# **Respiratory Failure in Pregnancy**



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# Disclosure

No conflicts of interestOff-label use of pharmaceutical agents

# Outline

Respiratory physiology in pregnancy

Respiratory failure in pregnancy

- Incidence
- Etiology
- Managmenent







# **Blood gases in late pregnancy**

рН	7.43		
PaCO <sub>2</sub>	30	mmHg	- hyperventilation
PaO <sub>2</sub>	105	mmHg	- normal a-A gradien
HCO <sub>3</sub> ⁻	20	mEq/L	- renal compensation

**Decreased oxygen reserve** 

- reduced FRC
- increase O<sub>2</sub> consumption



Cause of death	eath 2000–02		2003-05			2006-08			
	n	Rate	95% CI	n	Rate	95 % CI	n	Rate	95 % CI
Direct deaths									
Sepsis*	13	0.65	0.38-1.12	18	0.85	0.54-1.35	26	1.13	0.77-1.67
Pre-eclampsia and eclampsia	14	0.70	0.42-1.18	18	0.85	0.54-1.35	19	0.83	0.53-1.30
Thrombosis and thromboembolism	30	1.50	1.05-2.15	41	1.94	1.43-2.63	18	0.79	0.49-1.25
Amniotic fluid embolism	5	0.25	0.10-0.60	17	0.80	0.50-1.29	13	0.57	0.33-0.98
Early pregnancy deaths	15	0.75	0.45-1.25	14	0.66	0.39-1.12	11	0.48	0.27-0.87
Ectopic	11	0.55	0.30-0.99	10	0.47	0.25-0.88	6	0.26	0.12-0.58
Spontaneous miscarriage	1	0.05	0.01-0.36	1	0.05	0.01-0.34	5	0.22	0.09-0.52
Legal termination	3	0.15	0.05-0.47	2	0.09	0.02-0.38	0	0.00	
Other	0	0.00		1	0.05	0.01-0.34	0	0.00	
Haemorrhage	17	0.85	0.53-1.37	14	0.66	0.39-1.12	9	0.39	0.20-0.75
Anaesthesia	6	0.30	0.13-0.67	6	0.28	0.13-0.63	7	0.31	0.15-0.64
Other Direct	8	0.40	0.20-0.80	4	0.19	0.07-0.50	4	0.17	0.07-0.47
Genital tract trauma	1	0.05	0.01-0.36	3	0.14	0.05-0.44	0	0.00	
Fatty liver	3	0.15	0.05-0.47	1	0.05	0.01-0.34	3	0.13	0.04-0.41
Other causes	4	0.20	0.08-0.53	0	0.00		1	0.04	0.01-0.31
All Direct	106	5.31	4.39-6.42	132	6.24	5.26-7.41	107	4.67	3.86-5.64
Indirect									
Cardiac disease	44	2.20	1.64-2.96	48	2.27	1.71-3.01	53	2.31	1.77-3.03
Other Indirect causes	50	2.50	1.90-3.30	50	2.37	1.79-3.12	49	2.14	1.62-2.83
Indirect neurological conditions	40	2.00	1.47-2.73	37	1.75	1.27-2.42	36	1.57	1.13-2.18
Psychiatric causes	16	0.80	0.49-1.31	18	0.85	0.54-1.35	13	0.57	0.33-0.98
Indirect malignancies	5	0.25	0.10-0.60	10	0.47	0.25-0.88	3	0.13	0.04-0.41
All Indirect	155	7.76	6.63-9.08	163	7.71	6.61-8.99	154	6.72	5.74-7.87
Coincidental	36	1.80	1.30-2.50	55	2.60	2.00-3.39	50	2.18	1.65-2.88
Late deaths									
Direct	4			11			9		
Indirect	45			71			24		

Table 4 Characteristics of included studies according to country level of development					
Characteristic $(N = 41)^a$	Developing <sup>b</sup> $(n = 16)$	Developed <sup>b</sup> $(n = 25)$	p value		
Study duration (years), mean $\pm$ SD	$5.4 \pm 2.9$	$7.4 \pm 3.6$	0.06		
Participants	73 (30-1,902)	65 (18-754)	0.81		
Deliveries during study period	28,209 (5,764-822,591)	24.347 (2.224-82.623)	0.92		
Incidence of ICU admission during study period	2.7 (1.3-13.5)	3.0 (0.7-8.8)	0.52		
Maternal deaths (%)	14.0 (0.0-40.0)	$3.4(0.0-18.4)^{\circ}$	0.002		
Overall proportion of ICU admissions (%)	2.4 (0.5-16.0)	1.5 (0.4–12.0)	0.38		
Received mechanical ventilation (%)	41.0 (3.0-100.0)	41.5 (13.0-76.0)	0.60		
Hypertensive disease of pregnancy (%)	39.8 (10.0-74.0)	32.5 (13.0-88.0)	0.93		
Hypertensive disease of pregnancy (per 1,000 deliveries)	1.1 (0.2-6.7)	0.9 (0.2-4.7)	0.75		
Obstetric haemorrhage (%)	25.0 (8.5-53.0)	21.5 (5.0-46.5)	0.85		
Obstetric haemorrhage (per 1,000 deliveries)	0.8 (0.4–1.8)	0.6 (0.1-2.3)	0.27		
Sepsis/infection (%)	5.0 (0.0-17.0)	4.8 (0.0-24.0)	0.85		
Sepsis/infection (per 1,000 deliveries)	0.2(0.0-2.3)	0.1(0.0-0.9)	0.62		
Other direct obstetric complications (%)	4.5 (0.0-30.0)	5.8 (0.0-55.0)	0.31		
Other direct obstetric complications (per 1,000 deliveries)	0.1(0.0-1.6)	0.2(0.0-3.4)	0.95		
Non-obstetric diagnoses (%)	21.5 (6.5-43.0)	25.8 (0.0-47.0)	0.92		
Non-obstetric diagnoses (per 1,000 deliveries)	0.9(0.2-2.2)	0.7(0.0-3.0)	0.99		
Anaesthetic complications (%)	0.3 (0.0-26.0)	0.0(0.0-22.0)	0.83		
Anaesthetic complications (per 1,000 deliveries)	0.0 (0.0-0.5)	0.0 (0.0-0.6)	0.71		

Pollock et al, Int Care Med 2010, 36:1465

>About 1-2 per 1,000 deliveries

Account for about 1% of ICU admissions

Vast majority ICU admissions postpartum

- 90% postpartum
- 10% during pregnancy

Pregnancy - specific

Aggravated by pregnancy

Non - specific

## Pregnancy - specific

Preeclampsia (pulmonary edema)
Amniotic fluid embolism
Tocolytic pulmonary edema
Septic ARDS (chorioamnionitis)
Trophoblastic embolism
Fetal intrauterine surgery

> Aggravated t

> Non - specifi

Gastric acid aspiration
Venous thromboembolism
Pyelonephritis (producing ARDS)
Sepsis
Air embolism
Pneumonia (varicella, others)
Connective tissue disease
Cardiac failure

Pregnancy - specific

Aggravated by pregnancy

> Non - specific

# **Causes of Respiratory Failure**

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# ➢Pneumonia:

- Usual pneumonias occur, no change in incidence
- Complications more common
- Also:
  - Influenza
  - Varicella
  - HIV associated
  - Tuberculosis



## Causes of Respiratory Failure

## ➢Pneumonia:

- Management
  - do NOT avoid chest x-rays
  - avoid tetracyclines & quinolones, if possible
  - VZIG and acyclovir
  - Tamiflu (oseltamivir)
  - TB: INH, rifampin, ethambutol PZA (recommended by WHO) delay Rx of latent TB

# Influenza in Pregnancy

Increased risk of severe disease

7 – 9% of ICU patients (1% of population)

Major risks to fetus

Fever
Hypoxemia

Management

Oseltamivir
Optimize oxygenation

# **Cystic fibrosis**

 low risk with stable disease
 avoid pregnancy if (?) FVC < 50% pulmonary hypertension

increased perinatal mortality

 Management: nutrition antibiotics counseling

## **Other Chronic Lung diseases**

- eg. bronchiectasis, neuromuscular disease, restrictive lung disease
- little data
- Some may deteriorate (LAM, SLE)
- increasingly common request
- multidisciplinary team management

#### Case series: restrictive lung disease in 15 pregnancies





Lapinsky et al, Chest. 2014 Feb;145(2):394-8

## Lung function tests during pregnancy



Timing of Spirometry in pregnancy

Lapinsky et al, Chest. 2014 Feb;145(2):394-8

# Restrictive disease: Respiratory support



# Delivery - mode





## Restrictive disease in pregnancy

- Women with severe restrictive lung disease tolerate pregnancy reasonably well
- Careful monitoring & planning:
  - Oxygenation requirements
  - Small risk of ventilatory failure
  - Labour and delivery:
    - Timing
    - Potental difficulty with:
      - neuraxial anesthesia
      - airway management



# Pregnancy-specific conditions

# **Amniotic Fluid Embolism**

Rare: 1/8,000 to 1/80,000
 Catastrophic: mortality 10 - 86%

Presentation: cardiorespiratory collapse fetal distress cardiac arrest, seizures

Late effects: ARDS & DIC

# Amniotic Fluid Embolism

## > Hemodynamics:

pulmonary hypertension & biventricular dysfunction

## Diagnosis:

- Usually diagnosis of exclusion
- Not yet adequately validated:
  - Tryptase
  - Fetal squames and debris in pulmonary capillaries
  - Complement levels
  - Zinc coproporphyrin
  - Sialyl Tn antigen
  - C1 esterase inhibitor Tamura N, et al Crit Care Med. 2014;42:1392-6

# Amniotic Fluid Embolism

## Management:

- Supportive ventilation
  - fluid, inotropes
  - Rx DIC
- Deliver fetus
- Steroids ?
  - based on similarity with anaphylactic reaction
  - no supporting data

# ARDS in pregnancy

Important cause of maternal death
Pregnant women appear very susceptible:

Reduced serum albumin
Increased blood volume
Upregulation of components of the inflammatory response

Smith, et al. West J Med 1990, 153:508 Catanzarite, Obstet Gynecol Survey 1997, 52:381 Sheng et al. Crit Care Med. 2012 May;40(5):1570-7

# **ARDS in pregnancy**

pre-eclampsia
obstetric sepsis
amniotic fluid embolism
aspiration
major hemorrhage
placental abruption

Smith, et al. West J Med 1990, 153:508 Catanzarite, Obstet Gynecol Survey 1997, 52:381

# **Respiratory failure in pregnancy**

# Management

# **Respiratory failure in pregnancy**

## ICU Management

- Prepare the ICU !
- Non-invasive ventilation
- Intubation
- Conventional mechanical ventilation
- Non-conventional modes
- Other management issues
- Role of delivery

## **Respiratory failure in pregnancy**

## ➢ Prepare the ICU:

- Drugs: oxytocin, Hemabate, ergotamine
- Blood compat: send q4 days
- Equipment: Vaginal delivery Caesarean delivery Neonatal resuscitation



- Decisions: fetal resuscitation status
- Contact details: OB, anesthesia, neonatology



# **Non-invasive Ventilation**

## >Advantages

avoids the upper airway avoids sedation



## ≻Concerns

- nasal congestion
- reduced lower esophageal sphincter tone
- aspiration

# **Non-invasive Ventilation - Role**

## Acute respiratory failure

- Pulmonary edema (preeclampsia, cardiogenic)
- Other (eg. asthma, pneumonia)

# Chronic respiratory failure

- Neuromuscular disease
- Kyphoscoliosis
- Bronchiectasis



Bach. Am J Phys Med Rehabil 2003; 82:226

# **Endotracheal intubation in pregnancy**



Failed intubation 8x more common than non-pregnant patient

Affected by anatomical changes aspiration risk weight gain reduced oxygen reserve preeclampsia

Munnur et al, Crit Care Med, 2005, 33:S259



TIME TO HEMOGLOBIN DESATURATION WITH INITIAL  $F_AO_2 = 0.87$ 

Benumof et al, Anesthesiology 1997; 8:979 Baraka et al, Anesth Analg 1992; 75:757

# **Conventional Ventilation**

# Oxygenation optimize: PaO<sub>2</sub> > 90 mmHg ?

Ventilation
 normal PaCO<sub>2</sub> 30 mmHg
 permissive hypercapnia ?
 avoid alkalosis

## Pressure

- respiratory system compliance
- adequate PEEP

# **Blood Gas Targets in Pregnancy**



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As with any organ, oxygen delivery is determined by:

-Oxygen saturation -Hemoglobin -Cardiac output





## Oxygen Targets in Pregnancy

Modelling based on animal data: Maternal Sat 96% to 85% will result in fetal: 70% to 55% Meschia, Clin Chest Med 2011;32:15

Maternal hypoxemia (10% O<sub>2</sub>): no adverse effect on fetal monitoring Polvi et al. Obstet Gynecol. 1995;86:795

Winnipeg H1N1 experience: 6 pregnant women, initial sats 50 – 88%: 4/6 marked ischemic encephalopathy (but likely numerous confounding factors)

Oluyomi-Obi et al. J Obstet Gynaecol Can 2010;32:443



## CO<sub>2</sub> Targets in Pregnancy

- Over ventilation reduces uterine blood flow
  - effects of positive pressure on cardiac output
  - effects of resp alkalosis on UBF Levinson et al. Anesthesiology. 1974;40:340-7

• Low maternal PaCO<sub>2</sub> is associated with fetal hypoxia and acidosis, due to reduced uterine blood flow

Group	Maternal	Fetal	APGAR
hyperventilated	pH 7.5 PCO <sub>2</sub> 23	pH 7.34 PO <sub>2</sub> 23	6.9
hypoventilated	pH 7.36 PCO <sub>2</sub> 39	pH 7.29 PO <sub>2</sub> 29	8.4

Peng et al, Br J Anaesth 1972, 44:1173

# CO<sub>2</sub> Targets in Pregnancy

## Permissive hypercapnia

- Very limited data
- Produces fetal acidemia secondary to maternal acidemia, but NOT fetal hypoxemia
- Maternal PaCO<sub>2</sub> of 52 mmHg well tolerated

## Bicarbonate therapy

Crosses the placenta in humans (more so than in animal models)

Hollmen, Acta Anaesth Scan 1972, 221 Ivankovic et al, Am J Obstet Gynecol 1970

## **Less Conventional Ventilation**

Prone positioning
 no data on maternal or fetal effects

Nitric oxide
 little data, case reports in Pulm HTN

### ≻HFO

Recent experience during H1N1

# ➤ ECMO

Significant experience during H1N1

Nair, et al. Intensive Care Med. 2011;37:648-54

# Risks of an ICU stay to the fetus

## Risks of an ICU stay to the fetus

Review of 93 pregnant women admitted to ICU (Mayo Clinic 1995 - 2005)

### Fetal loss

- 1<sup>st</sup> trimester: 65% spontaneous abortion
- 2<sup>nd</sup> trimester: 43% fetal loss
- 3<sup>rd</sup> trimester: 5% fetal loss

### Risk factors for fetal loss:

- Maternal shock
- Maternal transfusion
- Lower gestational age

Cartin-Ceba et al, Crit Care Med 2008; 38:2746

## Risks of an ICU stay to the fetus

## Other potential risks:

- Maternal hypoxia
- Maternal hypotension
- Radiation exposure
- Maternal fever
- Drug therapy
- Maternal cardiac arrest

## H1N1 Winnipeg experience: 6 women with severe H1N1

Table 2. Maternal clinical management	and outcome, n (%)
Need for vasopressors	
Yes	4 (67)
No	2 (33)
Use of hemodialysis	
Yes	2 (33)
Tamiflu	6 (100)
Maternal outcomes	
Death	2 (33)
Survival	4 (67)
latrogenic medical complications	2 (33)

#### Oluyomi-Obi et al. JOGC 2010;32(5):443–447

#### Table 3. Obstetrical and neonatal management and outcome

Obstetric status and outcome		
Gestational age at end of pregnancy (n = 6), weeks	n (%)	
≤14	1 (16.7)	
15–28	1 (16.7)	
≥29	4 (66.6)	
Antenatal complications (n = 6)	n (%)	
Gestational hypertension	1 (16.5)	
PPROM	1 (16.5)	
Preterm labour	1 (16.5)	
Pregnancy outcome (n = 6)	n (%)	
SA	1 (16.7)	
Live birth	4* (66.6)	
Stillbirth	1 (16.7)	
Mode of delivery (n = 5)	n (%)	
SVD	2 (40)	
CS	3 (60)	
NICU admissions	3 (60)	
Length of NICU admission, days,		
Survivors (2)	mean 23.5	
Non-survivors (1)	2	
Neonatal outcomes (n = 4)	n (%)	
Death	1 (25)	
Survival	3 (75)	
Without sequelae of HIE	2 (50)	
With sequelae of HIE	1 (25)	
Evidence of HIE on investigation	2†	

### Sedation & NM blockade

- No completely "safe" drugs
- > Opiates: most OK
- Benzodiazepines: cross placenta, potential problems. We use midazolam, if needed
- Propofol: short term OK? Propofol syndrome in mother and fetus?

Hilton. J Neurosurg Anesthesiol. 2007;19:67-8

- Neuromuscular blockers: cross placenta
- Delivery: warn the neonatologist!

How do we ventilate in pregnancy?

# Is delivery beneficial to the mother?

## Retrospective review

➢ 4 ICUs, 2004 − 2014

#### 29 patients, ventilated while pregnant, >24 hr: Age (yr) 29.0 (±7.7) Gestation at admission (wk) 25.4 (±6.0)

#### **Indication for ICU admission**



# Ventilation during pregnancy

#### **Ventilation**

Ventilation durat	ion (days)	6.0 (± 8.2)
Highest PEEP	(cmH <sub>2</sub> O)	10.9 (± 4.4)
Highest Plateau	pressure (cmH <sub>2</sub> O)	27.3 (± 6.5)

	Day 1	<u>Day 2</u>
Tidal volume		
actual (ml)	446 (± 90)	452 (± 102)
by PBW (ml/kg)	7.9 (± 1.5)	8.1 (± 1.7)
<b>Compliance</b> (ml/cmH <sub>2</sub> O)	21.4 (± 9.2)	22.8 (± 8.6)

#### Distribution of worst blood gases in first 48 hr



Number of patients

#### Effect of Delivery



#### Effects of Delivery (n=10)



# Delivery of the fetus

Given the physiological changes, it may be considered that delivery of the pregnant women with respiratory failure is beneficial to the mother

## **Delivery of the fetus**

Given the physiological changes, it may be considered that delivery of the pregnant women with respiratory failure is beneficial to the mother

### $\succ$ NOT always the case:

- Some oxygenation improvement
- Some change in compliance or PEEP requirement

Tomlinson MW, et al. Obstet Gynecol. 1998; 91:108-11. Mabie WC, et al. Am J Obstet Gynecol 1992; 167:950-7 Lapinsky, et al. Int J Obstet Anesth 2015; 24:323

# **Delivery of the fetus**

## Given the physiological changes, it may be



> Delivery:

Tomlinson MW, et al. Obstet Gynecol. 1998; 91:108-11. Mabie WC, et al. Am J Obstet Gynecol 1992; 167:950-7 Lapinsky, et al. Int J Obstet Anesth 2015; 24:323

- If fetus is viable and at risk due to maternal hypoxia
- NOT purely to improved maternal condition

