La bronchiolite: ciò che dobbiamo realmente sapere e saper fare

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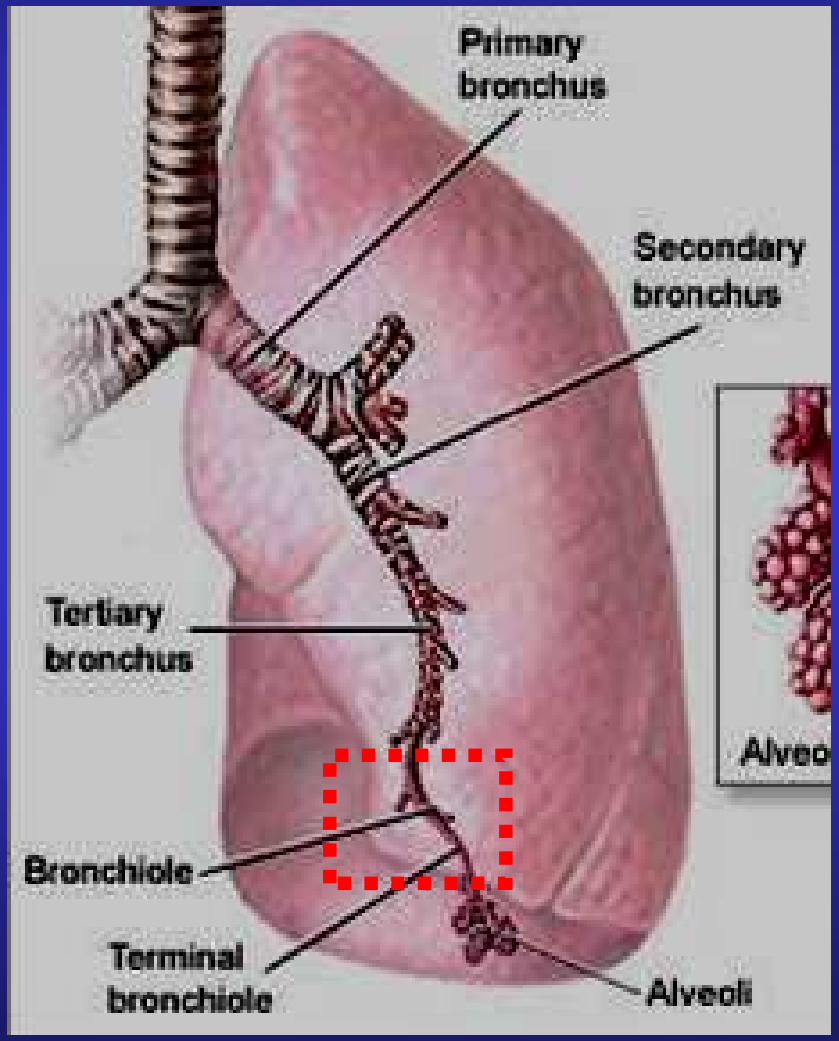
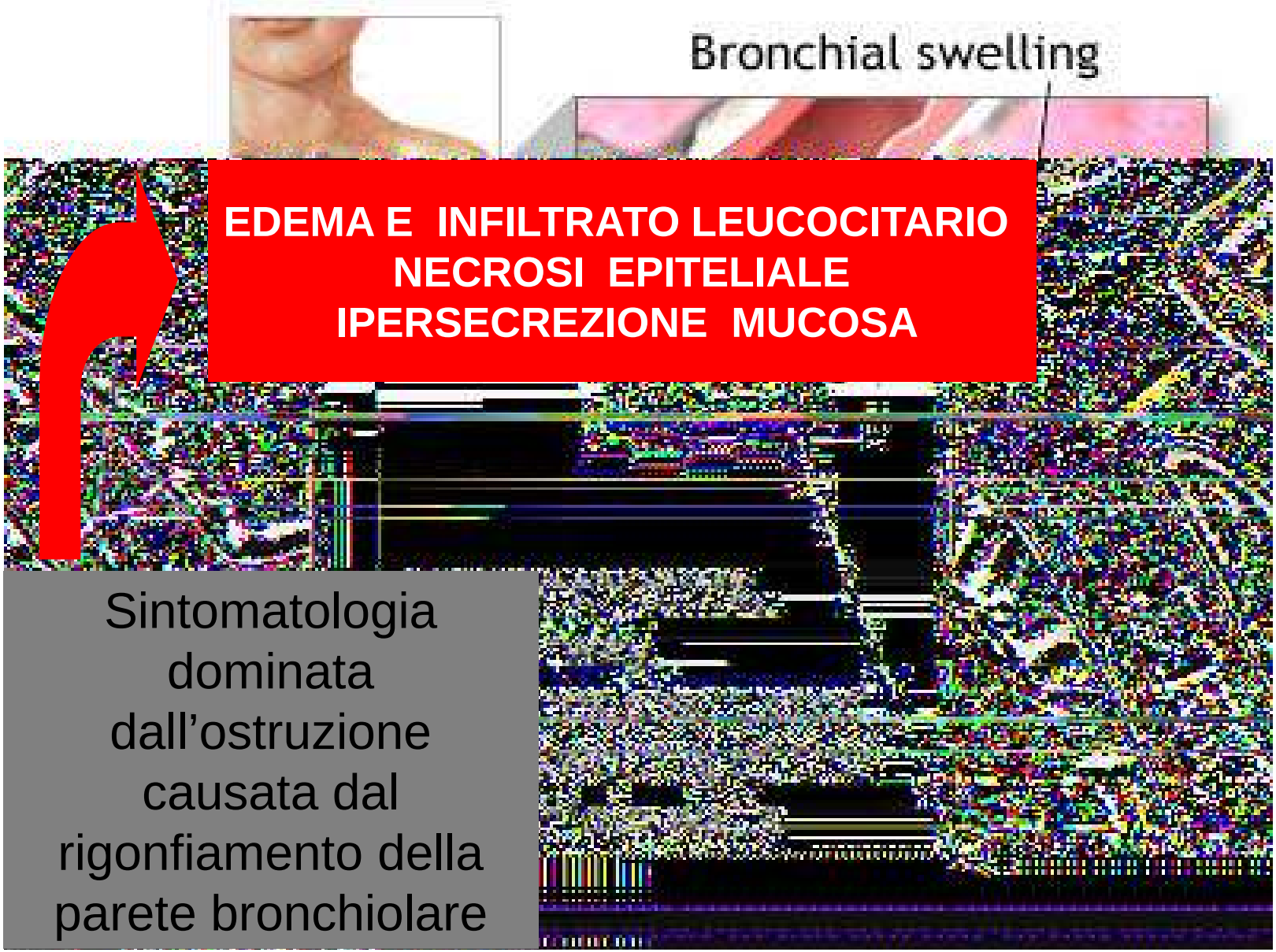
BRONCHIOLITE: DEFINIZIONE

- **Broncopatia ostruttiva acuta ad etiologia virale, a carattere epidemico stagionale**
- **Si presenta come una virosi discendente dell'apparato respiratorio**
- **Colpisce bambini di età < 2 anni (il 70% nei primi sei mesi)**



BRONCHIOLITE: FISIOPATOLOGIA



EDEMA E INFILTRATO LEUCOCITARIO
NECROSI EPITELIALE
IPERSECREZIONE MUCOSA

Sintomatologia dominata dall'ostruzione causata dal rigonfiamento della parete bronchiolare

BRONCHIOLITE: EZIOLOGIA

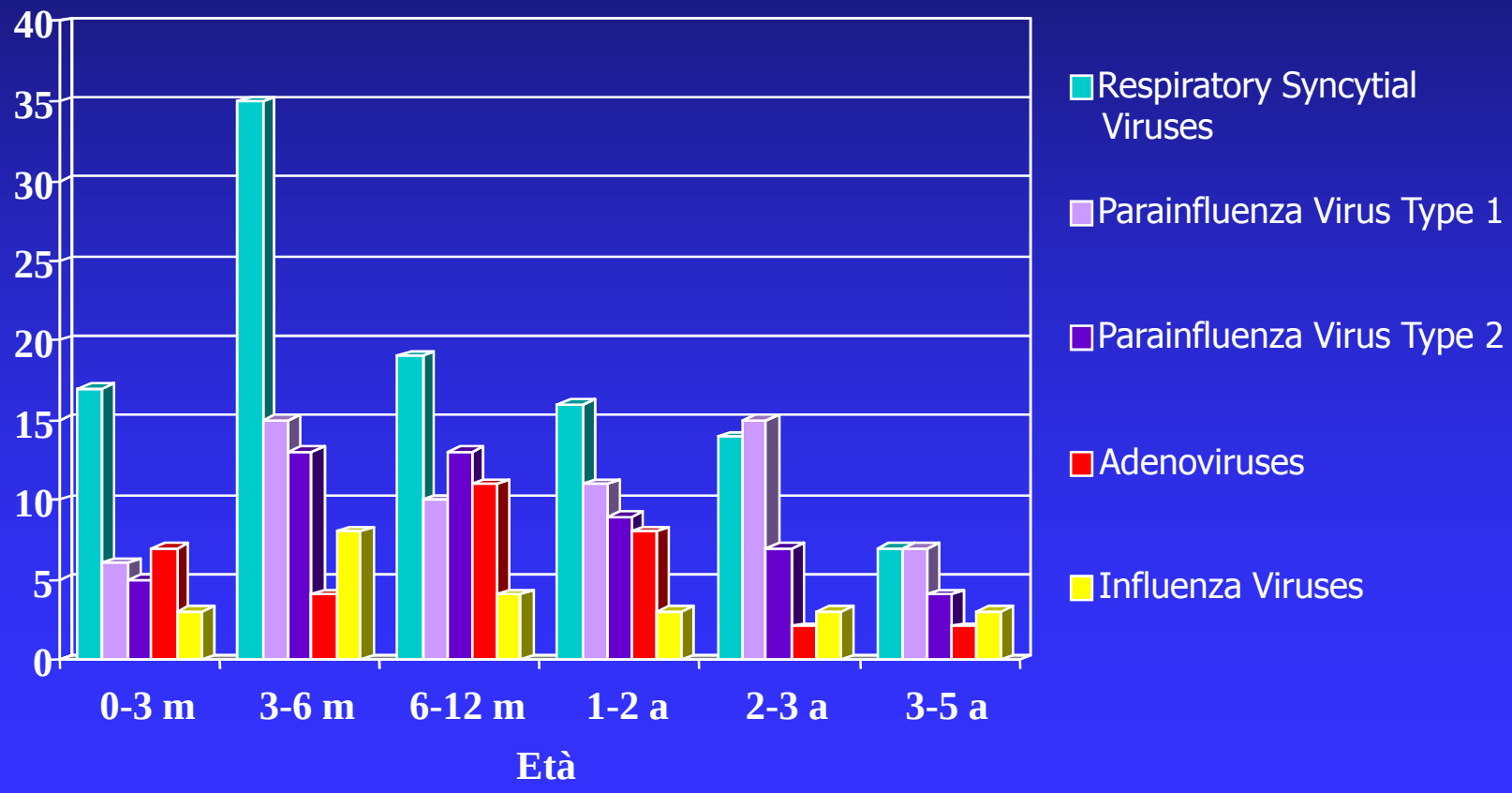
70-85 % ➡ VRS

15-30 % ➡ Parainfluenzae 1, 2, 3
Influenzae B
Adenovirus 1, 2, 5
Mycoplasma (nei bambini più grandi)

Grimpel E Arch Pediatr 2001

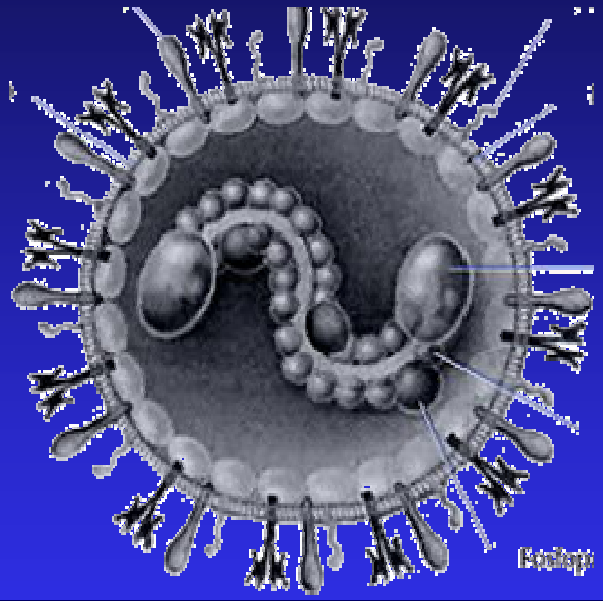
BRONCHIOLITE: EZIOLOGIA

Virus respiratori principali secondo l'età



BRONCHIOLITE: EZIOLOGIA

VIRUS RESPIRATORIO SINCIZIALE (VRS)



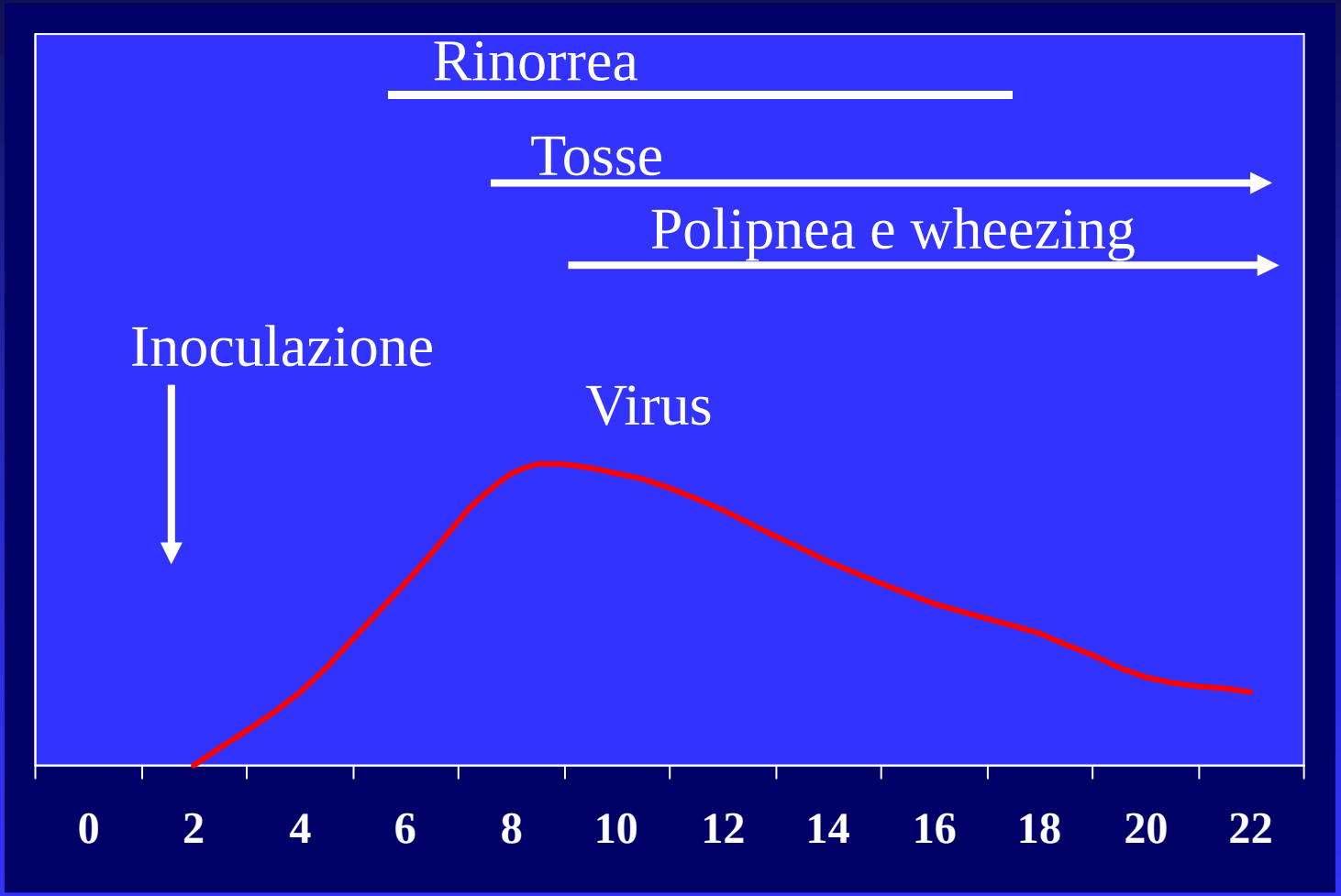
- Paramyxovirus , RNA unico filamento, Sottotipi A e B, con 10 proteine
- **Glicoproteina G** permette l'adesione alle cellule respiratorie
- **Glicoproteina F** responsabile della penetrazione del virus nella cellula ospite e della formazione di sincizi
- Infesta le cellule cilindriche epiteliali del naso e in 2-4 giorni può raggiungere le vie aeree inferiori; non da viremia.

BRONCHIOLITE: EZIOLOGIA

Trasmissione del VRS

- Il virus si diffonde con le secrezioni nasofaringee
- La porta di ingresso è data dalle mucose (congiuntivale, nasale e della bocca)
- Il VRS può sopravvivere fino a 7 ore in superfici non porose
- La trasmissione avviene abitualmente per diretto contatto; è possibile anche per contatto con le mani o con oggetti contaminati

MODELLO DI INFEZIONE PRIMARIA DI VRS IN BAMBINI IMMUNOCOMPETENTI



Giorni dopo l'inoculazione

BRONCHIOLITE: EPIDEMIOLOGIA

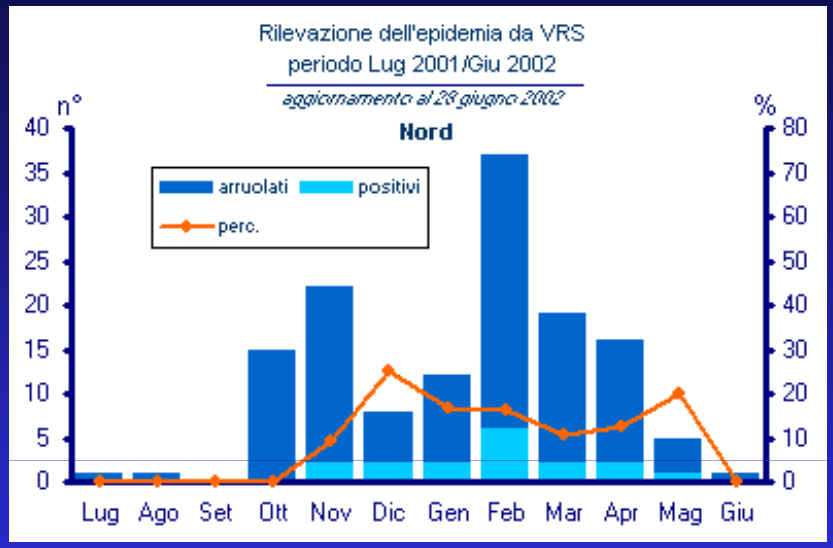
- 66 % dei bambini contraggono l'infezione da RSV nel 1°anno di vita, l'82% entro il 2°anno
- 40 - 50 % dei bambini infettati dal RSV sviluppa sintomi di infezioni delle basse vie respiratorie (bronchiolite, polmonite), di questi solo nell' 1-2% dei casi è necessario il ricovero ospedaliero
- 50 % presentano una reinfezione ogni anno (nel 45% dei bambini ospedalizzati)

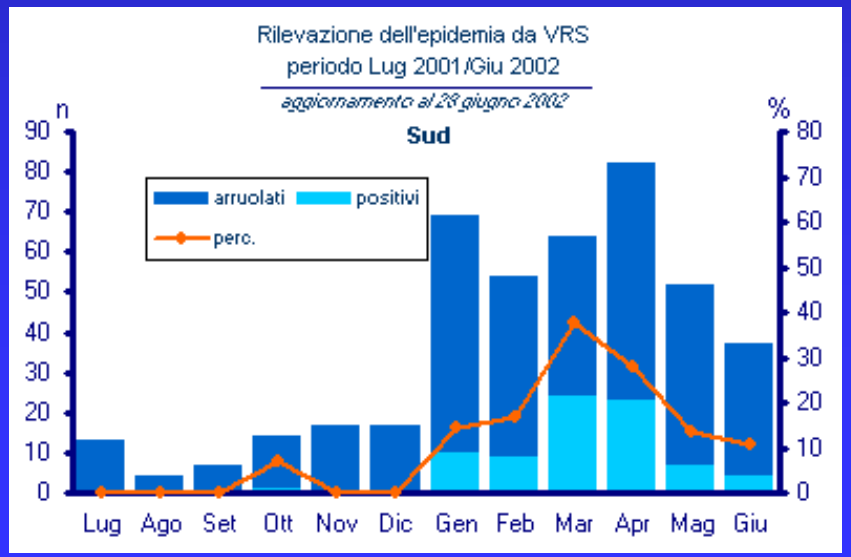
CDC 1998, Moylett E Hosp Med 1999

BRONCHIOLITE: EPIDEMIOLOGIA

OSSERVATORIO VRS

LUGLIO 2001-GIUGNO 2002





BRONCHIOLITE: DIAGNOSI

Bambini nei primi 2 a., periodo epidemico, prevalenza sesso M

Febbre *(possibile)*, **Rinite** → **Tosse**

↓ **dopo 1-3 giorni**

Difficoltà ad alimentarsi
Irrequietezza
Tachipnea
Rientramenti respiratori
Distensione toracica

→ **sibili e rantoli crepitanti diffusi in tutti i campi polmonari**

↓ **se l'infezione procede**

Peggioramento delle condizioni generali
> Dispnea
Comparsa di cianosi
> Tachipnea (> 70 atti/m')
Crisi di apnea

BRONCHIOLITE: DIAGNOSI

esami diagnostici

- Rx torace: inutile se non si sospettano atelettasie o pneumotorace *(non modifica il decorso della malattia – cat. evidenza 1a)*
- Es. di laboratorio: in caso di decisione per fluidoterapia, indici di flogosi?
- Test per RSV: utile solo per decidere isolamento e efficace nel ridurre l'uso improprio di antibiotici *(non modifica la terapia e la durata del ricovero – cat.evidenza 1a)*

BRONCHIOLITE: DIAGNOSI

SINTOMI E SEGNI PREDITTIVI DI GRAVITA'

- Elevazione termica
- > Frequenza respiratoria (> 60-70 atti/m')
- Condizioni generali compromesse
- Rifiuto dell'alimentazione
- Comparsa di cianosi
- Comparsa di crisi di apnea

Determinazione della Sa O_2 → migliore predittore di gravità

CRITERI DI OSPEDALIZZAZIONE

1) Condizioni generali compromesse

2) Apporto di liquidi inadeguato

3) FR>70 atti/min e/o SaO_2 < 92% e/o Cianosi e/o Apnee

4) Presenza di fattori di rischio:

Nati pretermine: *di età gestazionale inferiore alle 32 settimane, displasia broncopolmonare, con ventilazione meccanica in età neonatale.*

Patologie croniche: *Broncopatie croniche, Cardiopatie congenite, Deficit immunitario(congeniti, acquisiti), malattie metaboliche/neurologiche severe.*

Nato a termine sano: *età inferiore alle 6 settimane, esposizione al fumo passivo*

BRONCHIOLITE: TERAPIA

"Oxigen is important in bronchiolitis and there is little convincing evidence that any other therapy is consistently useful"

Reynolds and Cook J Pediatr 1963;62:1205

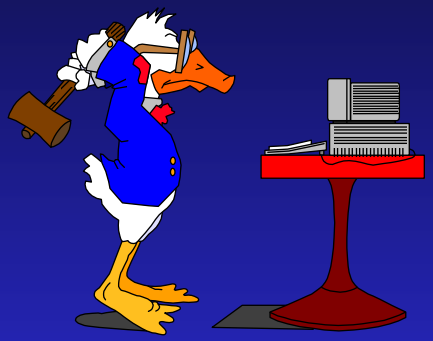
BRONCHIOLITE: TERAPIA

La bronchiolite è una malattia "self-limited"

E' indispensabile controllare e correggere l'idratazione, l'ossigenazione e lo stato di nutrizione del paziente *(categoria di evidenza Ia).*

- **Idratazione:** è raccomandata l'infusione di liquidi per via e.v. se il p. è clinicamente disidratato o non assume per os un minimo di 80cc/Kg/die di liquidi.
- **Nutrizione:** è raccomandata un'alimentazione regolare, adeguata all'età, sia per apporto calorico che di liquidi.
- **Ossigenazione:** è raccomandata la somministrazione di O2, se la saturazione è < 92% e per mantenerla comunque entro il 94%; la miscela di O2 deve essere riscaldata ed umidificata.

BRONCHIOLITE: TERAPIA



- BRONCODILATATORI
- CORTISONICI
- ANTIBIOTICI
- HELIOX
- ADRENALINA
- SOLUZ. SALINA IPERTONICA
- rhDNasi (desossiribonucleasi ricombinante umana)
- SURFACTANT

Bronchodilators for bronchiolitis.

Gadomski AM, Cochrane Database Syst Rev. 2010 Dec 8;12:CD001266

OBJECTIVES: To assess the effects of bronchodilators on clinical outcomes in infants with acute bronchiolitis.

MAIN RESULTS: We included 28 trials (1912 infants) with bronchiolitis. In 10 inpatient and 10 outpatient studies, oxygen saturation did not improve with bronchodilators (mean difference (MD) -0.45, 95% confidence interval (CI) -0.96 to 0.05, n = 1182). Outpatient bronchodilator treatment did not reduce the rate of hospitalization (12% in bronchodilator group versus 16% in placebo, odds ratio (OR) 0.78, 95% CI 0.47 to 1.29, n = 650). Inpatient bronchodilator treatment did not reduce the duration of hospitalization (MD 0.06, 95% CI -0.27 to 0.39, n = 349). In seven inpatient and eight outpatient studies, average clinical score decreased slightly with bronchodilators (standardized mean difference (SMD) -0.37, 95% CI -0.62 to -0.13, n = 1006). Oximetry and clinical score outcomes showed significant heterogeneity.
Adverse effects included tachycardia and tremors.

AUTHORS' CONCLUSIONS: Bronchodilators do not improve oxygen saturation, do not reduce hospital admission after outpatient treatment, do not shorten the duration of hospitalization and do not reduce the time to resolution of illness at home. The small improvements in clinical scores for outpatients must be weighed against the costs and adverse effects of bronchodilators.

Glucocorticoids for acute viral bronchiolitis in infants and young children.

Fernandes RM,Cochrane Database Syst Rev. 2010 Oct 6;(10):CD004878

OBJECTIVES: To review the efficacy and safety of systemic and inhaled glucocorticoids in children with acute viral bronchiolitis.

MAIN RESULTS: We included 17 trials (2596 participants); only two had low overall risk of bias. Baseline severity, glucocorticoid schemes, comparators and outcomes were heterogeneous. Glucocorticoids did not significantly reduce outpatient admissions by days 1 and 7 when compared to placebo (pooled risk ratios (RRs) 0.92; 95% CI 0.78 to 1.08; and 0.86; 95% CI 0.7 to 1.06, respectively). There was no benefit in LOS for inpatients (mean difference -0.18 days; 95% CI -0.39 to 0.04). Unadjusted results from a large factorial low risk of bias RCT found combined high-dose systemic dexamethasone and inhaled epinephrine reduced admissions by day 7 (baseline risk of admission 26%; RR 0.65, 95% CI 0.44 to 0.95; number needed to treat 11, 95% CI 7 to 76), with no differences in short-term adverse effects. No other comparisons showed relevant differences in primary outcomes.

AUTHORS' CONCLUSIONS: Current evidence does not support a clinically relevant effect of systemic or inhaled glucocorticoids on admissions or length of hospitalization. Combined dexamethasone and epinephrine may reduce outpatient admissions, but results are exploratory and safety data limited. Future research should further assess the efficacy, harms and applicability of combined therapy.

WITHDRAWN: Inhaled corticosteroids during acute bronchiolitis in the prevention of post-bronchiolitic wheezing.

Blom DJ Cochrane Database Syst Rev. 2011 Jan 19;1:CD004881

OBJECTIVES: The objective of this review was to evaluate the effect of inhaled corticosteroids, started during the acute phase of bronchiolitis, on the prevention of post-bronchiolitic wheezing.

MAIN RESULTS: Five studies matched the inclusion criteria, with a median Jadad score of 4 (Inter Quartile Range 3 to 4), involving 374 infants. Pooling of the data was limited, due to the clinical diversity of the studies. However, no effect of inhaled corticosteroids in the prevention of wheezing (diary records or GP diagnosed), hospital re-admissions or use of corticosteroids or bronchodilators could be demonstrated. Duration of therapy, length of follow up or causative agent (respiratory syncytial virus or not) did not influence the pooled effect. In the three studies that also evaluated the adverse events, none were reported.

AUTHORS' CONCLUSIONS: This review does not demonstrate an effect of inhaled corticosteroids given during the acute phase of bronchiolitis in the prevention of post-bronchiolitic wheezing. The small number of included participants and the inability to pool all clinical outcomes precludes us from making strong recommendations.

Antibiotics for bronchiolitis in children.

Spurling GK,Cochrane Database Syst Rev. 2007 Jan 24;(1):CD005189

BACKGROUND: Antibiotics are not recommended for bronchiolitis unless there is concern about complications such as secondary bacterial pneumonia. Despite this, they are used at rates of 34 to 99% in uncomplicated cases

SELECTION CRITERIA: Types of studies: single or double blind randomised controlled trials comparing antibiotics to placebo in the treatment of bronchiolitis. Types of participants: children under the age of two years diagnosed with bronchiolitis using clinical criteria (including respiratory distress preceded by coryzal symptoms with or without fever). Types of interventions: oral, intravenous, intramuscular or inhaled antibiotics versus placebo. Types of outcome measures: primary clinical outcomes: time for the resolution of symptoms/signs (pulmonary markers: respiratory distress; wheeze; crepitations; oxygen saturation; and fever). Secondary outcomes: hospital admissions; time to discharge from hospital; re-admissions; complications/adverse events developed; and radiological findings.

MAIN RESULTS: One study met our inclusion criteria. It randomised children presenting clinically with bronchiolitis to either ampicillin or placebo. The main outcome measure was duration of illness and death. There was no significant difference between the two groups for length of illness and there were no deaths in either group.

AUTHORS' CONCLUSIONS: This review found no evidence to support the use of antibiotics for bronchiolitis. This results needs to be treated with caution given only one RCT justified inclusion. It is unlikely that simple RCTs of antibiotics against placebo for bronchiolitis will be undertaken in future. Research to identify a possible small subgroup of patients presenting with bronchiolitis-like symptoms who may benefit from antibiotics may be justified. Otherwise, research may be better focussed on determining the reasons for clinicians to use antibiotics so readily for bronchiolitis, and ways of reducing their anxiety, and therefore their use of antibiotics for bronchiolitis.

Heliox inhalation therapy for bronchiolitis in infants.

Liet JM et. Al Cochrane Database Syst Rev. 2010 Apr 14;(4):CD006915

BACKGROUND: Acute viral bronchiolitis is associated with airway obstruction and turbulent gas flow. Heliox, a mixture of oxygen and the inert gas helium, may improve gas flow through high-resistance airways and decrease the work of breathing

MAIN RESULTS: We included four trials involving 84 infants under two years of age with respiratory distress secondary to bronchiolitis caused by respiratory syncytial virus (RSV) and requiring paediatric intensive care unit (PICU) hospitalisation. We found that infants treated with heliox inhalation had a significantly lower mean clinical respiratory score in the first hour after starting treatment when compared to those treated with air or oxygen inhalation (mean difference (MD) -1.15, 95% confidence interval (CI) -1.98 to -0.33, P = 0.006, n = 69). There was no clinically significant reduction in the rate of intubation (risk ratio (RR) 1.38, 95% CI 0.41 to 4.56, P = 0.60, n = 58), in the need for mechanical ventilation (RR 1.11, 95% CI 0.36 to 3.38, P = 0.86, n = 58), or in the length of stay in a PICU (MD = -0.15 days, 95% CI -0.92 to 0.61, P = 0.69, n = 58). No adverse events related to heliox inhalation were reported.

AUTHORS' CONCLUSIONS: Current evidence suggests that the addition of heliox therapy may significantly reduce a clinical score evaluating respiratory distress in the first hour after starting treatment in infants with acute RSV bronchiolitis. Nevertheless, there was no reduction in the rate of intubation, in the need for mechanical ventilation, or in the length of PICU stay. Further studies with homogeneous logistics in their heliox application are needed. Such studies would provide necessary information as to the appropriate place for heliox in the therapeutic schedule for severe bronchiolitis.

5% hypertonic saline with epinephrine is safe and may be effective in the treatment of bronchiolitis

Al-Ansari K et al J Pediatr 2010; 157:630-4

Participants 171 infants aged <18 months (mean age, 3.1 months) clinically diagnosed with bronchiolitis.

Intervention Infants were randomized in a DBPCT to receive nebulized 5%, 3%, or 0.9% (normal) saline with epinephrine every 4 hours.

Outcomes The primary efficacy outcome was improved bronchiolitis severity score at 48 hours. Safety was assessed by monitoring severity score and oxygen saturation with each treatment.

Main Results The primary outcome of this study suggests that higher levels of hypertonic saline may statistically improve severity scores at 48 hours for the 5% saline group compared with the 0.9% saline group. The mean severity score for the 3% saline group was intermediate. No adverse reactions or other safety concerns were identified.

Nebulized hypertonic saline solution for acute bronchiolitis in infants.

Zhang L. Cochrane Database Syst Rev. 2008:CD006458.

BACKGROUND: Airway edema and mucus plugging are the predominant pathological features in infants with acute viral bronchiolitis. Nebulized hypertonic saline solution may reduce these pathological changes and decrease airway obstruction.

MAIN RESULTS: We included four trials involving 254 infants with acute viral bronchiolitis (189 inpatients and 65 outpatients) in this review. Patients treated with nebulized 3% saline had a significantly shorter mean length of hospital stay compared to those treated with nebulized 0.9% saline (mean difference (MD) -0.94 days, 95% CI -1.48 to -0.40, P = 0.0006). The 3% saline group also had a significantly lower post-inhalation clinical score than the 0.9% saline group in the first three days of treatment (day 1: MD -0.75, 95% CI -1.38 to -0.12, P = 0.02; day 2: MD -1.18, 95% CI -1.97 to -0.39, P = 0.003; day 3: MD -1.28, 95% CI -2.57 to 0.00, P = 0.05). The effect of nebulized hypertonic saline in improving clinical score was greater among outpatients than inpatients. No adverse events related to 3% saline inhalation were reported.

AUTHORS' CONCLUSIONS: Current evidence suggests nebulized 3% saline may significantly reduce the length of hospital stay and improve the clinical severity score in infants with acute viral bronchiolitis

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice, F. Saitta et. al. Pediatrics - submitted

Lo scopo del nostro studio è stato quello di valutare l'efficacia della soluzione salina iperonica al 3% rispetto alla soluzione salina isotonica in associazione all'adrenalina nebulizzata in 109 bambini ospedalizzati per bronchiolite tra Novembre ed Aprile 2008 e 2009.

Criteri di inclusione:

età 1- 24 mesi; tachipnea (FR: >40 per età < 1 a; >30 per >1a); rientramenti respiratori, reperto ascoltatorio di sibili e/o rantoli crepitanti.

Criteri di esclusione:

cardiopatie, malattie infiammatorie croniche, pregressi episodi di wheezing, saturazione ossigeno in aria ambiente < 85%, coscienza obnubilata e/o insufficienza respiratoria tale da richiedere ventilazione meccanica.

Pazienti randomizzati in 2 gruppi:

Gruppo 1 : adrenalina 1,5 mg + soluzione salina 0,9% 4 ml.
Gruppo 2 : adrenalina 1,5 mg + soluzione salina 3% 4 ml.
ogni 8 ore per tutta la durata dell'ospedalizzazione.
Valutazione dello score clinico nei bambini prima dell'aerosolterapia e 30 minuti dopo l'aerosolterapia.
O^2 terapia a tutti

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice et. al. Pediatrics - submitted

FR	Rientramenti	Auscultazione	O_2Sat%	Punteggio
< 30	No	Murmure Vescicolare	> 96	0
31-45	Lievi (alle basi)	Wheezing fine espirazione e/o qualche crepitio	93-95	1
46-60	**Moderati** (intercostali, all'epigastrio	Wheezing in tutta l'espirazione e/o crepitii diffusi	89-92	2
> 60	**Gravi** (giugulo. Alitamento delle pinne nasali)	Wheezing udibili senza stetoscopio e/o marcata riduzione del MV	< 89	3

da Lowell DI Pediatrics 1997

S.I.P. Campania

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice et. al. Pediatrics - submitted

Baseline demographic and clinical characteristic of the 106 evaluated patients

	0.9% Saline solution Group I N= 54	3% Saline solution Group II N= 52	*P*-value
Gender- males, N (%)	35 (64)	34 (65)	N.S.╪
Age (mo.) mean ± SD	4.2± 1.6	4.8± 2.3	N.S.*
Baseline clinical severity mean ± SD	8.8± 1.5	8.5± 1.4	N.S.*
Days of illness at hospital admission, mean ± SD	3± 1.8	3.6±2.2	N.S.*
Baseline saturation %, mean ± SD	92.7 ± 3.9	93.5 ± 4.2	N.S.**
RSV serum positivity, N (%)	45 (83.3%)	42 (80.7%)	N.S.*

The percentages in round brackets are calculated over the total number of subjects reported at the top of column.
╪: Chi-squared test.
*: Mann-Whitney U test
**: t-test

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice et. al. Pediatrics – submitted

Clinical severity score for the two groups of patients at each day

	I day	II day	III day	*P*-value
Clinical severity scores, mean ± SD				
0.9% Saline solution Group I	8.8± 1.5	8.3± 1.7	7.7± 1.6	0.0001*
3% Saline solution Group II	8.5± 1.4	7.4± 1.6	6.5± 1.6	0.0001*
P-value	NS**	0.0045**	<0.005**	

*: Anova Friedman test
**: Mann-Whitney U test

I due trattamenti, riferiti ad i due gruppi, sono entrambi efficaci nel ridurre il CS-score; il CS-score si riduce in maniera diversa nei due gruppi, con maggior riduzione (stat. significativa) per il gruppo II.

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice et. al. Pediatrics - submitted

Clinical severity scores, before vs after inhalations, for each day

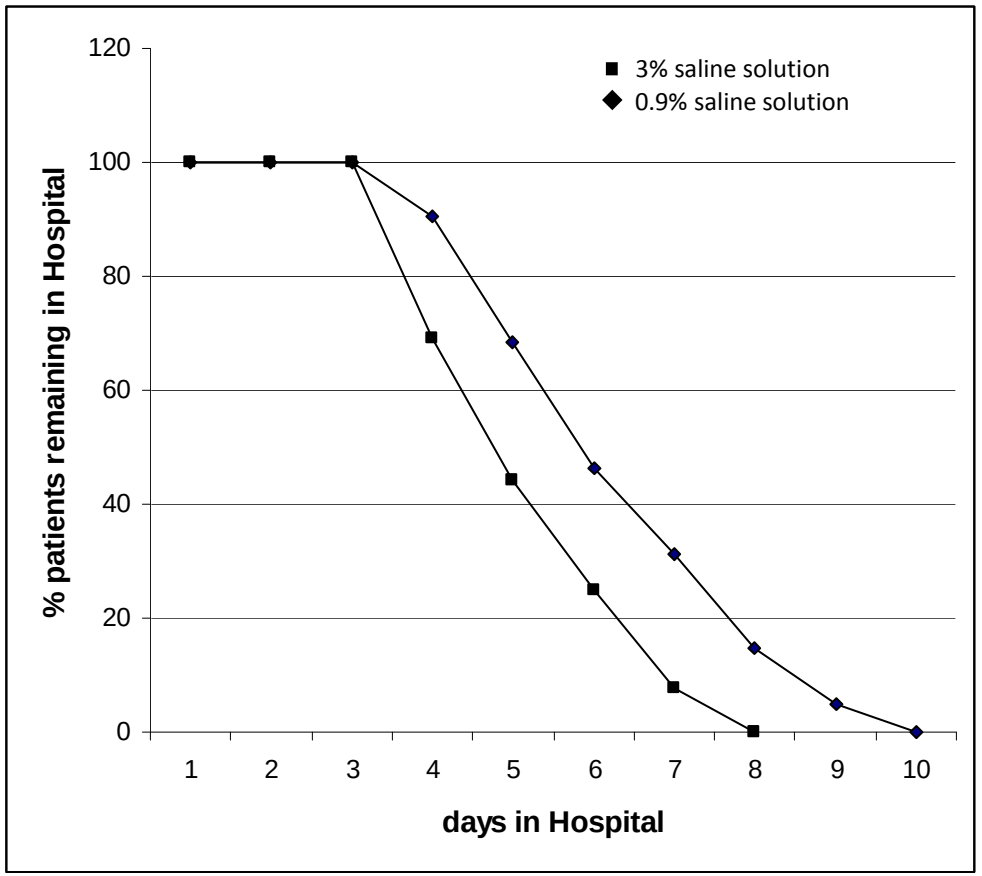
	I day		*P*-value	II day		*P*-value	III day		*P*-value
	baseline	after inh		before inh.	after inh.		before inh.	after iinh.	
0.9% Saline solution Group I	8.8± 1.5	8.8± 1.6	N.S	8.3± 1.7	8.2± 1.7	N.S	7.7± 1.6	7.6± 1.6	N.S.
3% Saline solution Group II	8.5± 1.4	8± 1.3	0.00002	7.4± 1.6	6.8± 1.4	0.00001	6.5± 1.6	5.8± 1.4	<0.00001

P value of Wilcoxon test

il CS-score prima e dopo inalazione, non si riduce in maniera significativa nel primo gruppo; si riduce in maniera significativa nel secondo gruppo, per tutti i giorni considerati.

Nebulized 3% Hypertonic Saline Solution and Epinephrine in Hospitalized Infants with Bronchiolitis

M. Miraglia del Giudice et. al. Pediatrics - submitted



I giorni di ospedalizzazione sono statisticamente differenti nei due gruppi:
gruppo A: mean: 5.6±1.6
gruppo B: mean: 4.9± 1.3

S.I.P. Campania

“Oxigen is important in bronchiolitis and there is little convincing evidence that any other therapy is consistently useful”

Reynolds and Cook J Pediatr 1963;62:1205

GRAZIE

SANTOBONO PAUSILIPON
AZIENDA OSPEDALIERA PEDIATRICA

L'INSUFFICIENZA RESPIRATORIA IN PEDIATRIA:
DALL'EMERGENZA IN PRONTO SOCCORSO ALL'ASSISTENZA DOMICILIARE

Napoli, 3-4 giugno 2011

SIMRI
Società Italiana per le Malattie Respiratorie Infantili

SIMEUP
Società Italiana Medicina Emergenza Urgenza Pediatrica

SIP
Società Italiana di Pediatria Sez. Campania