PREVENTION OF RSV IN NEONATES

SPEAKER
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K-MAX CME 29 june 2022

Dr Kumar Ankur

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Areas of Interest	ELBW, POCUS, VENTILATION
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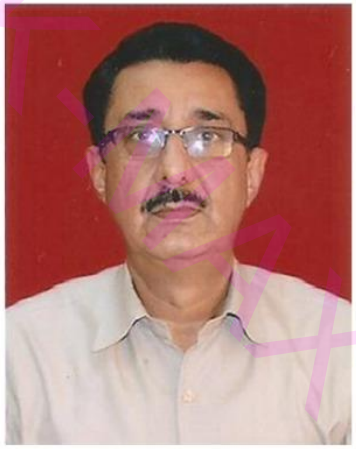
Super Speciality Hospital



NAME	**Dr (Col)Rajeev Kumar Thapar (Retd)**
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ACHIEVEMENTS	- Certified BLS instructor , Basic & Advance NRP instructor - NBE Examiner, Assessor & Appraiser - Fifty (54) Publications in National Journals - Contributed to IAP Neonatology Atlas Book(Two editions) - Chapters on HHHFNC and Neonatal Resuscitation -Manual of NICU protocols –Defense Services chapter NNF - IAP PG training module - Ex Secretary, IAP Disaster Management Group(2019-22) -Vice President , AOP, Noida (2023), -Member Research, Academy of Pediatrics, Noida (2024)

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RSV Prevention

Dr. Kumar Ankur

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India & Global ELBW Outcomes

- LMICs overall: ~34% ELBW survival
- ELGANs (<28 weeks): ~39% survival
- High-income (USA)
  - 24 weeks: ~64%
  - 28 weeks: ~94%

Antenatal Steroids
CPAP/NIV
Surfactant/ Nutrition

VLBW mortality in Indian NICUs: 15–41%

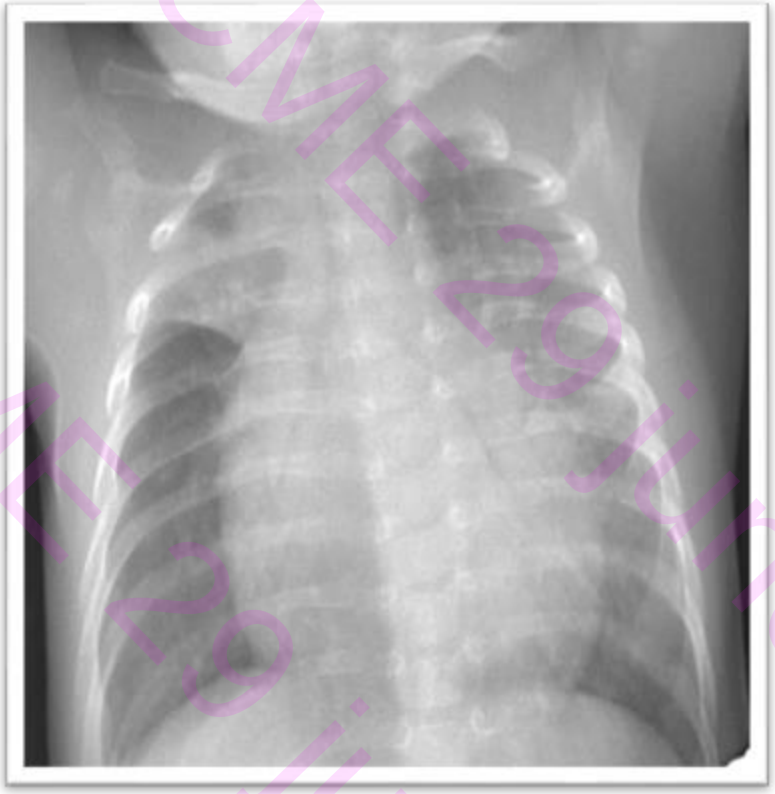
One South Indian NICU: ~79.5% survival for VLBW

D Chawla Ind Jour Peds 6th March 2021
Mosalli, *Journal of Clinical Neonatology* 13(1):p 14-18, Jan–Mar 2024

26 weeks, ANS/MgSO4- Em-LSCS (AREDF), 710 grams

DR-CPAP/LISA/NIV for 1 month /Discharge 2 kg.

Readmitted after 3 weeks with *LRTI* - NIV/ABX/2 weeks



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Major Respiratory Infections

- **RSV**: Most common; causes rehospitalization
- **Influenza**: Severe LRTI and death
- **Rhinovirus**: Wheezing and reactive airway disease
- **Bacterial pneumonia**: Increased risk post-NICU

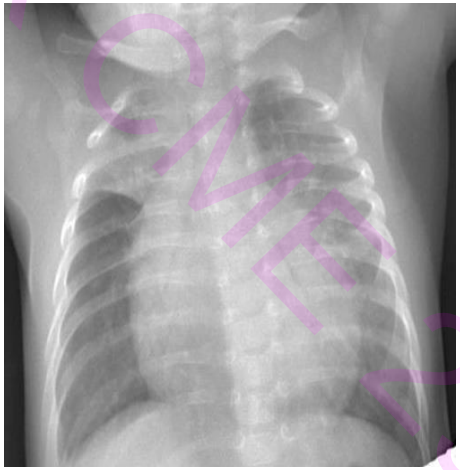
WHO 2023/Blanken et al ; NEJM 2013/Shi T et al 2017, Lancet

Case

26 weeks, ANS/MgSO4/EmLSCS, 710 grams

DR-CPAP/LISA/NIV for 1 month /2 kg.

Readmitted after 3 weeks with LRTI - NIV/ABX/2 weeks stay



After birth

RSV 1-2 years

Mother RSV+

Protection 1 month

WHO 2023/Blanken et al ; NEJM 2013/Shi T et al 2017, Lancet

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RSV

- **Community Acquired Pneumonia**
  - **USA - 37 %**
  - **LMIC- 31 %**
  - **Global Burden analysis**
    - **2 % of all death in < 5 years (46 % in less than 5 months)**
    - **3.6 % of all death between 28 days -6 month**
    - **8-15 % of all cause hospitalization (> 50 % receive inappropriate antibiotics)**

193 /WHO position paper on immunization to protect infants against RSV. WEEKLY EPIDEMIOLOGICAL RECORD, NO 22, 30 MAY 2025

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Global Data Highlights

- PT (< 29 weeks): 10-25 %
- PT+BPD/CLD: 25- 30%
- CHD: 15- 20 %
- Healthy Term infants: 1-3 %

- Rehospitalization rate: 20–40% in first year
- RSV affects up to 50% of ELBW infants
- Post-discharge infections contribute to mortality

WHO 2023/Blanken et al ; NEJM 2013/Shi T et al 2017, Lancet

Indian Data -2023

- 3x higher RSV hospitalization risk in pre terms <6 months
- 76% preterm re-admissions RSV-positive
- All ELBW (23–27 weeks) required respiratory support
- RSV detection in ELBW re-admissions: ~100%
- Median hospital stay: 14 days
- All RSV+ neonates discharged alive
- Seasonal Peak: September to November

Clinical Profile and Short-Term Outcomes in Neonates with RSV; Single-Center Study Vamshi Venkat M. Indian Pediatrics August 2024

Disease Spectrum - Prevalence

Incubation Period: 4-6 days

MILD 40 - 50 %	MODERATE to SEVERE 20 - 30 %	MV/Death Rare (0.1-0.5%)

Disease Spectrum	Estimated Prevalence (%)
Asymptomatic or Mild URTI	40–50%
Symptomatic URTI	20–30%
LRTI - Bronchiolitis	15–25%
LRTI - Pneumonia	2–5%
Apnea (neonates/preterms)	1–3%
Severe RSV (Hospitalization)	2–3%
ICU Admission	0.5–1%
Mechanical Ventilation	0.1–0.5%
Post-RSV Wheezing/Asthma	30–40% (of severe cases)

Hall CB et al, NEJM 2009/AAP RSV Guidelines/Lancet 2017

Diagnostic Tests

Test	Sample	Sensitivity	Specificity	Turnaround Time	Clinical Utility
RT-PCR	Nasopharyngeal swab/aspirate	95–100%	>98%	4–6 hours (Rapid: <2h)	Gold standard; best for high-risk infants
Rapid Antigen Tests (RADT/ELISA)	Nasopharyngeal swab	70–90%	>95%	15–30 minutes Yield decreases after Day 5 of symptoms	Best in children <2 yrs; lower yield in neonates
Direct Fluorescent Antibody (DFA)	Nasopharyngeal aspirate	60–80%	90–95%	2–4 hours	Moderate accuracy; labor-intensive
Viral Culture	Nasopharyngeal sample	50–70%	~100%	3–10 days	High specificity but slow; not for acute care
Serology (IgM/IgG)	Blood	Not reliable	Not reliable	Days–weeks	Not useful for acute diagnosis
Chest X-ray	Imaging modality	N/A	N/A	Immediate	Supports clinical diagnosis; non-specific
CBC/CRP/Procalcitonin	Blood	Non-specific	Non-specific	2–4 hours	To rule out bacterial co-infection

What are the Preventive strategies

- Antenatal
  - Antenatal RSV vaccine
- Postnatal – more than 17 vaccines under trial
  - IV Immunoglobulin (Respigan)-IV/Cost/Side effects
  - Postnatal monoclonal antibodies
    (Palivizumab and Nirsevimab)
- Infection
  - Mainly supportive
  - Rarely Antiviral

Goal of RSV immunization is not to prevent infection but rather to reduce the severity.

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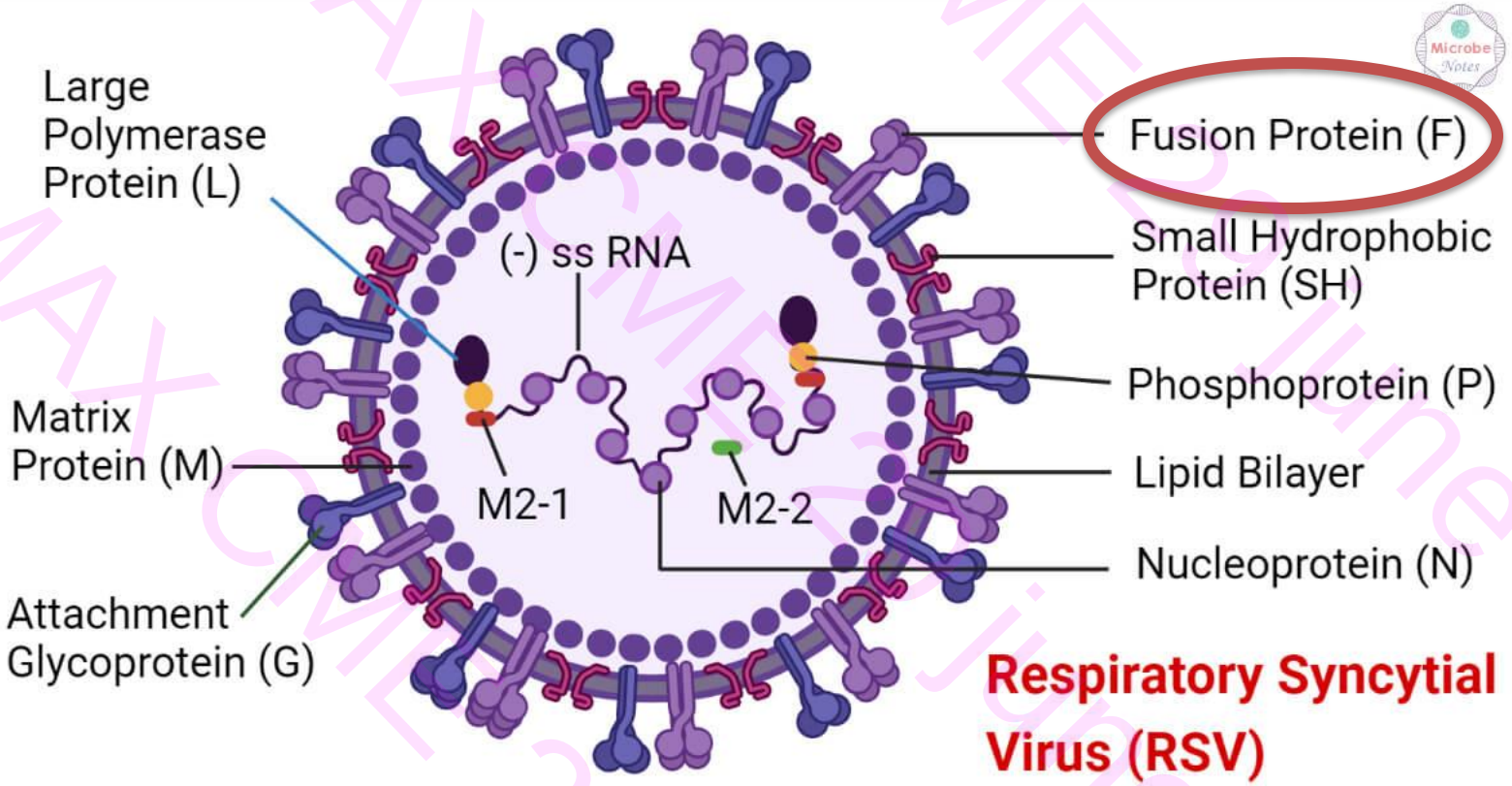
RSV



Binds F protein → blocks virus-cell fusion

Prevents syncytia formation and viral replication

Maternal RSV Vaccine – RSV Pre F

- RSV Pre F- Perfusion F protein Vaccine - Bivalent
- Given at 32–36 weeks gestation: 0.5 mL IM single dose.
- 82% efficacy vs severe RSV-LRTI in infants <90 days.
- 57% efficacy vs medically attended RSV-LRTI in <6 months.
- No Palivizumab needed if given 2 weeks before delivery
- Protects infants for ~6 months.

Not Available in India

CDC/ACOG/WHO position paper 30th May 2025

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Palivizumab: Evidence

- **Two pivotal trials included nearly 2800 of the most vulnerable patients**

IM-pact RSV Trial
1502 subjects

Preterm Infant/BPD

< 35 weeks
5 injections/ 5 months

FELTES TRIAL

HS – CHD

5 injections/ 5 months

The IMpact-RSV Study Group. Pediatrics. 1998;102(3):531-537.
Feltes TF, J Pediatr. 2003;143(4):532-540.

Outcomes

	IMpact	FELTES
Hospitalization all	78 % less stay	45 %
Hospitalization In BPD	39 % less stay	
Hospitalization In Very Preterm	72% less stay	
O2 needs	40% lesser days	57% fewer days
Absolute Reduction	5.8 %	4.4%

No differences in Mortality

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Indication as per NNF INDIA

- **Babies born a< 29 weeks *(< 33wk)* until 12 months.**
- **Babies >29 -32 weeks with BPD *(< 35 wk)***
- **Babies with (CHD) are at risk of congestive heart failure or on anti-failure medications, awaiting cardiac surgery, or CHD with moderate to severe PAH.**

Palivizumab may be considered

- **In babies with cystic fibrosis, post-tracheostomy, and immunocompromised babies.**

Bold : Other Infectious disease society recommendation

RSV Season in India

- Generally : 5 month duration
- In developed countries - seasonal trend.
- Pre COVID – fixed season; now its disrupted (irregular peak)
- There is limited information on RSV season in India.
- Recent studies from India have shown an increased incidence of RSV from July to November, with a smaller peak during December, January, and February.

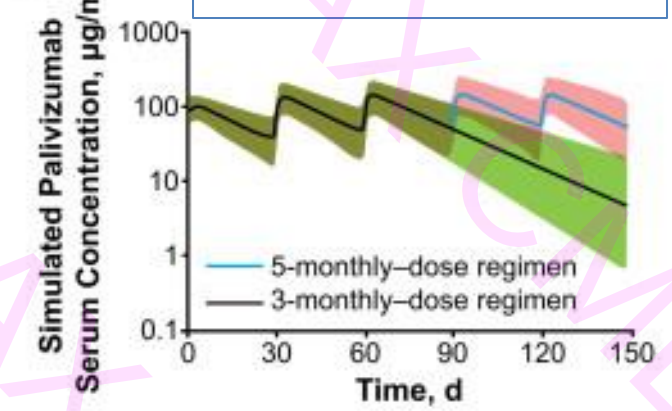
Vaccination Dose & Schedule

- ***Dose:*** **The dose is 15 mg/kg, once per month for 5 months; 15 mg/kg/dose has been shown to achieve a mean trough serum concentration that is associated with a 99% reduction of RSV.**
- **Should continue to receive prophylaxis after recovery from their acute infection.**
- **No issues with any any other vaccines if co administered (even on Day 1 of life)**

3 doses Vs. 5 Monthly doses

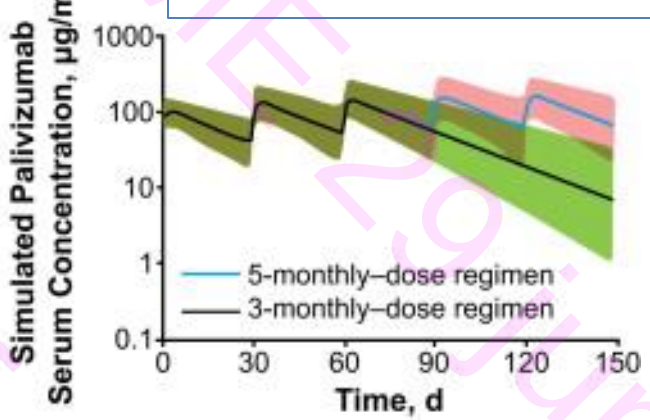
A

< 24 months with CLD



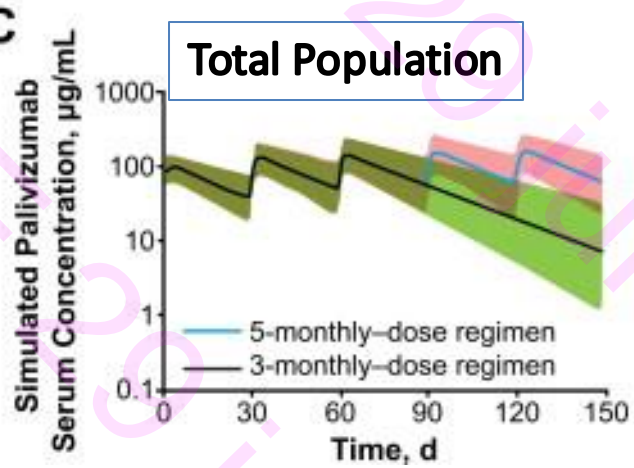
B

<35 weeks GA < 6 months



C

Total Population



Taiwan: 6 months

William V. La Via, Gerard F. Notario, Xiang-Qing Yu, Shringi Sharma, Peter A. Noertersheuser and Gabriel J. Robbie
Pulmonary Pharmacology & Therapeutics, 2013-12-01, Volume 26, Issue 6, Pages 666-671,

Safety Profile

- Common: fever, injection site rash, conjunctivitis , URI
- Serious: anaphylaxis, hypersensitivity, Arrythmia (rare),

Contraindicated in hypersensitive patients

Use caution with bleeding disorders

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Concern with Palivizumab: too many doses;

Any other options :

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Nirsevimab– Monoclonal Antibody

- Long acting (Half life: 63–73 d)- block virus entry in to the host
- Single-dose IM for infants entering RSV season.
- 50 mg (<5 kg), 100 mg (≥5 kg).
- 74.5% efficacy vs medically attended RSV-LRTI.
- 76.4% reduction in RSV hospitalizations in infants.
- Consistent protection across all gestational age & Cost effective

CDC Study	90 % effectiveness against hospitalization
European Study	83 % reduction in hospitalization

NEJM, 2023: Abrysvo & Nirsevimab trials.

- **Given at discharge for NICU infants born in RSV season.**
- **Reduces post-discharge RSV hospitalizations.**
- **Preferred over Palivizumab due to ease and longer coverage.**

FDA /CDC	2023
ACIP/AAP	2023; all infants < 8 months
EU & UK	2022
Canada	2023
India (sanofi/Dr reddy)	Launched -June 2025

US Department of Health and Human Services | Centers for Disease Control and Prevention | MMWR | March 7, 2024 | Vol. 73 | No. 9

- Both palivizumab and nirsevimab - passive immunity
- Both blocks viral replication.
- Both have been shown to drastically reduce the RSV
- Both have been approved by the FDA for preterm infants;
  - however, only nirsevimab is approved for all infants regardless of medical history through the first year of life.

Take Home Message

- Indicated for high-risk infants: preterms, CHD, CLD, immunocompromised. (Follow NNFI)
- Dose: 15 mg/kg IM monthly for up to **5 doses** per season. (P)
  - Single dose for Nirsevimab
- Reduces RSV hospitalizations by ~45–55%.
- Limitations: high cost, no impact on mortality.
- **Breast feeding (Decrease infection + less severe) / Hand Hygiene /Second hand Smoking**