and only in children older than 5 years

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Cromolyn Sodium

- Prophylaxis against acute attacks
- 2 - 4 weeks to produce clinical change- inhaled agent
- Inhibits release of mediators from mast cells
- No place in treatment of acute asthma

Anticholinergics

- Decrease bronchial smooth muscle tone and mucous gland secretion mainly in central airway, larynx and large bronchi
- Inhaled (ipratropium bromide)
- IV - atropine, glycopyrrolate
- May be less effective for chronic use in pediatric patients

Leukotriene Pathway Modifiers - 1

- 1st new drugs in 20 years for treatment of asthma
- Slow reactive substance of anaphylaxis - airway smooth muscle contraction by a non-histamine mechanism
- Leukotrienes induce edema, migration of eosinophils and stimulation of airway secretions via the 5-lipoxygenase pathway

Leukotriene Pathway Modifiers - 2

- Leukotriene receptor antagonist - Montelukast (Singulair^{R}) - 5 mg q hs (age 1-12 yrs)
- Indications for use
  - Exercise induced asthma
  - Aspirin induced asthma
  - First line therapy - may be chosen before inhaled glucocorticoids and decrease need for rescue beta agonists and oral glucocorticoids

Theophylline

- Methylxanthine - bronchodilator - inhibits adenosine mediated bronchoconstriction
- Synergistic with $beta_2$ agonists
- Narrow therapeutic index - 10-20 ug/ml
- Toxicity - headaches, tremors, seizures, arrhythmias

Asthma Treatment in Children Aged 0-2 years -1

- Consider a diagnosis of asthma if >3 episodes of reversible bronchial obstruction have been documented within the previous 6 months
- Intermittent β2 agonists are first choice (inhaled, jet nebulizers in the US and oral in Europe) despite conflicting evidence
- LTRA daily controller therapy for viral wheezing (long- or short-term treatment)

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Asthma Treatment in Children Aged 0-2 years -2

- Nebulized or inhaled (metered-dose inhaler and spacer) corticosteroids as daily controller therapy for persistent asthma, especially if severe or requiring frequent oral corticosteroid therapy
- Evidence of atopy/allergy lowers the threshold for use of ICS and they may be used as first-line treatment in such cases
- Use oral corticosteroids (e.g. 1-2 mg/kg prednisone) for 3-5 days during acute and frequent recurrent obstructive episodes

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Asthma Treatment in Children Aged 3-5 years - 1

- ICS are the first choice, budesonide 100-200 ug x 2 or fluticasone 50-125 ug x 2 by MDI
- Short-acting β2 agonists, salbutamol 0.1 mg/dose or terbutaline 0.25 mg/dose 1-2 puffs at 4-h intervals as needed
- LTRA can be used as monotherapy instead of ICS if symptoms are intermittent or mild persistent

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Asthma Treatment in Children Aged 3-5 years -2

- If full control is not achieved with ICS, add LTRA-montelukast 4 mg granules or 4 mg chewing tablet
- If control still not achieved consider the following (nonsequential) options:
  - Add LABA at least intermittently (although note lack of published evidence supporting use in this age group)
  - Increase ICS dose
  - Add theophylline

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Long Term Management of Severe Asthma - 1

- Education
- Monoclonal antibody therapy – Omalizumab binds to IgE – age 12 and older with severe allergic asthma and IgE sensitivity to inhaled allergens – subQ q 2-4 weeks decreases risk of severe exacerbations
- Subcutaneous injection or sublingual immunotherapy – immune modulation – can be used in children as young as 3 years of age

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Long Term Management of Severe Asthma - 2

- Spirometry -yearly assessment of lung function – PEF and FEV1 (obstruction)
  - Exercise testing
- Exhaled nitric oxide – good marker of eosinophilic airway inflammation – optimizes ICS treatment, may identify those in whom ICS can be safely reduced or withdrawn

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Severity of Asthma	Symptoms	Treatment
Mild	Infrequent brief Good exercise tolerance, asymptomatic in-between, infrequent nocturnal symptoms	1. Inhaled β agonist 2. Oral β agonist in infants and young children
Moderate	Symptoms > 2 per week Decreased exercise tolerance Exacerbations last several days Symptoms at night 2 or 3 x a week	1. Cromolyn Na 2. Inhaled corticosteroids 3. β agonists for acute attacks 4. Leukotriene pathway modifiers
Severe	Continued symptoms Limited activity Frequent exacerbations Nocturnal symptoms every night Hospitalization	1. Oral plus inhaled corticosteroids 2. β agonists 3. Theophylline

Preoperative Evaluation - 1

- Severity of disease correlates with risk of respiratory complications intraoperatively
  - Age at onset
  - Frequency
  - Typical attack
  - Attacks that require steroids, hospitalization, intubation or care in ICU
  - Coexisting lung disease - BPD, prematurity, cystic fibrosis

Preoperative Evaluation - 2

- Precipitants to exacerbation - exercise, cold air, dry air, upper or lower tract infection, smoke, GE reflux
- Therapy maximized
- Current medications
- Supplemental medication taken during exacerbation

Preoperative Evaluation - 3

- Physical Exam
  - Wheezing
  - Prolonged expiratory phase
  - Increased work of breathing (nasal flaring, accessory muscle use, tachypnea)
- Lab Data
  - Room air oxygen saturation with pulse oximeter
  - Chest x-ray - specific pulmonary pathology eg pneumonia
  - ABG - normal in mild asthma
  - PFT - spirometry- obstructive pattern - increased CV, FRC and decreased FEV_1 and FVC

URI

- Increased airway reactivity
- Mucosal edema
- Airway plugging
- Postpone 4 - 6 weeks

Anesthetic Risk Factors in Children

- Preliminary data indicate asthmatic children are 5.5 times more likely to experience wheezing perioperatively than nonasthmatics and are more likely to have perioperative respiratory complications

L Caramico, et al. Anesth Analg 1997;84:S183.

Incidence of Perioperative Complications

Perioperative complications	Asthmatic n=111 (%)	Nonasthmatic n=824 (%)	Relative Risk 95% CI
Any wheezing	12 (11%)	12 (2%)	5.5 (2.4-12.5)
Cough - I	6 (5%)	3 (0.4%)	12.5 (3.1-50.9)
Stridor - P	3 (3%)	3 (0.4%)	6.8 (1.2-42)
SpO_2 <95% - P	5 (5%)	6 (0.7%)	6.4 (1.9-21)
SpO_2 <95% - PO	2 (2%)	2 (0.2%)	10 (2.8-36)

I=intraoperative; P=PACU; PO=postoperative day 1.

Risk Factors for Wheezing in Asthmatic Patients (n=111)

Variable	Wheezing (n=12)	No Wheezing (n=99)	p value
URI ≤1 mo ago	9 (75%)	36 (36%)	0.01
Last attack ≤1 yr	9 (75%)	45 (46%)	0.05
Last attack ≤1 mo	8 (67%)	26 (26%)	0.004

DISCUSSION: These preliminary data indicate that asthmatic children are 5.5 times more likely to experience wheezing perioperatively than nonasthmatics, and are more likely to have perioperative respiratory complications.

Preoperative Management Therapy Maximized

- Mild asthma- nebulized beta $_2$ agonist prior to surgery
- Moderate asthma- regular use of beta $_2$ agonist one week prior to surgery and addition of an inhaled or oral anti-inflammatory agent
- Severe asthma- frequent or recent asthma exacerbation-oral prednisone 1 mg/kg (60 mg max.) for 3-5 days prior to surgery or oral dexamethasone 0.6 mg/kg (16 mg max.) or methylprednisolone 1mg/kg for 48 hours prior to surgery

Zachary CY, et al. Ann Allergy Asthma Immunol 1996;77:468-72
Qureshi F, et al. J Pediatr 2001;139:20-26

Corticosteroid Administration

- Currently taking oral or intravenous corticosteroids or have had 3 courses in the past year or one course in the previous 4 to 6 months need supplementation
- Hydrocortisone 1 mg/kg IV
- Emergency surgery - IV steroids will decrease airway inflammation within several hours and are indicated

Preoperative Preparation and Induction

- Premedication - oral midazolam 0.5-1 mg/kg or IV 0.05-0.1 mg/kg
  -no adverse effects in mild to moderate asthma

  Kil N et al. Pediatr Dent. 2003;25:137-42

- Intravenous glycopyrrolate (0.01 mg/kg) or atropine (0.02 mg/kg)

Induction Agents - 1

- Thiopental may release histamine
  - Airway instrumentation may cause bronchospasm
- Ketamine - smooth muscle relaxation and bronchodilation
  - In the actively wheezing child (especially with hemodynamic instability), may be the agent of choice -increased airway secretions
  - Profound depression of airway reflexes

Induction Agents - 2

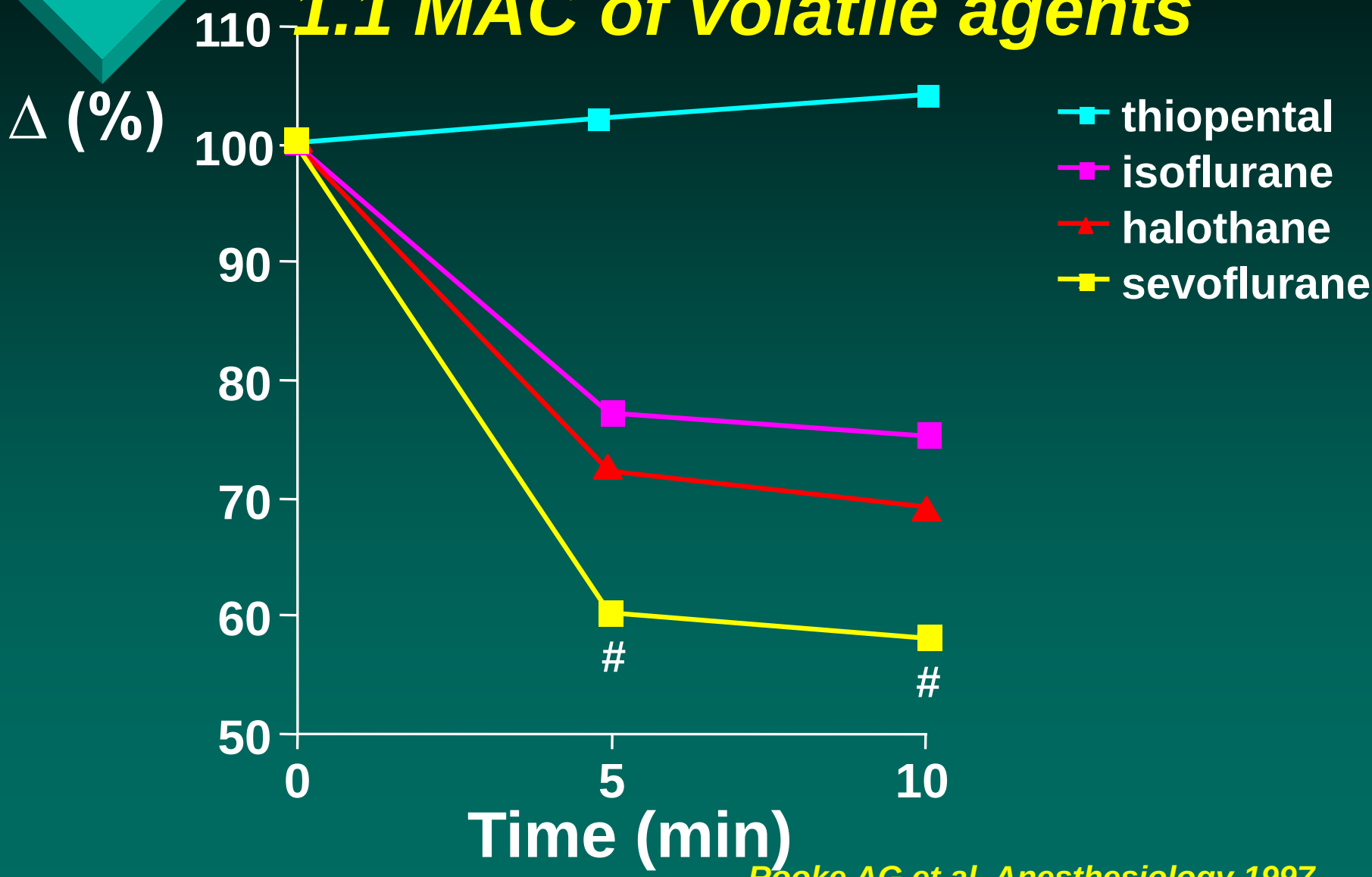
- Propofol
  - Less incidence of wheezing after intubation as compared to thiopental
  - Profound depression of airway reflexes
  - Agent of choice in the hemodynamically stable patient
- Etomidate - not protective
- Lidocaine - IV, 1 - 1.5 mg/kg 1-3 min prior to intubation
  - Prevents reflex bronchoconstriction, better than spraying of the airway

Induction Agents - 3

- Halothane
  - Bronchodilation
  - Cardiac dysrhythmias with adrenergic agents or methylxanthines
- Isoflurane, Desflurane
  - Bronchodilation--desflurane less bronchodilation than sevoflurane

    Goff MJ et al. Anesthesiology 2000;93:404-8
  - Breath holding/laryngospasm
- Sevoflurane
  - Bronchodilation
  - Decreased laryngospasm and dysrhythmias

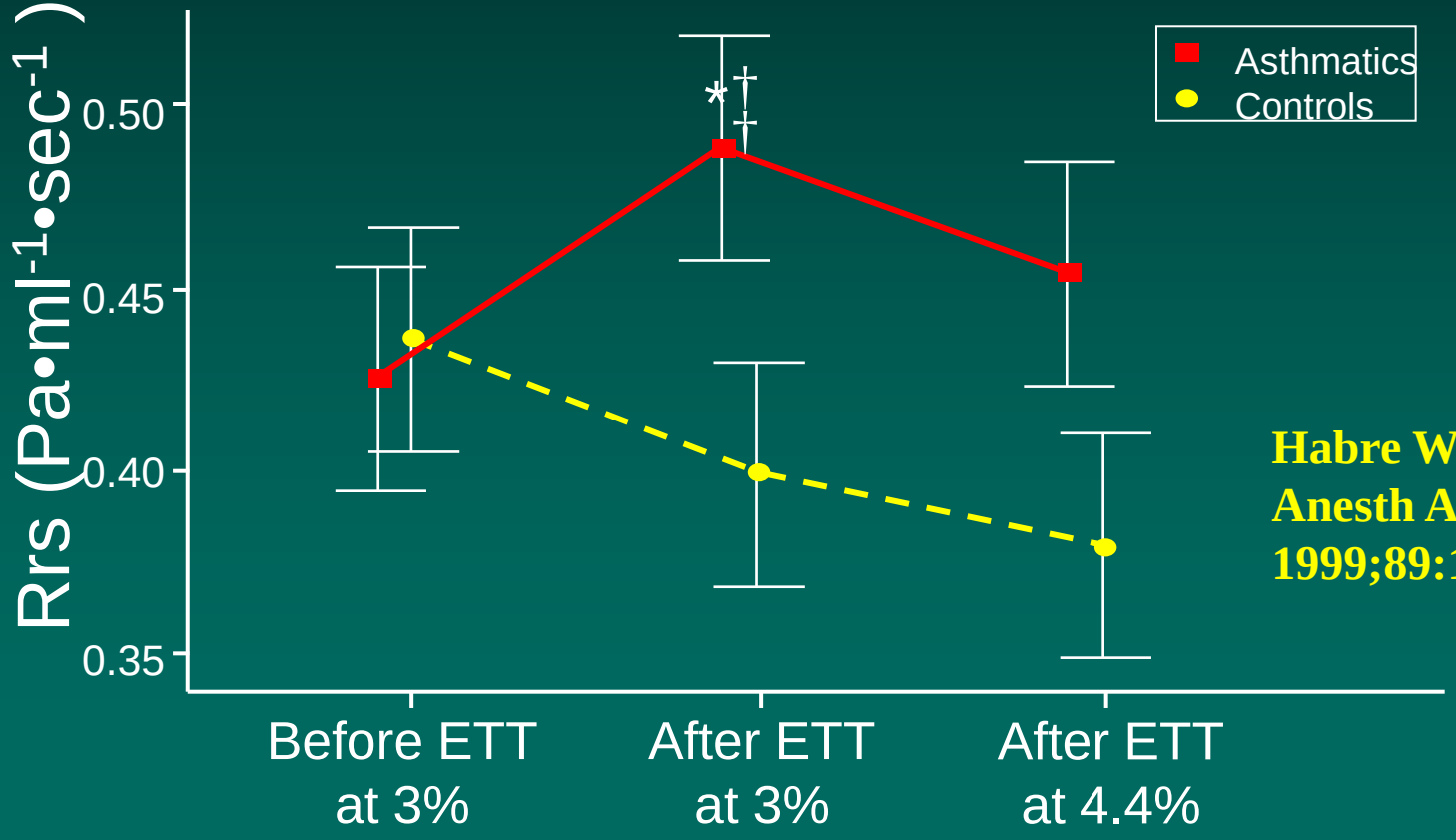
Airway resistance after tracheal intubation 1.1 MAC of volatile agents



Rooke AG et al. Anesthesiology 1997

Respiratory Mechanics in Children with and without Asthma

44 children, 22 asthmatics, 22 controls
Induction sevo. 8% + 50% N_2O - sevo 3% (preETT vol.) - trach. intubation at 5%
Spontaneous ventilation at 3% (1.2 MAC) followed by 4.2% (1.7 MAC)



Habre W et al., Anesth Analg 1999;89:1177

Respiratory Mechanics in Children with and without Asthma

When comparing children with and without asthma, tracheal intubation under sevoflurane was associated with an increase in respiratory system resistance in asthmatic children

Habre W et al., Anesth Analg 1999;89:1177

In children anesthetized with propofol, sevoflurane 1 MAC slightly decreased airway resistances (NS)

Habre W et al., ASA 2007;A1615

Salbutamol Prevents the Increase of Respiratory Resistance Caused by Tracheal Intubation During Sevoflurane Anesthesia in Asthmatic Children

Pietro Scalfaro, MD, Peter D. Sly, MD, FRACP, Craig Sims, FANZCA and Walid Habre, MD

Anesth Analg 2001;93:898-902

Data

- 30 children ASA I or II with mild to moderate asthma and wheezing in the last 12 mo
- Salbutamol or placebo 30-60 minutes prior to inhalation induction with sevoflurane
- Airway opening pressure and flow measured before and after insertion of oral endotracheal tube
- Respiratory system resistance **decreased 6.0%** with salbutamol and **increased 17.7%** in the placebo group

Desflurane but Not Sevoflurane Impairs Airway and Respiratory Tissue Mechanics in Children with Susceptible Airways

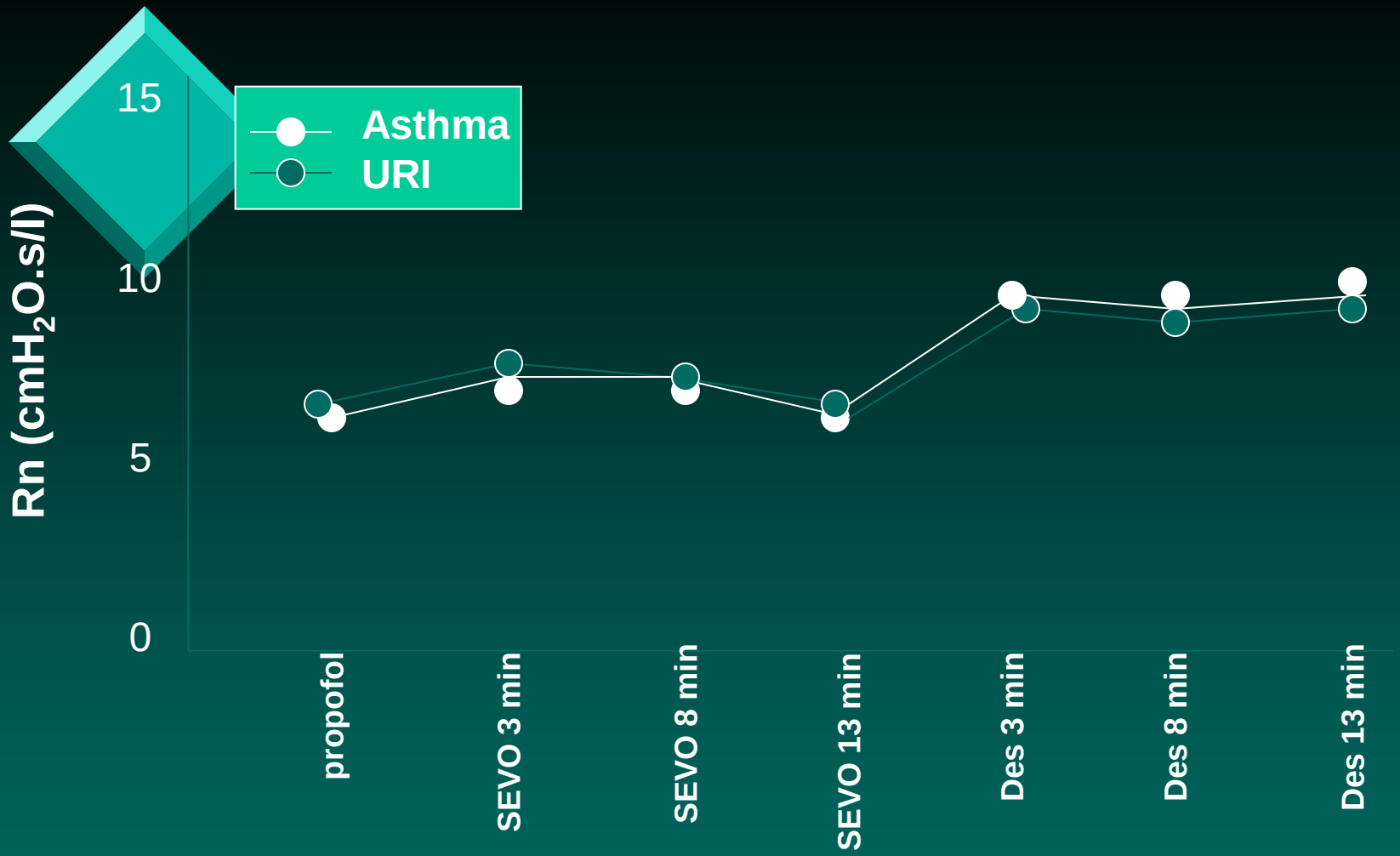
Britta S. von Ungern-Sternberg, M.D.,
Sonja Saudan, M.D.,
Ferenc Petak, Ph.D., et al

Anesthesiology 2008;108:216-24.

Data

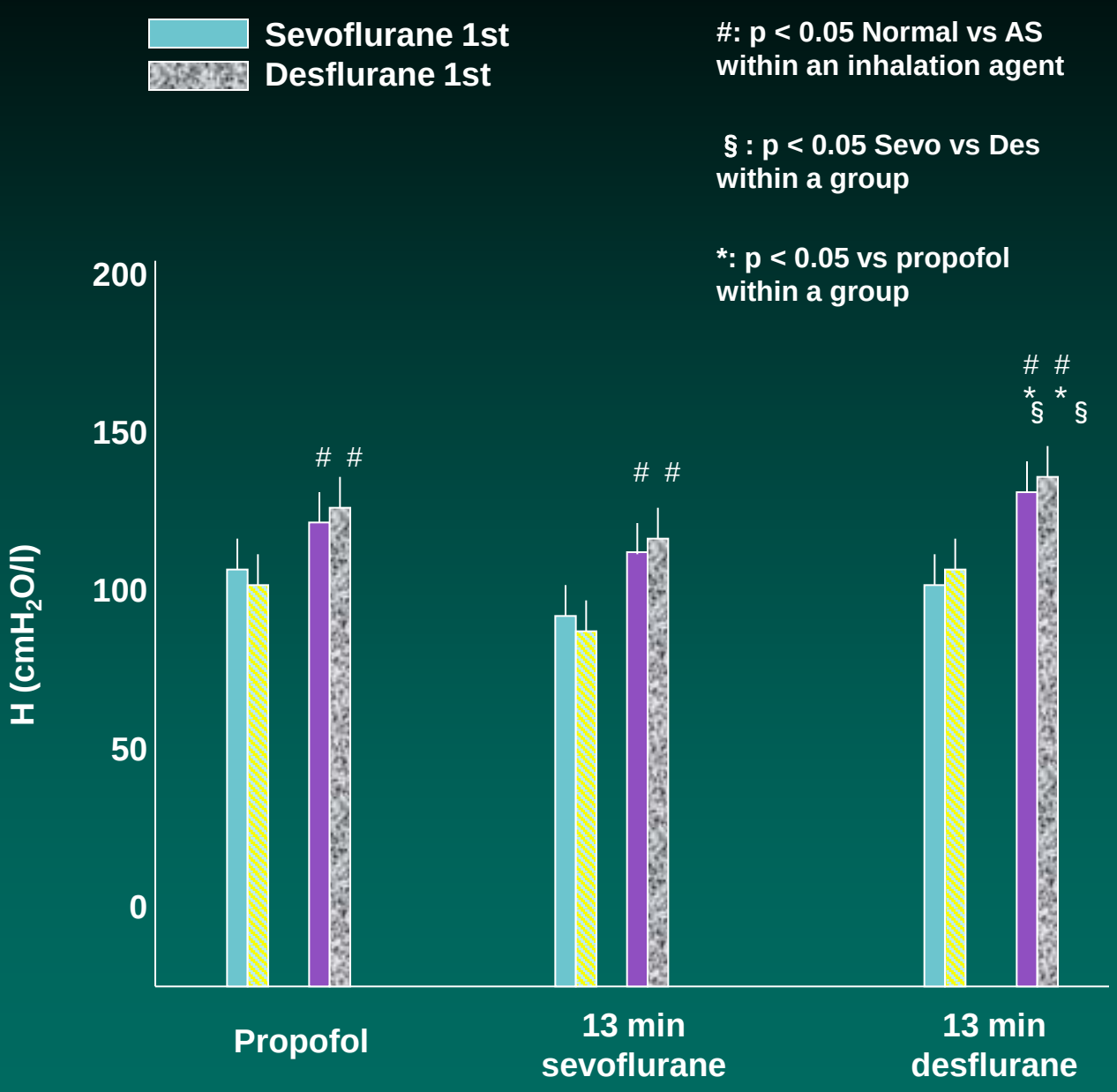
- 40 children, average age - 39 months, 20 children (Group C), 20 children (Group AS)
- Airway susceptibility (Group AS) - 10 children with asthma, 10 children with URI in past 2 weeks
- Baseline propofol anesthetic and either addition of desflurane or sevoflurane
- 4 asthmatics had salbutamol treatment the morning of surgery

Anesthesiology 2008:108:216-24



Changes in the airway resistance (Rn) during sevoflurane (sevo 3 min-sevo 13 min) and desflurane (des 3 min-des 13 min) administration in children with susceptible airways due to asthma or recent upper respiratory tract infection (URI). Data are mean ± SEM (n = 10 in each group). * $P < 0.05$ *versus* propofol.

Anesthesiology 2008;108:216-24.



Airway resistance (Rn), inertance (I), and tissue damping (G) and elastance (H) in children with normal airways (*open and cross-hatched bars with white background)* and with airway susceptibilities (AS, *open and cross-hatched bars with gray background)* during propofol, and 13 min after sevoflurane and desflurane administration in children receiving either sevoflurane (*open bars)* or desflurane (*cross-hatched bars)* first. Data are mean ± SEM (n = 10 for each column). # *P* <0.05, normal *versus* bronchial hyperreactivity for a given inhalation agent. § *P* <0.05, sevoflurane (Sevo) *versus* desflurane (Des) within a group. * *P* <0.05 *versus* propofol within a group.

Anesthesiology 2008;108:216-24.

Airway Resistance at the Different Assessments for Children with Doctor-diagnosed Asthma

	Propofol	Sevo 3 min	Sevo 8 min	Sevo 13 min	Des 3 min	Des 8 min	Des 13 min	Salbutamol
Mean	6.5	6.7	6.4	6.0	10.0	10.1	10.2	No
SD	2.1	2.2	1.9	1.6	2.7	2.9	2.9	
Mean	7.0	7.6	7.2	6.8	11.5	11.1	11.5	Yes
SD	2.3	2.0	1.9	1.9	3.5	2.7	3.6	

Randomization to anesthetic agent and salbutamol therapy on day of surgery is indicated.
Des = desflurane; sevo = sevoflurane

Anesthesiology 2008;108:216-24.

Muscle Relaxants

- Atracurium and

  d-tubocurarine release histamine should be avoided
- Vecuronium, Rocuronium , Cisatracurium - agents of choice
- Reversal with neostigmine
  - Doesn't cause bronchospasm if combined with atropine or glycopyrrolate

NSAIDS and Asthma

- Safe to use acetaminophen, ibuprofen, and ketorolac
- Caution in patients with nasal/ethmoidal polyposis with asthma and aspirin sensitivity (Samter's triad)
- Avoid in severe asthmatics?

PRACTALL consensus report Allergy 2008;63:5-34

Other Caveats

- Avoid endotracheal intubation whenever possible
- Mask or LMA (manipulation of larynx can precipitate bronchospasm)
- Humidify gases - dry gas can provoke bronchospasm
- Avoid histamine releasing drugs - meperidine, morphine, atracurium
- Regional analgesia to avoid pain and allow deep breathing
- Always reverse neuromuscular blockade

Extubation

- Deep extubation if nature of surgery and anatomy of the airway allow
- Lidocaine - blocks afferent irritant vagal pathways and may directly relax airway smooth muscle - 1-1.5 mg/kg IV may be given for prophylaxis of bronchospasm
- Atropine 0.02 mg/kg

Intraoperative Bronchospasm

- Light anesthesia
- Kinked ET tube
- Tension Pneumothorax
- Endobronchial intubation
- Increased airway secretions
- Pulmonary edema
- Aspiration
- Anaphylaxis

Treatment of Intraoperative Bronchospasm - 1

- 100% oxygen administration
- Deepen the anesthetic with a volatile agent, propofol or ketamine
- Administer an inhaled beta 2 agonist, albuterol, it may take 10-20 administrations until bronchospasm is relieved or tachycardia limits further use

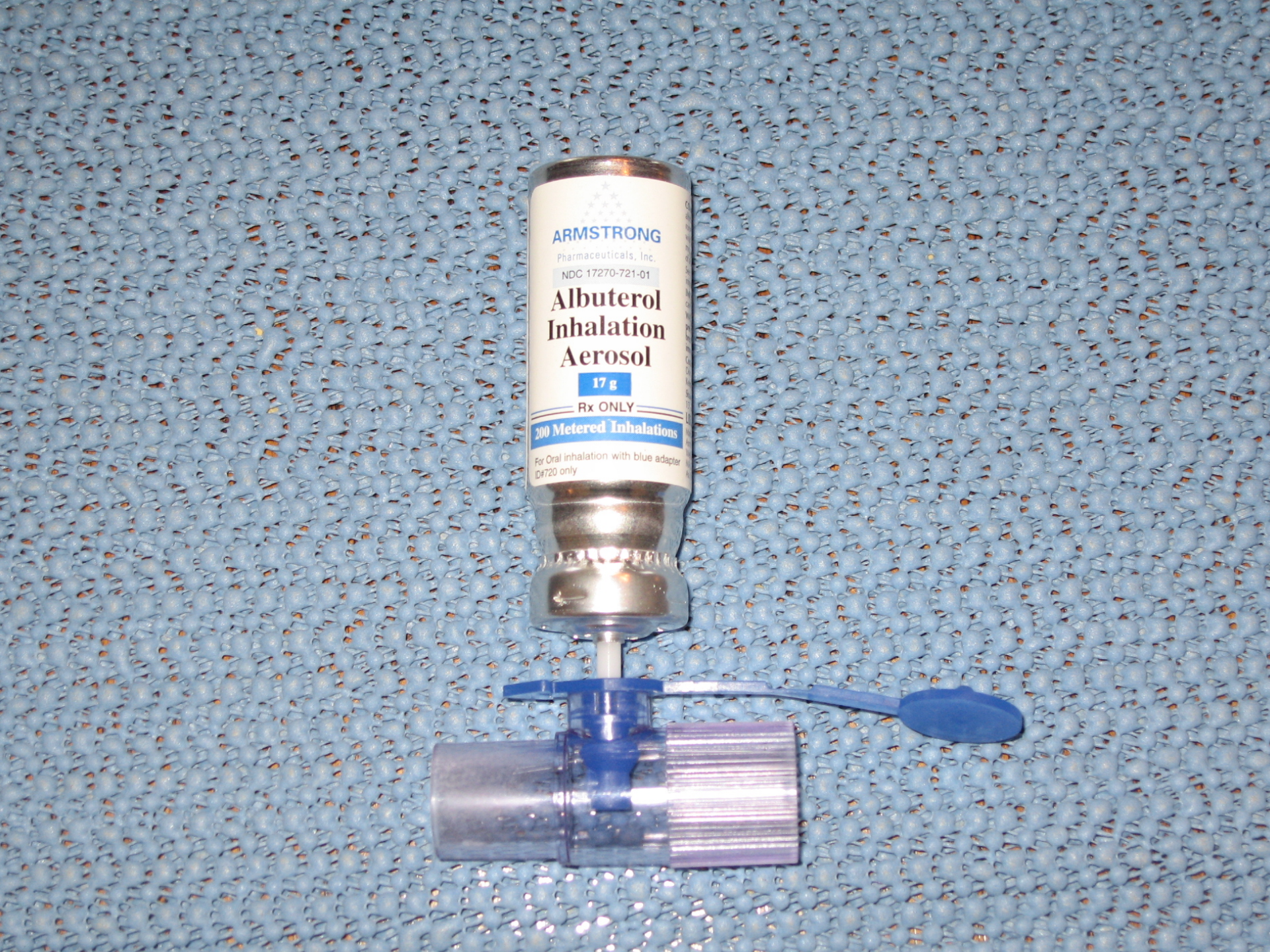
Delivery of Beta-2 Agonists in Intubated Patients

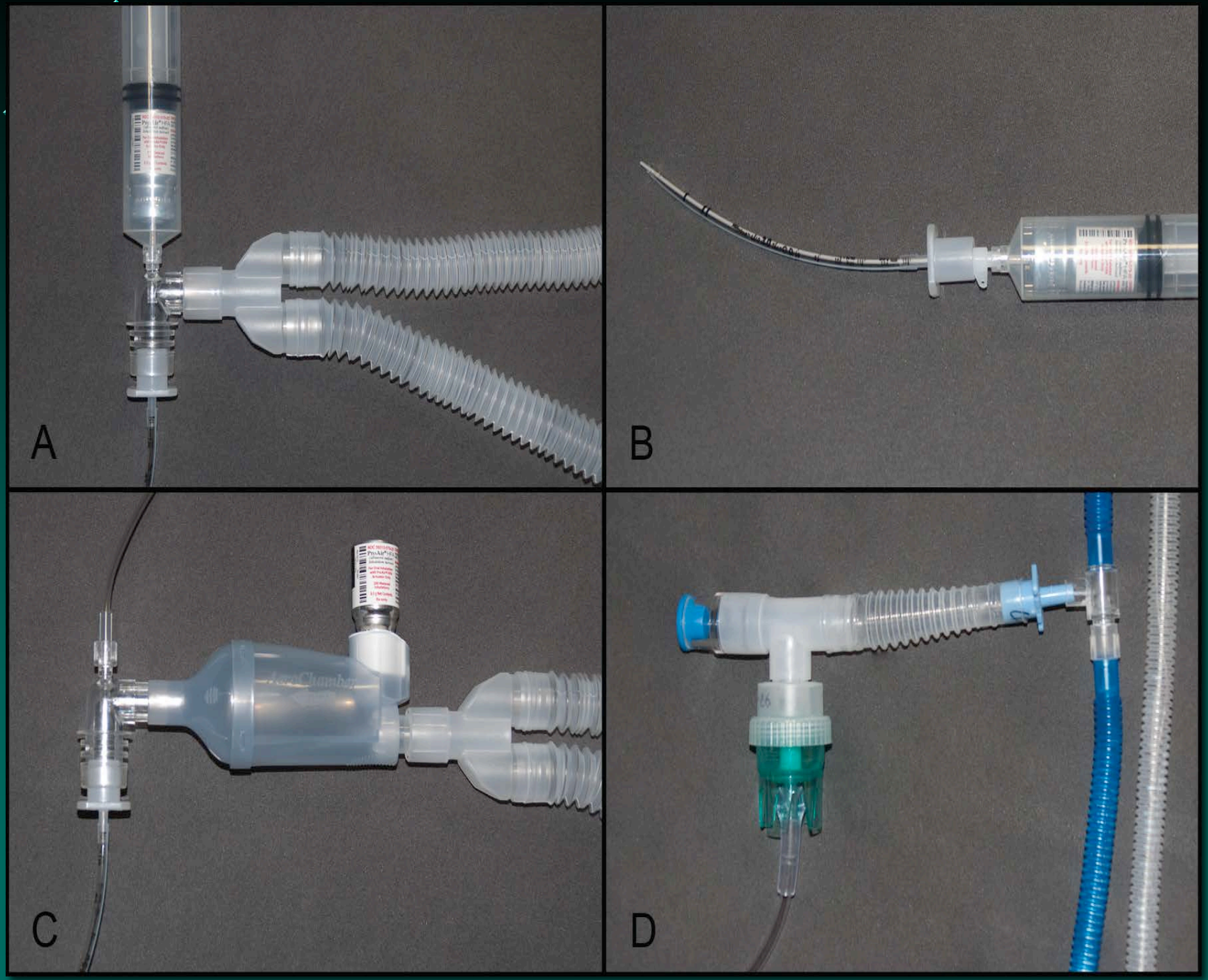
- Delivery by MDI through 3.0-6.0 mm ID tracheal tube is low (2.5-12.3% of discharged dose)
- May be increased 10 fold by actuating the canister into a 19 G distally placed catheter
- May also increase toxicity - to avoid
  - 1) Only one puff at a time
  - 2) Puff to puff intervals should be 2-5 min apart
  - 3) Maximum cumulative puffs = 1/5 kg
  - 4) Continuous ECG monitoring

Taylor RH et al Anesthesiology 1991;74:360-63


ALBUTEROL
INHALATION AEROSOL
17 grams
MAX
BD
2oz


ALBUTEROL
17 grams


ARMSTRONG
Pharmaceuticals, Inc.
NDC 17270-721-01
Albuterol
Inhalation
Aerosol
17 g
Rx ONLY
200 Metered Inhalations
For Oral inhalation with blue adapter
ID#720 only


A
B
C
D

Treatment of Intraoperative Bronchospasm - 2

- IV corticosteroids- methylprednisolone 1-2mg/kg or hydrocortisone 1-3 mg/kg
- IV lidocaine 1.0 to 1.5 mg/kg and/or atropine 0.02 mg/kg
- Sub Q epinephrine 10µg/kg, terbutaline 5-10µg/kg or IV epinephrine or isoproterenol
- Pressure controlled ventilation- low inflating pressure, prolonged expiratory time