

SALA VIOLANTE/GINEVRA

## URGENZE RESPIRATORIE

Moderatori: Salvatore Maggiore - Giorgio Carbone

# Gabriele Valli

Quando si parla di asma grave?



XII congresso nazionale

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RICCIONE 13-15 MAGGIO 2022



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# Quando si parla di Asma Grave?

Gabriele Valli, MD

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XII congresso nazionale

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## CASO 1

Donna di 55 anni, giunge in PS per la comparsa di difficoltà respiratoria e respiro sibilante. Sa di essere asmatica e prende regolarmente terapia inalatoria con formeterolo e budesonide.

Ha avuto un recente episodio febbrile, circa 4 giorni prima, da allora ha dovuto aumentare le inalazioni fino a 4-6 al giorno.

Ha iniziato a prendere autonomamente il bentelan. Non è nuova a questi episodi, tutti gli anni, nei mesi invernali, è costretta a fare dei cicli di corticosteroidi per via sistemica e



## CASO 2

Ragazzo di 30 anni, non ha mai sofferto di disturbi respiratori. Sa di essere allergico ai pollini e alle polveri per cui per brevi periodi durante la primavera prende dell'antistaminico per prevenire gli episodi di rinite.

Ha aiutato un amico a svuotare una cantina e mentre lavoravano ha cominciato ad accusare

# GLOBAL STRATEGY FOR ASTHMA MANAGEMENT AND PREVENTION

## STARTING TREATMENT

in adults and adolescents with a diagnosis of asthma

Track 1 is preferred if the patient is likely to be poorly adherent with daily controller ICS-containing therapy is recommended even if symptoms are infrequent, as it reduces the risk of severe exacerbations and need for OCS.



### FIRST ASSESS:

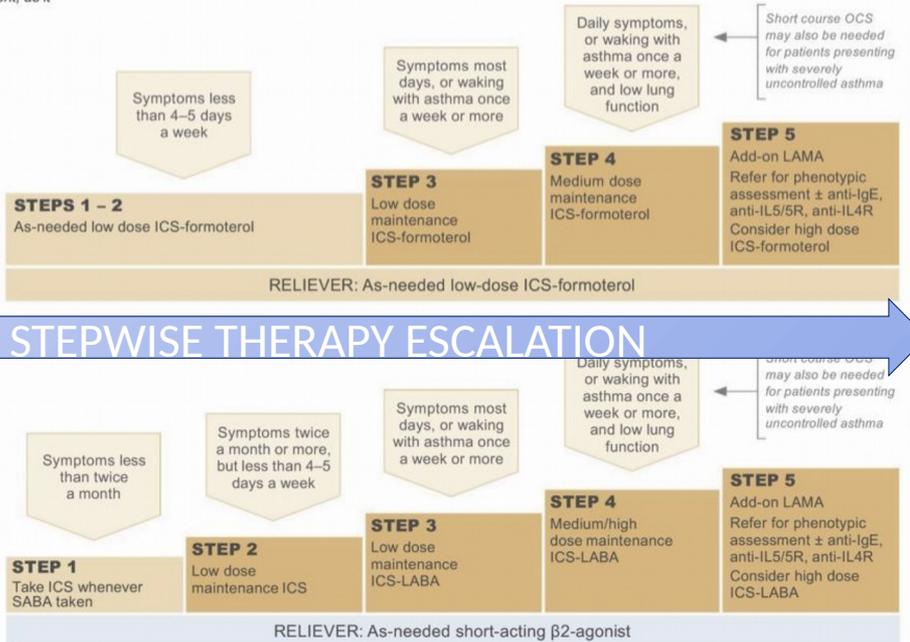
- Confirm diagnosis
- Symptom control and modifiable risk factors, including lung function
- Comorbidities
- Inhaler technique and adherence
- Patient preferences and goals

### START HERE IF:

**CONTROLLER and PREFERRED RELIEVER** (Track 1). Using ICS-formoterol as reliever reduces the risk of exacerbations compared with using a SABA reliever

### START HERE IF:

**CONTROLLER and ALTERNATIVE RELIEVER** (Track 2). Before considering a regimen with SABA reliever, check if the patient is likely to be adherent with daily controller therapy



Le linee guida sulla gestione dell'asma si focalizzano sul controllo dei sintomi.

I pazienti sono «**pazienti gravi**» quando hanno uno scarso controllo dei sintomi e necessitano di terapie farmacologiche via via più complesse

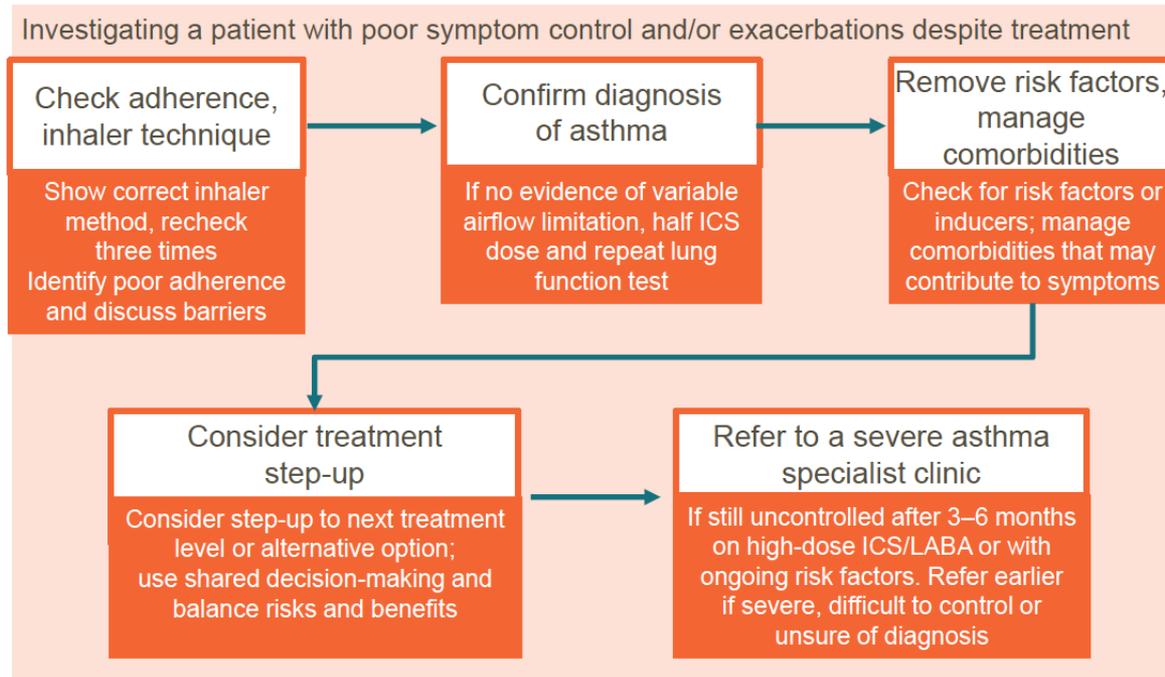
# Definizione di Asma Grave secondo le attuali linee guida

	Exacerbations in previous year	FEV1	Symptoms control	Therapy	OCS
Enfumosa	≥1 (requiring OCS)	Not required	Not required	≥1200 µg beclometasone or equivalent	Not required
WHO	>2	FEV1 <60%	Poor	Maximal dose	Daily
TENOR	≥2 (requiring OCS) <sup>a</sup>	Not required	Not required	≥3 drugs <sup>a</sup>	>5 mg prednisone or equivalent
ATS-ERS and GINA	≥2 (requiring OCS) or ≥1 hospitalization <sup>a</sup>	FEV1 < 80% FEV1/ FVC < LLN <sup>a</sup>	ACQ >1.5, ACT<20 <sup>a</sup>	≥1000 µg beclometasone or equivalent	>50% of previous year <sup>a</sup>
U-Biopred	≥2 (requiring OCS)	Not required	ACQ >1.5 or equivalent score	≥1000 µg fluticasone or equivalent <sup>a</sup>	Daily use <sup>a</sup>
NICE	1 life threatening or 2 hospitalization <sup>a</sup>	FEV1 < 70% <sup>a</sup>	Not required	≥1000 µg beclometasone or equivalent	>50% of previous year (>7.5 mg prednisone or equivalent) <sup>a</sup>

**Table 1.** Principal criteria of severe asthma in guidelines and main clinical trials. OCS: oral corticosteroid; FEV1: forced expiratory volume in 1 s. a. Refers to the presence of at least one of these

- Frequenza delle riacutizzazioni
- Grado di ostruzione bronchiale
- Controllo dei sintomi
- Uso di alte dosi di corticosteroidi

# Percorso clinico del paziente con Asma Grave secondo le Linee Guida ERS/ATS



ICS, inhaled corticosteroid; LABA, long-acting  $\beta$ -agonist

*L'interesse all'identificazione di questi pazienti come «**gravi**» è legato alla possibilità di indirizzare il malato ad una valutazione specialistiche ed all'accesso alle cure con i farmaci biologici*

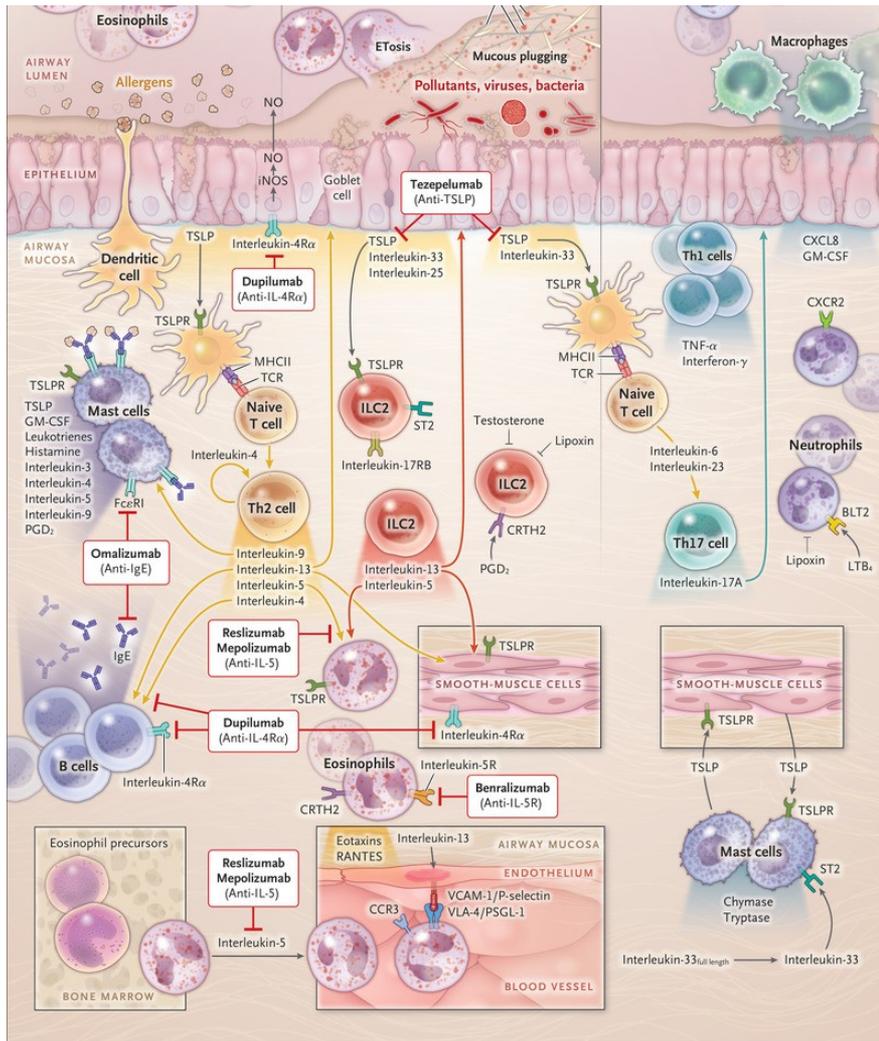
# Meccanismi infiammatori alla base dell'asma bronchiale grave

## Reazione Infiammatoria modulata da Th2

- Innescata da cellule dendritiche epiteliali
- mediata da IgE, Mastociti ed Eosinofili
- Coinvolge fattori chemiotattici e interleukine antagonizzabili con immunoglobuline specifiche
- Reversibile, caratterizzata da elevata variabilità e silente nelle fasi inter-critiche
- Buona risposta ai corticosteroidi

## Reazione Infiammatoria modulata da Th1

- Innescata da macrofagi
- mediata da neutrofili con attivazione delle cellule fibroblastiche e innesco del remodelling interstiziale
- Caratterizzata da scarsa reversibilità, frequenti riacutizzazioni ed infezioni respiratorie
- Scarsa risposta alla terapia corticosteroides



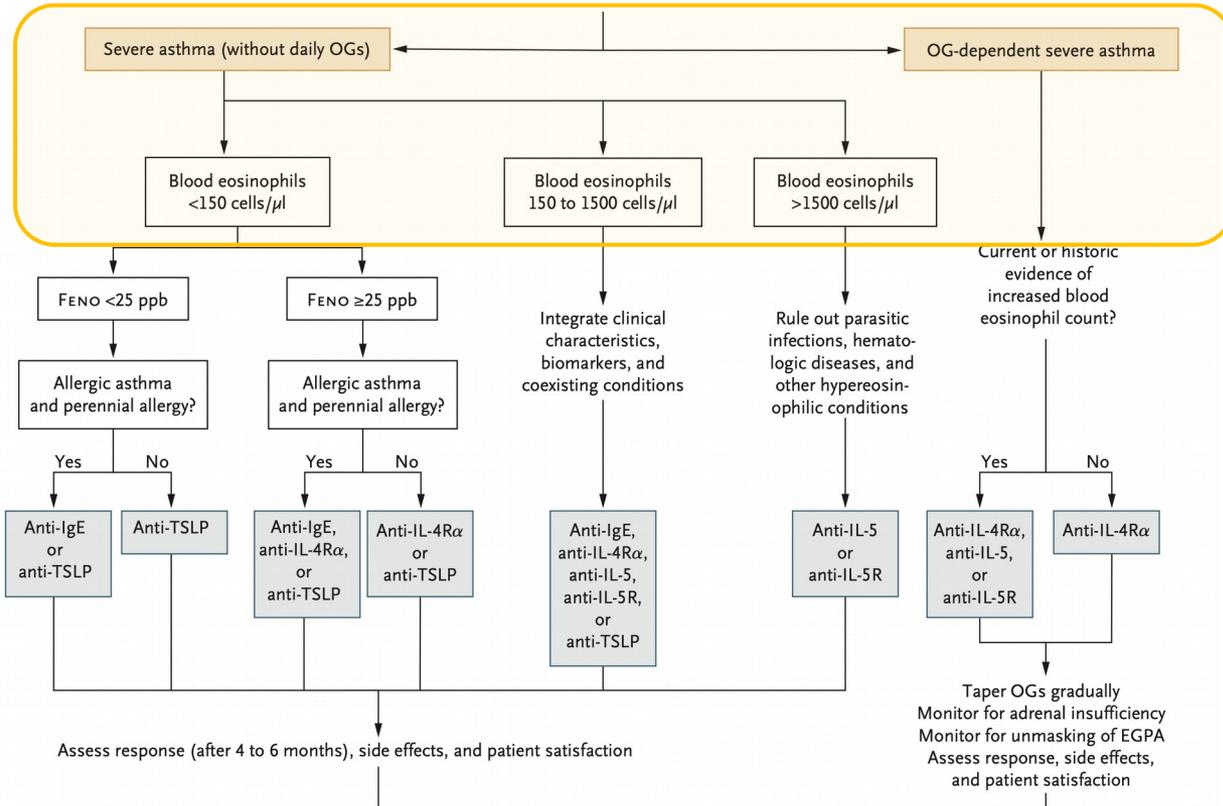
# Terapia monoclonale nei pazienti asmatici gravi

Nella scelta del tipo di terapia biologica è fondamentale valutare il tipo di reazione infiammatoria che sostiene l'ipereattività bronchiale del paziente.

Risultano fondamentali:

- La risposta ai corticosteroidi
- L'attivazione degli eosinofili

*Questi due parametri, facilmente recuperabili anche in emergenza, possono indicare il tipo di risposta infiammatoria sottostante*



Assess response (after 4 to 6 months), side effects, and patient satisfaction

Taper OGs gradually  
Monitor for adrenal insufficiency  
Monitor for unmasking of EGPA  
Assess response, side effects, and patient satisfaction



e paz



più

La paziente viene trattata con corticosteroidi sistemici e terapia inalatoria.

Subito dopo il trattamento riferisce già un miglioramento dei sintomi.

Viene ricoverata in OBI da cui verrà dimessa dopo 2 giorni di osservazione

Il paziente, dopo circa 30min di attesa va in arresto respiratorio.

Viene intubato e ricoverato in rianimazione

Verrà dimesso in buone condizioni dopo 15 giorni di ricovero di cui 5 in terapia intensiva

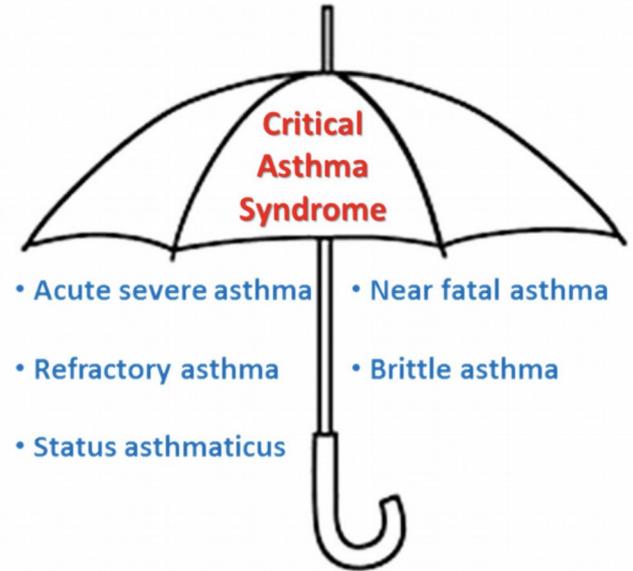
costretta a fare dei cicli di corticosteroidi per via sistemica e

Mentre lavoravano a cominciare ad accusare

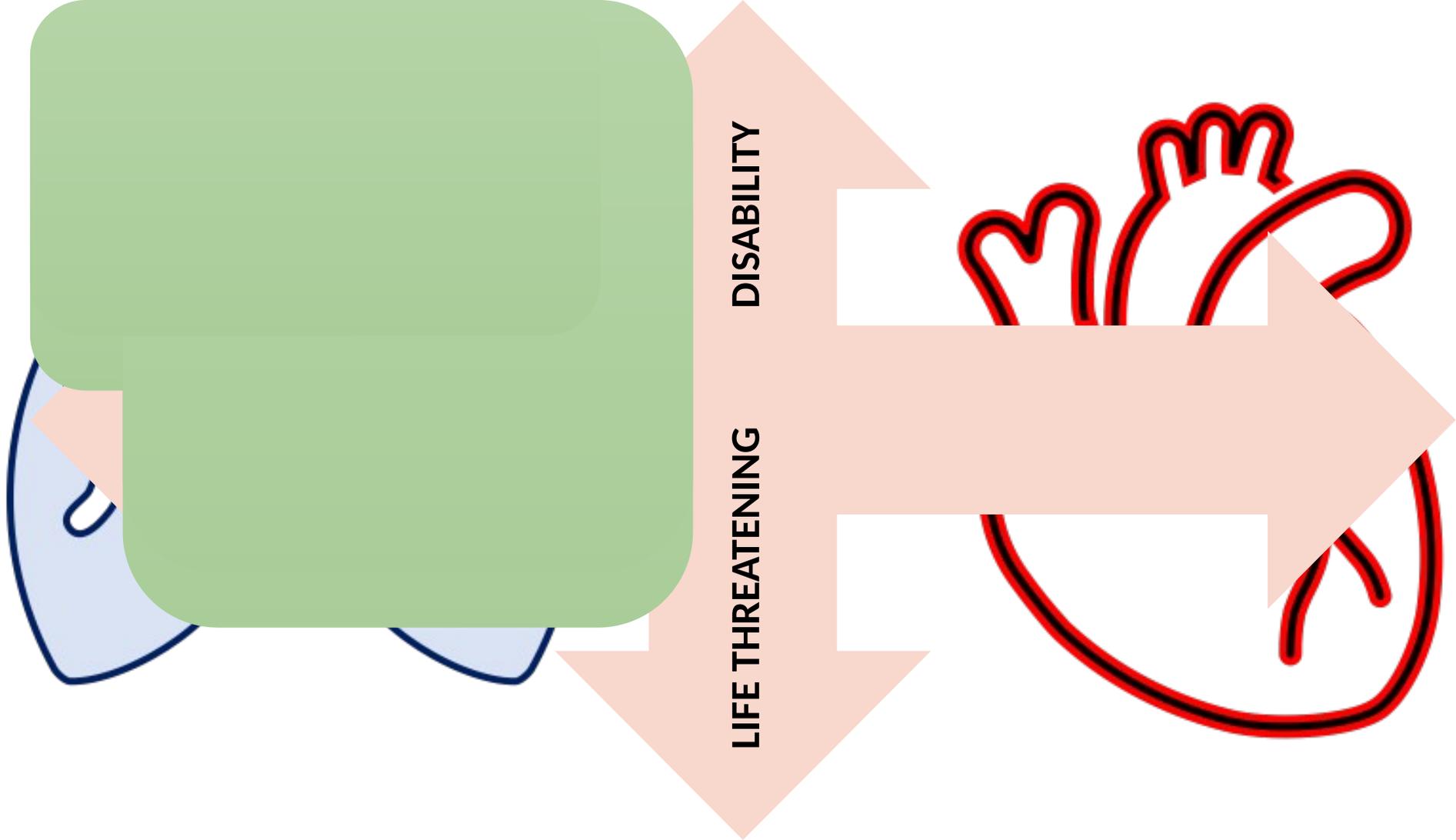
## Definition of Critical Asthma Syndromes

Nicholas Kenyon • Amir A. Zeki • Timothy E. Albertson •  
Samuel Louie

Nel 2015 Kenyon e coll. Introducono per la prima volta la definizione di «Critical Asthma Syndrome» una definizione che raccoglie tutte le condizioni «life threatening»



**Fig. 1** Critical asthma syndrome (CAS) is an umbrella term that represents many other terms historically and currently used to describe acute and severe life-threatening exacerbations



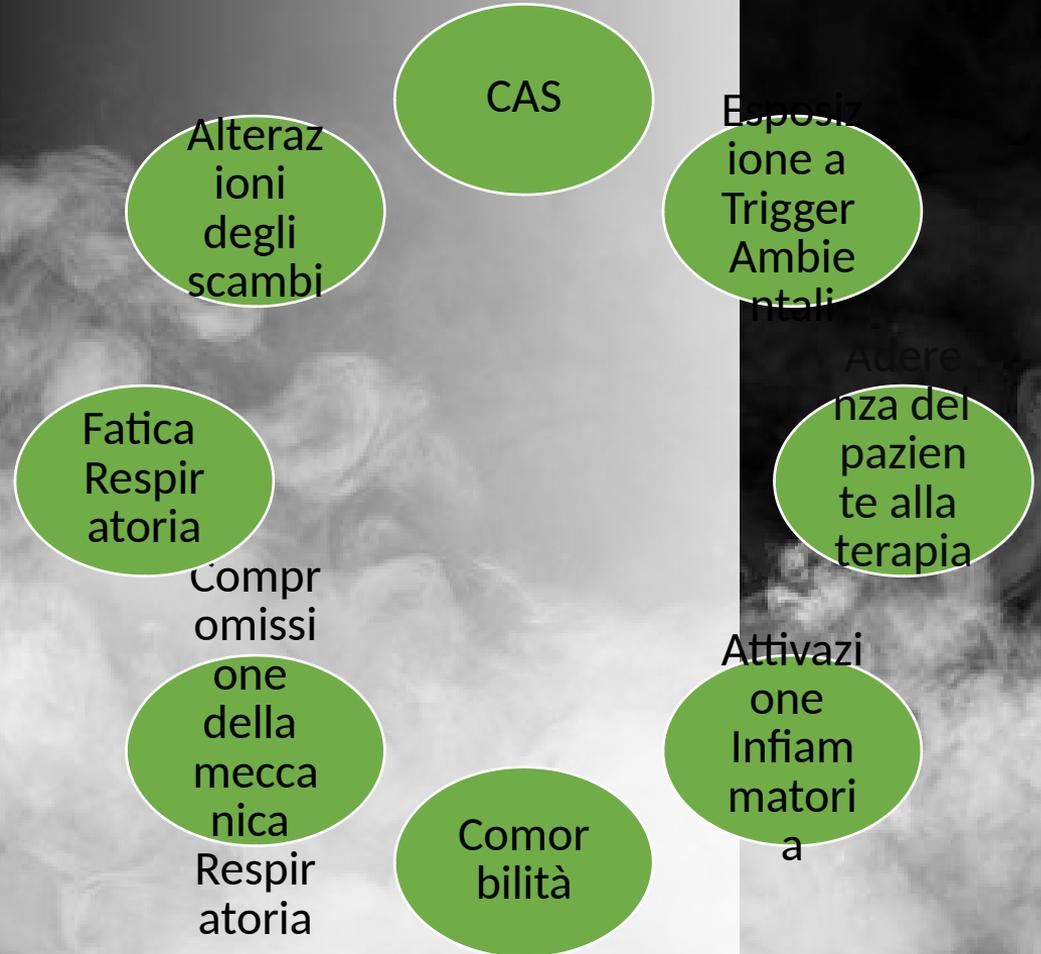
**LIFE THREATENING**

**DISABILITY**



# Riconoscere la Critical Asthma Syndrome

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# Fisiopatologia di un attacco d'asma

Trigger Ambientale  
(allergene, ozono, virus...)

Reazione infiammatoria Th2 mediata:

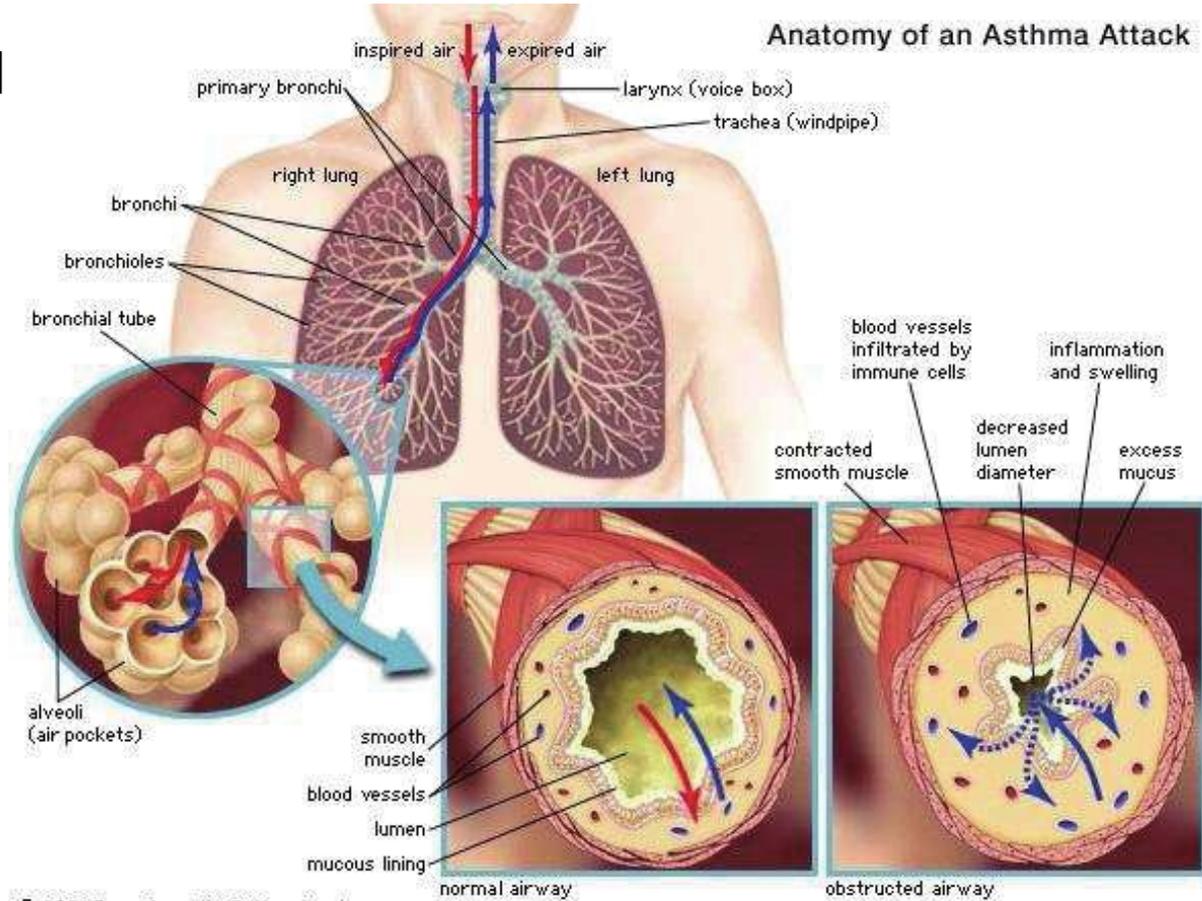
TERAPIA BIOLOGICA

BRONCODILATATORI

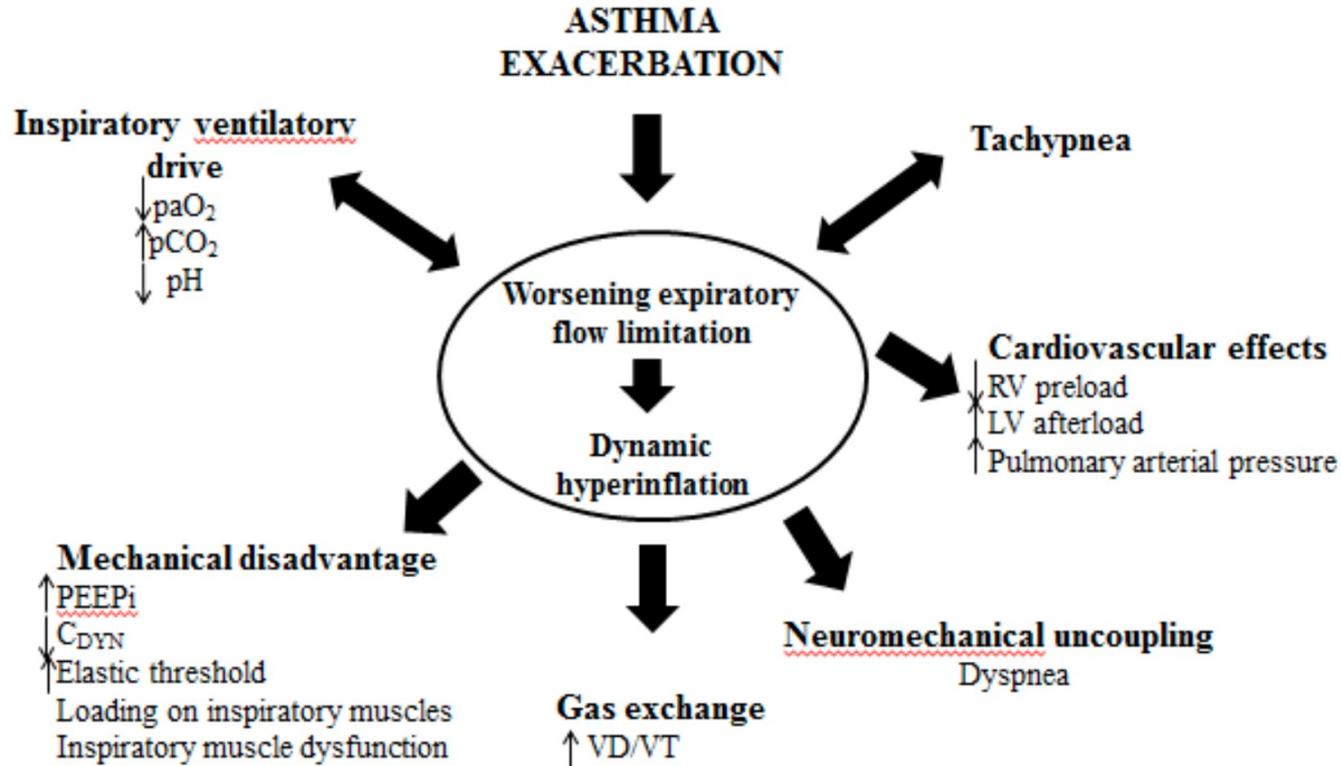
CORTICOSTEROIDI

O<sub>2</sub> E VENTILAZIONE ASSISTITA

V/Q *mistmach*



© 2001 Encyclopædia Britannica, Inc.



**Figure 6.** Pathophysiological changes due to dynamic hyperinflation.

# Management of Life-Threatening Asthma: Severe Asthma Series.

Garner O, Ramey JS, Hanania NA.

*Chest.* 2022 Feb 23:S0012-3692(22)00395-6.

**TABLE 1 ]** Simplified Severity Score for Acute Asthma<sup>4</sup>

Sign or Symptom	Severity Score		
	Mild	Moderate	Severe
Pulse rate, beats/min	< 90	91-119	> 120
Wheezing	Absent	Present	Present
Rales	Absent	Present	Present
Prolonged expirium	Absent	Present	Present
Oxygen saturation, %	95-100	90-94	< 89
Use accessory muscles	Absent	Present	Present
Minimal no. of parameters required to qualify for categories	Any 3 of the above	Any 3 of the above or the use of accessory muscles only	Any 3 of the above or oxygen saturation of < 89% only

# Importanza dei parametri emogasanalitici

## Livello 1

- Ostruzione lieve
- Normale scambio dei gas
- Paucisintomatico

## Livello 2

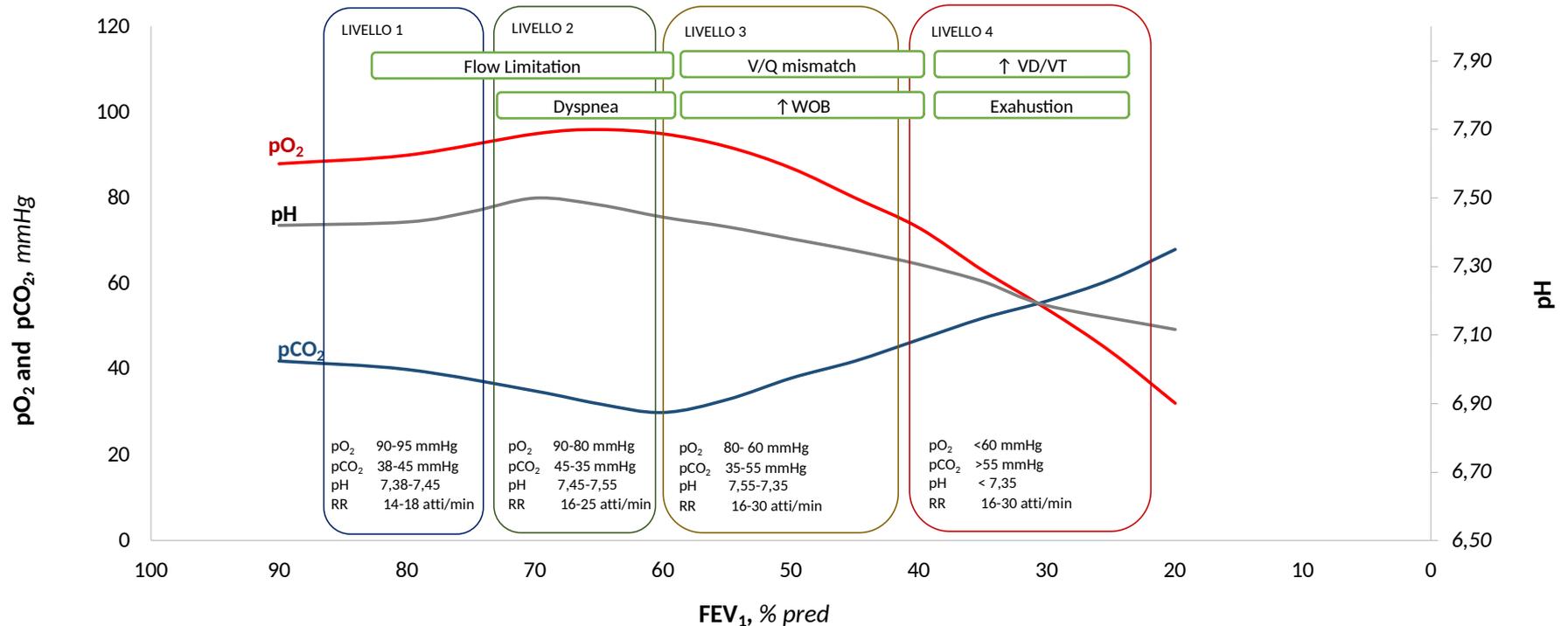
- Ostruzione moderata
- Alcalosi Respiratoria
- Sibili, Tosse

## Livello 3

- Ostruzione severa
- Ipossia con pH e  $pCO_2$  normali
- Dispnea

## Livello 4

- Ostruzione non reversibile
- Ipercapnia
- Confusione, Bradipnea



### SEGNI DI FATICA RESPIRATORIA

- Fr > 25 atti/min
- Respiro Paradosso
- Muscolatura Accessoria

### SEGNI DI COMPROMISSIONE EMODINAMICA

- FC > 120
- PAS < 100
- Diaforesi

### SEGNI V/Q MISMATCH

- SpO<sub>2</sub> < 92%
- pH < 7.35
- pCO<sub>2</sub> > 45 mmHg

### SEGNI ESAURIMENTO

- Confusione
- Silenzio Respiratorio
- La<sup>-</sup> > 2.0 mmol/L



**RAPIDA PROGRESSIONE DEI SINTOMI (<6hr)**  
**Check every 30 min**

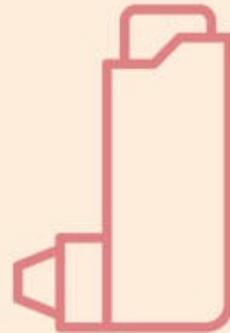
# Razionale della terapia

Massimizzare la  
funzione

Ridurre il lavoro  
respiratorio

Migliorare gli scambi dei  
gas

Spegnere il processo  
infiammatorio





## ORIGINAL RESEARCH

# The Effect of Low-Dose Ketamine in Treating Acute Asthma Attack; a Randomized Clinical Trial

Mehrdad Esmailian<sup>1</sup>, Mahboubeh Koushkiyan Esfahani<sup>1\*</sup>, Farhad Heydari<sup>1</sup>

1. Emergency Medicine Research Center, Al-Zahra Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

**Table 2:** Comparing mean change in peak expiratory flow rate (PEFR) in different groups

Group	PEFR		Change	P*
	Before	After		
Placebo	336.2 ± 101.5	352.1 ± 101.2	16.0 ± 30.5	Ref
0.3 mg/kg ketamine	325.3 ± 48.1	367.3 ± 56.9	42.0 ± 23.0	0.17
0.4 mg/kg ketamine	396.4 ± 89.4	443.6 ± 67.9	52.9 ± 45.0	0.02
0.5 mg/kg ketamine	320.6 ± 91.9	431.9 ± 80.2	111.3 ± 62.8	< 0.001

\*, significance level has been reported based on comparison with the placebo group. Data were presented as mean ± standard deviation.

in PEFR compared to 0.3mg/kg dose (df: 3, 88; F = 23.8; p < 0.001). **Conclusion:** It seems that administration of 0.4 - 0.5 mg/kg doses of intravenous ketamine followed by infusion of the same dose during 30 minutes can be effective for rapid recovery of PEFR in patients with mild to moderate asthma.

**Keywords:** Ketamine; asthma; efficiency; peak expiratory flow rate; emergency service, hospital

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# Emergency treatment of status asthmaticus with enoximone

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## Editor's key points

- Enoximone is a phosphodiesterase III inhibitor, primarily used in treatment of heart failure.
- The author presents a case report of eight patients with status asthmaticus refractory to treatment.
- Enoximone was effective in all these patients in reversing bronchospasm.
- Enoximone may have a role in refractory status asthmaticus in preventing tracheal intubation and mechanical ventilation.

This report describes the treatment of eight patients with status asthmaticus, six of whom were already maximally treated. They were consequently treated with enoximone, a selective phosphodiesterase III inhibitor, in their refractory phase. Bronchodilatation in these patients was immediate. No side-effects were observed. Enoximone appears to be a valuable addition to the treatment of status asthmaticus. I.V. administration bypasses inhalation incapability in severe asthma. It is likely to reduce or altogether prevent the need for resorting to secondary or tertiary high-tech therapy such as mechanical ventilation or anaesthetics, thus avoiding complications, as well as for transfers to specialized intensive care units. Not only do these aspects enable substantial cost savings, but they also may spare the patient a lot of anguish and a prolonged recovery.

**Keywords:** asthma; enoximone; intensive care; respiratory factors

Accepted for publication: 13 December 2013



## Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure

*Eur Respir J* 2017; 50: 1602426

*Question 3: Should NIV be used in ARF due to acute asthma?*

### Recommendation

Given the uncertainty of evidence we are unable to offer a recommendation on the use of NIV for ARF due to asthma.

BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults

*Davidson AC, Banham S, Elliott M, et al. Thorax* 2016;71:ii1–ii35.

### Evidence statement

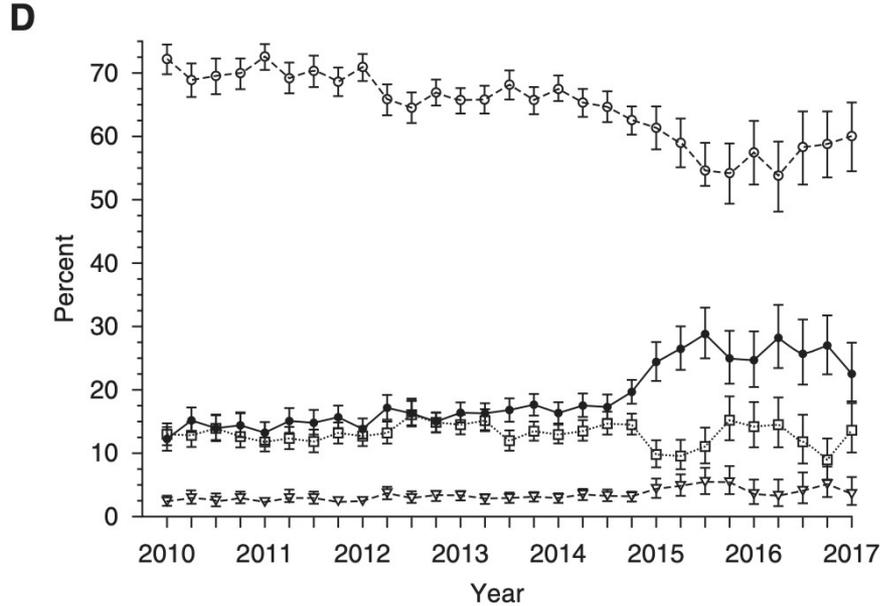
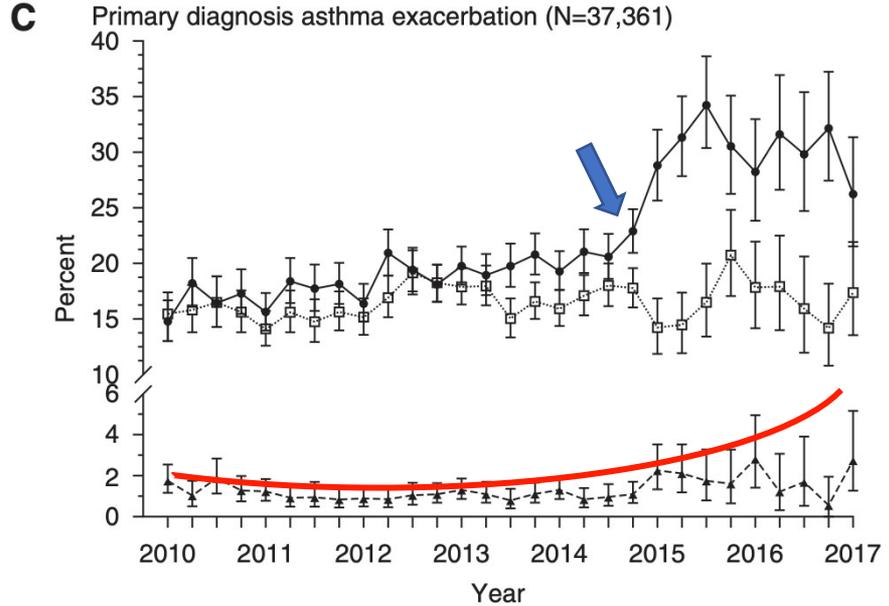
There is insufficient evidence to support the use of NIV in AHRF in acute asthma (Level 3).

### Recommendation

39. NIV should **NOT** be used in patients with acute asthma exacerbations and AHRF (Grade C).

# Noninvasive Ventilation Use in Critically Ill Patients with Acute Asthma Exacerbations

Meghan D. Althoff<sup>1</sup>, Fernando Holguin<sup>1</sup>, Fan Yang<sup>2</sup>, Gary K. Grunwald<sup>2</sup>, Marc Moss<sup>1</sup>, R. William Vandivier<sup>1</sup>, P. Michael Ho<sup>3,4</sup>, Tyree H. Kiser<sup>5</sup>, and Ellen L. Burnham<sup>1</sup>



**Conclusions:** Noninvasive ventilation use during asthma exacerbation was associated with improved outcomes but should be used cautiously with acute comorbid conditions.



Migliorare gli scambi dei gas



# Compassionate Use of a Single Dose of Benralizumab in a Near-Fatal Asthma Exacerbation.

Pérez de Llano L, Blanco Cid N, Ortiz Piquer M, Dacal Rivas D.

*Pneumology Service, Hospital Lucus Augusti, Lugo; EOXI Lugo, Cervo e Monforte, Lugo, Spain*



Spegnere il processo  
infiammatorio

Table. Blood Gas Values and Respiratory Mechanics Before and After Administration of Benralizumab<sup>a</sup>

Variables	Days Before and After Administration											
	-4	-3	-2	-1	0	+1	+2	+3	+4	+5	+6	+7
pH	7.29	7.31	7.32	7.37	7.37	7.31	7.35	7.32	7.34	7.34	7.41	7.45
PaCO <sub>2</sub>	52	61	70.3	61.5	72.5	82.1	78.8	83.6	75.8	63.7	53.6	42.6
PaO <sub>2</sub>	46.5	99.5	103	69.2	61.4	59	52.8	98.8	93.6	158	76.2	93
FiO <sub>2</sub> (%)	50	39	34	34	39	43	42	46	44	39	39	43
TV (mL)	536	442	484	512	466	507	500	531	615	722	816	585
MV (L/min)	12.3	10.5	11.4	12.2	10.5	9.6	7.3	9.2	9.9	10.4	9.7	11.7
PIP (cm H <sub>2</sub> O)	41	35	36	35	30	29	41	36	24	22	25	23
mAWP (cm H <sub>2</sub> O)	15	15	18	17	11	13	18	18	12	13	17	14
PEEP (cm H <sub>2</sub> O)	6	6	10	9	1	6	12	10	5	10	10	8
Raw (cm H <sub>2</sub> O/L/sg)	126.83	114.28	94.73	88.52	108.57	100	189.04	117.39	72.72	51.92	49.48	46.15

Abbreviations: FiO<sub>2</sub>, fraction of inspired oxygen; mAWP, mean airway pressure; MV, minute ventilation; PCO<sub>2</sub>, indicates partial pressure of carbon dioxide; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; pO<sub>2</sub>, partial pressure of oxygen; Raw, airway resistance; TV, tidal volume.

<sup>a</sup>Green rows: relevant mechanical ventilation parameters, lung mechanical characteristics, and arterial blood gas values. Yellow column: day zero, administration of dose of benralizumab. Amber column: day 4 after benralizumab injection when we observed improvement in mechanical ventilation measurements.

Conclusioni





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