OPTIMALISASI LUARAN JANIN PADA PERSALINAN PRETERM

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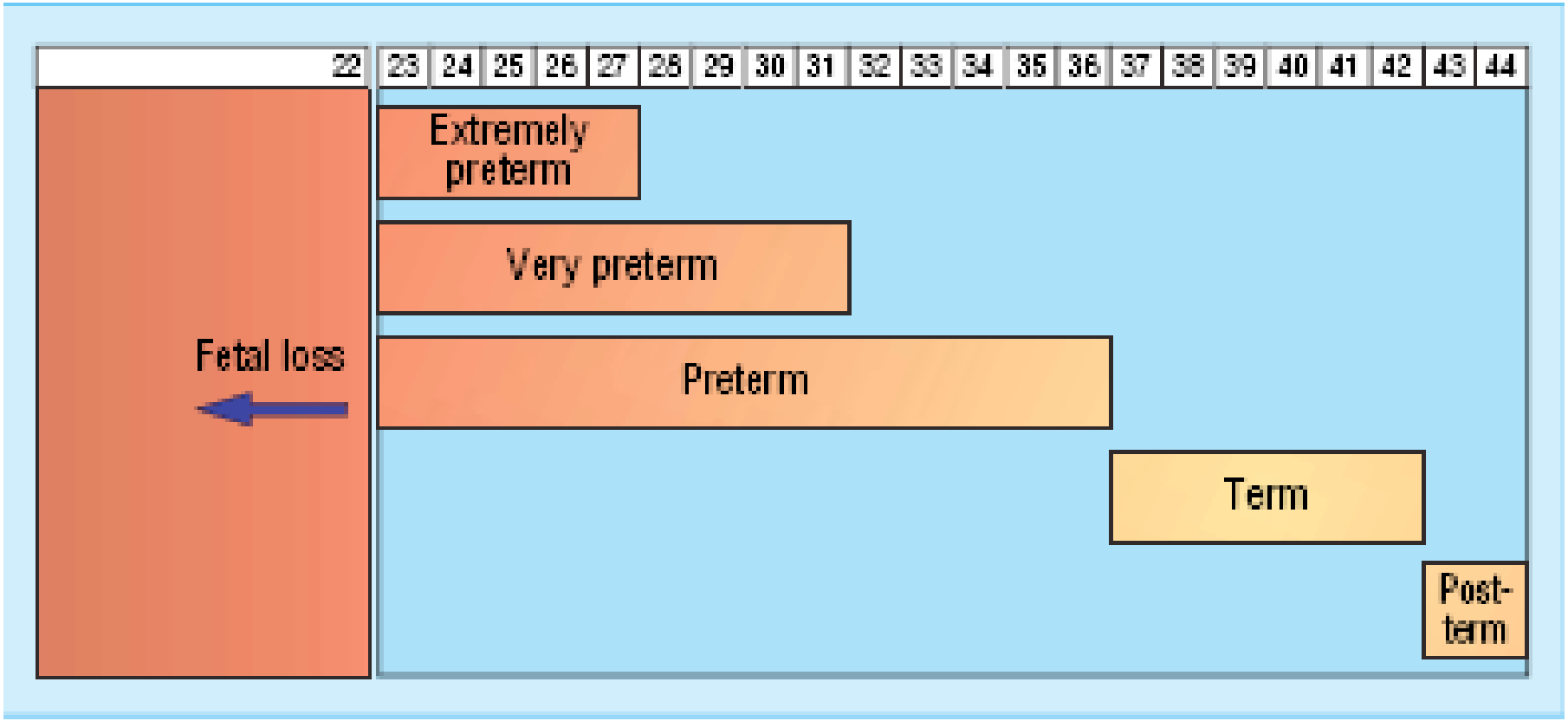
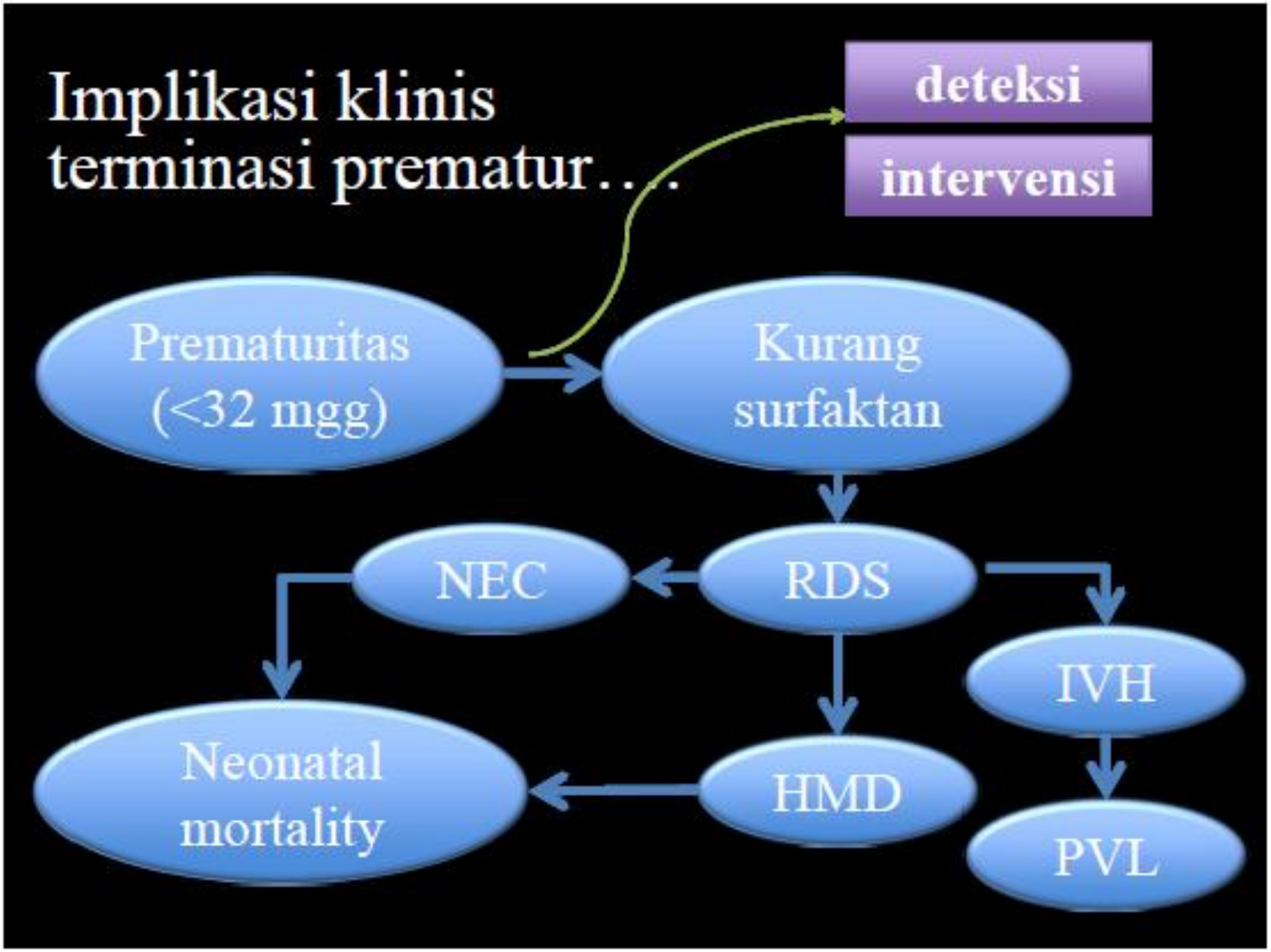


- Definitions of Preterm, according to gestational age
- Tucker J, McGuire W. Epidemiology of preterm birth. *BMJ* 2004;329;675-678

Problems on the preterm outcome

- Perinatal mortality
- Serious neonatal morbidity
  - CNS Injuries
- Moderate to severe childhood disability

Lumley J. Defining the Problem: the Epidemiology of Preterm Birth. *Br J Obstet Gynaecol*. 2003;110(Suppl 20):3-7


Implikasi klinis terminasi prematur….
deteksi
intervensi
Prematuritas (<32 mgg)
Kurang surfaktan
NEC
RDS
IVH
Neonatal mortality
HMD
PVL

Komplikasi Bayi Prematur

Permasalahan jangka pendek dan jangka panjang pada bayi prematur dengan VLBW		
Organ / sistem yang terganggu	Permasalahan jangka pendek	Permasalahanjangka panjang
Paru	Sindrom gagal napas, kebocoran udara, displasia bronkopulmonar , henti napas	Displasia bronkopulmonar , asma, penyakit paru reaktif
Gastrointestinal / nutrisi	Hiperbiliribunemia, intoleransi makanan, enterokolitis nekrotikans, gagal tumbuh	Failure to thrive short-bowel syndrome, kolestasis
Imunologi	Hospital-acquired infection, defisiensi imun, infeksi perinatal	Respiratory syncytial virus infection Bronkiolitis
Sistem saraf pusat	Perdarahan intraventrikel, periventricular white-matter injury, hidrosefalus	Cerebral palsy, hidrosefalus, atrofi serebral , keterlambatan perkembangan saraf, gangguan pendengaran
Mata	Retinopati prematuritas	Kebutaan, retinal detachment, miopia, strabismus
Kardiovaskular	Hipotensi, PDA, hipertensi pulmonal	Hipertensi pulmonal, hipertensi pada usia dewasa
Ginjal	Ketidakseimbangan cairan dan elektrolit, gangguan keseimbangan asam basa	Hipertensi pada usia dewasa
Hematologi	Anemia iatrogenik , kebutuhan untuk trasfusi anemia pada prematuritas	
Endokrin	Hipoglikemia, rendahnya hormon tiroksin (transien), defisiensi kortisol	Gangguan regulasi glukosa , peningkatan resistensi insulin

Tocolytic therapy in Preterm Labor

Sumber: Strong Perifax February 27, 2002

Drug	Dose	Side Effects	Contraindiacations
Terbutaline (Brethine)	25 mg q 30 min up to 1 mg over 4 hr	Cardiac arrhythmias, Pulmonary edema, Hypotension, myocardial Ischemia, tachycardia, Anxiety, tremulousness	Cardiac arrhythmias, Poorly-controlled Thyroid disease, diabetes
Magnesium Sulfate	4 to 6 gm IV bolus over 20 min, then 2 to 4 gm/hr	Flushing, lethargy, Headache, muscle Weakness, dry mouth, Diplopia, pulmonary Edema, cardiac arrest, Respiratory insufficiency	Myasthenia gravis
Ca Channel blockers (Nifedipine)	20 mg po loading dose, then 10 to 20 mg po q4 to 6 hr	Flushing, headache, Dizziness, nausea, Transient hypotension	Cardiac disease, use Caution with renal Disease, maternal Hypotension, avoid Concomitant use with $MgSo_4$
Prostaglandin Synthetase inhibitors	Indomethacin Loading dose – 50 Mg rectally or 50 To 100 mg orally, Then 25 to 50 mg Orally q 4 hr for 48 hr	Nausea, heartburn Fetal : Renal Insufficiency, premature, Closure of ductus Arteriosus, Oligohydramnios Neonate : pulmonary Hyper tension, Necrotizing Entero colitis	Significant renal or Hepatic impairment

PEMILIHAN TOKOLITIK

- Pertimbangan:
  - usia kehamilan
  - pengaruh obat tokolitik pada bayi
  - efek lanjut pada ibu
- Tiga pilihan pengelolaan persalinan preterm:
  - Menghentikan proses persalinan dan menunggu sampai bayi aterm
  - Menunda persalinan sampai 48-72 jam untuk meningkatkan maturitas paru janin
  - Tetap membiarkan persalinan berlangsung karena ibu kemungkinan akan mendapatkan efek tidak bagus bila tokolitik diberikan.

– Pemberian tokolitik dapat diberikan jangka panjang sampai bayi mencapai aterm bila :

- Umur kehamilan antara 18 – 34 minggu
- BB janin kurang dari 2000 gram,
- Kulit ketuban masih utuh
- Dilatas serviks kurang dari 4 cm
- Kulit ketuban tidak menonjol
- Janin pada keadaan biofisikal baik.
- Kontraksi uterus berlangsung dengan jarak < 10 menit.

– Kontra indikasi dapat dikelompokkan sbb :

- Terdapat solusio plasenta
- IUFD
- Gawat janin
- Kelainann kongenital mayor (diagnosis USG)
- Pre Eklamsia berat yang progresif
- Penyakit ibu yang yang mengindikasikan terminasi kehamilan.
- Ketruban sudah pecah lama
- Penyakit jantung yang menahun

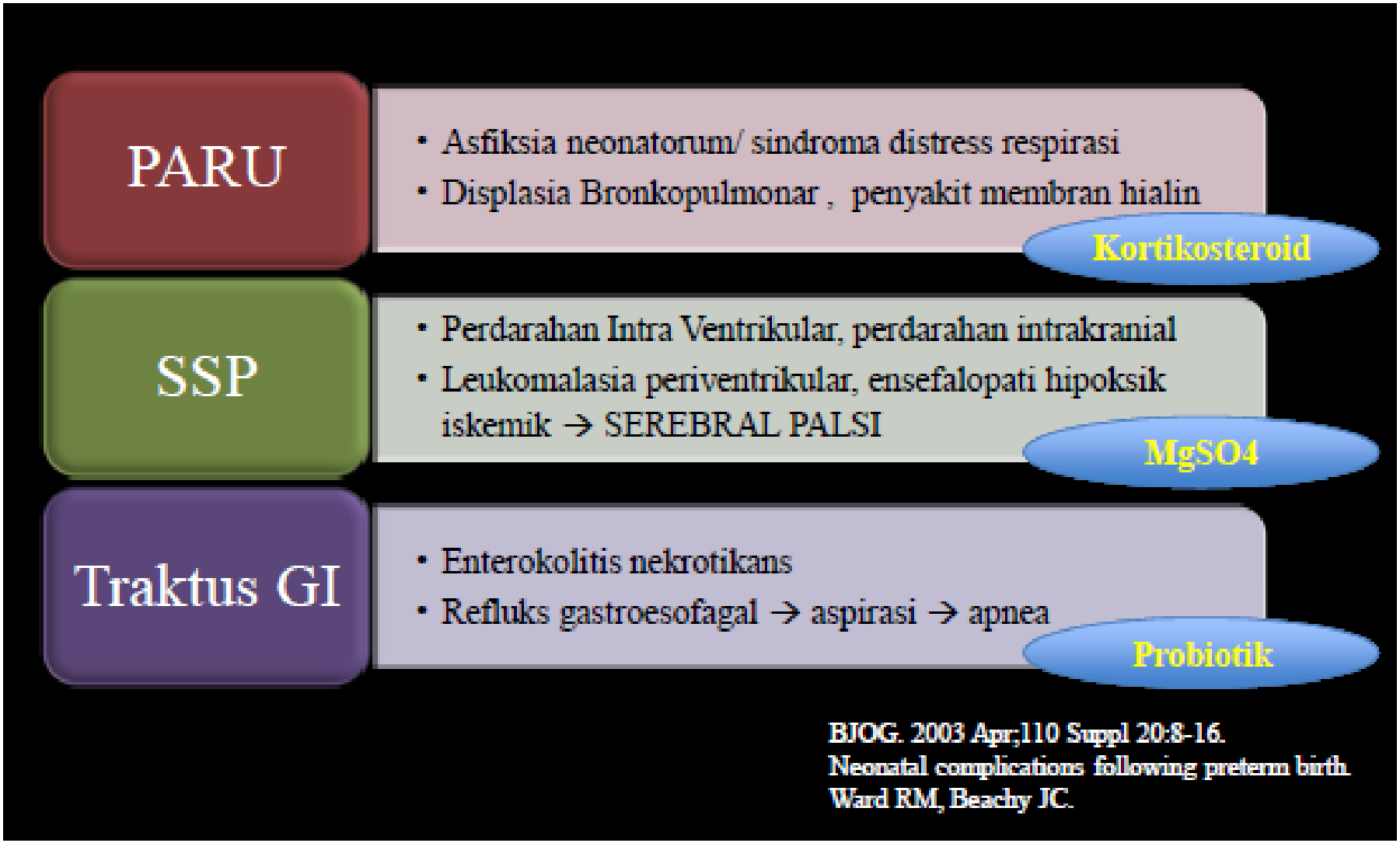
The Use of Progesterone for Prevention of Preterm Birth

Recommendations

1. Women at risk for PTL should be encouraged to participate in studies on the role of progesterone in reducing the risks of preterm labour. (I-A)
2. Women should be informed about the lack of available data for may neonatal outcome variables and about the lack of comparative data on dosing and route of administration. Women with short cervix should be informed of the single large RCT showing the benefit of progesterone in preventing PTL. (I-A)
3. Women and their caregivers should be aware that a previous preterm labour and/or short cervix (< 15 mm at 22-26 weeks gestation) on transvaginal ultrasound could be used as an indication for progesterone therapy. The therapy should be started after 20 weeks gestation and stopped when the risk of prematurity is low. (I-A)
4. On the basic of the data from the RCTs and meta-analysis, it is recommended that in cases where the clinician and the patient have opted for the use of progesterone the following dosages should be used:
   - For prevention of PTL in women with history of previous PTL: 17 alpha-hydroxyprogesterone 250 mg IM weekly (IB) or progesterone 100 mg daily vaginally. (I-A)
   - For prevention of PTL in women with short cervix < 15 mm detected on transvaginal ultrasound at 22-26 weeks progesterone 200mg daily vaginally. (I-A)

J Obstet Gynaecol Can 2008:30(1):67-71

KOMPLIKASI BAYI PREMATUR



RESPIRATORY IMMATURITY

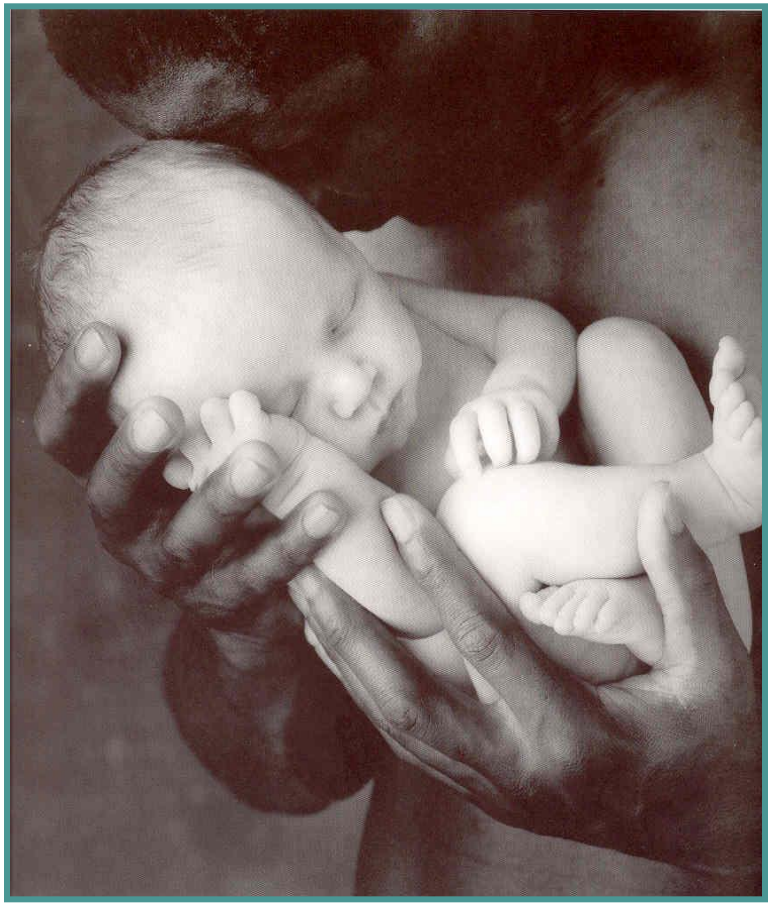
- ***RDS affect 40–50% of babies born before 32 weeks.***
- ***Liggins 1972: antenatal corticosteroids prior to preterm delivery reduces the incidence of RDS.***

Corticosteroids: Mechanism

- A variety of biochemical systems within the type II pneumocyte are regulated by glucocorticoids
- Occupancy of glucocorticoid receptors in target cells increase from 25% to > 75% after betamethasone treatment
- Increased lung compliance and maximal lung volume are achieved independent of surface active material

Effectiveness of antenatal corticosteroid therapy

The optimal treatment–delivery interval for administration of antenatal corticosteroids is more than 24 hours but fewer than seven days after the start of treatment.



Pemberian kortikosteroid…

Kapan ?	• High Risk of Preterm delivery • 28-34 minggu • 32-34 minggu (optimal) • > 34 minggu
Preparat/ cara pemberian	• Deksametasone 6 g/12 jam (4x)/ Im • Betametasone 12 g/24 jam (2x)/ Im
Pengulangan	• Interval terdekat 1 minggu • Maksimal 3x

Multiple doses *may lead to:*

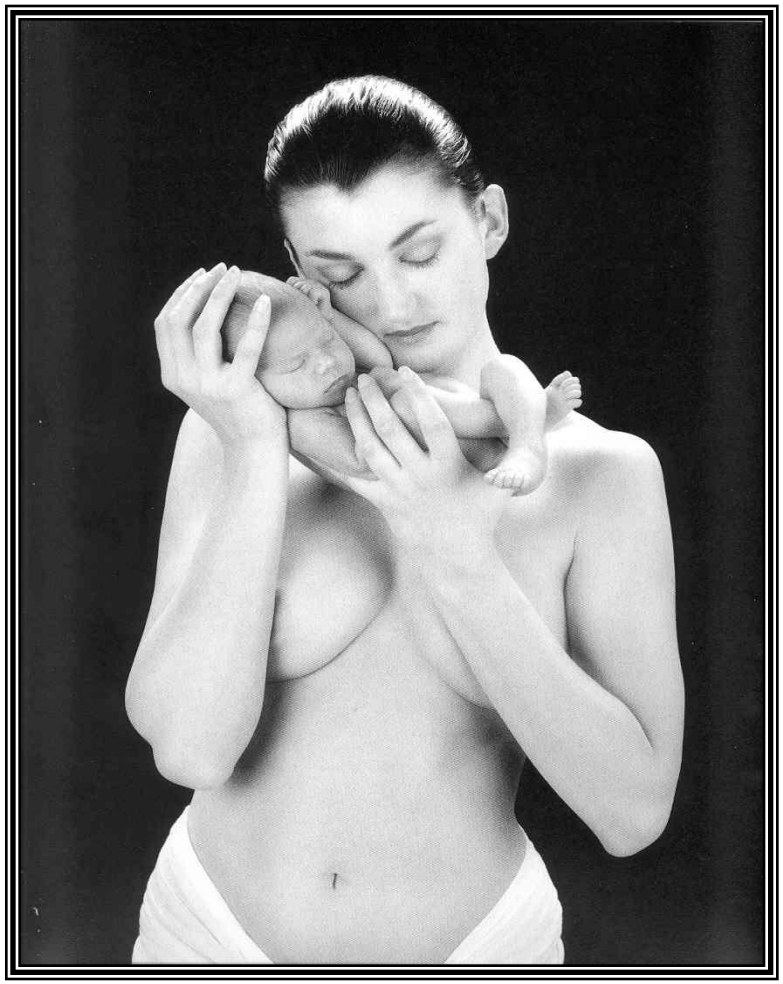
- ***Growth delay,***
- ***Brain developmental delay,***
- ***Lung development problems,***
- ***Necrotizing enterocolitis,***
- ***Maternal and neonatal sepsis,***
- ***Adrenal gland insufficiency and***
- ***Placental infarction.***

(Banks et al, 1999)

Safety

The use of a single course of antenatal corticosteroids

Does not associated with any significant maternal or fetal adverse effects.



Contraindications and precautions

- *Corticosteroid therapy is **contraindicated** if a woman suffers from **systemic infection** including **tuberculosis.***
- *Caution is advised if suspected **chorioamnionitis** is diagnosed.*

SUSUNAN SARAF PUSAT

Preterm Birth And CNS Injuries

Pathologically :2 CNS injuries :

(1) Intraventricular Hemorrhage (IVH)

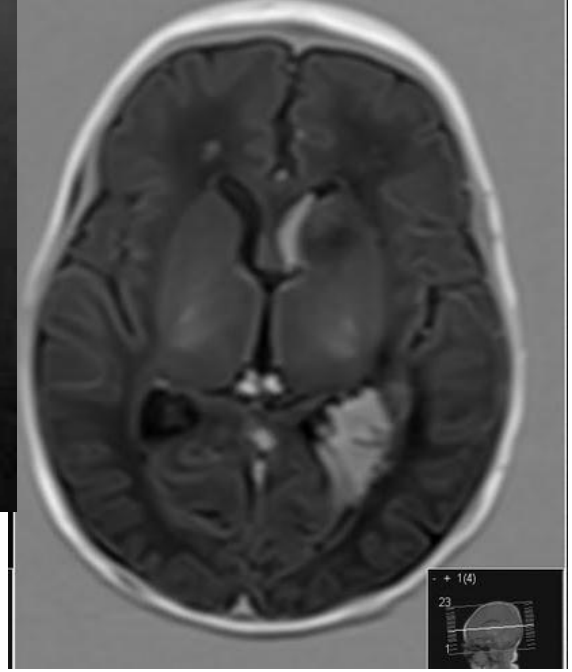
Usually diagnosed by ultrasound (U/S)

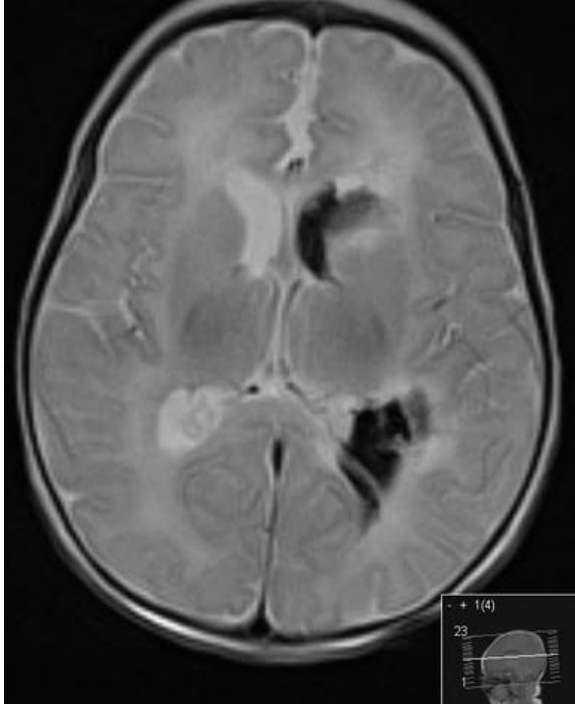
(2) White Matter Injury.

Usually diagnosed by MRI

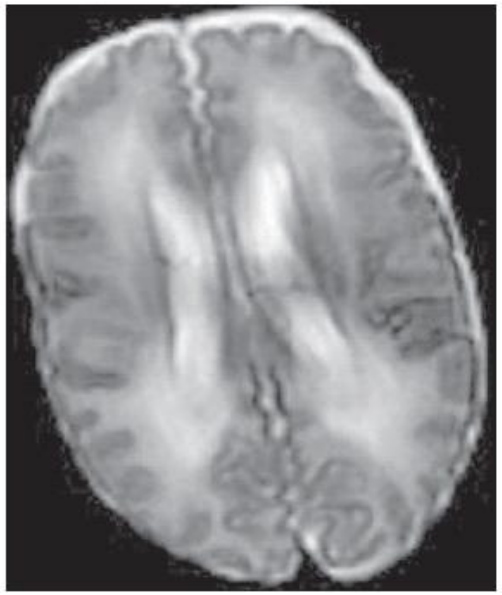
SOGC Clinical Practice Guideline No. 258, May 2011

Tran cranial U/S
I.V. Hemorrhage





MIR left lateral I.V. Hemorrhage T1 &T2



MRI T2 White Matter Injury

Preterm Birth And CNS Injuries

Clinically: The most frequent adverse

CNS outcomes are

1-Cerebral palsy **(CP)**

2-Cognitive impairment

3-Blindness,deafness & developmental delay.

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Spastic CP


Spastic CP


Ataxic CP

Cerebral Palsy (CP)

The Magnitude Of The Problem

- CP is the most common cause of severe motor disability in childhood
- CP increases inversely according to G. age:

All live births : 0.25 %

Compared with infants at term the CP risk is:

- At 34-36 weeks : 3 fold
- At 30-33 weeks : 8- 14 fold
- At 28-30 weeks : 46 fold
- At < 28 weeks : 80 Fold

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MgSO4 Use in Obstetrics

- **Eclampsia**: Prophylaxis & management*
- **Tocolysis** :No longer recommended **
- **Fetal neuroprotection** in preterm delivery

  : A new evidence &validation

*Altman et al,Lancet, 90-10877(9321)359;2002 Duley et al ,. Lancet 1995;345(8963):1455–63.

*Magee et al.,SOGC Clinical Practice Guideline no. 206, March 2008

** Doyle et al Cochrane Database Syst Rev 2009;(1):CD004661

The Mechanism Of Neuroprotective Effect

- **The mechanism is not well understood**
- **potential neuroprotective actions include:**
  - **Antioxidant effects**
  - **Reduction in pro-inflammatory cytokines**
  - **Inhibition of calcium influx into cells**
  - **Stabilization of membranes**
  - **Increased cerebral blood flow**
  - **Prevention of large blood pressure fluctuations**

Gathwala ,. Neuronal protection with magnesium. Indian J Pediatr 2001;68:417–9

Marret et al ., Semin Fetal Neonatal Med. 2007;12(4):311.

Hyagriv & Katherine .,UpToDate 19.3: January 2012

The 3 large, well-done RCTs (Placebo)

Trial & No.	Inclusion	Dose of MgSO4	Significant reduction of CP
ACTOMgSO4 Crowther et al (2003) n.:1062 Australia	< 30 Ws	4 g Loading then1 g/h	Moderate to severe CP (3.4% Vs 6.6 %)
BEAM Rouse et al , N Engl J Med. 2008;359(9):895 n.2241 USA	24-31 Ws cost $25 million and took 10 years	6 g loading then 2 g/h	Moderate to severe CP (1.9% Vs 3.5 %)
PREMAG Marett et al., Gy. Ob. Fertil. 2008;36(3):278 n.573 France.	<33 Ws	Single 4 g loading	Death & gross motor dysfunction (0.6% Vs 0.4%)

MgSO4 significantly ↓risk of CP in early preterm birth

What Is The Recommended Dose ?

- 4g Mg SO4 IV loading dose, over 30 minutes, followed by a maintenance infusion of 1g/ hours until birth or for 24 hours, whichever comes first. .(II-2B)
- Mg SO4 should be started, ideally within 4 hours before birth .(II-2B)

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What is the Imminent Preterm Birth

Imminent preterm birth" is defined as a high likelihood of birth due to one or both of the following conditions (II-2):

1-Active labour with ≥ 4 cm of cervical dilation, with or without PPROM.

2-Planned preterm birth for fetal or maternal indications.

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What Is The Cut-off Gestational Age For MgSO4 ?

Although there is controversy about upper G. age ,antenatal MgSO4 should be considered from viability to < 32 weeks. (II-1B)

If antenatal MgSO4 has been started, tocolysis should be discontinued. (III-A)

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Should MgSO4 Course Be Repeated ?

There is insufficient evidence that a repeat course of antenatal MgSO4 should be administered. (III-L)

Should Delivery Be Delayed To Give MgSO4 Course?

Delivery should not be delayed if there are maternal and/or fetal indications for emergency delivery. (III-E)

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TAKE HOME MESSAGE

- Kortikosteroid tetap menjadi modalitas utama pematangan janin pada terminasi prematur oleh karena PEB
- Proteksi otak dan saluran cerna dengan pemberian magnesium sulfat dan prebiotik antenatal dapat direkomendasikan
- Janin adalah individu utuh dan bukan semata organ paru saja sehingga maturitas organ vital lain wajib diperhatikan