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มหาวิทยาลัยศรีนครินทรวิโรฒ

Rationale use of Bronchodilator in Reactive Airways Disease

Somboon Chansakulporn, MD
Division of Allergy and Immunology, Department of Pediatrics
Srinakharinwirot University

ด.ช. ไทย อายุ 3 ปี ไอ หอบ มา 6 ชม. ก่อนมา รพ.

2 วัน ก่อน เริ่มมีอาการน้ำมูกใส ไอเล็กน้อย ไข้ต่ำๆ แม่บอกว่า เคยเป็นแบบนี้มา 2 รอบตั้งแต่อายุ 1½ ปี มักเป็นตามหลังอาการหวัด

PE: active, dyspnea, BT 38.2°C, RR 50 /min

HEENT: clear rhinorrhea, mild injected pharynx

Lung: generalized expiratory wheezing, poor air entry

แพทย์ได้ให้การรักษาด้วยการให้ salbutamol nebulization x 2 ครั้ง ห่างกัน 20 นาที

Lung: clear, no wheezing, good air entry

ท่านจะให้การวินิจฉัยอะไรเบื้องต้น :

A. Reactive airway disease

B. Viral-induced wheezing

C. Asthma

What is Reactive Airways Disease (RAD)?

- Not a diagnosis !!!
- A nondiagnostic term that described the following symptoms in young children:
  - Recurrent wheeze, cough, sputum production or dyspnea
- Practical use of this term
  - Young children (under 5 years old) with wheezing (1st or 2nd episodes)
  - Other asthma-like symptoms in the setting of viral lower respiratory infections (Viral-induced wheezing)
  - Uncomfortable to diagnose asthma on initial presentation

Douglas LC, Feder KJ. Pediatrics. 2017;139(1):e20160625.
Fahy JV, O'Byrne PM. Am J Respir Crit Care Med. 2001;163:822–823.
Douros K, Everard ML. Front Pediatr. 2020 May 5;8:218.

Reactive Airways Disease (RAD)

- Preschool wheezing / asthma (which was treated as asthma)
- Interchangable terms
  - "Asthma-like symptoms" or "Recurrent wheeze"
  - Bronchial hyper-responsiveness (BHR)
  - Viral-induced wheezing
  - Transient asthma

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RAD or Asthma?

Clinical Outcomes for Young Children Diagnosed With Asthma Versus Reactive Airway Disease

- Retrospective cohort analysis, university-based general pediatrics practice
- 403 children (2–7 yo), diagnosed with RAD or asthma

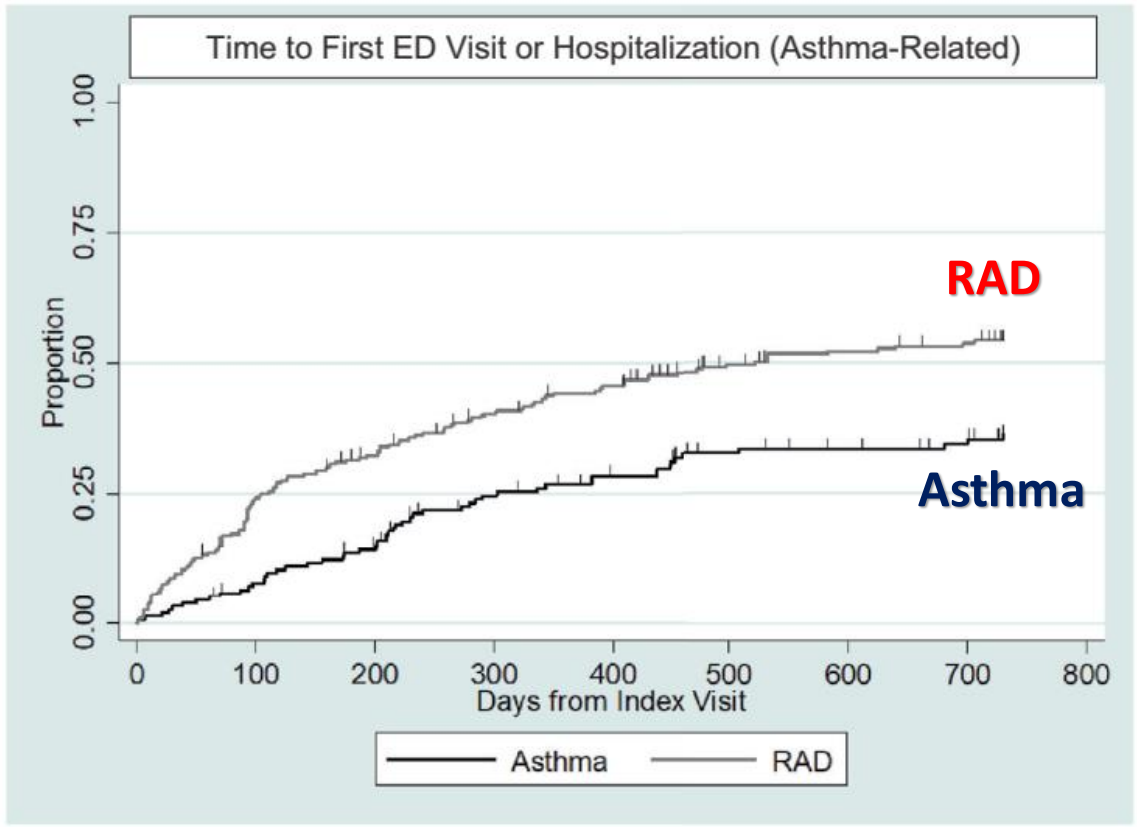
Table 1. Patient and Index Visit Characteristics

	Full Sample				Patient With 24 Months of Follow-Up			
	Overall n = 403	RAD n = 249	Asthma n = 154	*P* Value*	Overall n = 300	RAD n = 186	Asthma n = 114	*P* Value*
Sex (male)	259 (64%)	163 (66%)	96 (62%)	.525	200 (67%)	130 (70%)	70 (61%)	.130
Race (Black)	269 (67%)	172 (69%)	97 (63%)	.207	198 (66%)	129 (69%)	69 (61%)	.117
Ethnicity (Hispanic)	100 (25%)	60 (24%)	40 (26%)	.672	79 (26%)	49 (26%)	30 (26%)	.996
Age at index visit (mo)	23 (16)	18 (13)	30 (17)	**<.001**	20 (13)	16 (10)	26 (14)	**<.001**
Index visit location								
ED	107 (27%)	87 (35%)	20 (13%)	**<.001**	83 (28%)	67 (36%)	16 (14%)	**<.001**
General pediatrics clinic	273 (68%)	146 (59%)	127 (82%)		206 (69%)	112 (60%)	94 (82%)	
Hospital	21 (5%)	16 (6%)	5 (3%)		10 (3%)	7 (4%)	3 (3%)	
Specialist clinic	2 (0%)	0 (0%)	2 (1%)		1 (0%)	0 (0%)	1 (1%)	
History of wheezing before index visit (Y/N)	151 (37%)	80 (32%)	71 (46%)	**.005**	105 (35%)	56 (30%)	49 (43%)	**.023**
Bronchiolitis co-diagnosed at index visit (Y/N)	46 (11%)	43 (17%)	3 (2%)	**<.001**	36 (12%)	34 (18%)	2 (2%)	**<.001**

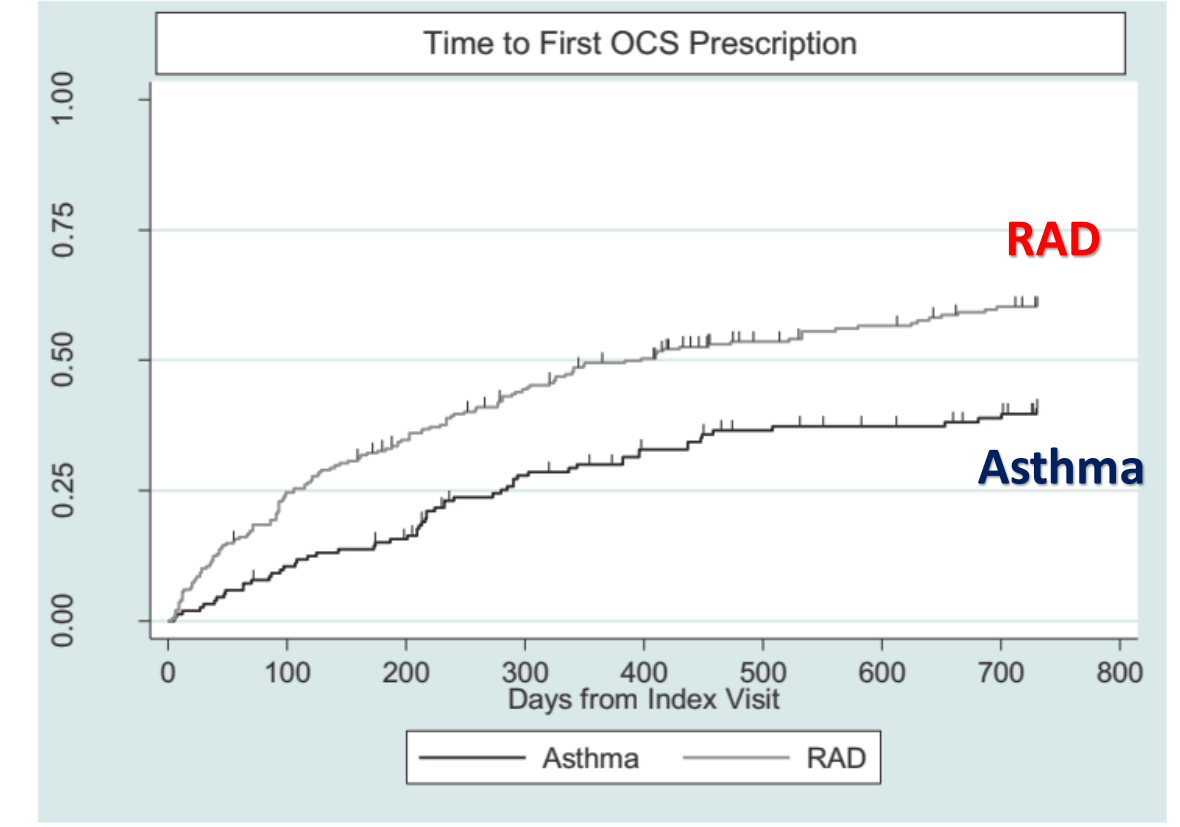
RAD indicates reactive airway disease; ED, emergency department.
Data presented as mean (SD) or N (%).
*Pearson Chi-square test, Fisher exact test, or *t* test.

Frey SM, et al. Acad Pediatr. 2022;22(1):37-46.

Clinical Outcomes for Young Children Diagnosed With Asthma Versus Reactive Airway Disease



Log-Rank Test: $p < 0.001$
Wilcoxon Test: $p < 0.001$



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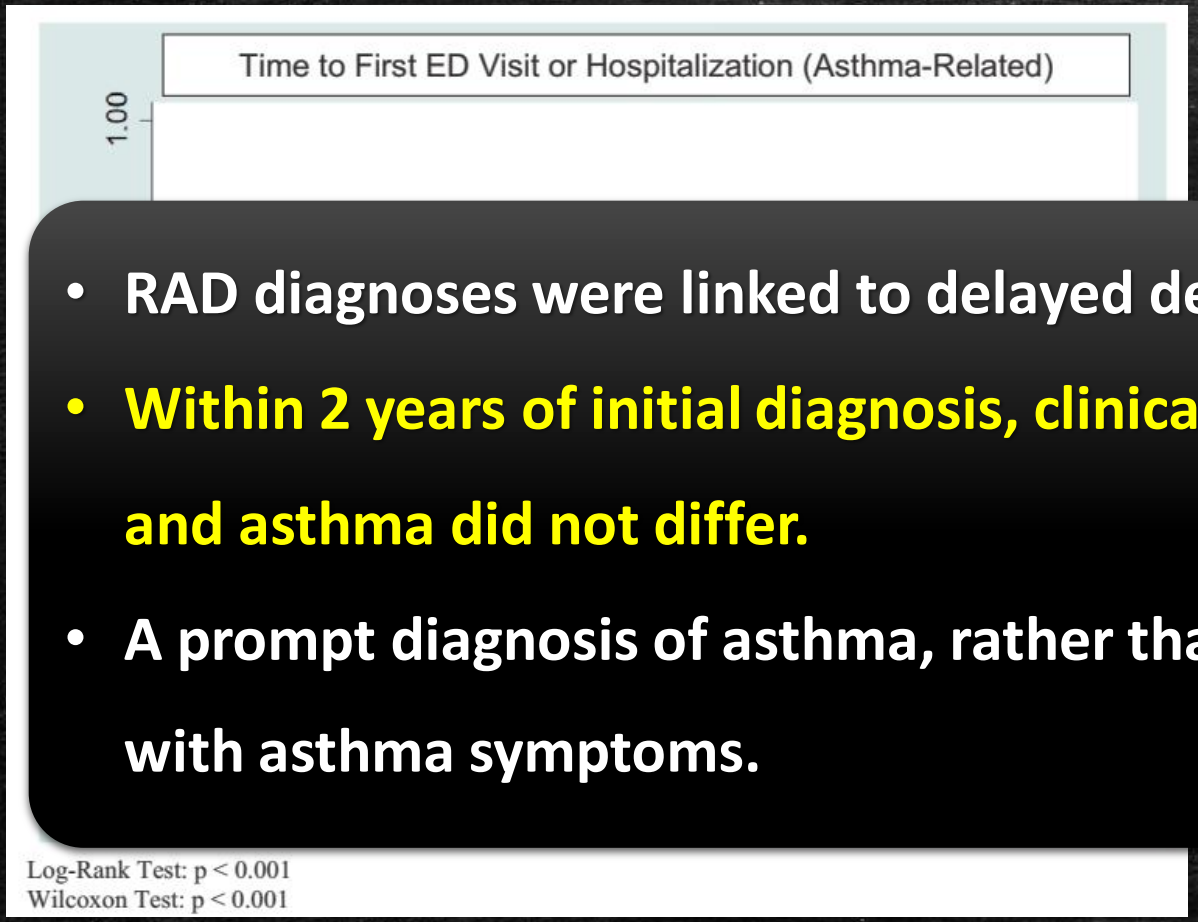
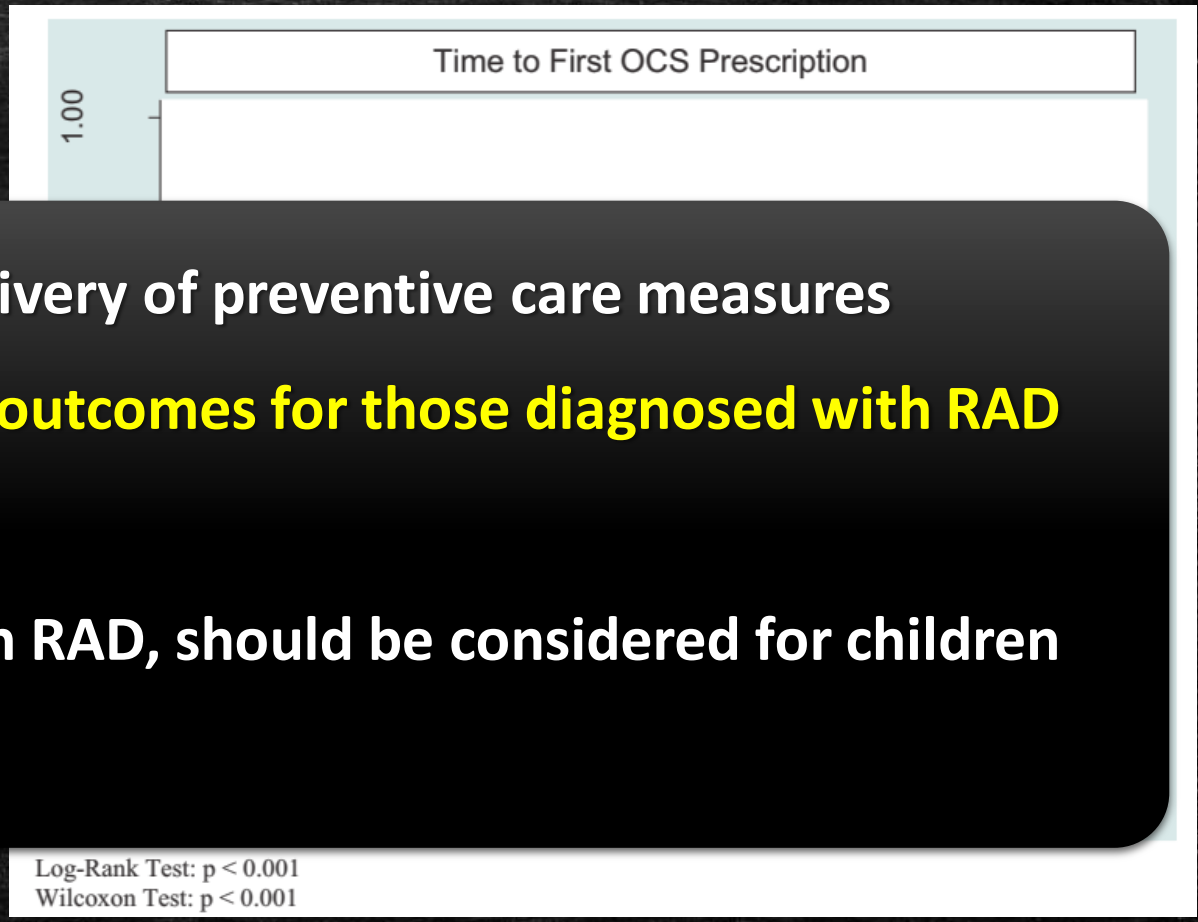
Clinical Outcomes for Young Children Diagnosed With Asthma Versus Reactive Airway Disease





- RAD diagnoses were linked to delayed delivery of preventive care measures
- **Within 2 years of initial diagnosis, clinical outcomes for those diagnosed with RAD and asthma did not differ.**
- A prompt diagnosis of asthma, rather than RAD, should be considered for children with asthma symptoms.

Frey SM, et al. Acad Pediatr. 2022;22(1):37-46.

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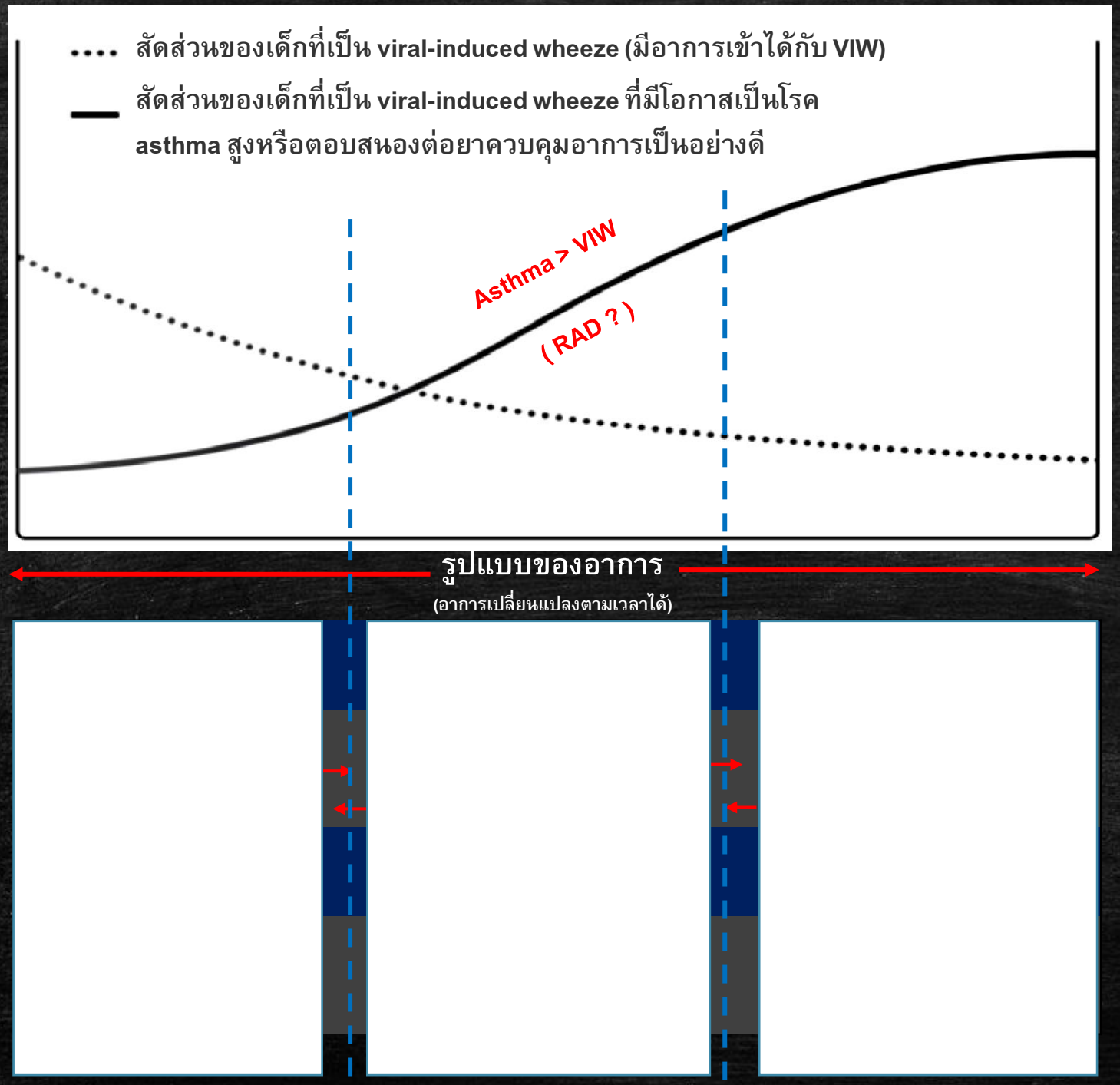
Children with RAD:
How to diagnosed Asthma in RAD



100%

Asthma

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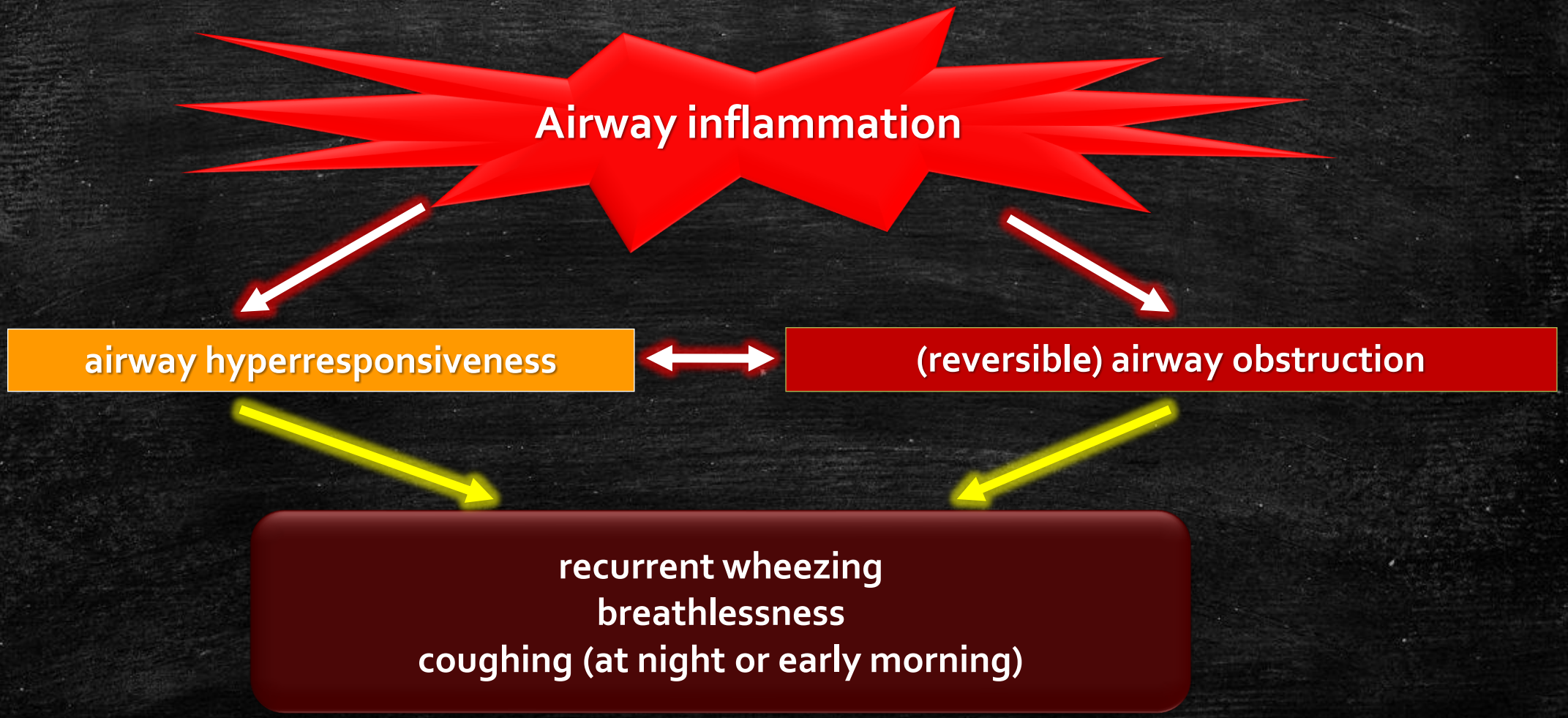
Clinical diagnosis of Asthma in young children

GINA 2022

Pathophysiology of Asthma / Recurrent wheezing



GINA 2022

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RAD and Viral infection as triggers

RSV- and RV-induced bronchiolitis Vs recurrent wheeze: A systematic review and meta-analysis

Healthy control | RSV-bronchiolitis

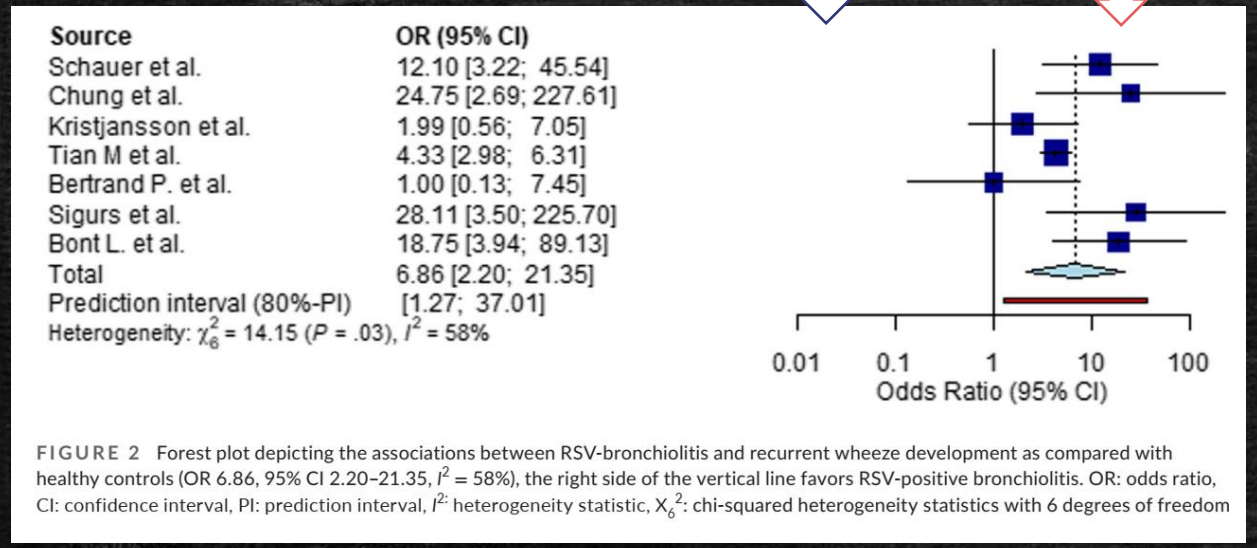


FIGURE 2 Forest plot depicting the associations between RSV-bronchiolitis and recurrent wheeze development as compared with healthy controls (OR 6.86, 95% CI 2.20–21.35, I^2 = 58%), the right side of the vertical line favors RSV-positive bronchiolitis. OR: odds ratio, CI: confidence interval, PI: prediction interval, $I^{2:}$ heterogeneity statistic, X_6^2: chi-squared heterogeneity statistics with 6 degrees of freedom

RSV-bronchiolitis | RV-bronchiolitis

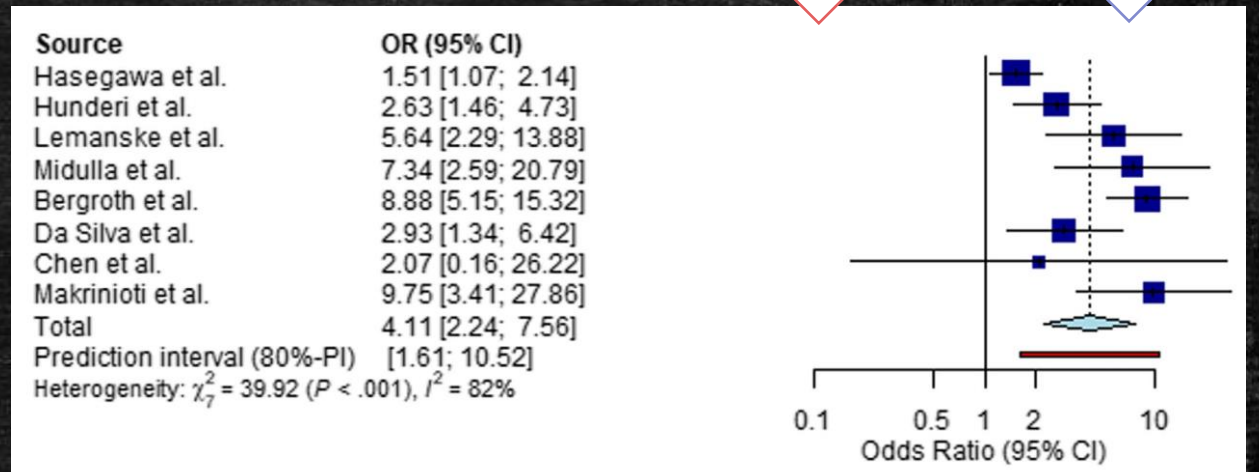


FIGURE 3 Forest plot depicting the associations between RSV-bronchiolitis and recurrent wheeze development as compared with RV-bronchiolitis (OR 4.24; 95% CI 2.15–8.36, I^2 = 85%), the right side of the vertical line favors RV-positive bronchiolitis. OR: odds ratio, CI: confidence interval, PI: prediction interval, $I^{2:}$ heterogeneity statistic, X_6^2: chi-squared heterogeneity statistics with 6 degrees of freedom

- Infant RV-bronchiolitis group were more likely to develop recurrent wheeze than RSV-bronchiolitis group
- OR 4.11 (95% CI 2.24–7.56)

Makrinioti H, et al. Pediatr Allergy Immunol. 2022;33(3):e13741.

RSV- and RV-induced bronchiolitis Vs asthma:
A systematic review and meta-analysis

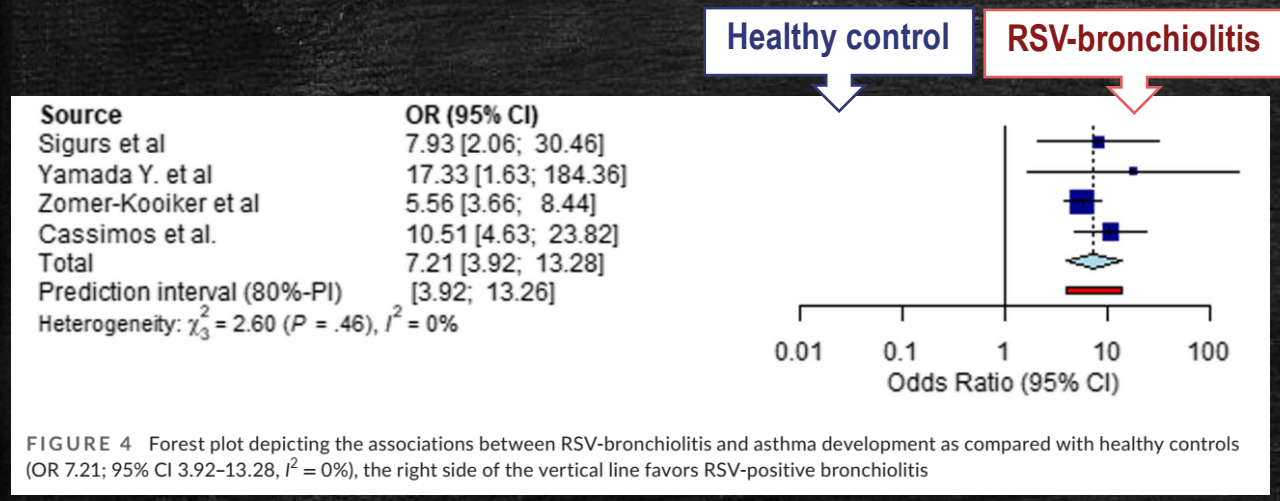


FIGURE 4 Forest plot depicting the associations between RSV-bronchiolitis and asthma development as compared with healthy controls (OR 7.21; 95% CI 3.92–13.28, I^2 = 0%), the right side of the vertical line favors RSV-positive bronchiolitis

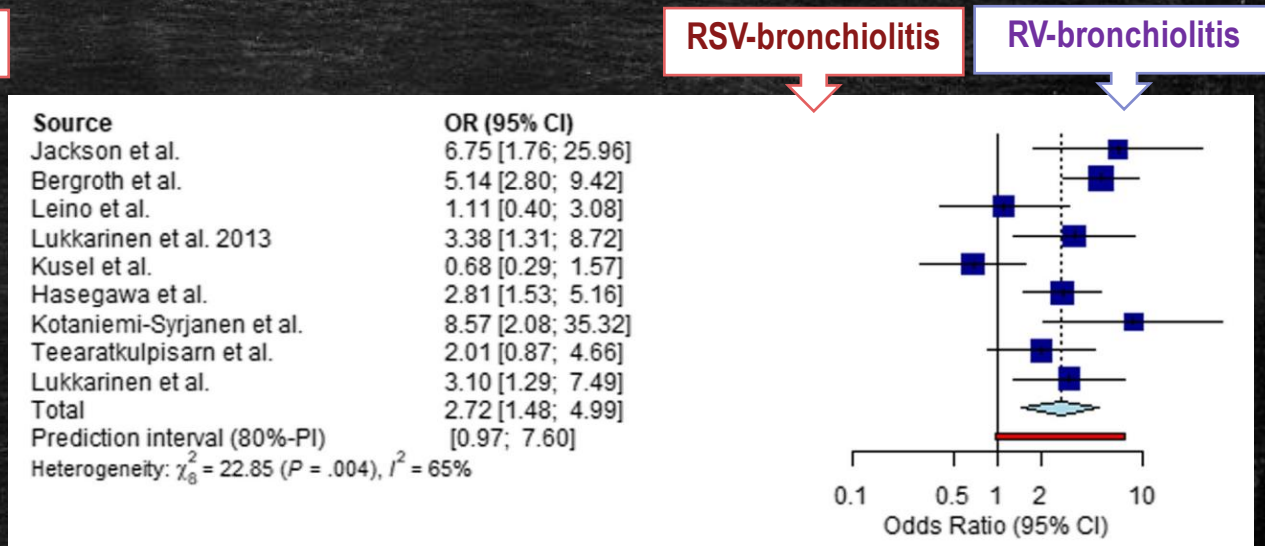


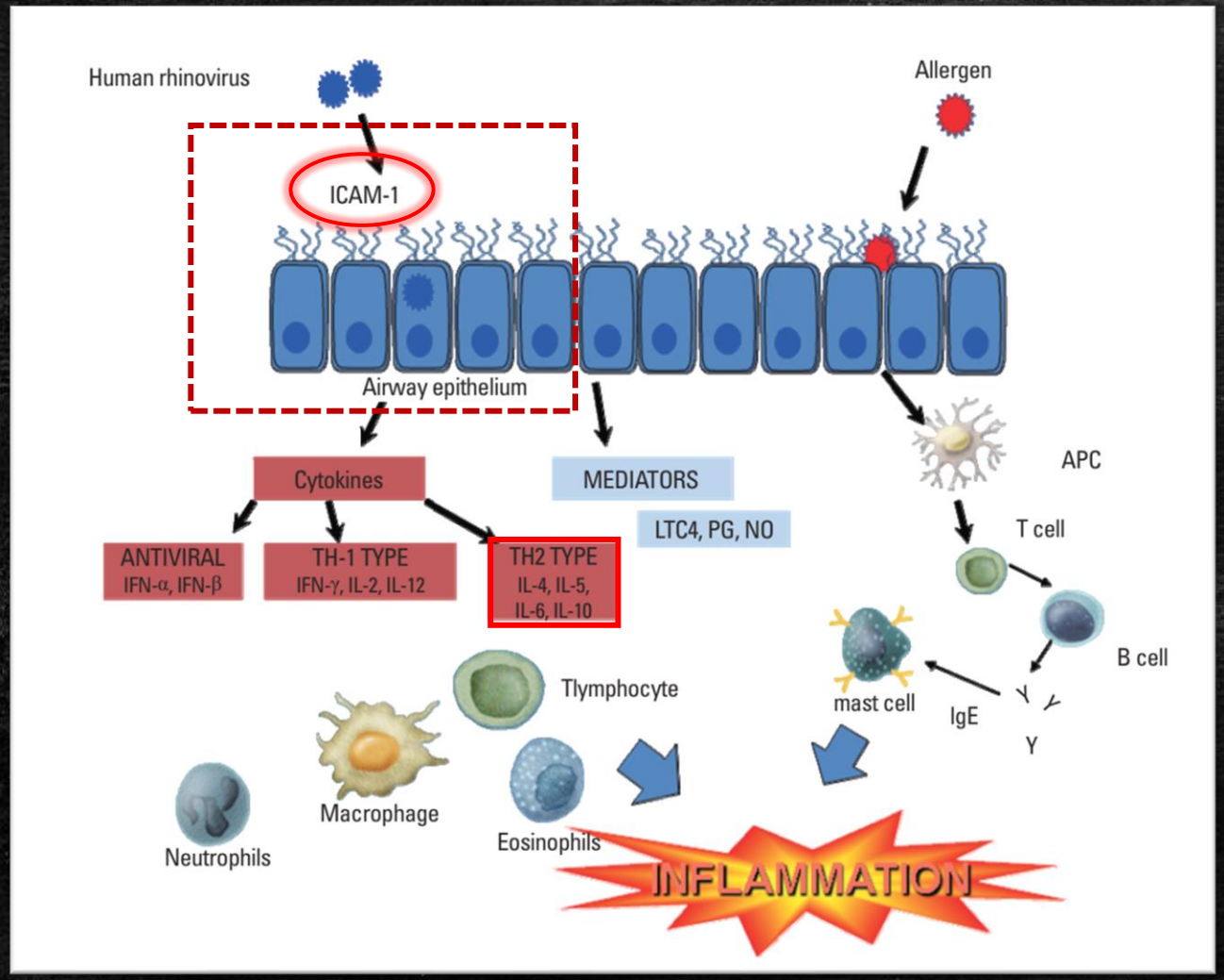
FIGURE 6 Forest plot depicting the associations between RSV-bronchiolitis and asthma development as compared with RV-bronchiolitis (OR 2.72; 95% CI 1.48–4.99, I^2 = 65%) the right side of the vertical line favors RV-positive bronchiolitis. OR: odds ratio, CI: confidence interval, PI: prediction interval, $I^{2:}$ heterogeneity statistic, X_8^2: chi-squared heterogeneity statistics with 8 degrees of freedom

- Infant RV-bronchiolitis group were more likely to develop asthma than RSV-bronchiolitis group
- OR 2.72 (95% CI 1.48–4.99)

Makrinioti H, et al. Pediatr Allergy Immunol. 2022;33(3):e13741.

How does rhinovirus induce airway hyper-responsiveness?

Mechanisms of rhinovirus-induced airway inflammation.

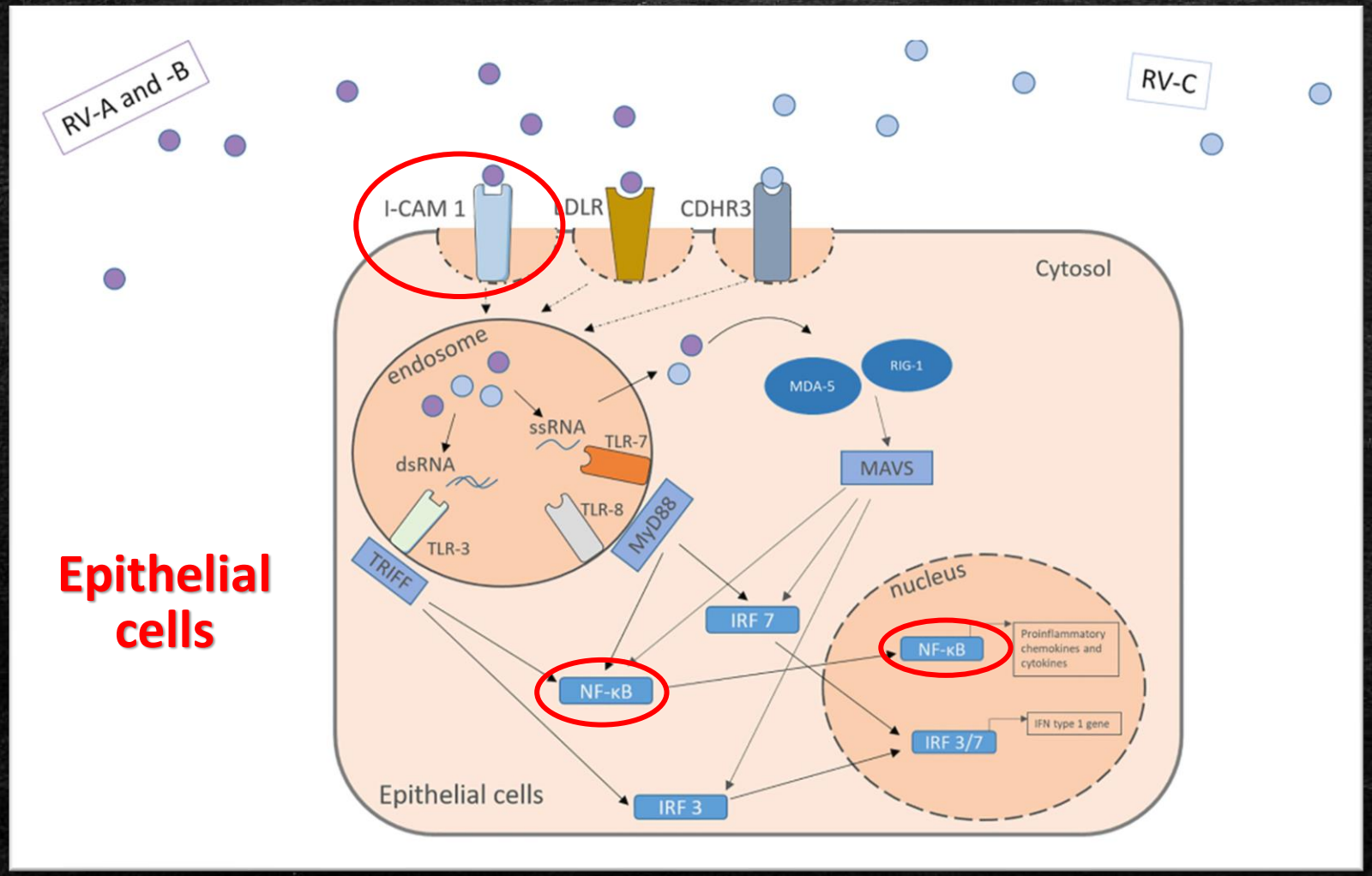


Rhinovirus

- **Induced airway inflammation through** activated macrophage, neutrophils **and** eosinophils
  - Mucous hypersecretion
  - SM contraction → wheezing

Kum WK, Gern JE. Allergy Asthma Immunol Res. 2012;4(3):116-21.

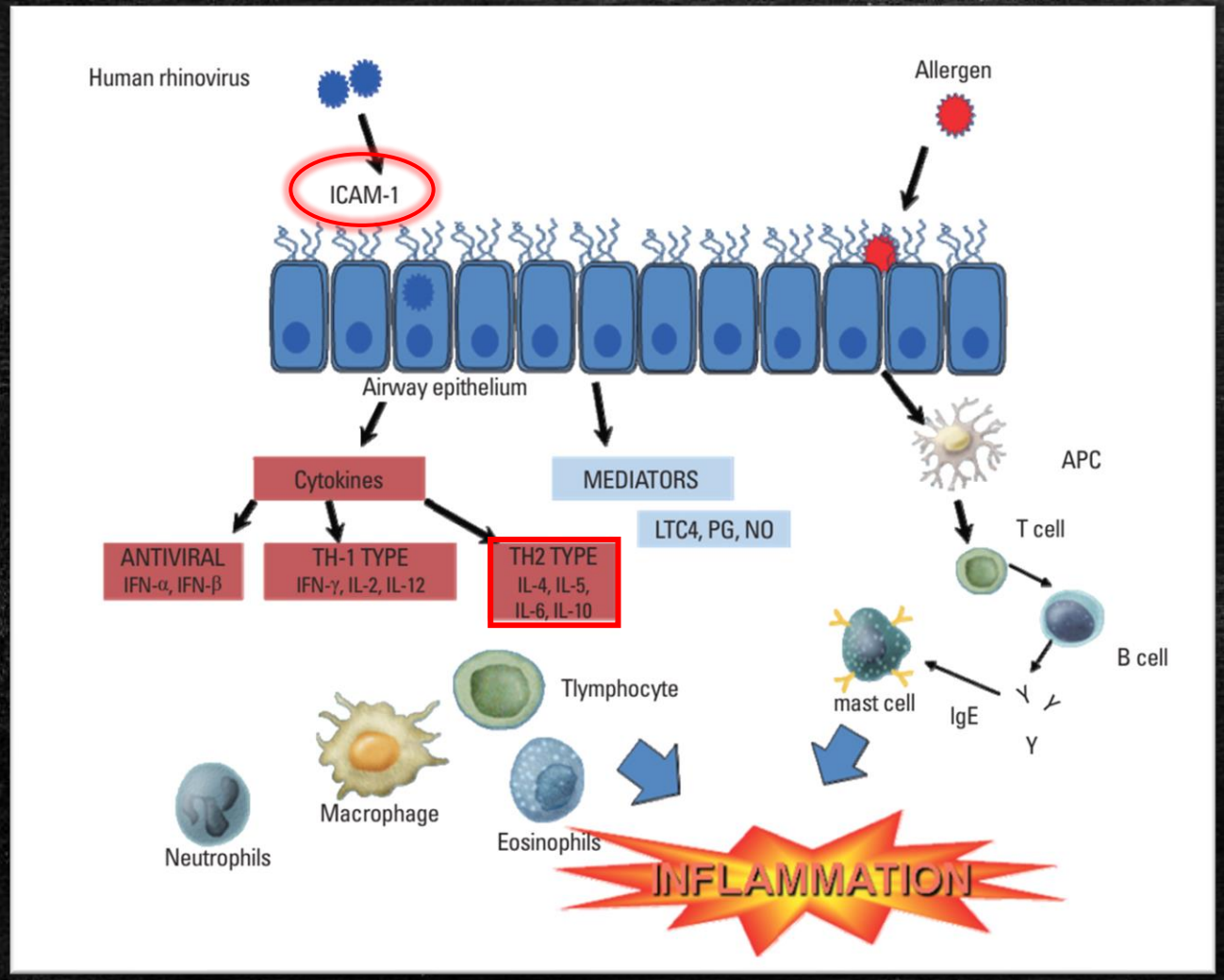
Mechanism of RV infection



Epithelial cells

Yang Z, et al. Front Immunol. 2021;12:731846.

Mechanisms of rhinovirus-induced airway inflammation.



Rhinovirus

- **Induced airway inflammation through** activated macrophage, neutrophils **and** <u>eosinophils</u>
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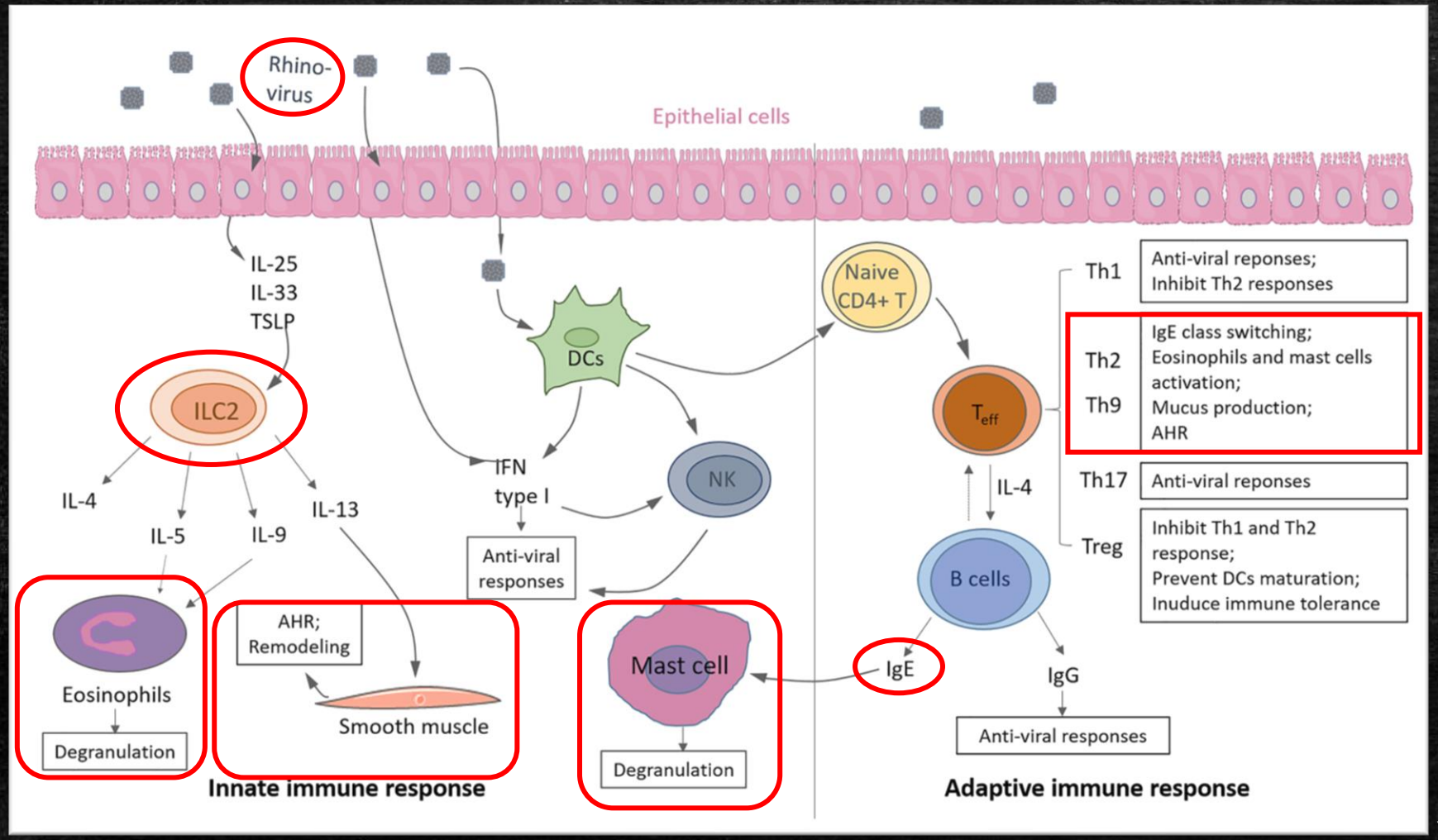
  - SM contraction → wheezing

Kum WK, Gern JE. Allergy Asthma Immunol Res. 2012;4(3):116-21.

Immune response to Rhinovirus in Asthma



Yang Z, et al. Front Immunol. 2021;12:731846.

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The role of bronchodilator in RV infection: What is the evidences?

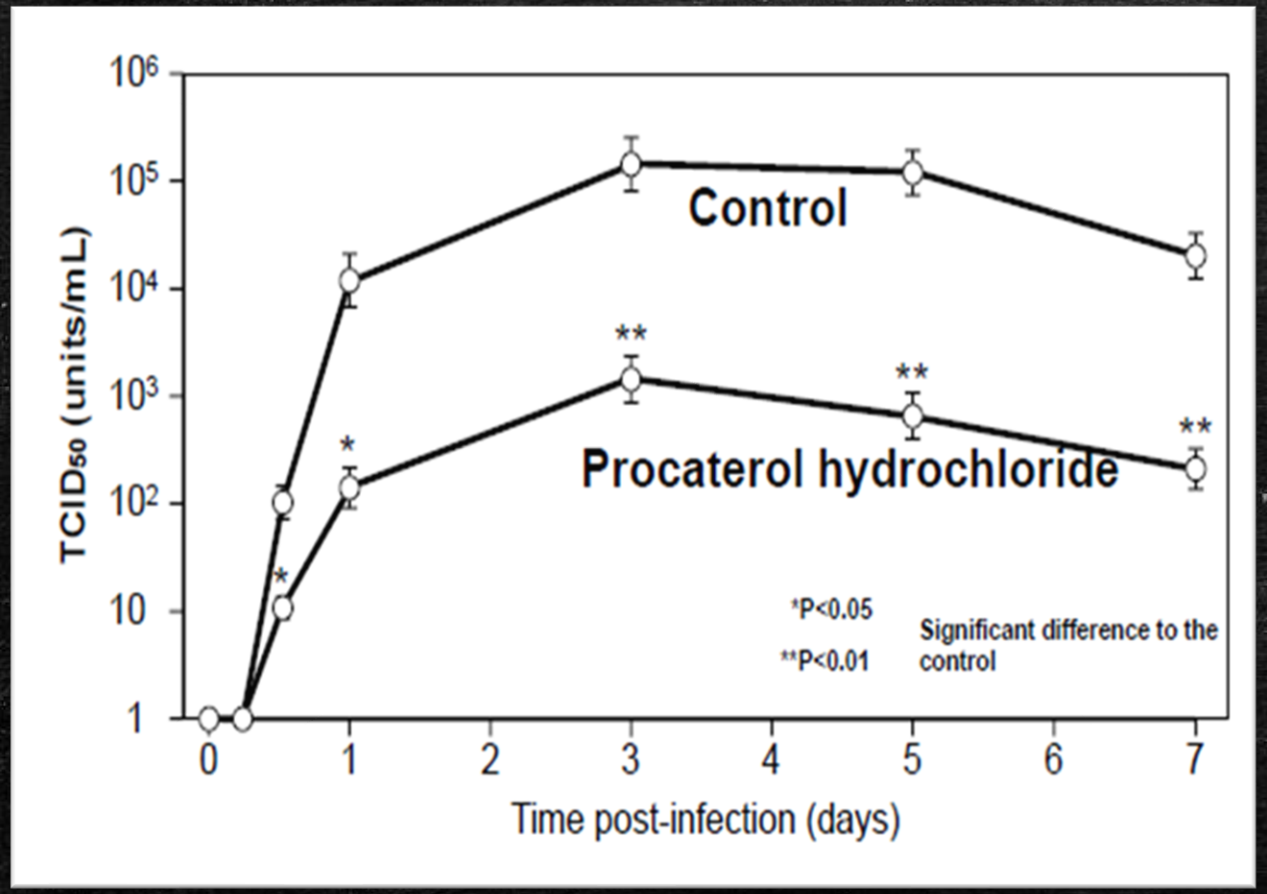
Procaterol inhibits rhinovirus infection in primary cultures of human tracheal epithelial cells

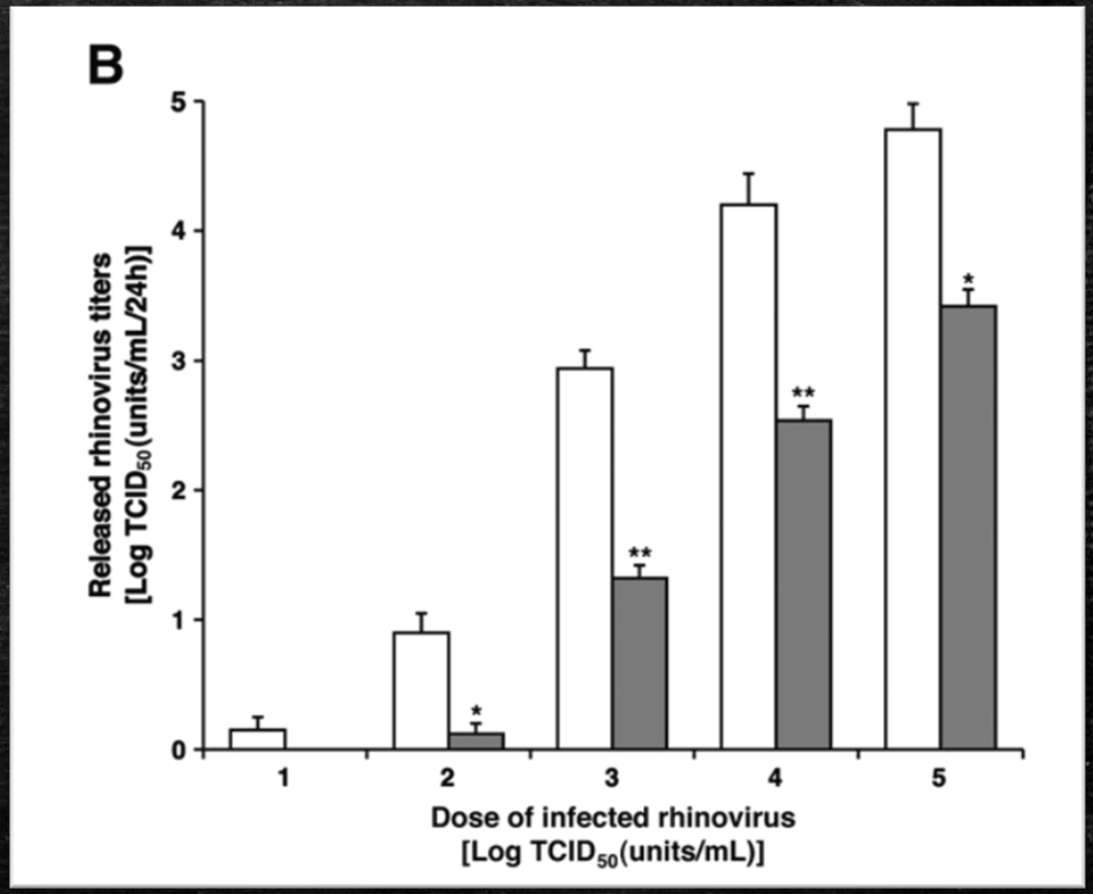
Mutsuo Yamaya [a,*], Hidekazu Nishimura [b], Yukimasa Hatachi [c], Motoki Yoshida [d], Hidenori Fujiwara [e], Masanori Asada [d], Katsutoshi Nakayama [f], Hiroyasu Yasuda [g], Xue Deng [g], Takahiko Sasaki [h], Hiroshi Kubo [a], Ryoichi Nagatomi [i]

- Human tracheal epithelial cell culture (human embryonic fibroblast cells)
  - Obtained from 41 patients (73±3 yr; 15 F, 26 M) without asthma
- Study intervention – pretreat with study medication for 3 days
  - Procaterol hydrochloride 0.1 μM
  - Vehicle
  - Selective β_2-adrenergic receptor antagonist (ICI 118551) 10 min before procaterol 0.1 μM
- Infected with Type 14 rhinovirus → cultured at 33°C in 5% CO_2–95% air for 7 days
- Outcome:
  - The quantification of rhinovirus RNA (detected cDNA with Quiagen kit and real-time PCR)
  - Measurement of ICAM-1 expression
  - Measurement of changes in acidic endosomes
  - NF-kappa B assay
  - Cyclic AMP assay

Yamaya M, et al. Eur J Pharmacol. 2011;650(1):431-44.

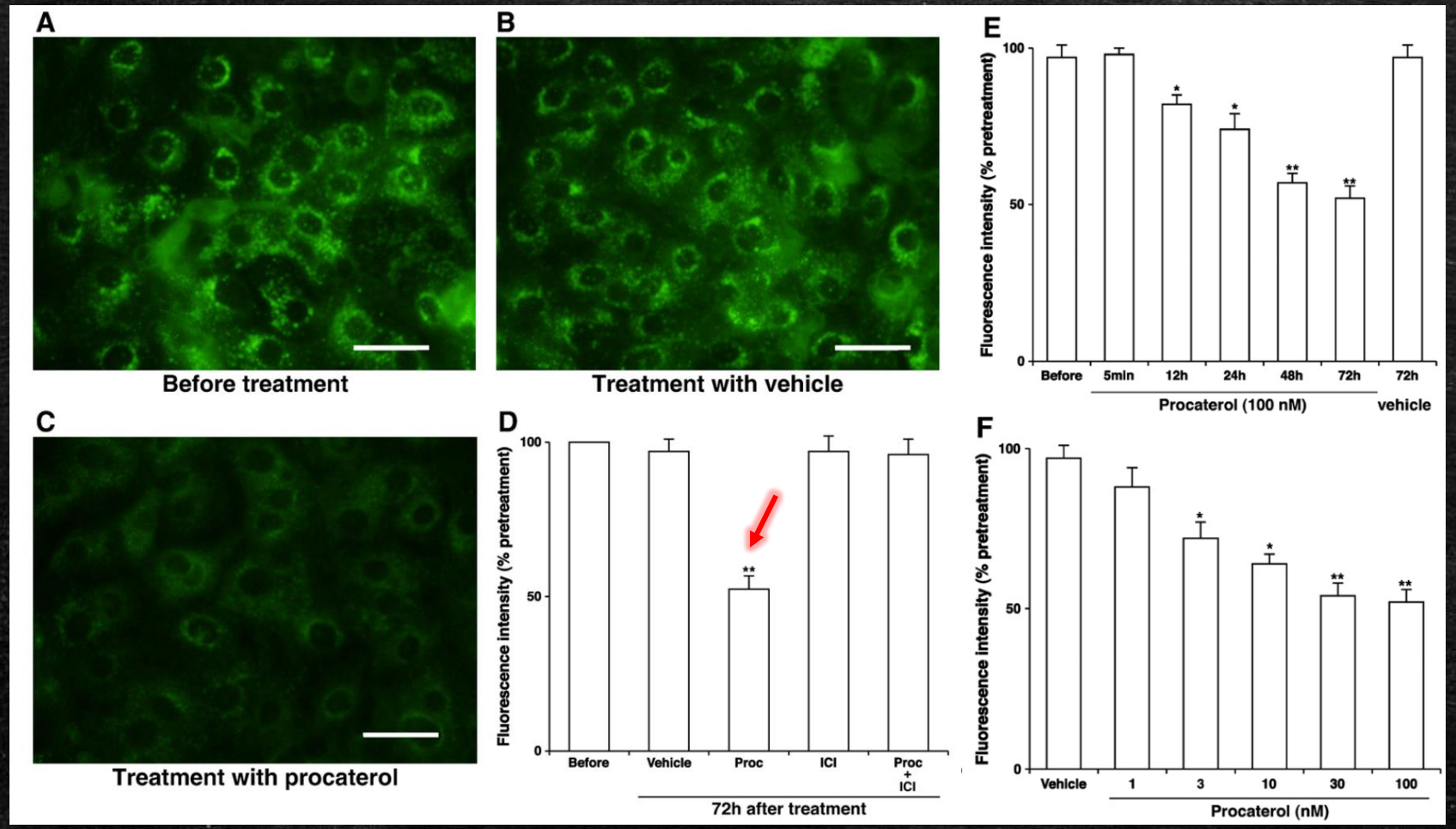
Effects of procaterol on RV and the acidification of RV endosomes

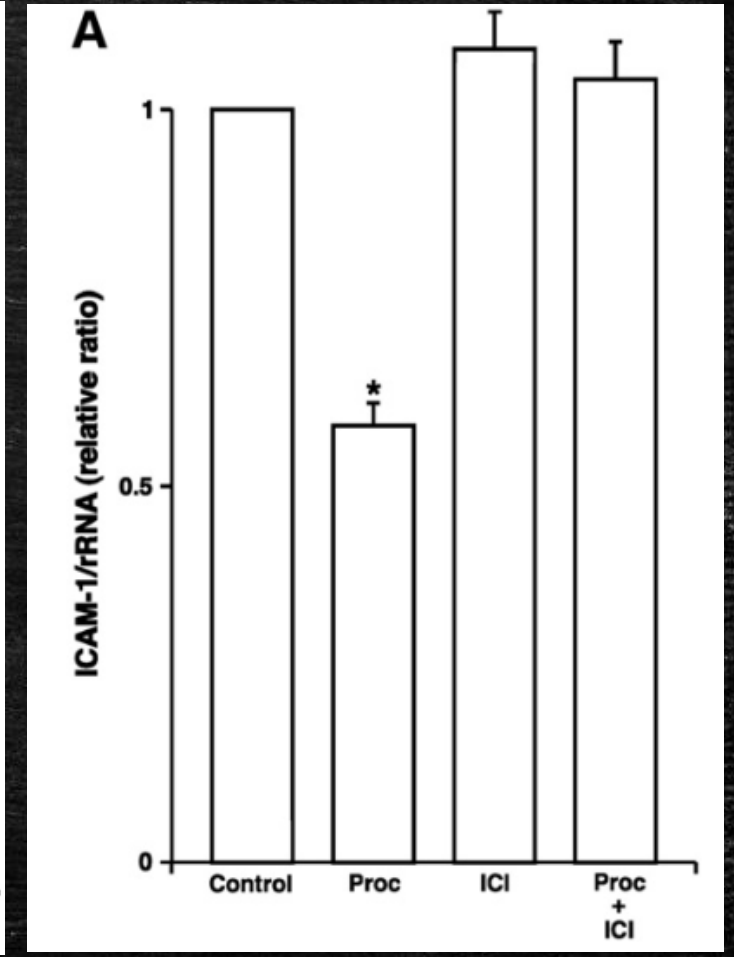




Yamaya M, et al. Eur J Pharmacol. 2011;650(1):431-44.

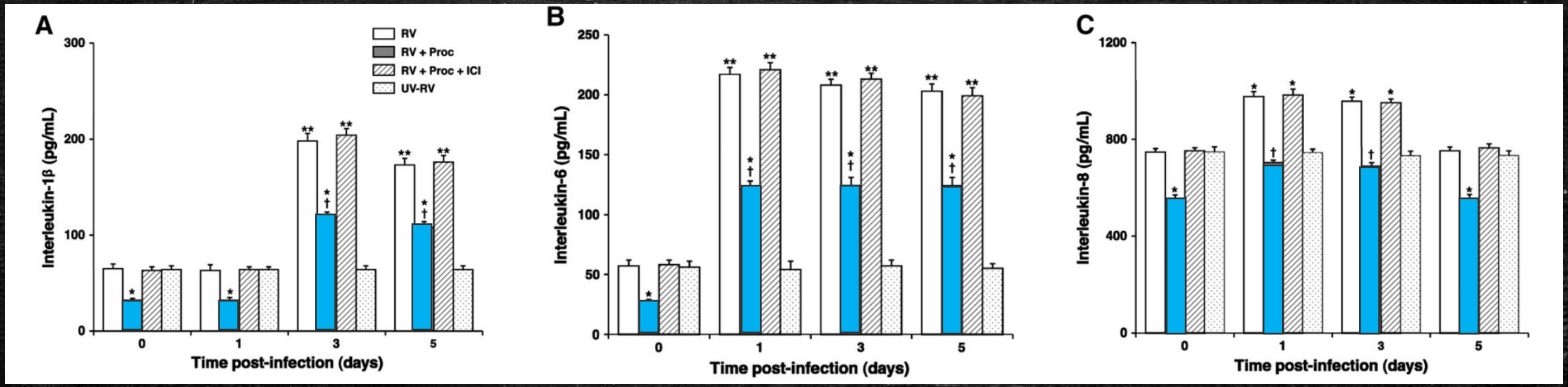
Effects of procaterol on the acidification of RV endosomes and ICAM-1 expression





Yamaya M, et al. Eur J Pharmacol. 2011;650(1):431-44.

Effects of procaterol on cytokine production with RV infection



Procaterol reduced the type 14 rhinovirus infection-induced secretion inflammatory cytokines (IL-1β, IL-6, and IL-8).

Yamaya M, et al. Eur J Pharmacol. 2011;650(1):431-44.

Procaterol inhibits rhinovirus infection in primary cultures of human tracheal epithelial cells

Mutsuo Yamaya [a,*], Hidekazu Nishimura [b], Yukimasa Hatachi [c], Motoki Yoshida [d], Hidenori Fujiwara [e], Masanori Asada [d], Katsutoshi Nakayama [f], Hiroyasu Yasuda [g], Xue Deng [g], Takahiko Sasaki [h], Hiroshi Kubo [a], Ryoichi Nagatomi [i]

What the study found on the efficacy of procaterol!!!

- Reduced the expression of ICAM-1 (the receptor for type 14 rhinovirus).
- Reduced the number of acidic endosomes in the cells (where RV RNA enters into the cytoplasm).
- Inhibited the activation of NF-κB proteins including p50 and p65 in the nuclear extracts.
- Increased the cytosolic amount of the inhibitory kappa B-α and cAMP levels.
- Reduced RV infection-induced secretion inflammatory cytokines (IL-1β, IL-6, and IL-8).

Yamaya M, et al. Eur J Pharmacol. 2011;650(1):431-44.

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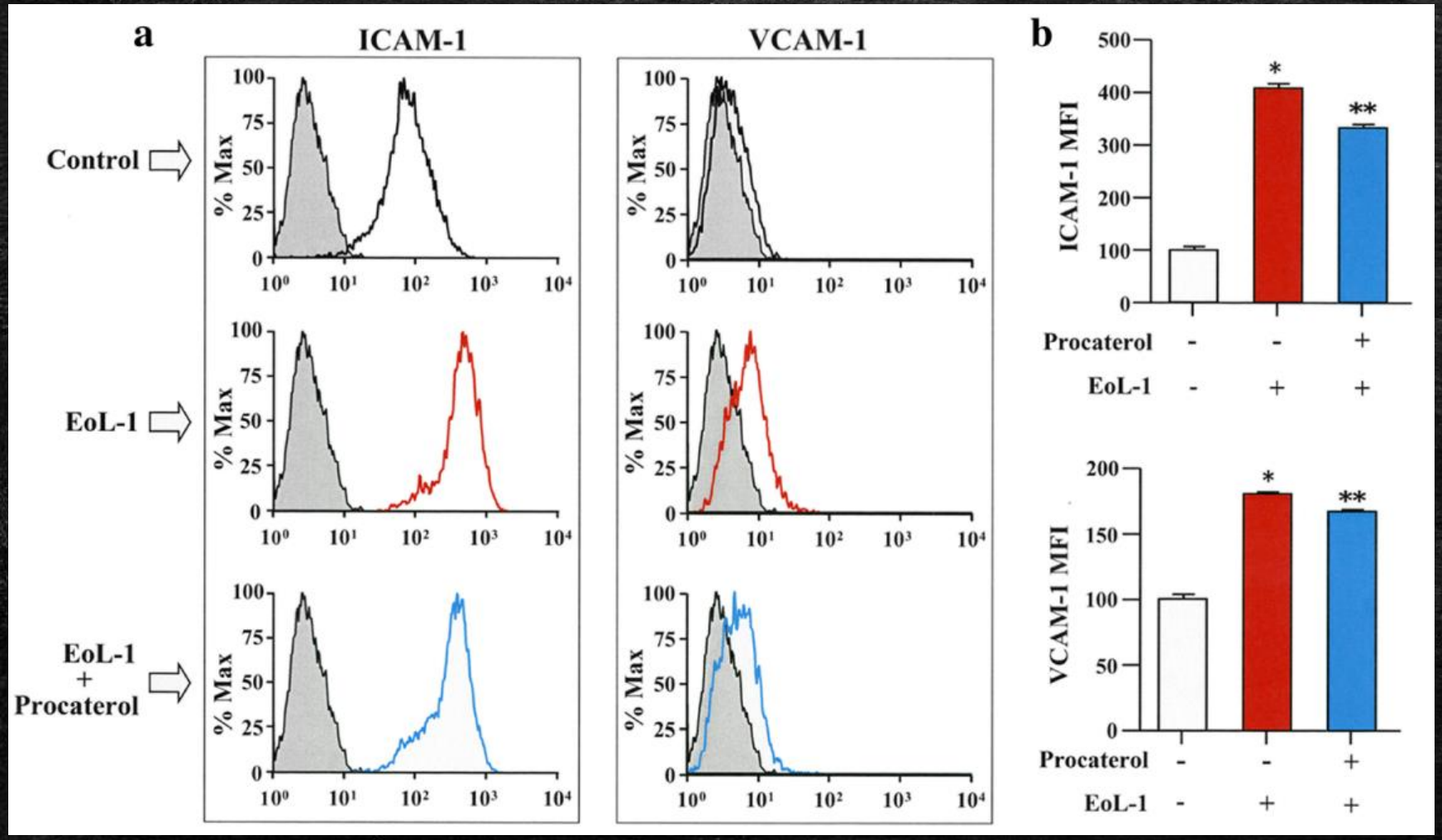
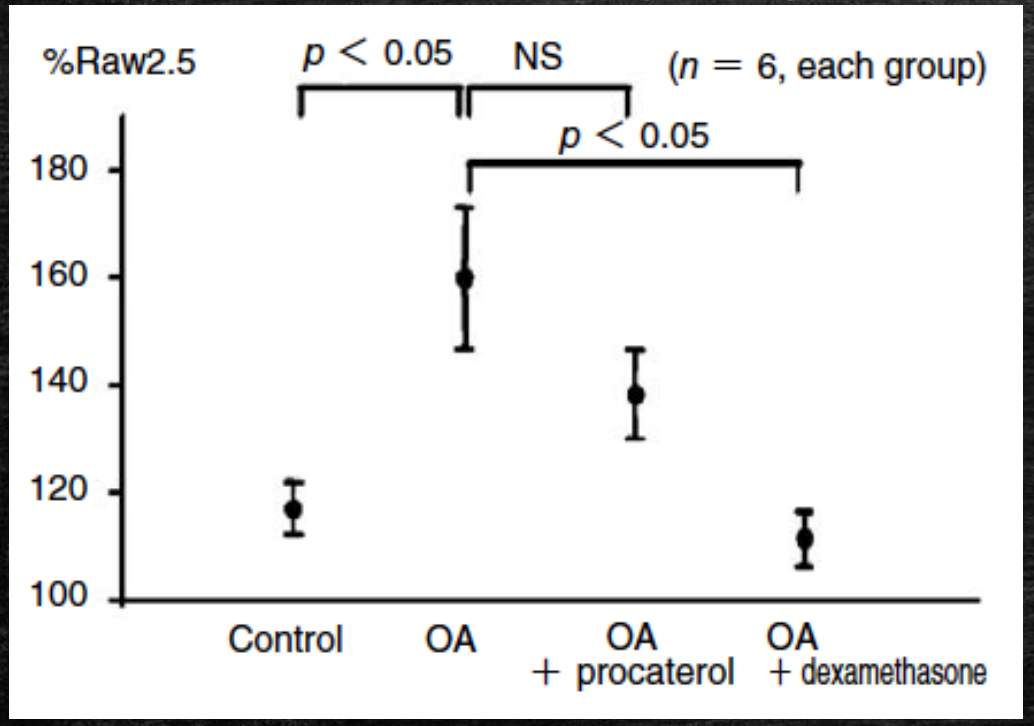
Airway inflammation in RAD:
Role of Bronchodilators

β_2 adrenergic agonist : Suppresses eosinophil-induced EMT of bronchial epithelial cells

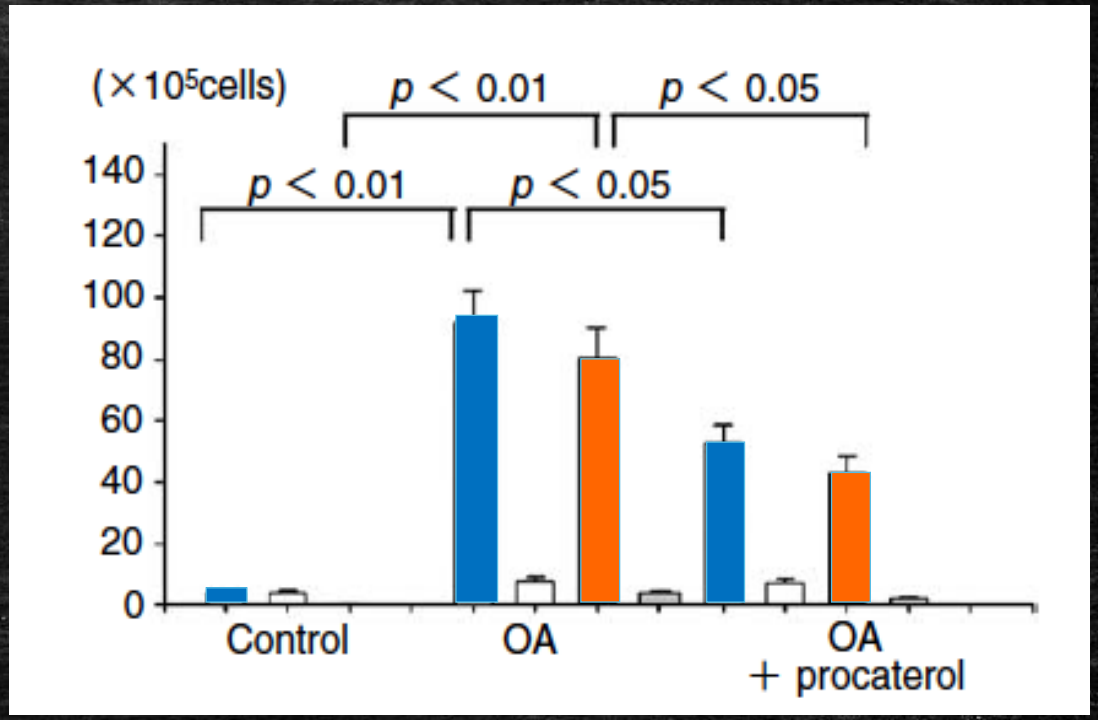


Kainuma K, et al. Respir Res. 2017;18(1):79.

Effect of Procaterol on airway inflammation and hyperresponsiveness



Airway resistant

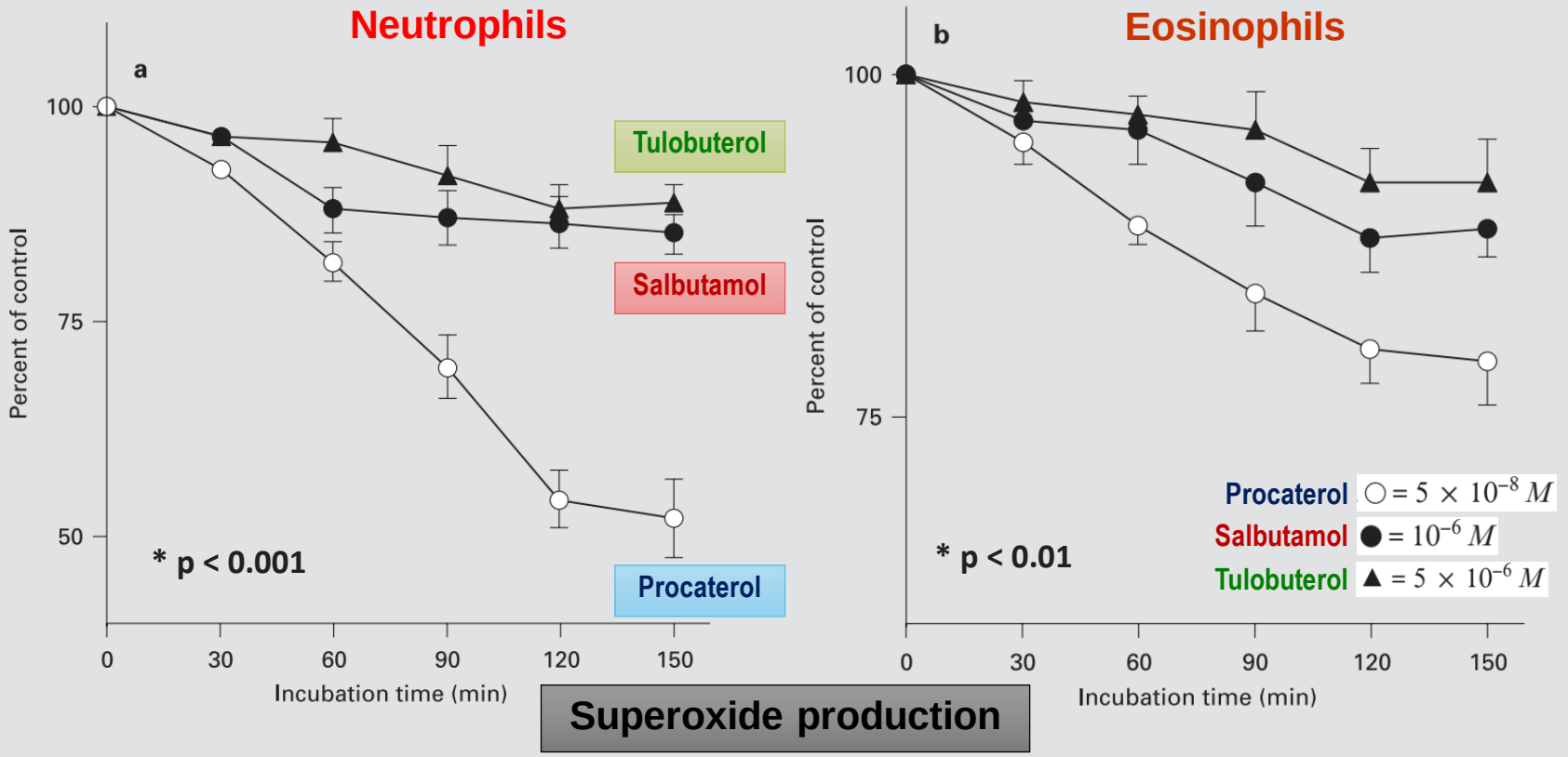


BAL fluid

Eosinophil
Total cell

Tashimo H, et al. Allergol Int. 2007;56(3):241-7.

β_2-agonists: Comparative inhibitory effects of superoxide anion (O_2^-) production (In vitro)



Superoxide production

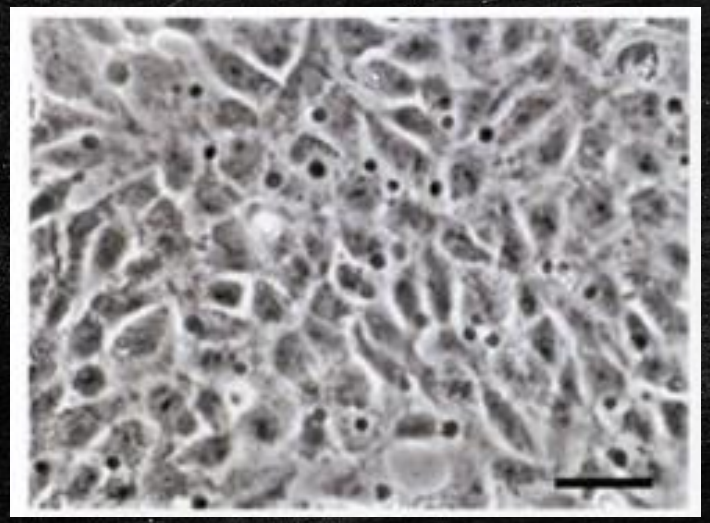
The suppressive effect of superoxide production

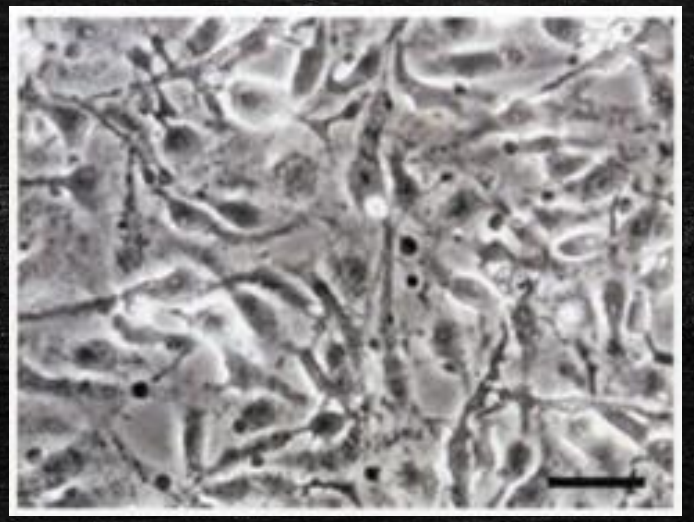
- **Procaterol >>> Salbutamol > Tulobuterol**
- **Neutrophils >> Eosinophils**

Yasui K, et al. Int Arch Allergy Immunol. 2006;139(1):1-8.

Airway remodeling: Effect of eosinophils

- Epithelial-mesenchymal transition (EMT)
  - Mechanism that increased number of myofibroblasts → AW remodeling
- Eosinophils contact with bronchial epithelial cells → induced AW remodeling
  - Increases TGF-β_1 → promote EMT

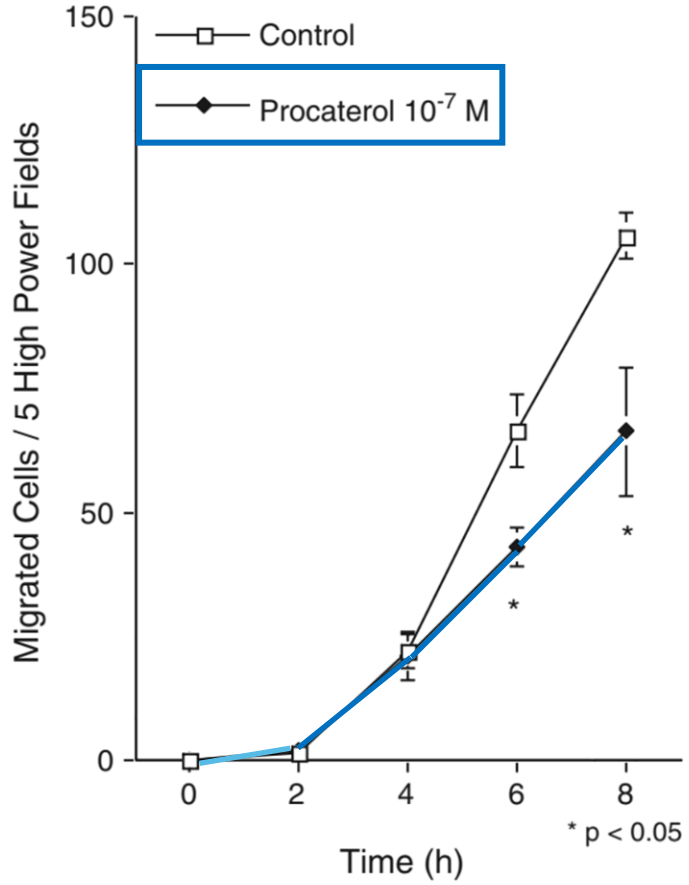


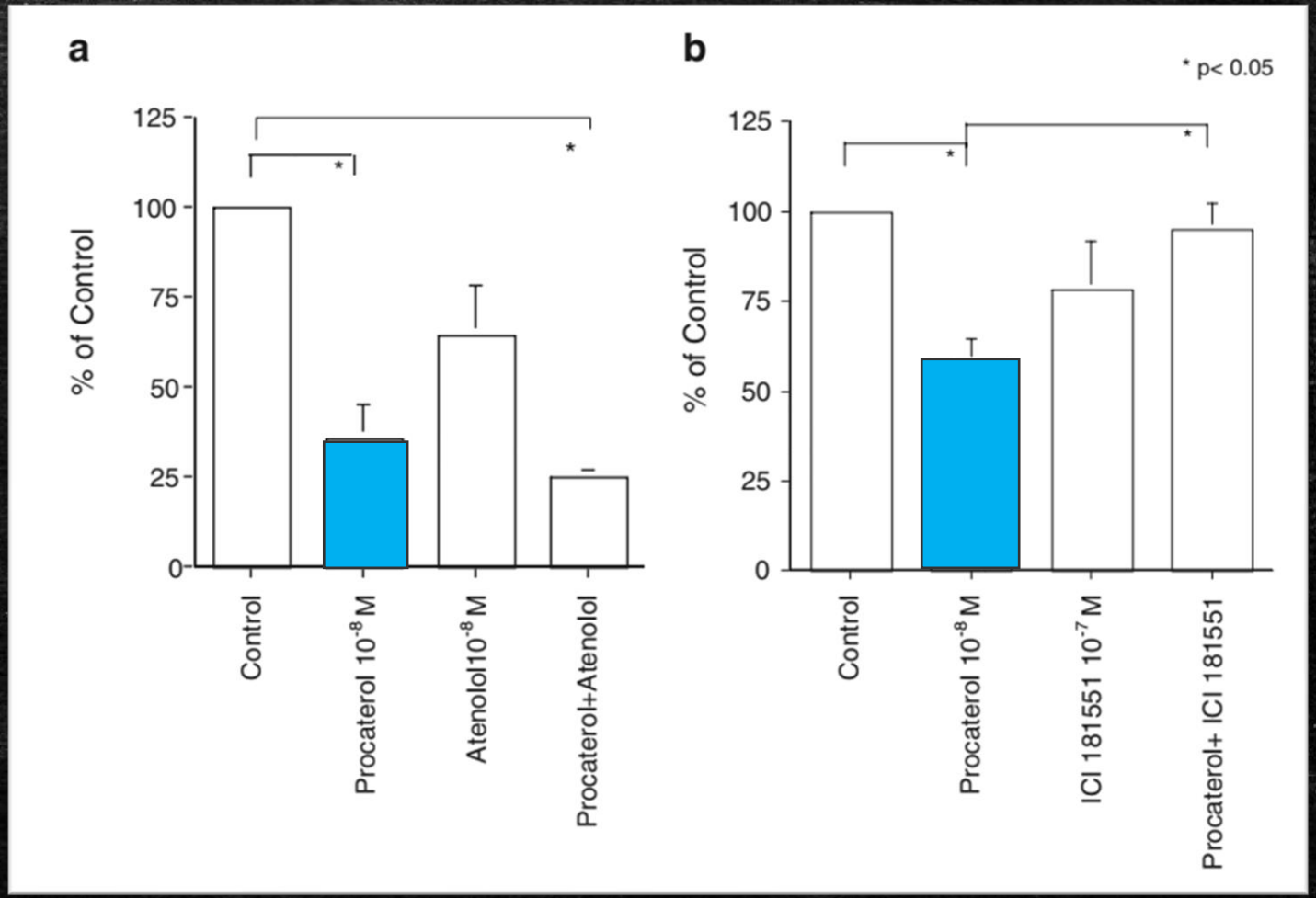


Yasukawa A , et al. **PLoS ONE. 2013;8:e64281**

Procaterol Inhibits Lung Fibroblast Migration

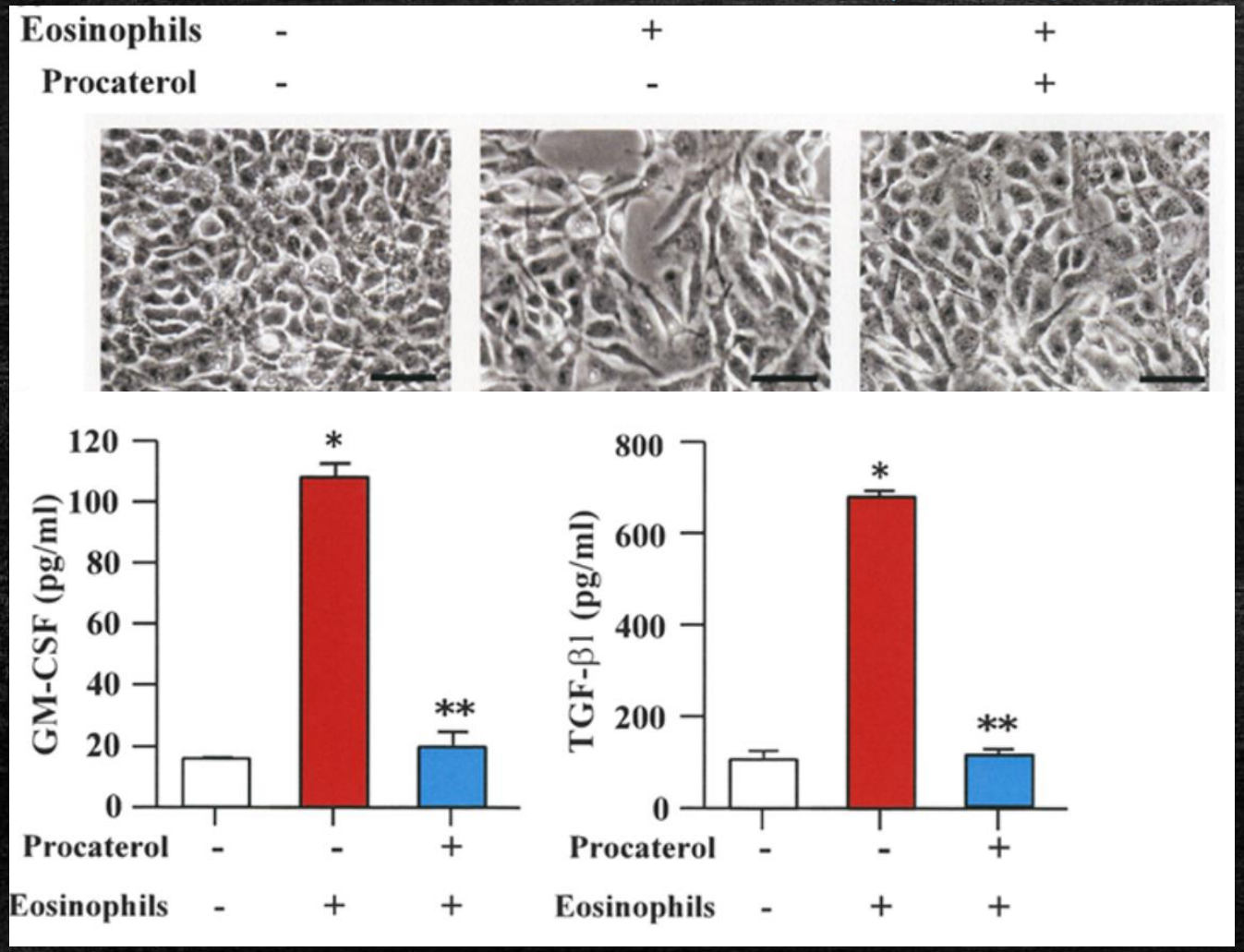
Tadashi Kohyama,[1,3,4] Yasuhiro Yamauchi,[1] Hajime Takizawa,[2] Susumu Itakura,[1]
Sumiko Kamitani,[1] Masashi Desaki,[1] Shin Kawasaki,[1] and Takahide Nagase[1]





Kohyama T, et al. Inflammation. 2009;32(6):387-92.

β_2 adrenergic agonist : Suppresses eosinophil-induced EMT of bronchial epithelial cells



Bronchial epithelial cells

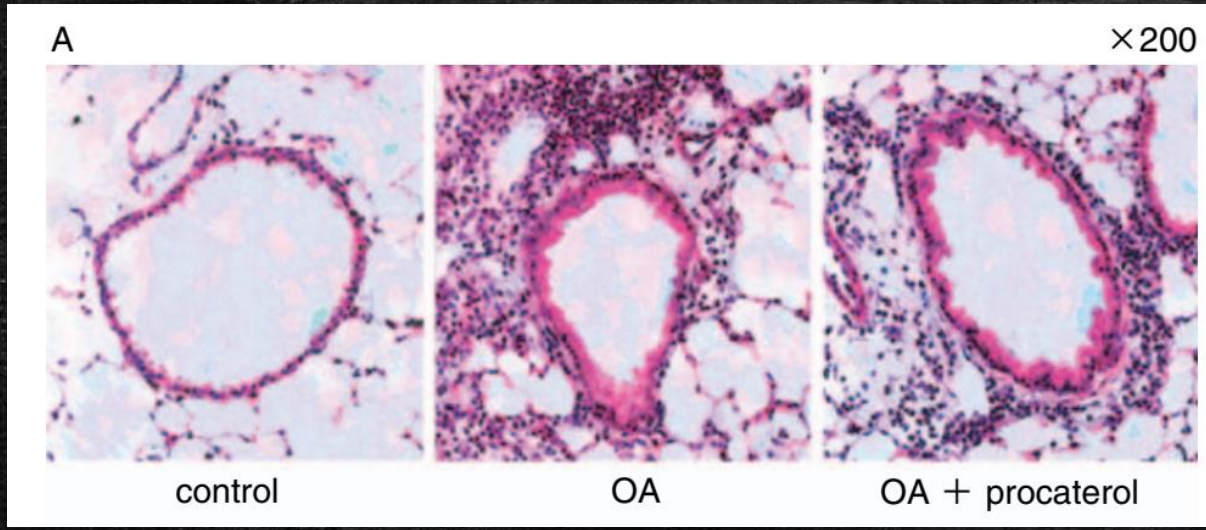
- From Riken Cell Bank (Tsukuba, Japan)
- Incubated with human eosinophils 24 hr.
- Pre-treated with procaterol for 1 hr.

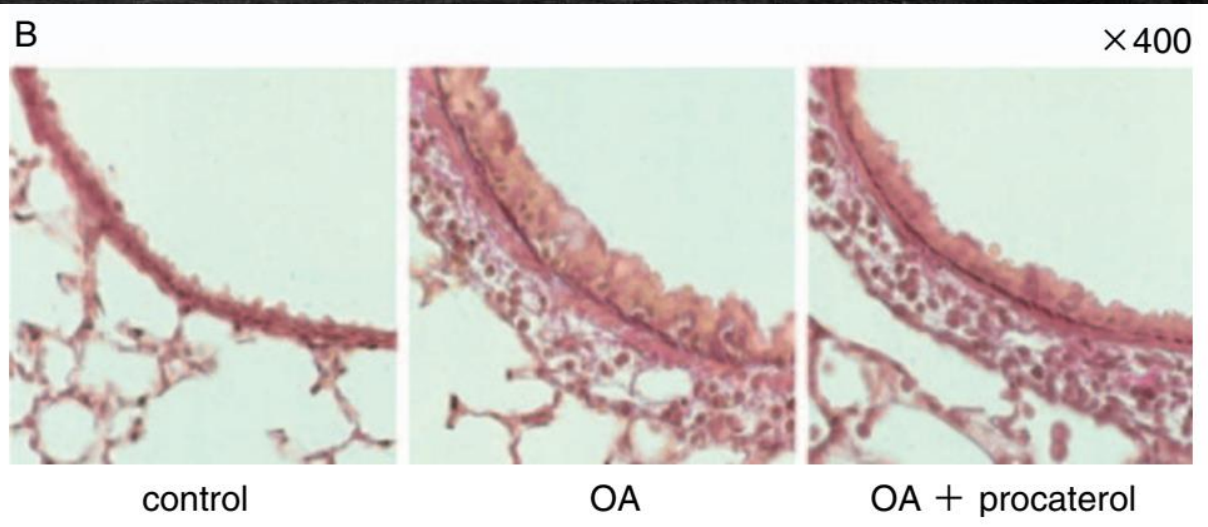
Outcome

- TGF-β_1 and GM-CSF level
- The expression of adhesion molecules (ICAM-1 and VCAM-1)
- fibroblast-like morphology

Kainuma K, et al. Respir Res. 2017;18(1):79.

Airway Inflammation Vs Airway remodeling:
Effect of procaterol





Deceased infiltration of eosinophils in the submucosal area in procaterol-treated Mice.

Reduced subepithelial fibrosis (represents airway remodeling), after procaterol treatment.

Tashimo H, et al. Allergol Int. 2007;56(3):241-7.

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มหาวิทยาลัยศรีนครินทรวิโรฒ

RAD and Wheezing with Cough: Evidences of Bronchodilators

Treatment of wheezing: Procaterol VS Albuterol

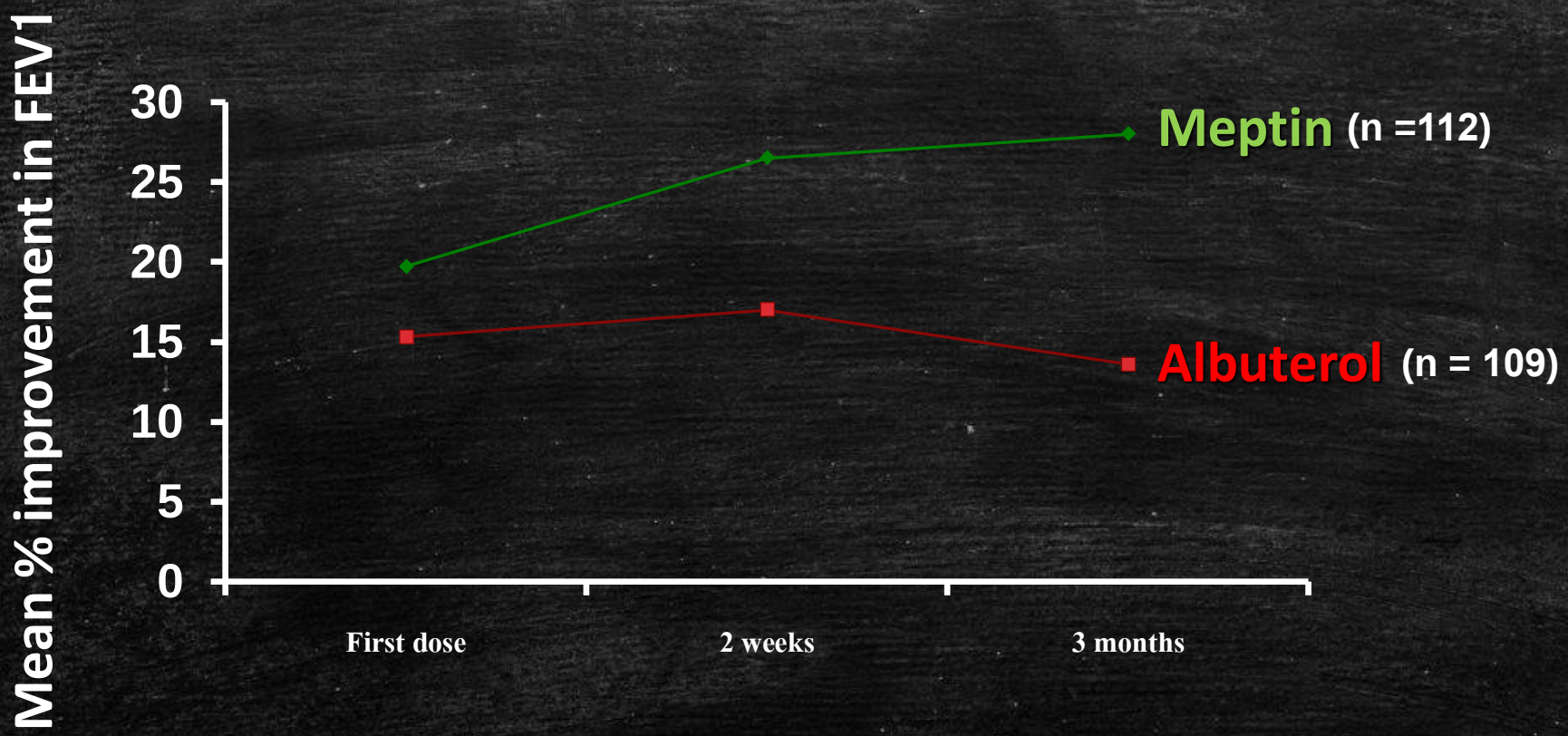
A comparison of oral procaterol and albuterol in reversible airflow obstruction

T L Petty [1], M L Brandon, W W Busse, P Chervinsky, W Schoenweter, A Beaupre, L P Boulet, J Mazza

- Multicenter, randomized, double-blind study
- N = 223 patients (mild to moderate, reversible bronchial airway obstruction)
- Duration: 12 weeks
- Intervention:
  - Procaterol 0.05 mg bid for 2 wk followed by 0.10 mg bid for 10 wk (N = 112)
  - Albuterol 2 mg tid for 2 wk followed by 4 mg tid for 10 wk (N = 109)
- Outcome: Spirometry at 2 wk, 2 months, and 3 months of treatment

Petty TL, et al. Am Rev Respir Dis. 1988 Dec;138(6):1504-9.

A Comparison of Oral Procaterol and Albuterol:
FEV1 after treatment

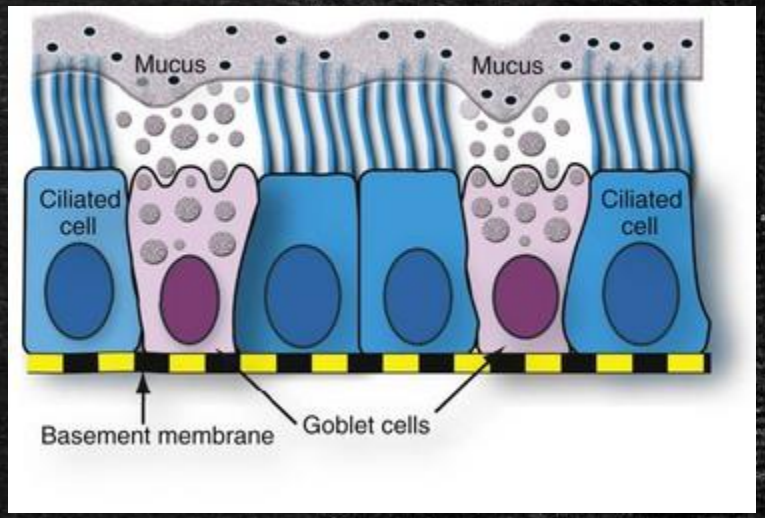


Petty TL, et al. Am Rev Respir Dis. 1988;138(6):1504-9.

β-adrenergic agonists:
Effect on mucociliary clearance

The mucociliary clearance apparatus

- Well-coordinated system → clearing the lung of bacteria and foreign particulate matter
  1. **Airway secretory cells:** produce a sol and gel (mucus) fluid layer on the airway surface
  2. **Ciliated cells:** propel the mucus out of the lung towards the mouth
- Measured by following the rate of egress of deposited, radiolabeled markers by gamma camera

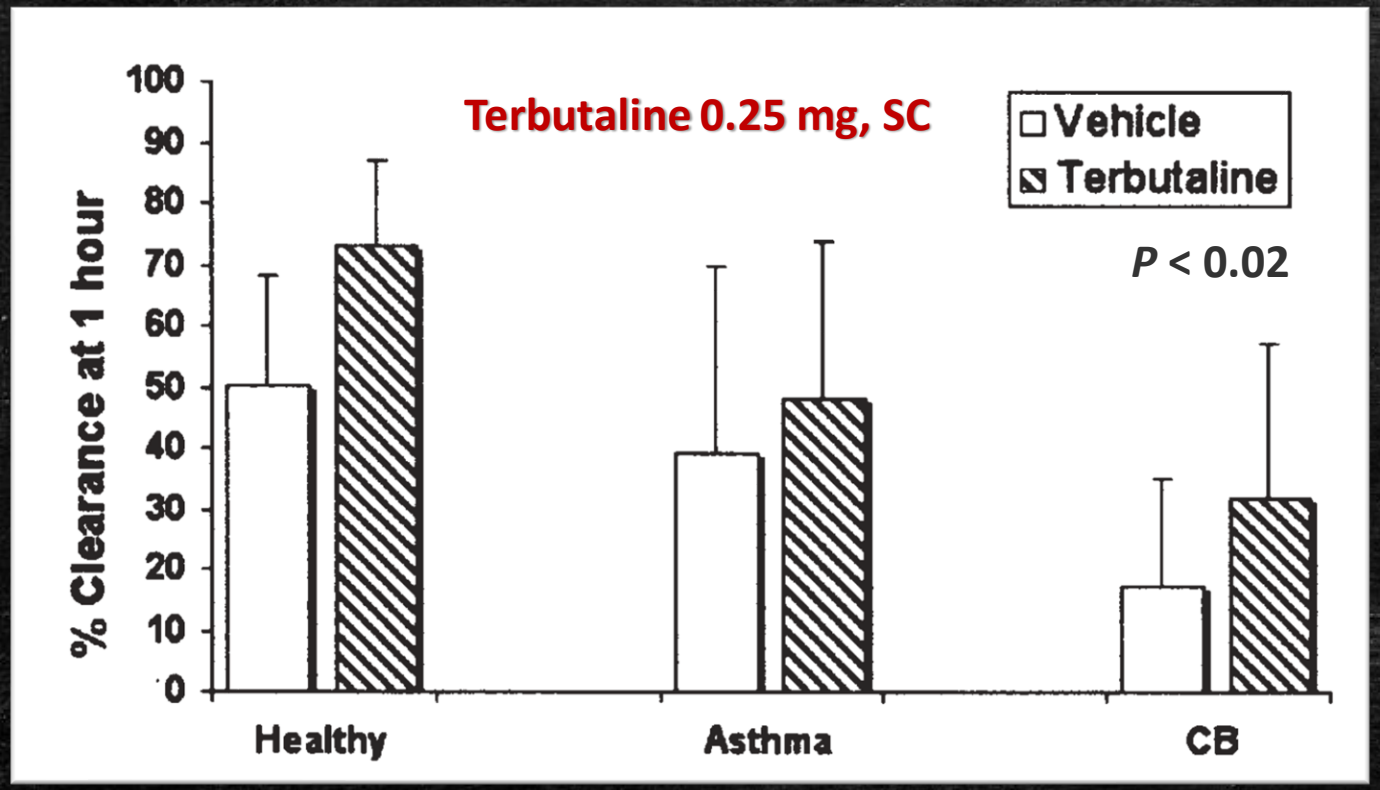


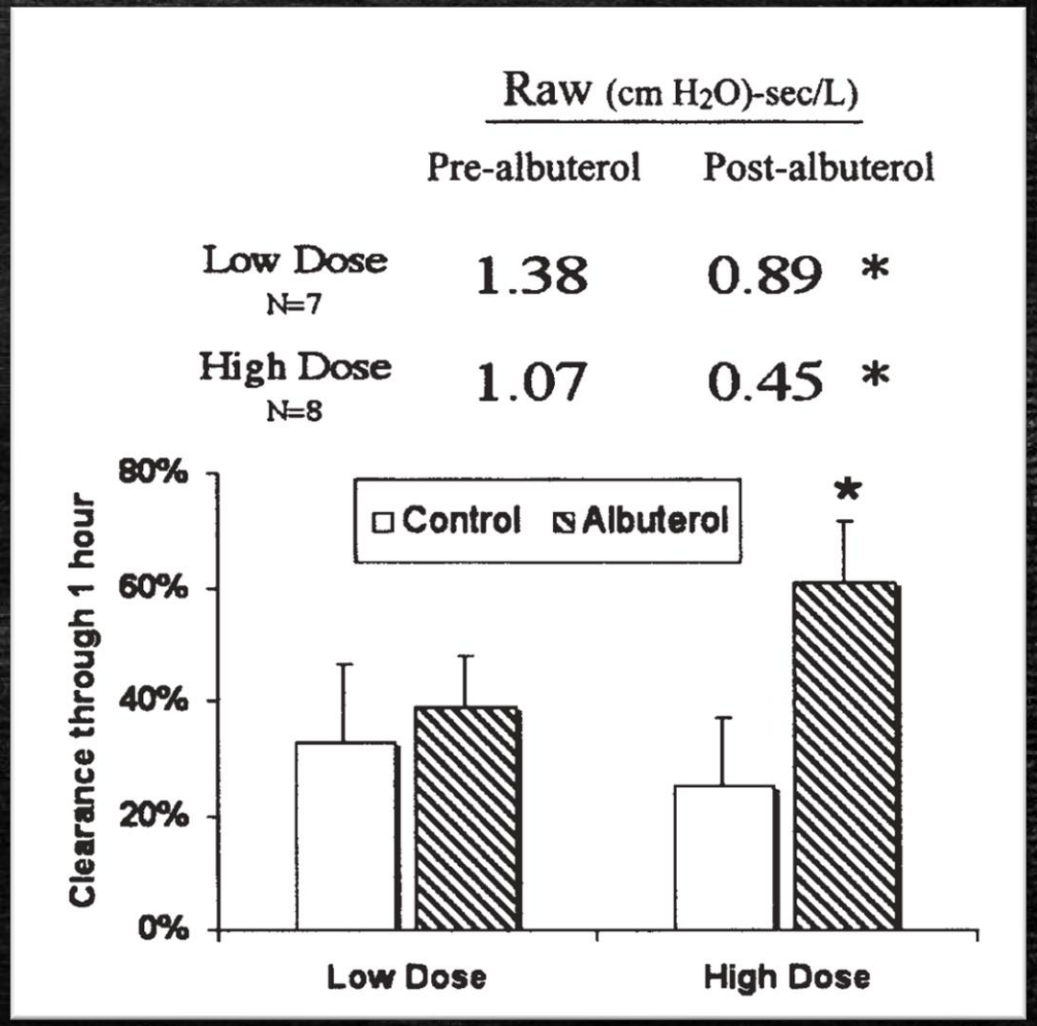
Short acting β-adrenergic agonists

- Enhance mucociliary clearance rates in various lung diseases (eg, asthma, chronic bronchitis, and cystic fibrosis)

Bennett WD. J Allergy Clin Immunol. 2002;110(6 Suppl):S291-7.

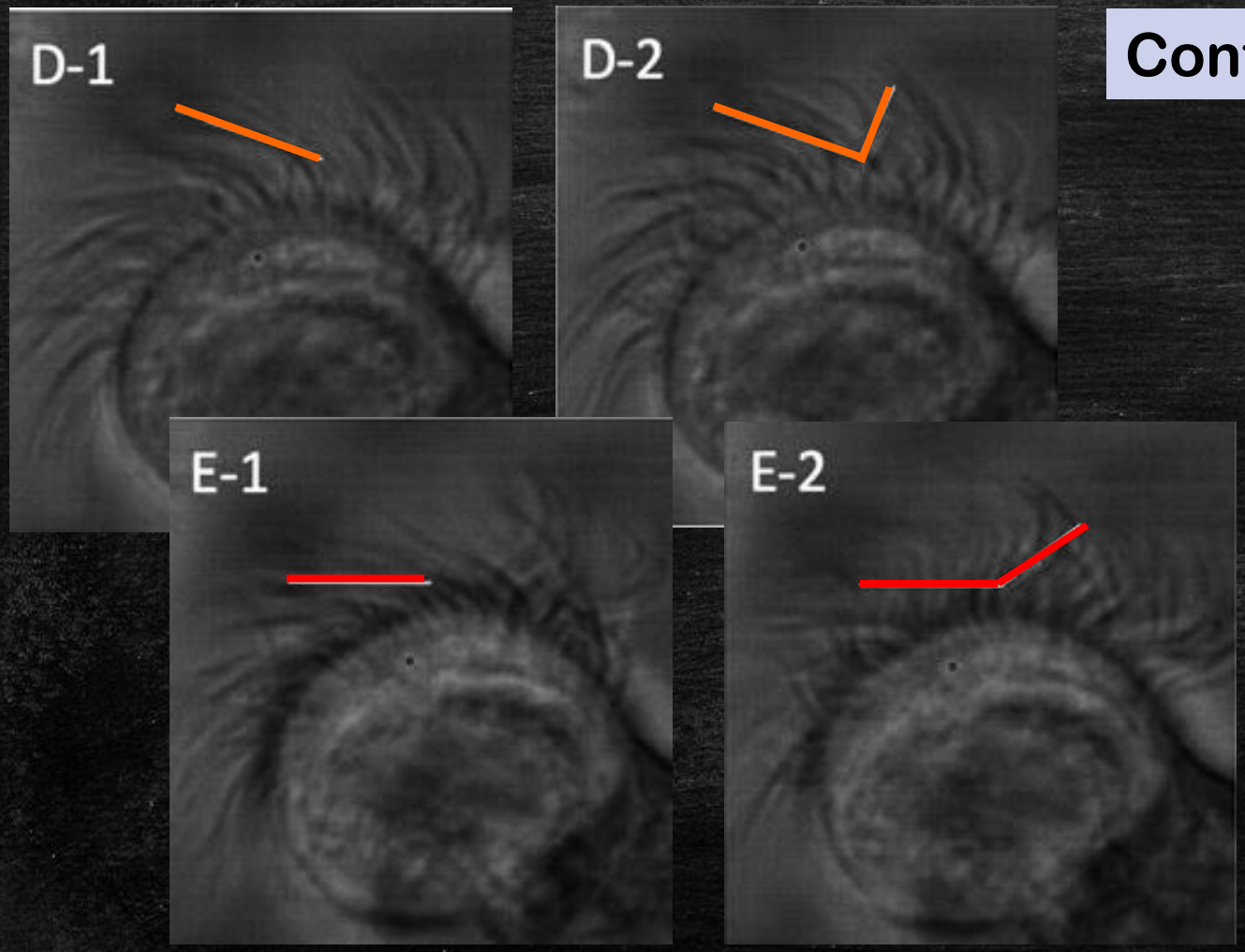
β-adrenergic agonists:
Effect on mucociliary clearance





Bennett WD. J Allergy Clin Immunol. 2002;110(6 Suppl):S291-7.

Effect of Procaterol: Mucociliary clearance



Control

Procaterol on ciliary transport rate (increased ciliary bend amplitude)

- 10 pM - increased 37%
- 10 nM - increased 70%

Procaterol NB

Komatani-Tamiya N, et al. Cell Physiol Biochem. 2012;29(3-4):511-22.

Original Article

Safety and efficacy of ambroxol hydrochloride in combination with procaterol hydrochloride in pediatric pneumonia treatment and their effects on TNF-α, IL-6, and IL-18

Weiping Xiang, Ling Yao, Zhonggan Zhou

Case-control study of treatment in 86 children (aged 3.10 ± 0.51 yo) with pneumonia for 10 days

- **Group A: routine pediatric pneumonia treatment**
  Group B: routine pediatric pneumonia treatment + ambroxol hydrochloride with procaterol hydrochloride
- **Routine pediatric pneumonia treatment = anti-inflammatory drugs, antibiotics (cefazolin and penicillin sodium), vitamin C, cooling +/- aminophylline for bronchospasm)**
- **Ambroxal hydrochloride: PO, tid (10 mg; 3 m-1 y / 15 mg; 2-3 y / 30 mg; > 4 y)**
- **Procaterol hydrochloride: PO tid (12.5 µg; < 5 y / 25 µg; > 5 y)**
- **Outcomes: Symptom scores, changes in plasma TNF-α, IL-6, and IL-18 levels, pulmonary function (FEV1 and FVC)**

Xiang W, Yao L, Zhou Z. Int J Clin Exp Med 2020;13(10):7951-7.

Efficacy of ambroxol hydrochloride in combination with procaterol hydrochloride in pediatric pneumonia

Table 2. Time of disappearance of clinical symptoms associated with children in group A and group B

Group	Group A (n=43)	Group B (n=43)	t	P
Cough disappearance time	7.01 ± 1.43	3.04 ± 1.36	13.190	< 0.001
Wheezing disappearance time	7.20 ± 1.25	4.05 ± 1.62	10.090	< 0.001
Defervescence time	7.18 ± 1.44	3.95 ± 1.26	11.070	< 0.001
Rale disappearance time	6.82 ± 1.08	3.02 ± 1.17	15.650	< 0.001

Table 3. Cough scores before and after treatment in children in group A and group B

Group	Group A (n=43)	Group B (n=43)	t	P
Before treatment	5.23 ± 1.68	5.42 ± 1.90	0.491	0.625
After treatment	2.68 ± 1.42	1.26 ± 0.23	6.473	< 0.001
t	7.801	9.374		
P	< 0.001	< 0.001		

The cough disappearance time, wheezing disappearance time, defervescence time, and rale disappearance time of group B were shorter than those of group A

- The cough scores of both groups were lower after treatment.
- The cough score of group B after treatment being lower than before treatment compare with group A

Xiang W, Yao L, Zhou Z. Int J Clin Exp Med 2020;13(10):7951-7.

Efficacy of ambroxol hydrochloride in combination with procaterol hydrochloride on TNF-α, IL-6, and IL-18 in pediatric pneumonia

Table 4. TNF-α before and after treatment in children in group A and group B

Group	Group A (n=43)	Group B (n=43)	t	P
Before treatment	13.14 ± 2.15	13.01 ± 2.47	0.260	0.795
After treatment	7.02 ± 2.48	4.28 ± 1.99	5.651	< 0.001
t	5.207	8.580		
P	< 0.001	< 0.001		

Table 5. IL-6 before and after treatment in children in group A and group B

Group	Group A (n=43)	Group B(n=43)	t	P
Before treatment	48.39 ± 2.69	49.13 ± 1.06	1.678	0.097
After treatment	36.46 ± 2.16	28.49 ± 1.24	20.980	< 0.001
t	6.135	8.508		
P	< 0.001	< 0.001		

Table 6. IL-18 before and after treatment in children in group A and group B

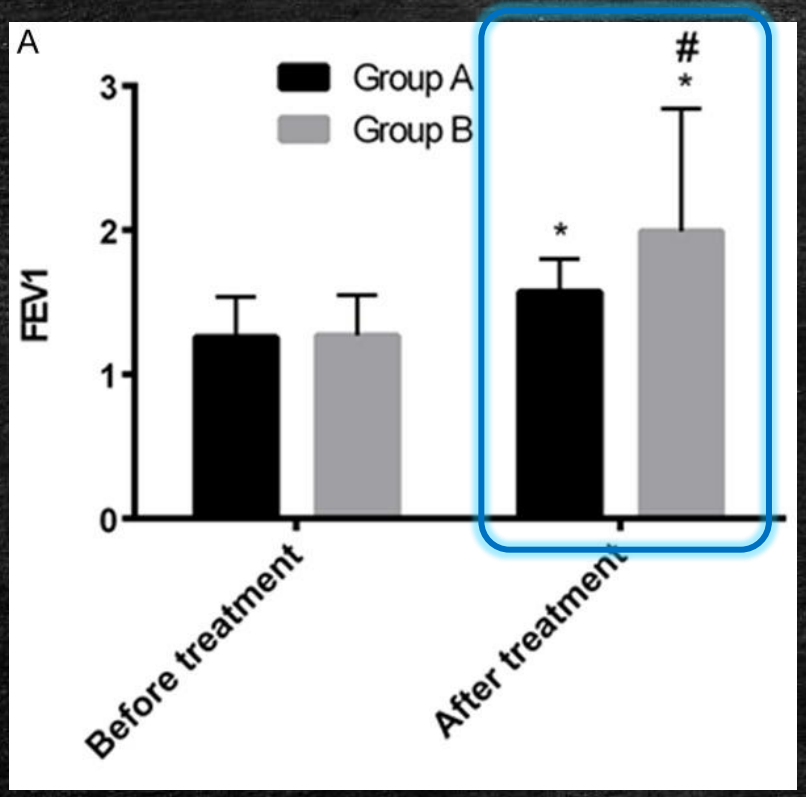
Group	Group A (n=43)	Group B (n=43)	t	P
Before treatment	320.19 ± 58.29	319.45 ± 56.41	0.054	0.957
After treatment	302.18 ± 46.09	236.29 ± 39.08	7.150	< 0.001
t	7.542	9.014		
P	< 0.001	< 0.001		

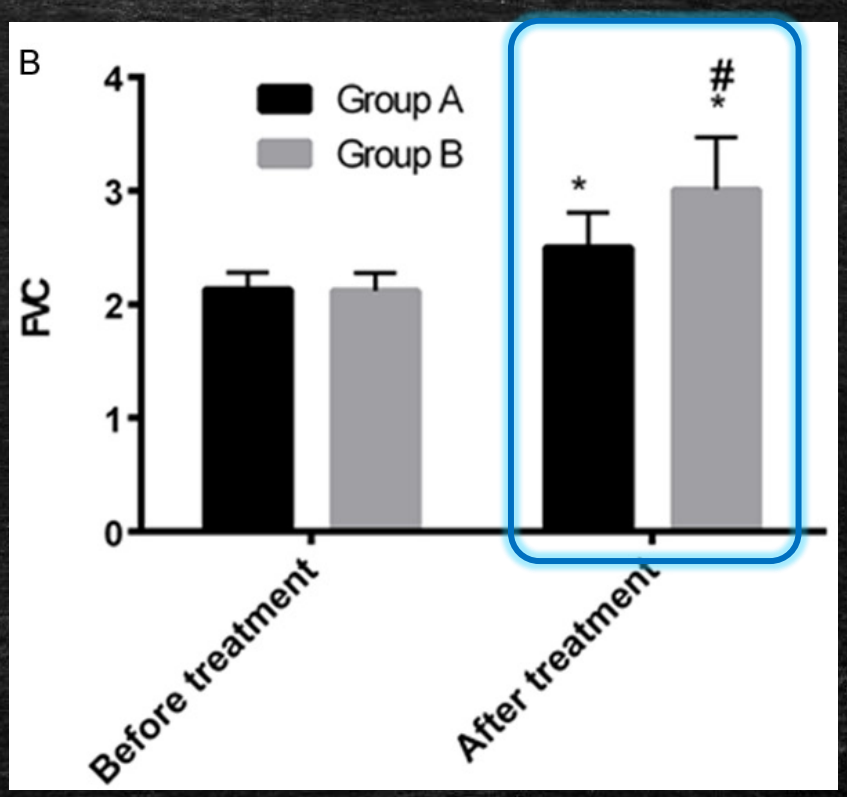
Inflammatory marker during pneumonia (TNF-α, IL-16 and IL-18)

- **the plasma level of group B after treatment being lower than that of group A**

Xiang W, Yao L, Zhou Z. Int J Clin Exp Med 2020;13(10):7951-7.

Efficacy of ambroxol hydrochloride in combination with procaterol hydrochloride on TNF-α, IL-6, and IL-18 in pediatric pneumonia





Pulmonary function (FEV1 and FVC) of group B were higher than those in group A after treatment ($P < 0.001$)

Xiang W, Yao L, Zhou Z. Int J Clin Exp Med 2020;13(10):7951-7.

Original Article

Safety and efficacy of ambroxol hydrochloride in combination with procaterol hydrochloride in pediatric pneumonia treatment and their effects on TNF-α, IL-6, and IL-18

Weiping Xiang, Ling Yao, Zhonggan Zhou

คณะแพทยศาสตร์
มหาวิทยาลัยศรีนครินทรวิโรฒ

The combination of ambroxol hydrochloride and procaterol hydrochloride in pediatric pneumonia treatment showed

- Better clinical symptoms (cough, wheezing, rale disappearance, and defervescence time periods)
- Better alleviation of pulmonary inflammation
- Better regulation of pulmonary function

This combination can improve the clinical efficacy of treatments in children with pneumonia to a certain extent and is worthy of wide clinical promotion.

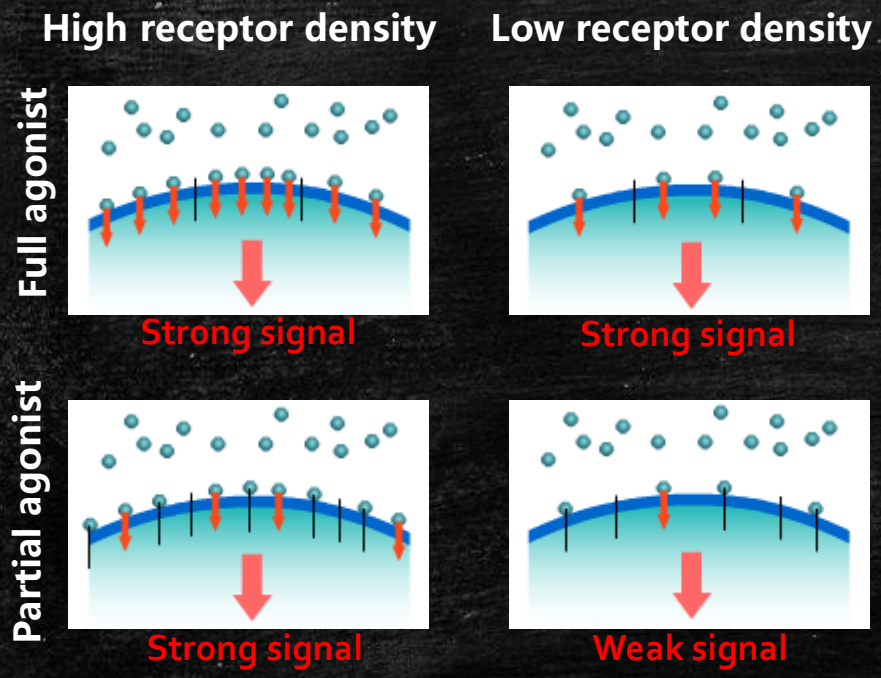
Xiang W, Yao L, Zhou Z. Int J Clin Exp Med 2020;13(10):7951-7.

Short-acting β2-Agonist: All generation

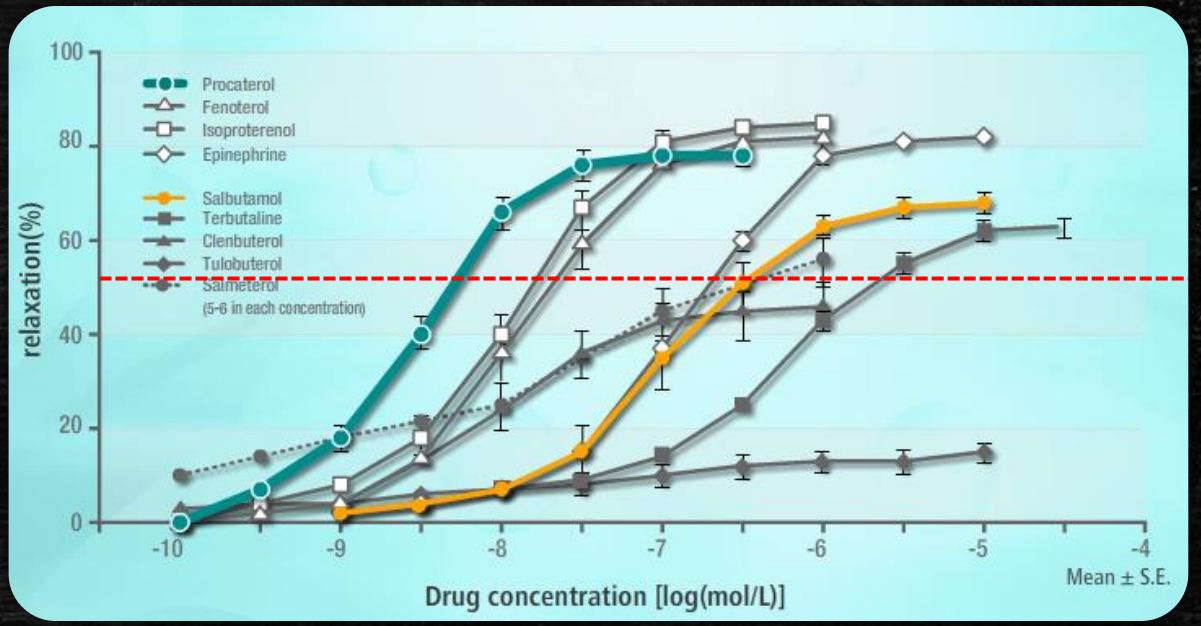
	รุ่นที่ 1	รุ่นที่ 2	รุ่นที่ 3
กลุ่มยาขยายหลอดลม	Adreneline, Ephedrine	Salbutamol, Terbutaline	Procaterol
ความเฉพาะเจาะจง	α, β1, β2	β2 > β1	β2 >>> β1
	ไม่มีรูปยาเม็ด	mg	µg
ประสิทธิภาพในการขยายหลอดลม			
ความเร็วในการออกฤทธิ์		0.5 – 1 hr	น้อยกว่า 30 นาที
ระยะเวลาในการออกฤทธิ์		2-7 hr	10-12 hr
อาการไม่พึงประสงค์		ใจสั่น มือสั่น (5-10%)	ใจสั่น มือสั่น (1-5%)
บัญชียาหลักแห่งชาติ		✓	✓

Full agonist & strong broncho-dilating effects

- **Full agonist：** only need 5% receptor density can reach 100% broncho-dilating effect
- **Partial agonist：** even with 100% receptor density, it can not reach full broncho-dilating effect



Relaxant effects of β2 adrenoceptor on severe precontraction

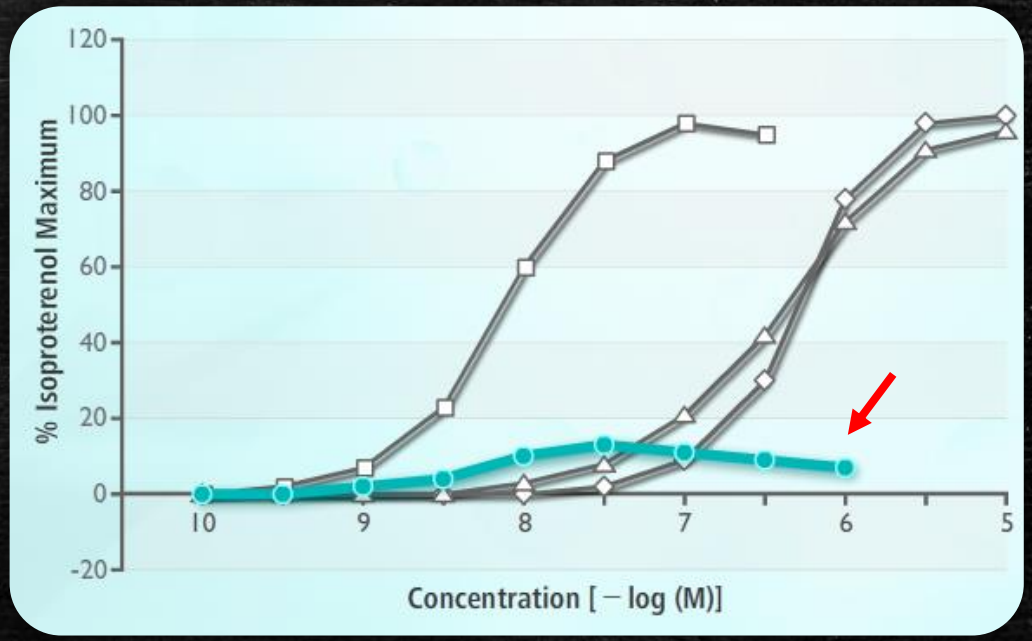


β_2 selectivity of bronchodilators

name	Bronchitis (β2) EC50	left atrium (β1) EC50	B1 effect	B2 selectivity (β2/β1)
Procaterol	11.1	0.0001	3	111,000
Salmeterol	5.0	0.0001	4	50,000
Clenbuterol	2.0	0.0001	2	20,000
Salbutamol	0.48	0.0004	14	1,200
Formoterol	25.0	0.05	100	500
Terbutaline	0.08	0.0003	35	267
Fenoterol	0.9	0.005	100	180
Orciprenaline	0.05	0.01	89	5
Isoprenaline	1.0	1.0	100	1

Highly selectivity for β2 receptor,

Less Cardiac side effects

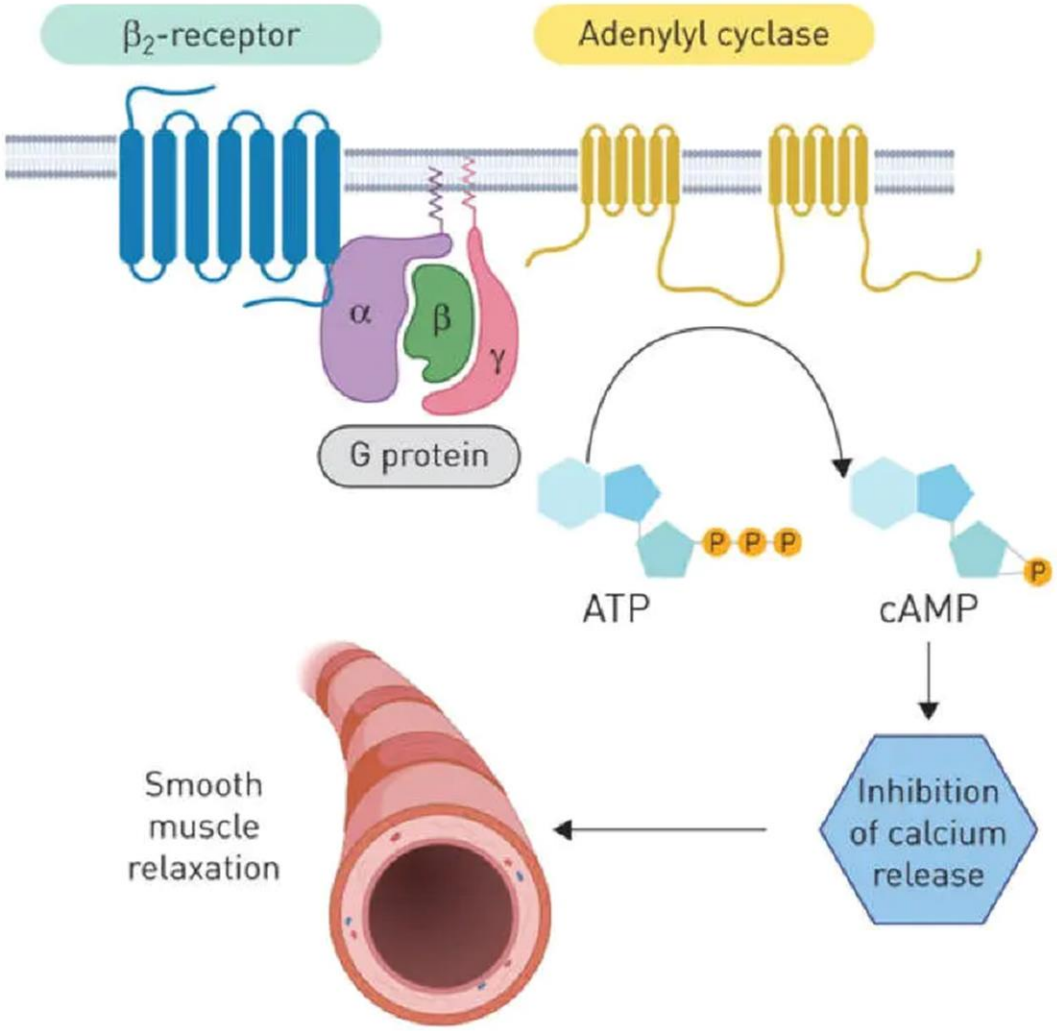


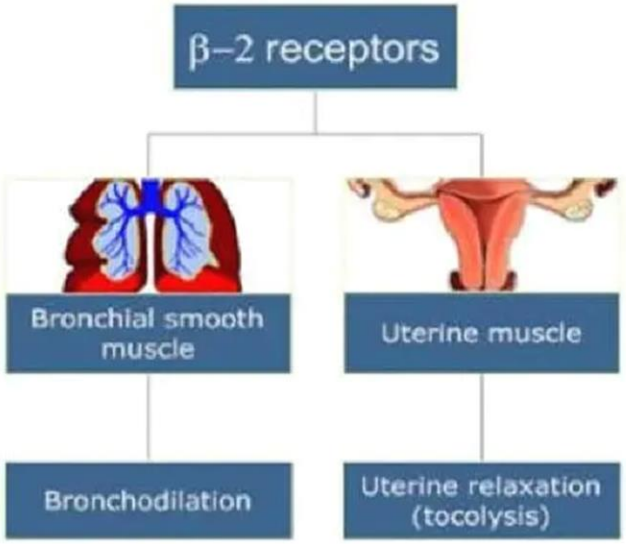
Positive inotropic responses

Yuichiro Kamigawa rt al. International Review of Asthma 1999;1(4):34.

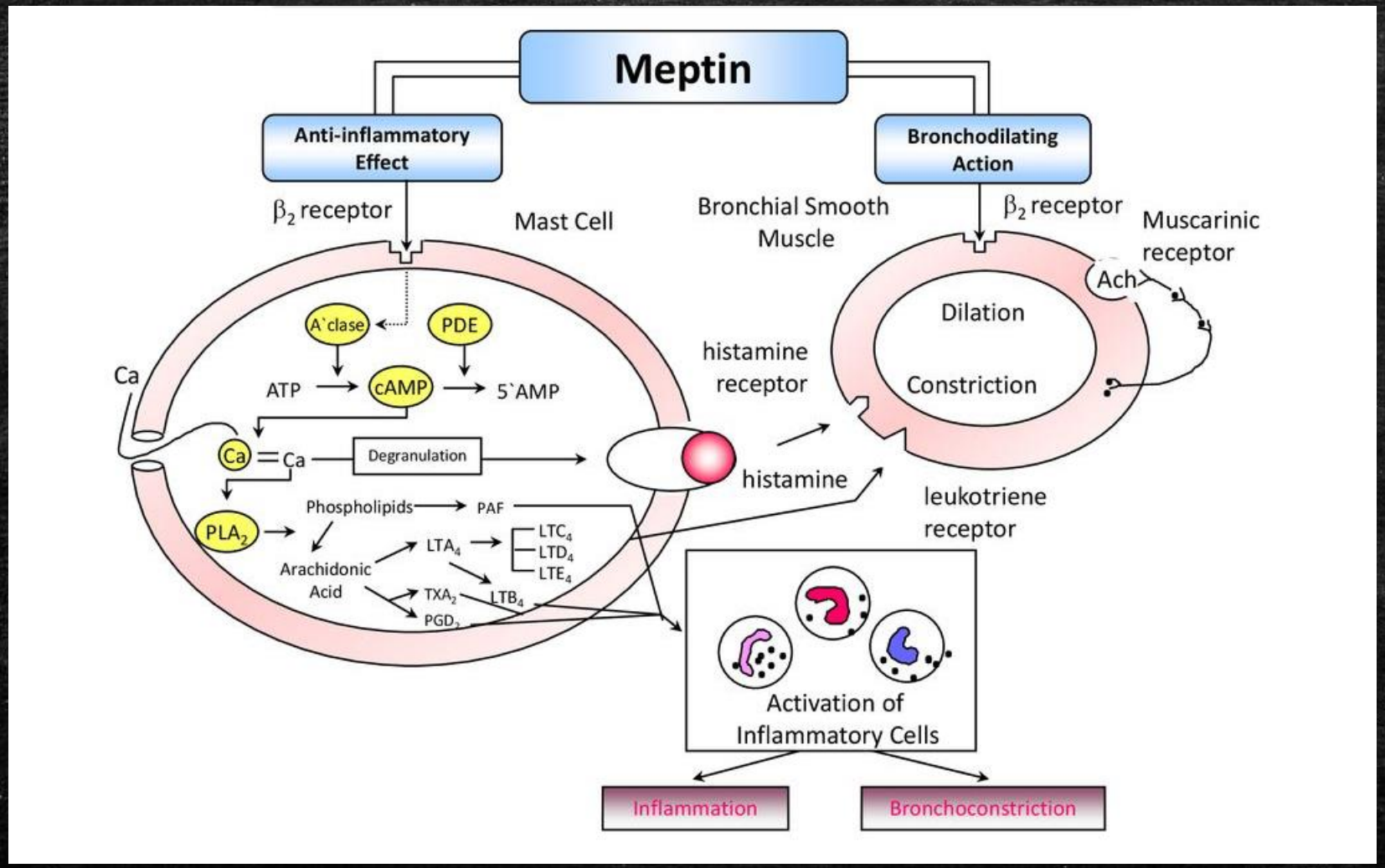
Selective agonists of beta adrenergic receptors 2

1. Terbutaline
2. Clenbuterol
3. Salbutamol
4. Salmeterol
5. Pirbuterol
6. Isoetarine
7. Orciprinaline





Procaterol: Mechanism of Action



❖ **Meptin Tab, Mini, Syrup**
be listed in National List of Essential Medicines
from year 2004 and also in year 2017

กลุ่มยา 3 Respiratory system

3.1 Bronchodilators

3.1.1 Adrenoceptor agonists

1.	Procaterol hydrochloride	syr	ก
2.	Salbutamol sulfate	tab, aqueous sol, DPI, MDI, sol for nebulizer	ก
3.	Terbutaline sulfate	tab, syr, sterile sol	ก
4.	Terbutaline sulfate	sol for nebulizer	ก
5.	Procaterol hydrochloride	tab	ข

Take home messages (1)

- RAD is a symptomatic diagnosis of recurrent wheezing in preschool child.
- Most of RAD-diagnosed children become asthma, since preschool asthma are difficult to diagnose.
- Early viral respiratory infections, especially RSV and rhinovirus (RV), are the significant risk factors for asthma development.
- RV infections cause airway inflammation and hyper-responsiveness which can be presented as recurrent wheezing or RAD.

Take home messages (2)

- Bronchodilator, eg; procaterol:
  - has an anti-viral effect especially in inhibiting RV infections by reducing RV adhesion molecules, acidification of RV endosomes and reducing inflammatory cytokine production.
  - reduces eosinophilic infiltration and fibroblast migration.
  - may help to prevent airway remodeling.
- Procaterol is the option of bronchodilator that helps in reducing RAD symptoms which are wheezing and coughing (improves mucociliary clearance and when using in combination with ambroxal)

Thank you for your attention

The End