WISC 2012 Hyderabad, India 6-9 December

2012 WAO International Scientific Conference

WAO WORLD ALLERGY ORGANIZATION

A World Federation of Allergy Asthma and Clinical Immunology Societies

ANAPHYLAXIS, ASTHMA AND PREGNANCY

SANDRA N. GONZÁLEZ DÍAZ, MD, PhD

FAAAAI, FACAAI, SLAAI 2010-2012

WAO WORLD ALLERGY ORGANIZATION

SLaai Sociedad Latinoamericana de Alergia, Asma e Inmunología

CENTRO REGIONAL DE ALERGIA E INMUNOLOGÍA CLÍNICA

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- Director of the Residency Program in Allergy and Clinical Immunology, Regional Centre of Allergy and Clinical Immunology, University Hospital of Monterrey, NL since 1990
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- Director of Fundraising Department, University Hospital since 2007
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  Past President of the Mexican Association of Allergy and Clinical Immunology (CMICA) 2005-2007
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- Past president UNASMA (International Asthma Foundation) M2007-2011
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- Faculty of Medicine, U.A.N.L 1977-1983. Monterrey, NL Mexico
- Specialty of Internal Medicine, University Hospital, UANL Monterrey, N.L.1986 – 1988
- Fellowship in Pediatric Allergy and Immunology Clíínica, UCSD, University of San Diego, California, USA, 1987-1988
- Subspecialty in Allergy and Clinical Immunology, University Hospital UANL , Monterrey, N. L.1988 – 1990
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UNIVERSIDAD AUTONOMA DE NUEVO LEON
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WAO White Book on Allergy

WORLD ALLERGY ORGANIZATION
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- More than 300 million people have asthma
- Females are 10% more likely than males to be diagnosed as having asthma in their lifetime
- Asthma is the most prevalent chronic disorder to complicate pregnancy
- Asthma affect 3.7 to 12 percent of pregnant women

Pawankar R, Canonica GW, Holgate ST, Lockey RF. WAO White Book on Allergy. 2011

WOMEN WITH ASTHMA

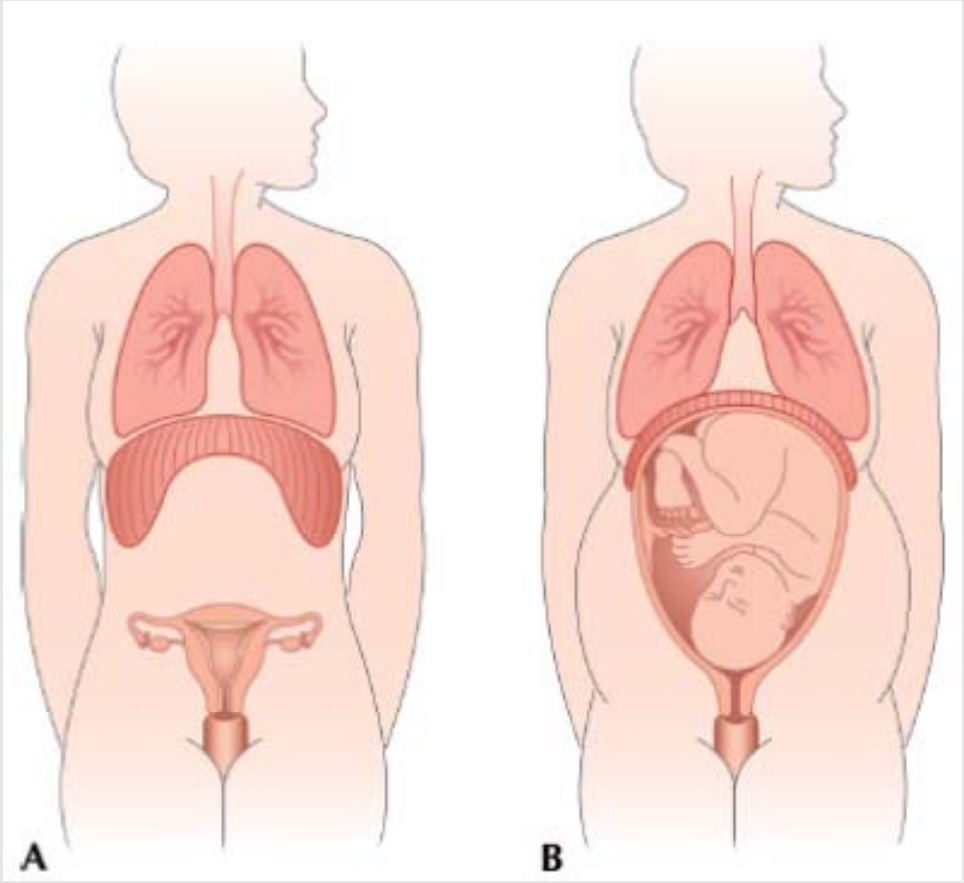
INFLUENCING FACTORS:

- Sex Hormones
- Menstrual cycle
- Pregnancy
- Obesity
- Smoking

Ann Allergy Asthma Immunol. 2006;96:655–665.

PHYSIOLOGICAL CHANGES DURING PREGNANCY

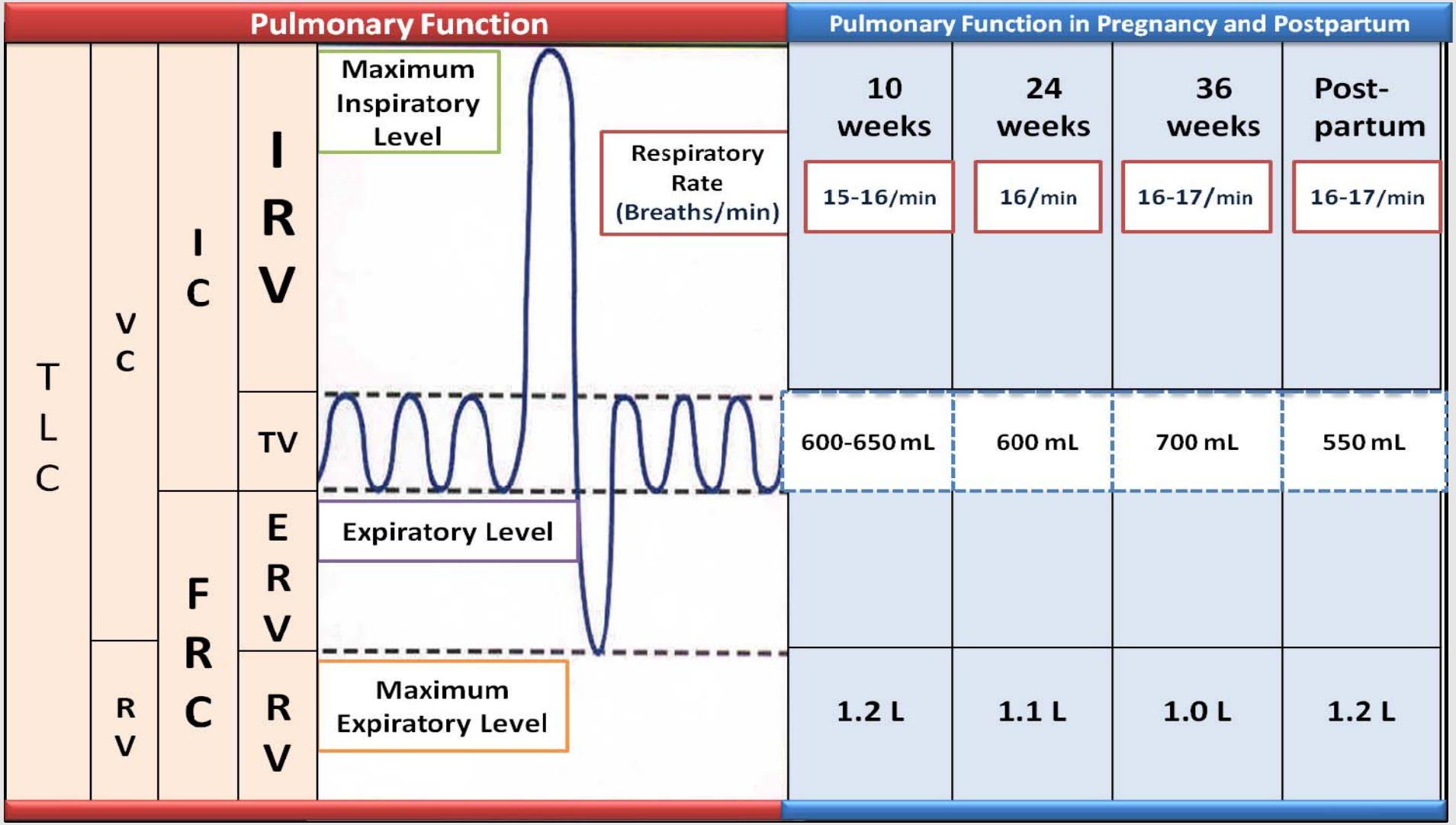
- **The diaphragm is raised 4 cm**
- **The diameter of the rib cage increases 2 cm**
- **The circumference is increased 6 cm**



Uterine enlargement restricts diaphragmatic excursion, reducing residual volume and functional residual capacity

Gluck MD. The Effect of Pregnancy on the Course of Asthma. Immunol Allergy Clin N Am 26 (2006) 63– 80

PULMONARY PHYSIOLOGICAL CHANGES IN PREGNANCY AND POSTPARTUM



Abbreviations: TLC, Total Lung Capacity; VC, Vital Capacity; RV, Residual Volume; IC, Inspiratory Capacity; FRC, Functional Residual Capacity; IVR; Inspiratory Reserve Volume; TV, Tidal Volume; ERV, Expiratory Reserve Volume.

The impact of estrogen and progesterone on asthma

Catherine L. Haggerty, PhD, MPH*; Roberta B. Ness, MD, MPH*; Sheryl Kelsey, PhD*; and Grant W. Waterer, MBBS, FRACP, FCCP†

Ann Allergy Asthma Immunol 2003;90:284–291.

Pregnancy and immunology: selected aspects

G. William Palmer, MD and Henry N. Claman, MD

Ann Allergy Asthma Immunol 2002;89:350–359.

Women with asthma: a review of potential variables and preferred medical management

Nancy K. Ostrom, MD

Ann Allergy Asthma Immunol. 2006;96:655–665.

Gender difference, sex hormones, and immediate type hypersensitivity reactions

- The course of allergic diseases varies unpredictably during pregnancy
- **Estrogens** effects on mast cell activation and allergic sensitization
- **Progesterone** is shown to suppress histamine release but potentiate IgE induction

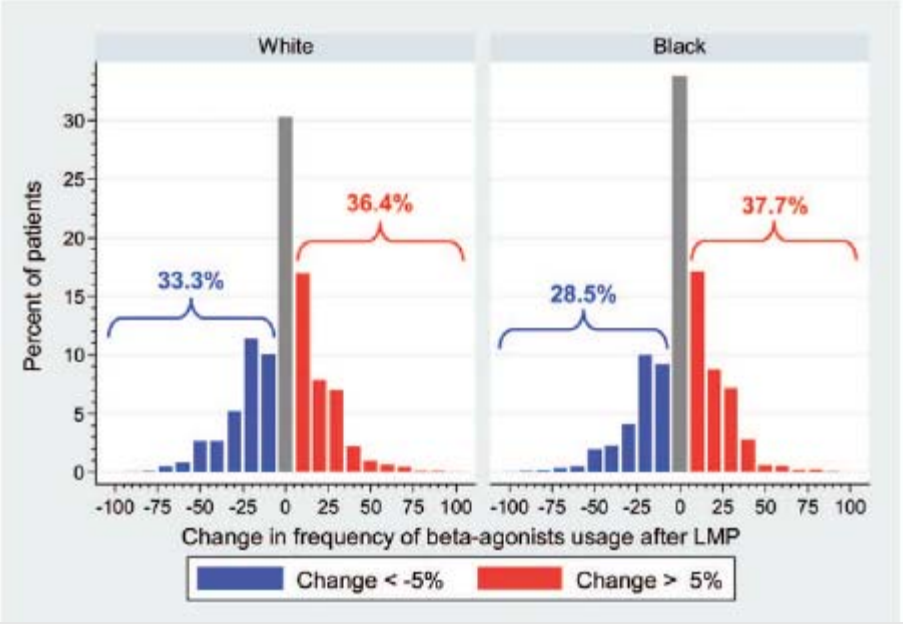
Chen W. et al. Allergy. 2008 Nov;63(11):1418-27.

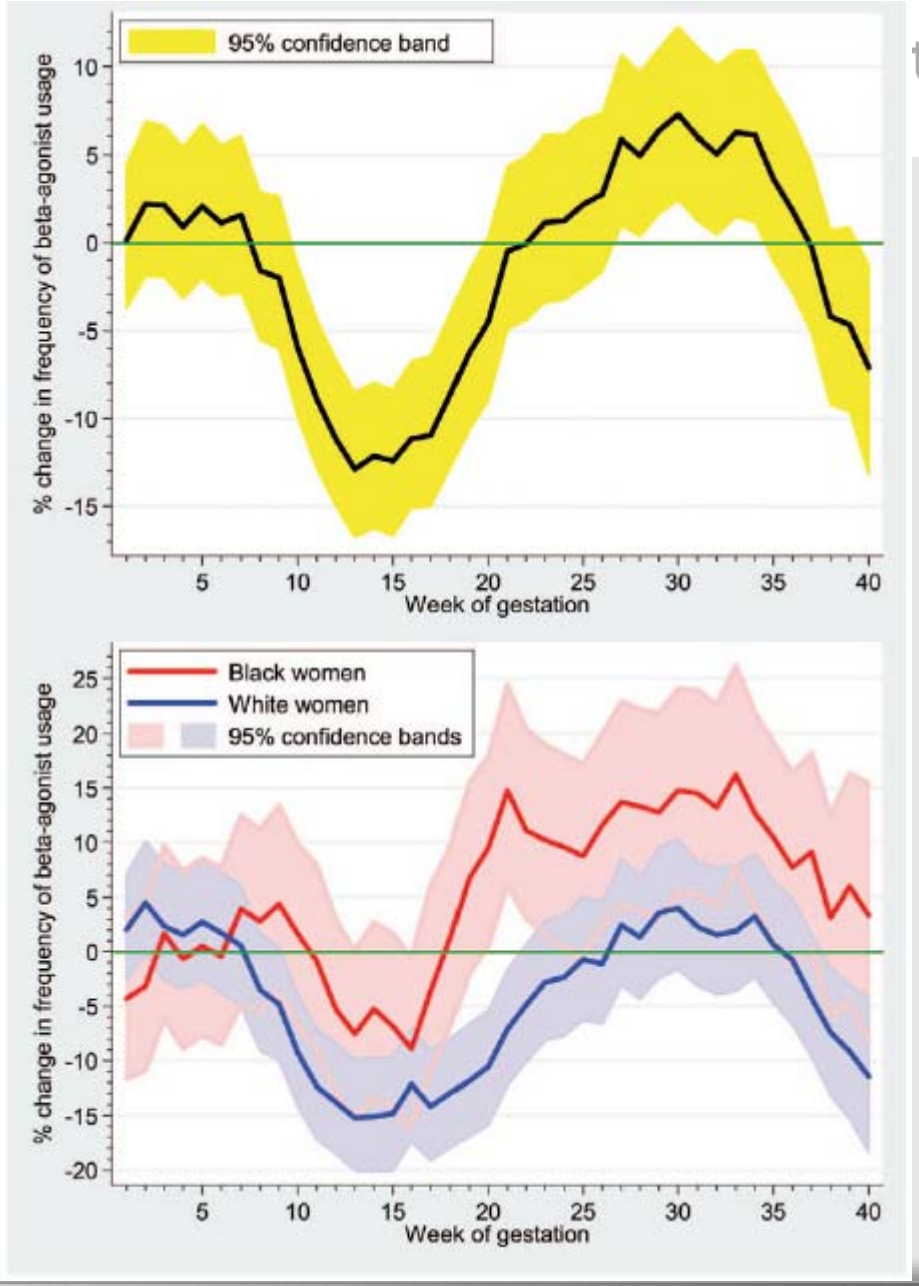
ASTHMA

It is the most common medical issue that can complicate pregnancy

Increased risk
Perinatal mortality
Pre eclampsia
Premature delivery
Low birth weight

NAEPP Expert Panel Report. Managing Asthma During Pregnancy: Recommendations for Pharmacologic Treatment—2004 Update. J ALLERGY CLIN IMMUNOL JANUARY 2005

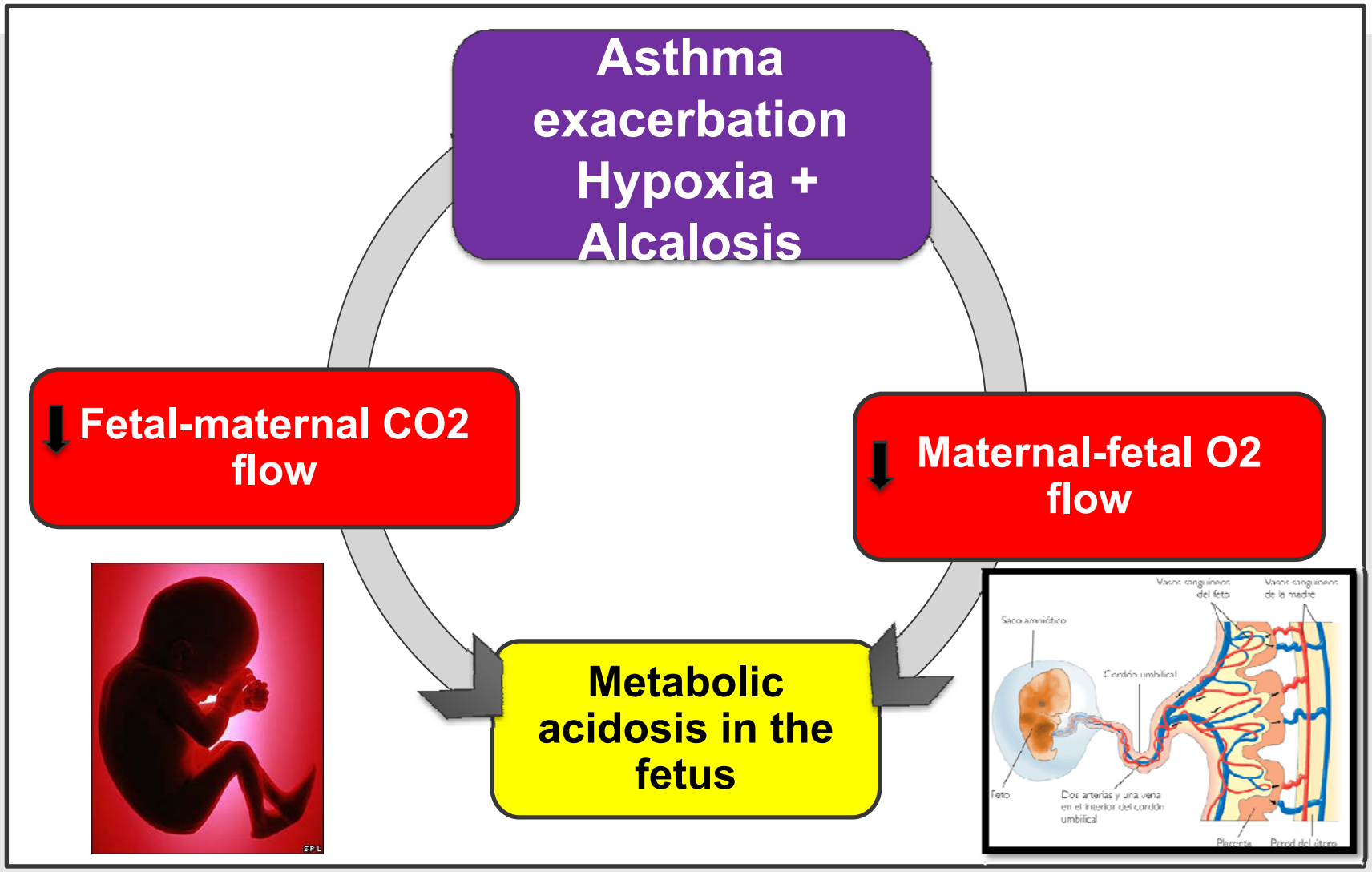




Exacerbations are most likely to occur between weeks 24 and 36, with exacerbations unlikely beyond week 37, including during delivery

Ann Allergy Asthma Immunol 2002;89:350–359

Maternal-fetal risk in asthma exacerbation



J Allergy Clin Immunol 2008;121:1379-84

Uncontrolled asthma and *exacerbations* are potentially dangerous to the fetus

Asthma exacerbations during the first trimester of pregnancy and the risk of congenital malformations among asthmatic women

Lucie Blais, PhD,[a,b] and Amélie Forget, MSc[a,b] *Montreal, Quebec, Canada*

J Allergy Clin Immunol 2008;121:1379-84

Risk of perinatal mortality associated with asthma during pregnancy: a 2-stage sampling cohort study

Marie-Claude Breton, MSc*; Marie-France Beauchesne, PharmD*†; Catherine Lemière, MD, MSc†; Évelyne Rey, MD, MSc‡; Amélie Forget, MSc†; and Lucie Blais, PhD*†

Ann Allergy Asthma Immunol. 2010;105:211–217.

High doses of inhaled corticosteroids during the first trimester of pregnancy and congenital malformations

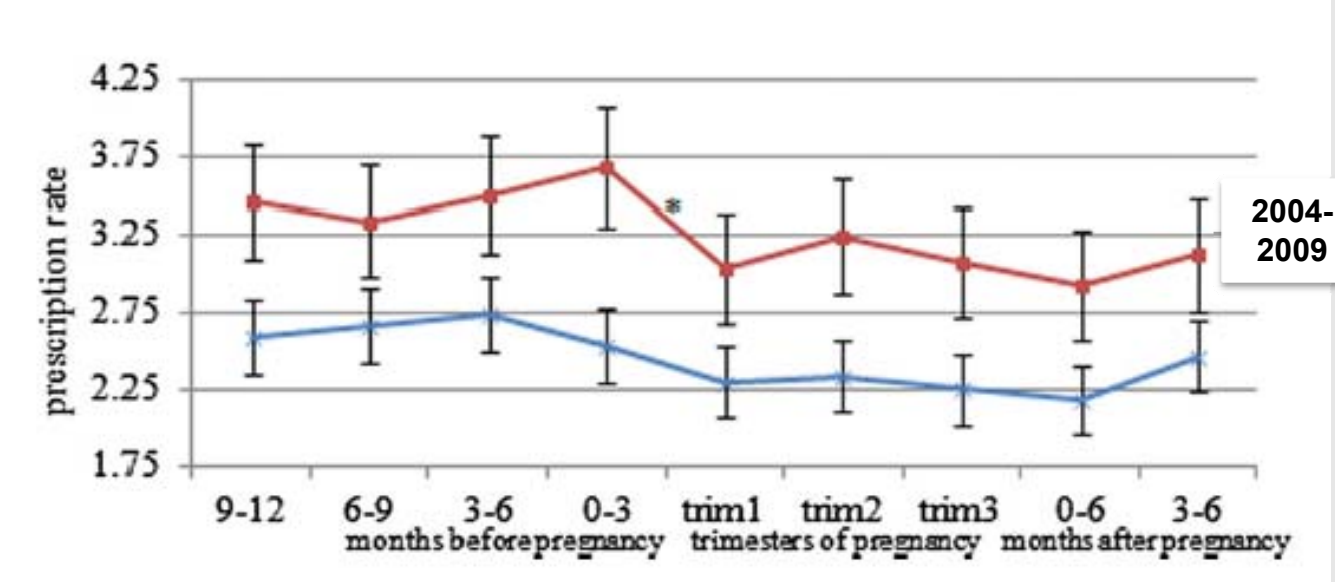
Lucie Blais, PhD,[a,c,d] Marie-France Beauchesne, PharmD,[a,c,d] Catherine Lemière, MD, MSc,[b,c] and Naoual Elftouh, MSc[c] *Montreal, Quebec, Canada*

J Allergy Clin Immunol 2009;124:1229-34

A population analysis of prescriptions for asthma medications during pregnancy

Priscilla A. Zetstra–van der Woude, MSc,[a] J. Sebastiaan Vroegop, MD,[b] H. Jens Bos,[a] and Lolkje T. W. de Jong–van den Berg, Prof Dr[a] *Groningen, The Netherlands*

Some studies indicate that women stop or change their asthma medications when they become pregnant



J Allergy Clin Immunol 2012

KEY POINT OF ASTHMA DURING PREGNANCY

National Asthma Education and Prevention Program

J Allergy Clin Immunol 2005;115:34-46.

- Asthma is considered the most common serious medical problem that could complicate pregnancy
- During pregnancy the severity of asthma often changes.
- The focus of asthma treatment in pregnant women is achieve the control of symptoms and maintenance of normal lung function.
- Poorly controlled of asthma resulting in increased perinatal mortality, increased prematurity and low birth weight.
- Acute exacerbations should be treatment aggressively in order to avoid fetal hypoxia. Treatment should include supplement oxygen, β-2 agonist and systemic corticosteroids.
- The evidence suggests that the risks of uncontrolled asthma are greater than any known risks from medication

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE
NATIONAL ASTHMA EDUCATION AND PREVENTION PROGRAM
ASTHMA AND PREGNANCY WORKING GROUP

QUICK REFERENCE
NAEPP EXPERT PANEL REPORT
Managing Asthma During Pregnancy:

Pharmacologic therapy using stepwise approach to achieve full control of symptoms and maintenance of pulmonary function.

J Allergy Clin Immunol 2005;115:34-46.

ASTHMA MEDICATIONS FOR USE IN PREGNANCY BASED IN FDA CATEGORIES

FDA Category	Drug Group	Active	Dosage (most used)
Pregnancy Category B	ICS	Budesonide	DPI: 200 mcg/inhalation
	Mast cell stabilizer	Cromolyn Nedocromyl	MDI: 1mg/puff MDI: 2mg/puff
	Leukotriene modifier	Montelukast Zafirlukast	4mg granules; 5, 10mg tablets 10, 20mg tablets
	Anticholinergic agents	Ipratropium	MDI: 18mcg/puff
	Anti IgE monoclonan antibody	Omalizumab	150mg/vial
Pregnancy Category C	ICS	Beclomethasone Mometasone Fluticasone Triamcinolone	HFA: 40 or 80 mcg/puff DPI:50, 100, 250mcg/inhalation 100mcg/puff
	Leikotriene modifier	Zileuton	600mg tablets
	Methylxanthines	Theophylline	100, 200, 300, 400 mg capsules extended release 125mg, 250mg tablets
	Short-acting β2- adrenergic agonist	Albuterol	MDI: 90mcg/puff
	Long-acting β2- adrenergic agonist	Formoterol Salmeterol	DPI: 9mcg/inhalation; 12mcg capsules MDI: 21mcg/puff; DPI: 50mcg/blister
	Combination products	Fluticasona/ Salmeterol	DPI: 100/50, 250/50, 500/50 mcg/blister

Abbreviation: FDA, Food and Drug Administration; ICS, Inhaled Corticosteroids; DPI, Dry Powder Inhaler; MDI, Metered Dose Inhaler; HFA, Hydrofluoroalkane; mg, milligrams; mcg, micrograms.

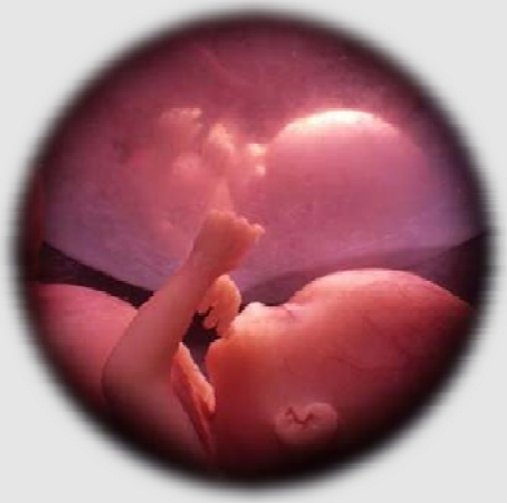
Gluck. Asthma Controller therapy during Pregnancy. Am J Obstetrics & Ginecology. No 192 January 2005

Asthma Severity	Mild Intermitent Asthma	Mild Persistent Asthma	Moderate Persistent Asthma	Severe Persistent Asthma	Exacerbated asthma during pregnancy
Symptoms /Day	≤ 2 days/week	> 2 days/week but < daily	Daily	Continual	•Oxygen flow to maintain O2 Saturation ≥ 95%
Symptoms /Night	≤ 2 nighst/month	> 2 nights/month	> 1night/week	Frequent	•Inhaled short acting β2-agonist every 20 min in firts hour
Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited	• Systemic (oral or IV) CS
PEF o FEV1 PEF Variability	≥ 80% < 20%	≥ 80% 20-30%	>60% - <80% >30%	≤ 60% >30%	•Add albuterol plus inhaled ipratropium in moderate-severe exacerbation
Steps of Recomendation	**Step 1**	**Step 2**	**Step 3**	**Step 4**	•Maintain continuous mathernal-fetal monitoring until patient stabilized
Drugs options recommended	Short acting inhaled β2-agonist as needed	Prefered: Low-doses ICS* Alternative treatment: cromolyn, Leukotriene receptor antagonist or sustained-release theophyline§	Prefered treatment: Either Low-doses ICS* and Long-acting inhaled β2- agonist OR Medium doses ICS* OR Medium doses ICS* and Long-acting inhaled β2- agonist Alternative treatment: Low-doses ICS* and either Theophyline§ or Leukotriene receptor antagonist OR Medium-doses ICS* and either Theophyline§ or Leukotriene receptor antagonist	Prefered treatment: High doses ICS* and Long-acting inhaled β2- agonist and if needed Oral corticosteroid Alternative treatment: High doses ICS and sustained release Theophyline§	•Re evaluate, categorized and act •Discharge home giving patient education and written action plan •Continue course of oral systemic corticosteroid, and start ICS* or increase dose for patients on ICS*
Patient education and enviromental control in all steps of treatment					
Levels of Asthma Control§	**Controlled**	**Partly controled**		**Very poorly controlled**	
Gradual stepwise reduction up to maintain the smallest step that achieves symptoms control		If control is not maintained, consider step up			
Quick Reliefe (All patients)	Short-acting bronchodilatador: 2-4 puff short-acting inhaled β2-agonist, up to 3 treatment at 20-minutes intervals. Course of systemic corticosteroid may be needed. Increasing use of short-acting inhaled β2-agonist may indicate the need to initiate (increase) Long-term control therapy.				Maintain contac with clinician for follow up intructions

ANAPHYLAXIS DURING PREGNANCY

- The true incidence of anaphylaxis during pregnancy is unknown

- Anaphylaxis during pregnancy, labor, and delivery can be catastrophic for the mother and, especially, the infant



Patient

- **Case: Anaphylactic shock in a pregnant women with untreated asthma**

- K.A.C.
- Female
- 29 years old
- Pregnancy of 18 weeks gestation
- Emergency Department
- University Hospital
- Monterrey, Mexico.

Admission to emergency department

- She was cleaning the home and feels multiple ant bites on her arms and legs.

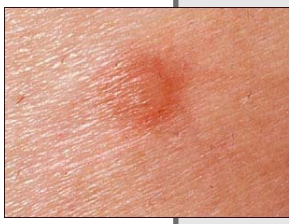
- **Immediately presented**:
- Generalized intching
- Cough and sore throat
- Difficulty breathing
- Dizziness
- Nausea

Admission Patient conditions

- Blood Pressure 80/40 mmHg
- Hearth rate 117 x min
- Breath Rate 24 x min
- Temperature 36.5 °C
- O2 Saturation: 90%

Weight: 112 kg
Height: 1.61 m
CMI: 43.2 kg/m2

Skin: Approximately 12-15 erythematous papules with central pustule in arms and legs, with aedema, pain and generalized intching.
Respiratory: bilateral diffuse wheezing
Gastrontestinal: nausea
Cardiovascular system: hypotension, tachycardia.
Central Nervous System: Anxious, dizziness and confusion.



Anaphylaxis during pregnancy

F. Estelle R. Simons, MD, FRCPC,[a] and Michael Schatz, MD, MSc[b] *Winnipeg, Manitoba, Canada, and San Diego, Calif*

TABLE II. Clinical criteria for diagnosis of anaphylaxis during pregnancy

Anaphylaxis is highly likely when any 1 of the following 3 criteria is fulfilled:

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized urticaria, itching or flushing, swollen lips-tongue-uvula)

AND at least 1 of the following:

1. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced peak expiratory flow, hypoxemia)
2. Reduced blood pressure or associated symptoms of end-organ dysfunction (eg, hypotonia [collapse], syncope, incontinence)

OR

2. Two or more of the following that occur rapidly after exposure to *a likely allergen* for that patient* (minutes to several hours):
   1. Involvement of the skin-mucosal tissue (eg, generalized urticaria, itch-flush, swollen lips-tongue-uvula)
   2. Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, hypoxemia)
   3. Reduced blood pressure or associated symptoms (eg, hypotonia [collapse], syncope, incontinence)
   4. Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting)

OR

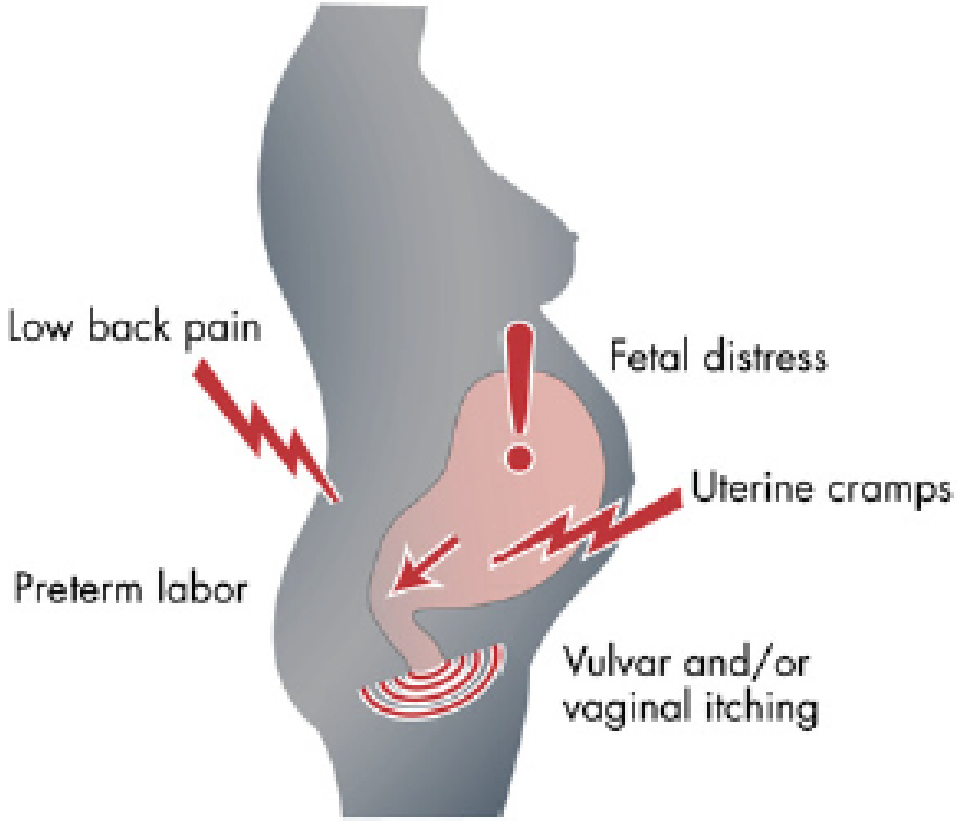
3. Reduced blood pressure after exposure to *known allergen* for that person* (minutes to several hours) defined as systolic blood pressure of <90 mm Hg or >30% decrease from that person's baseline value†‡

TABLE III. Symptoms and signs of anaphylaxis during pregnancy

Skin, subcutaneous tissue, and mucosa*†
Flushing, itching, urticaria (hives), angioedema, morbilliform rash, pilor erection
Periorbital itching, erythema, edema, conjunctival erythema, tearing
Itching and/or swelling of lips, tongue, palate, uvula, external auditory canals, palms, and soles
Respiratory*
Nasal itching, congestion, rhinorrhea, sneezing
Throat itching, tightness, dysphonia, hoarseness, dry staccato cough, stridor
Lower airways: increased respiratory rate, shortness of breath, chest tightness, deep cough, wheezing
Cyanosis
Respiratory arrest
Gastrointestinal*
Abdominal pain, dysphagia, nausea, vomiting (stringy mucus), diarrhea
Cardiovascular system*
Chest pain
Tachycardia, bradycardia (less common), other dysrhythmias, palpitations
Hypotension, feeling faint, incontinence, shock
Cardiac arrest
Central nervous system*
Aura of impending doom, uneasiness; headache (before epinephrine), altered mental status, dizziness, confusion, tunnel vision, loss of consciousness
Other*
Intense itching of the vulvar/vaginal regions, uterine cramps, low back pain, **fetal distress, preterm labor**
Metallic taste in mouth

Simons E, Schatz M. Anaphylaxis during pregnancy. J Allergy Clin Immunol 2012

Potential symptoms and signs of anaphylaxis during pregnancy



Simons E, Schatz M. Anaphylaxis during pregnancy. J Allergy Clin Immunol 2012

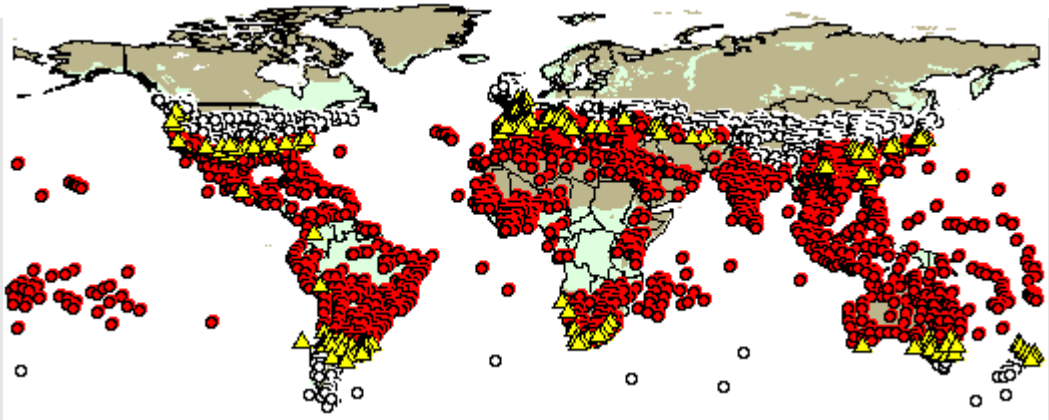
TRIGGERS

TABLE I. Etiology of anaphylaxis during pregnancy

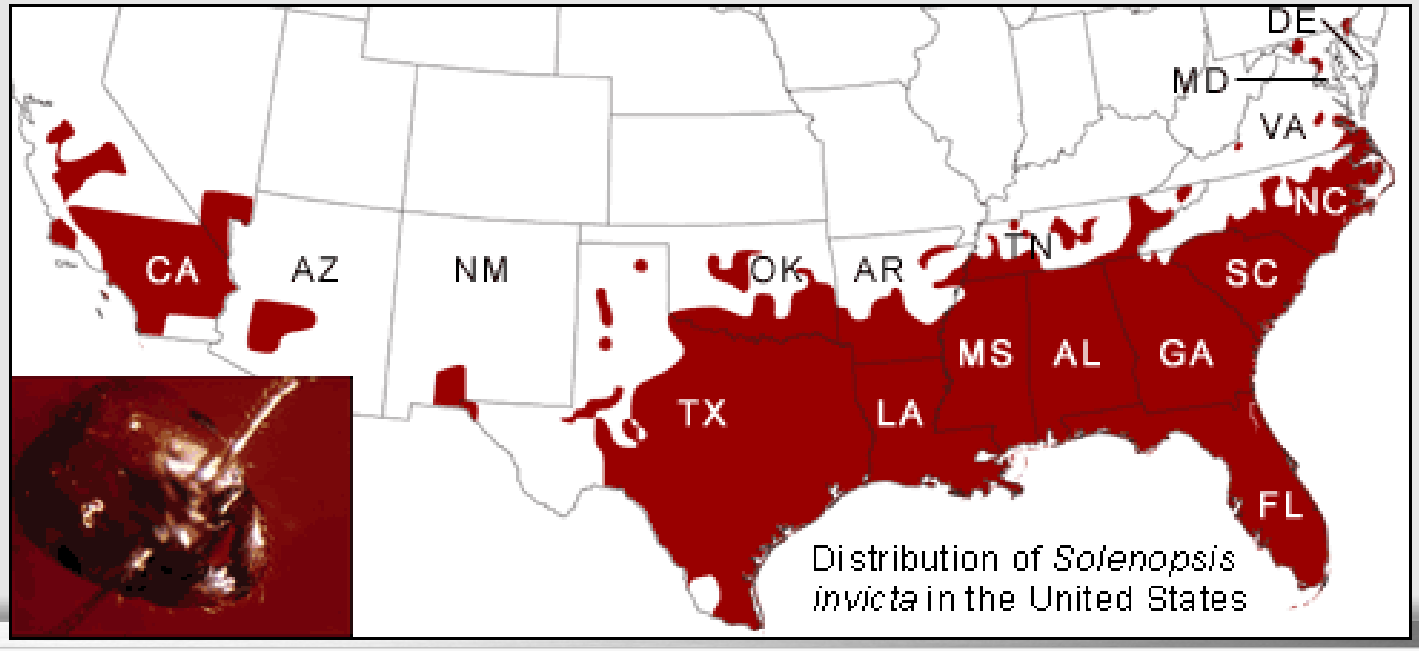
First 3 trimesters, before labor and delivery
Foods
Stinging insect venoms
Medications*
Biologic agents, including allergen immunotherapy
NRL
Other†
Labor and delivery
Antibiotics‡
NRL
Neuromuscular blockers
Oxytocin
Local anesthetics
Transfusion of blood or blood products

F. Estelle R. Simons, Ledit R. F. Ardusso et al J Allergy Clin Immunol 2011;127:587-93

Potential global range expansion of the invasive fire ant

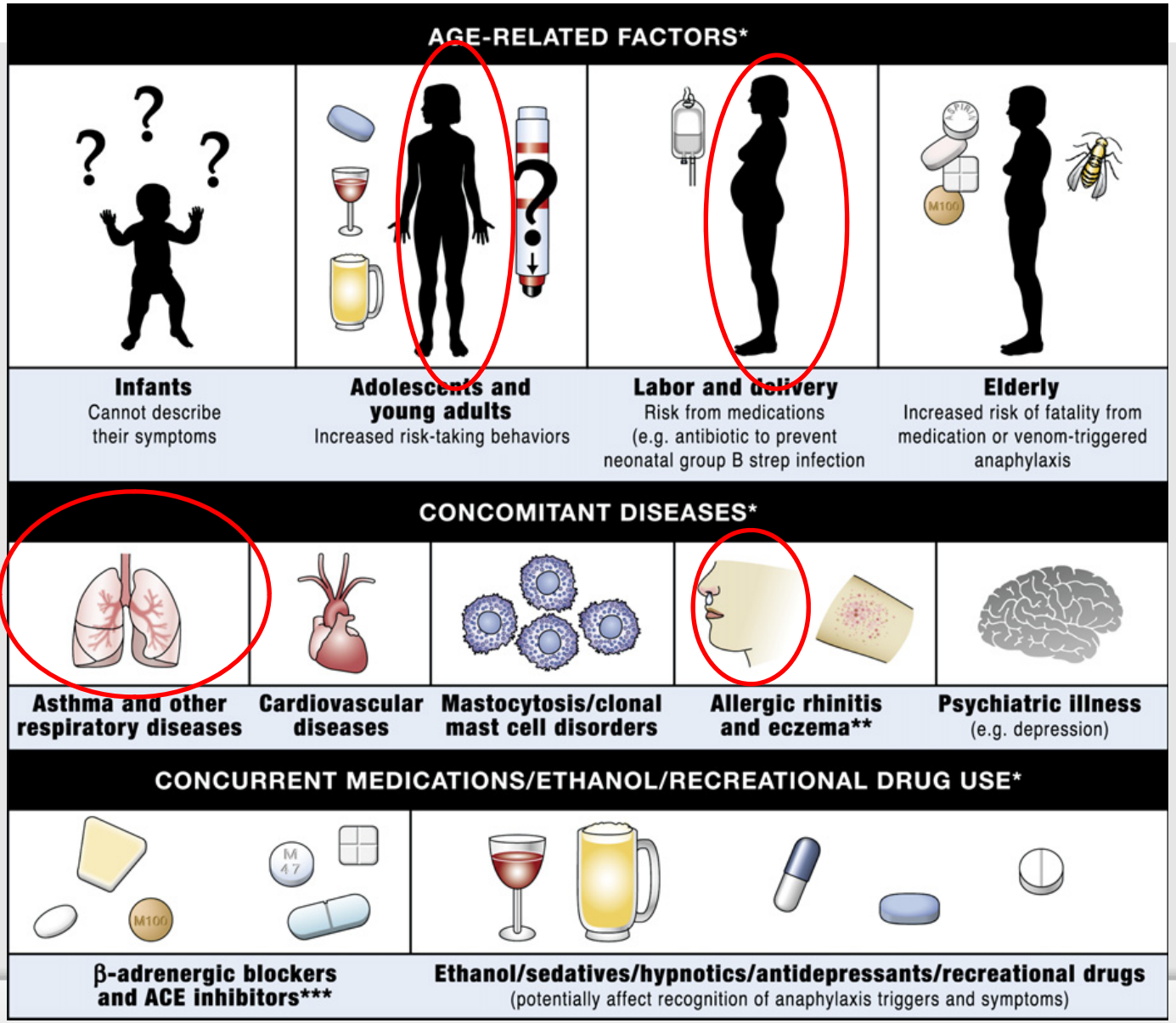


***S. invicta* populations are limited by arid conditions as well as cold temperatures.**



Morrison, L.W., S.D. Porter, E. Daniels, and M.D. Korzuhkin. Potential global range expansion of the invasive fire ant, Solenopsis invicta. Biological Invasions 6: 183-191. 2004

Factors associated with severity and fatality



F. Estelle R. Simons, Ledit R. F. Ardusso et al J Allergy Clin Immunol 2011;127:587-93

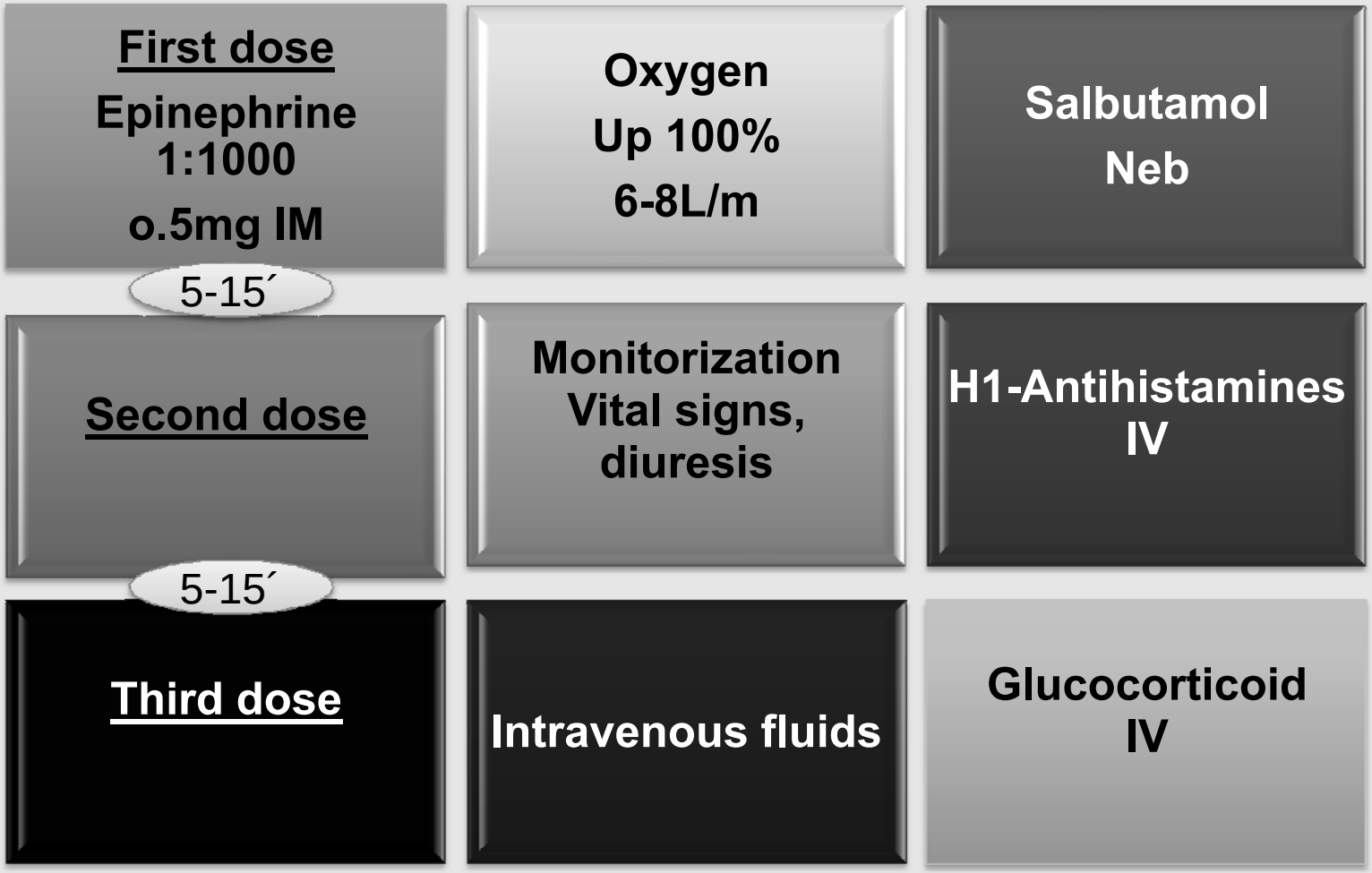
TABLE IV. Differential diagnosis of anaphylaxis during pregnancy

A. First 3 trimesters, before labor and delivery
Common diagnostic dilemmas, such as acute asthma, acute generalized urticaria, acute angioedema, syncope/fainting, panic attack, acute anxiety attack
Postprandial syndromes, such as scombroidosis, pollen-food allergy syndrome (oral allergy syndrome), monosodium glutamate reaction, sulfite reaction, food poisoning
Upper airway obstruction (other forms), such as nonallergic angioedema (no accompanying urticaria or itching): includes hereditary angioedema types I, II and III
Shock (other forms), such as hypovolemic, septic, cardiogenic
Nonorganic diseases, such as vocal cord dysfunction, hyperventilation, psychosomatic episode, Munchausen stridor
Other: excess endogenous histamine, such as mastocytosis/clonal mast cell disorder; flush syndromes, such as carcinoid syndrome; certain tumors; system capillary leak syndrome
B. Labor and delivery
Pulmonary embolism (thrombotic) and pulmonary edema
Cardiac conditions (acquired and congenital)*
Hypotension caused by spinal block, local anesthetic, or hemorrhage, for example, secondary to abruptio placentae or uterine rupture
Cerebrovascular accident
AFE
Preeclampsia/eclampsia-associated symptoms, such as laryngopathia gravidarum and seizures
Other

Simons E, Schatz M. Anaphylaxis during pregnancy. J Allergy Clin Immunol 2012

Basic management of anaphylaxis

J Allergy Clin Immunol 2012



Place the woman in her left side and elevate her lower extremities

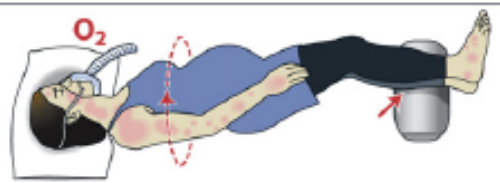
Treatment of anaphylaxis during pregnancy

1) Have a written emergency protocol for anaphylaxis recognition and treatment.
2) Remove exposure to the trigger, if possible, e.g. discontinue an intravenous medication.
3) Assess circulation, airway, breathing, mental status, skin, and body weight (mass).
4) Call for help: resuscitation team (hospital) or emergency medical services (community).

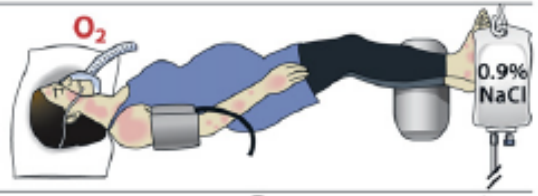
5) Inject epinephrine (adrenaline) 0.3 mg intramuscularly in the mid-outer thigh.

6) Give high-flow supplemental oxygen.

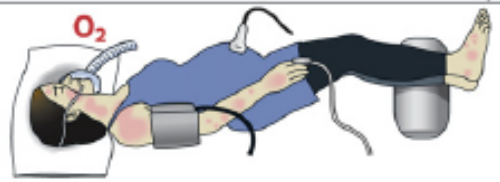
7) Position the mother on her left side, and elevate her lower extremities.



8) Maintain a minimum maternal systolic blood pressure of 90 mm Hg, to ensure adequate placental perfusion.



9) Continuously monitor maternal heart rate, blood pressure, oxygenation, and fetal heart rate (electronically).



10) When indicated, perform cardiopulmonary resuscitation with continuous chest compressions and rescue breathing.

11) When indicated, perform emergency Cesarean delivery.

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G & O Evaluation

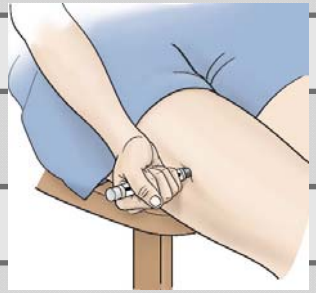
- Obstetric ultrasound
- Continuous Electronic Fetal Monitoring

Report:

- Fetal viability
- Heart rate and fetal movement
- No uterine contractions
- Placenta integrates

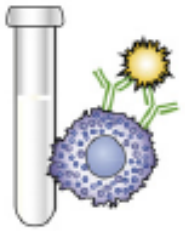
Evolution and discharge

- Good response to treatment
- Normal vital signs and fetal monitoring
- Remained under observation at least 24 hours
- Written Emergency Plan
- EPIPEN prescribing
- Tracking allergist's office



Anaphylaxis during pregnancy: Risk assessment and risk reduction

Confirm anaphylaxis trigger(s)

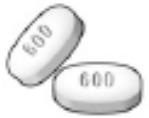


Measure allergen-specific IgE

DEFER allergen skin tests, if possible

Avoidance and immunomodulation

Avoid known allergens



DEFER medication desensitization; if possible, substitute drug from different class

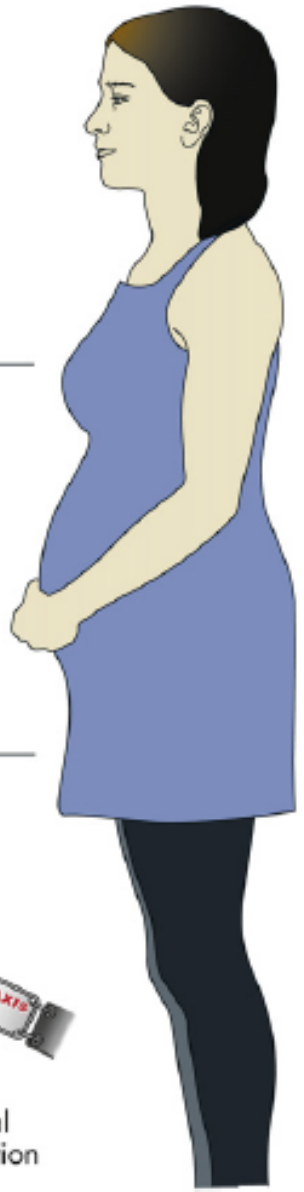
DEFER initiation of allergen immunotherapy; if possible, continue maintenance immunotherapy without dose increases

Emergency preparedness

Epinephrine autoinjector and training for use

Anaphylaxis emergency action plan; education

Medical identification



Simons E, Schatz M. Anaphylaxis during pregnancy. J Allergy Clin Immunol 2012

Conclusions

- Asthma is considered the most common serious medical problem that could complicate pregnancy
- Anaphylaxis during pregnancy, labor, and delivery can be catastrophic for the mother and, especially, the infant.
- Allergy/immunology specialists should play an important role in the prevention of anaphylaxis and asthma in pregnancy
- Prospective interdisciplinary studies of anaphylaxis and asthma during pregnancy are needed.