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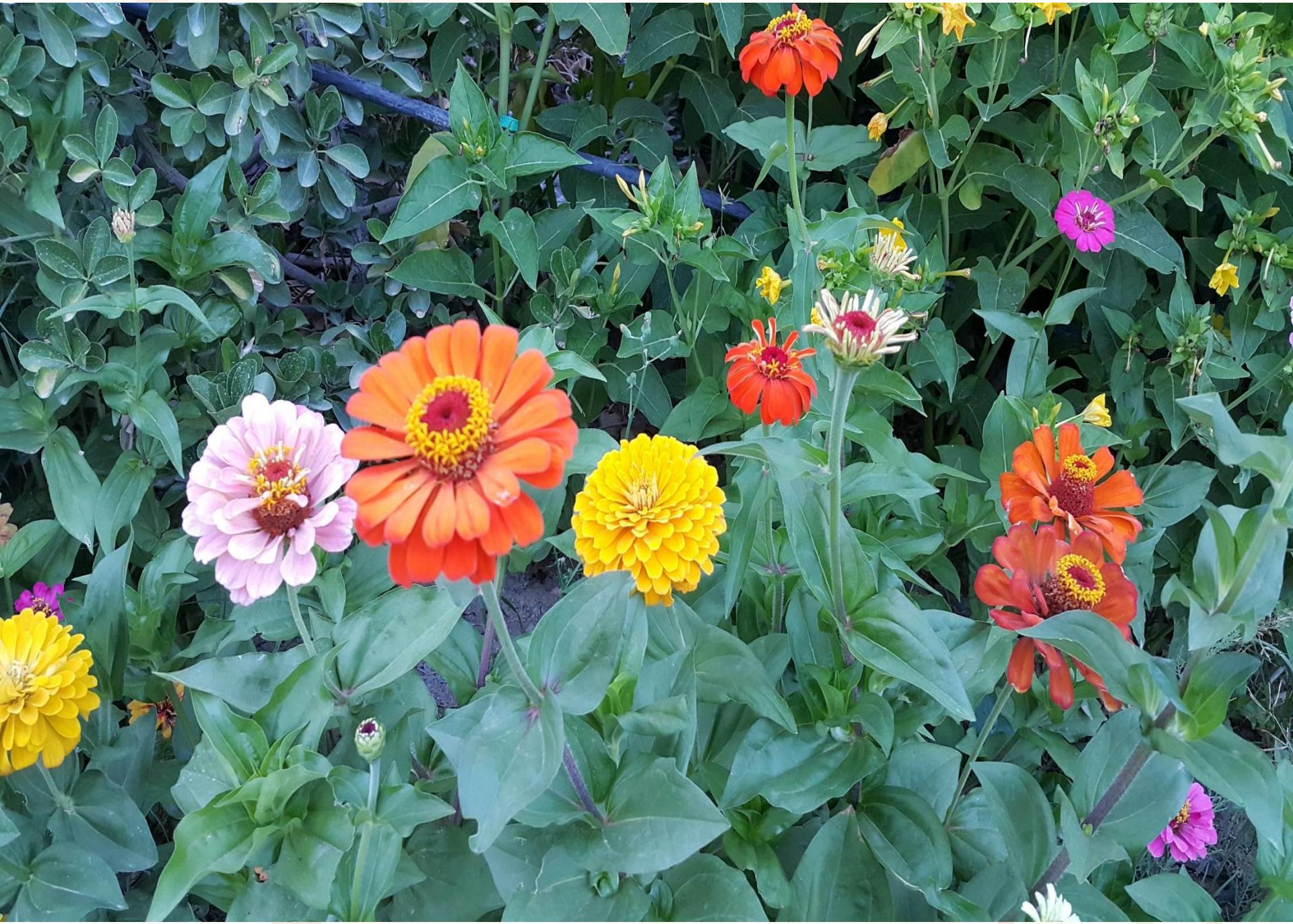


Hypertension in Pregnancy

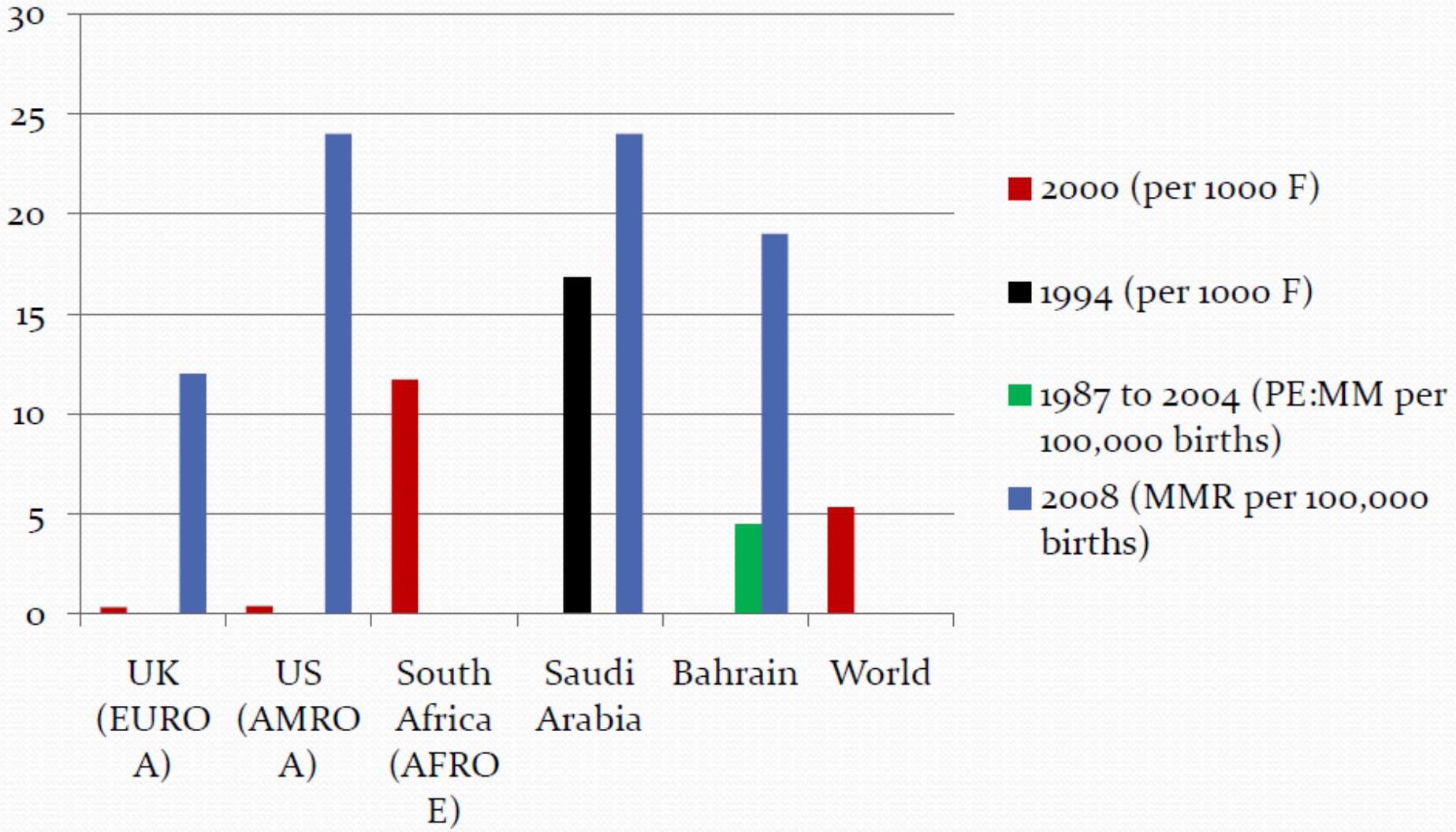
Dr. Mahboubeh Valiani

Assistant Professor of IUMS

Definition & Etiology

- Complicates 10-20% of pregnancies
- Elevation of BP ≥140 mmHg systolic and/or ≥90 mmHg diastolic, on two occasions at least 6 hours apart.

Preeclampsia – Incidence



Incidence

3% of pregnancies.

– Epidemiology

More common in primigravida

There is 3-4 fold increase in first degree relatives of affected women.

Preeclampsia - Definition

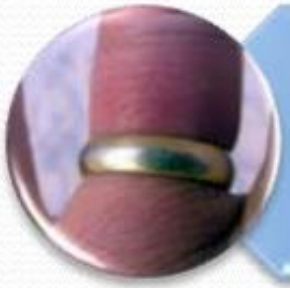
- Presence of

Hypertension

- SBP ≥ 140 or DBP ≥ 90
- 2 readings 6 hours apart
- > 20/52 gestation

Proteinuria

- ≥ 1+ Urine dipstick (not sensitive)
- ≥ 300 mg / 24



Nondependent Edema

- Hand
- Face
- Not sensitive or specific

Categories

- Chronic Hypertension
- Gestational Hypertension
- Preeclampsia
- Preeclampsia superimposed on Chronic Hypertension

Hypertension in Pregnancy

Hypertension in Pregnancy

>140 or 90 mmHg
2 consecutive times 6 hours apart
Pregnant patient

Pregnancy Induced Hypertension

>20/52

Chronic Hypertension

<20/52

Gestational Hypertension

-ve protrinuria

Preeclampsia

+ proteinuria (≥300mg/24 or 1+)
+/- nondependant edema (face & hands)

Eclampsia

+ unexplained grand mal seizures

Conception

1st Trimester Miscarriage

Pre-eclampsia

Prematurity

1st Trimester >> 2nd Trimester >> 3rd Trimester

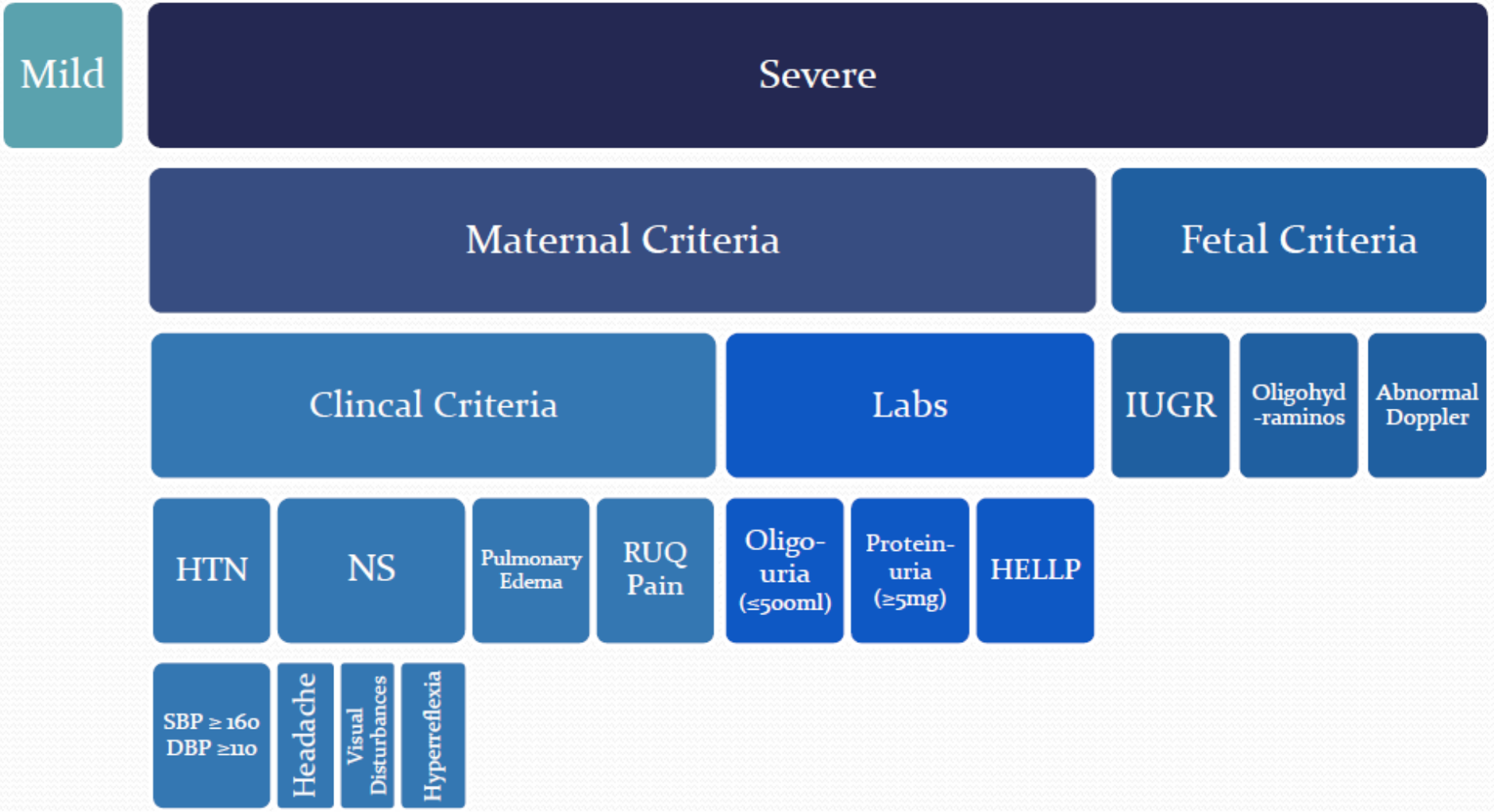
Implantation

2nd Trimester Miscarriage

Growth restriction

Still Birth

Preeclampsia - Classification



Preeclampsia

- Definition = New onset of hypertension and proteinuria after 20 weeks gestation.
  - Systolic blood pressure ≥140 mmHg OR diastolic blood pressure ≥90 mmHg
  - Proteinuria of 0.3 g or greater in a 24-hour urine specimen
  - Preeclampsia before 20 weeks, think MOLAR PREGNANCY!
- Categories
  - Mild Preeclampsia
  - Severe Preeclampsia
- Eclampsia
  - Occurrence of generalized convulsion and/or coma in the setting of preeclampsia, with no other neurological condition.

Preeclampsia

- **Severe Preeclampsia must have one of the following:**
  - **Symptoms of central nervous system dysfunction = Blurred vision, scotomata, altered mental status, severe headache**
  - **Symptoms of liver capsule distention = Right upper quadrant or epigastric pain**
  - **Nausea, vomiting**
  - **Hepatocellular injury = Serum transaminase concentration at least twice normal**
  - **Systolic blood pressure ≥160 mm Hg or diastolic ≥110 mm Hg on two occasions at least six hours apart**
  - **Thrombocytopenia = <100,000 platelets per cubic millimeter**
  - **Proteinuria = 5 or more grams in 24 hours**
  - **Oliguria = <500 mL in 24 hours**
  - **Severe fetal growth restriction**
  - **Pulmonary edema or cyanosis**
  - **Cerebrovascular accident**

Chronic Hypertension

- "Preexisting Hypertension"
- Definition
  - Systolic pressure ≥ 140 mmHg, diastolic pressure ≥90 mmHg, or both.
  - Presents before 20th week of pregnancy or persists longer then 12 weeks postpartum.
- Causes
  - Primary = "Essential Hypertension"
  - Secondary = Result of other medical condition (ie: renal disease)

Prenatal Care for Chronic Hypertensives

- Electrocardiogram should be obtained in women with long-standing hypertension.
- Baseline laboratory tests
  - Urinalysis, urine culture, and serum creatinine, glucose, and electrolytes
  - Tests will rule out renal disease, and identify comorbidities such as diabetes mellitus.
  - Women with proteinuria on a urine dipstick should have a quantitative test for urine protein.

Treatment for Chronic Hypertension

- **Avoid treatment in women with uncomplicated mild essential HTN as blood pressure may decrease as pregnancy progresses.**
- **May taper or discontinue meds for women with blood pressures less than 120/80 in 1st trimester.**
- **Reinstitute or initiate therapy for persistent diastolic pressures >95 mmHg, systolic pressures >150 mmHg, or signs of hypertensive end-organ damage.**
- **Medication choices = Oral methyldopa and labetalol.**

Gestational Hypertension

- Mild hypertension without proteinuria or other signs of preeclampsia.
- Develops in late pregnancy, after 20 weeks gestation.
- Resolves by 12 weeks postpartum.
- Can progress onto preeclampsia.
  - *Often when hypertension develops <30 weeks gestation.*
- Indications for and choice of antihypertensive therapy are the same as for women with preeclampsia.

Preeclampsia superimposed on Chronic Hypertension

- Affects 10-25% of patients with chronic HTN
- Preexisting Hypertension with the following additional signs/symptoms:
  - **New onset proteinuria**
  - **Hypertension and proteinuria beginning prior to 20 weeks of gestation.**
  - **A sudden increase in blood pressure.**
  - **Thrombocytopenia.**
  - **Elevated aminotransferases.**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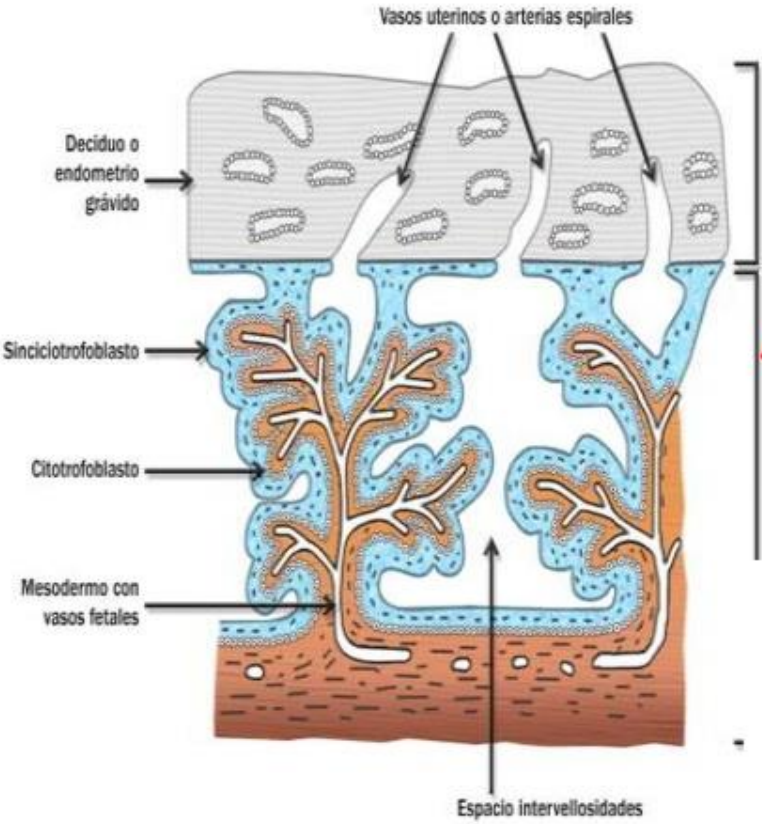
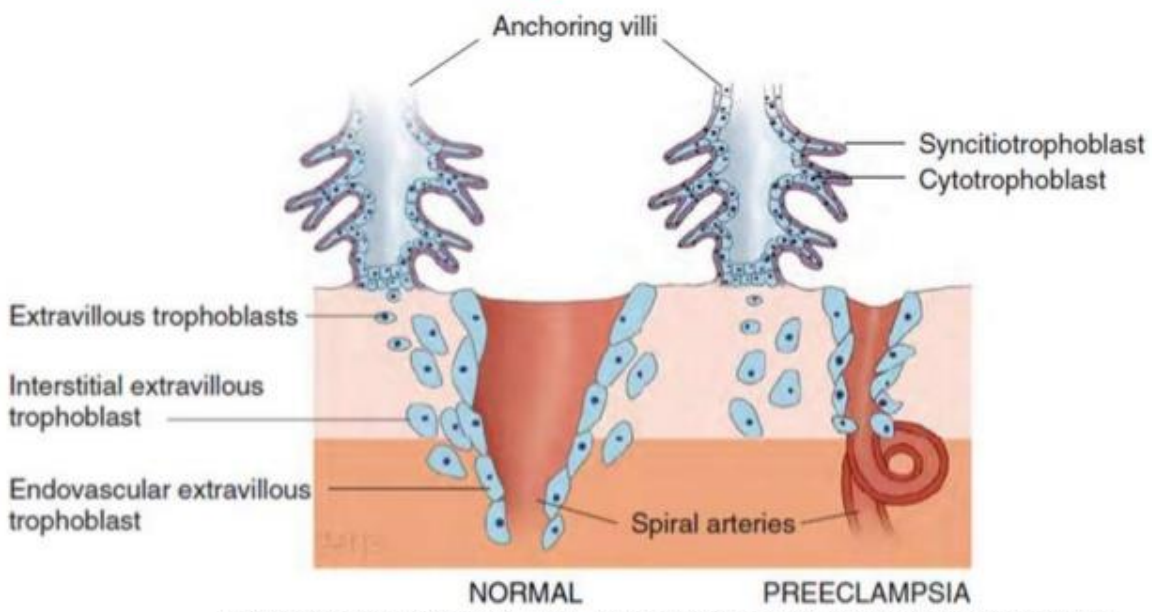
Preeclampsia – Pathology (1)

- Vascular Theory
  - Poorly perfused placenta
    - Abnormal placentation
    - Maternal microvascular disease
    - 'Relative': due to hyperplacentosis
  - → placental ischemia
  - → release of factors by placenta
  - → cascade
  - → damage maternal vascular endothelium

Síndromes Hipertensivo del Embarazo

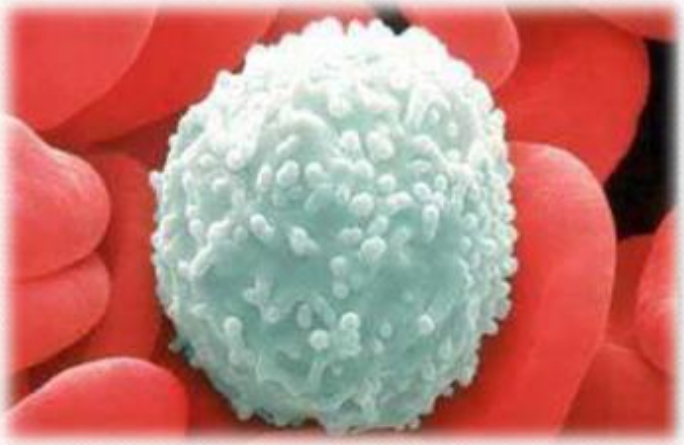


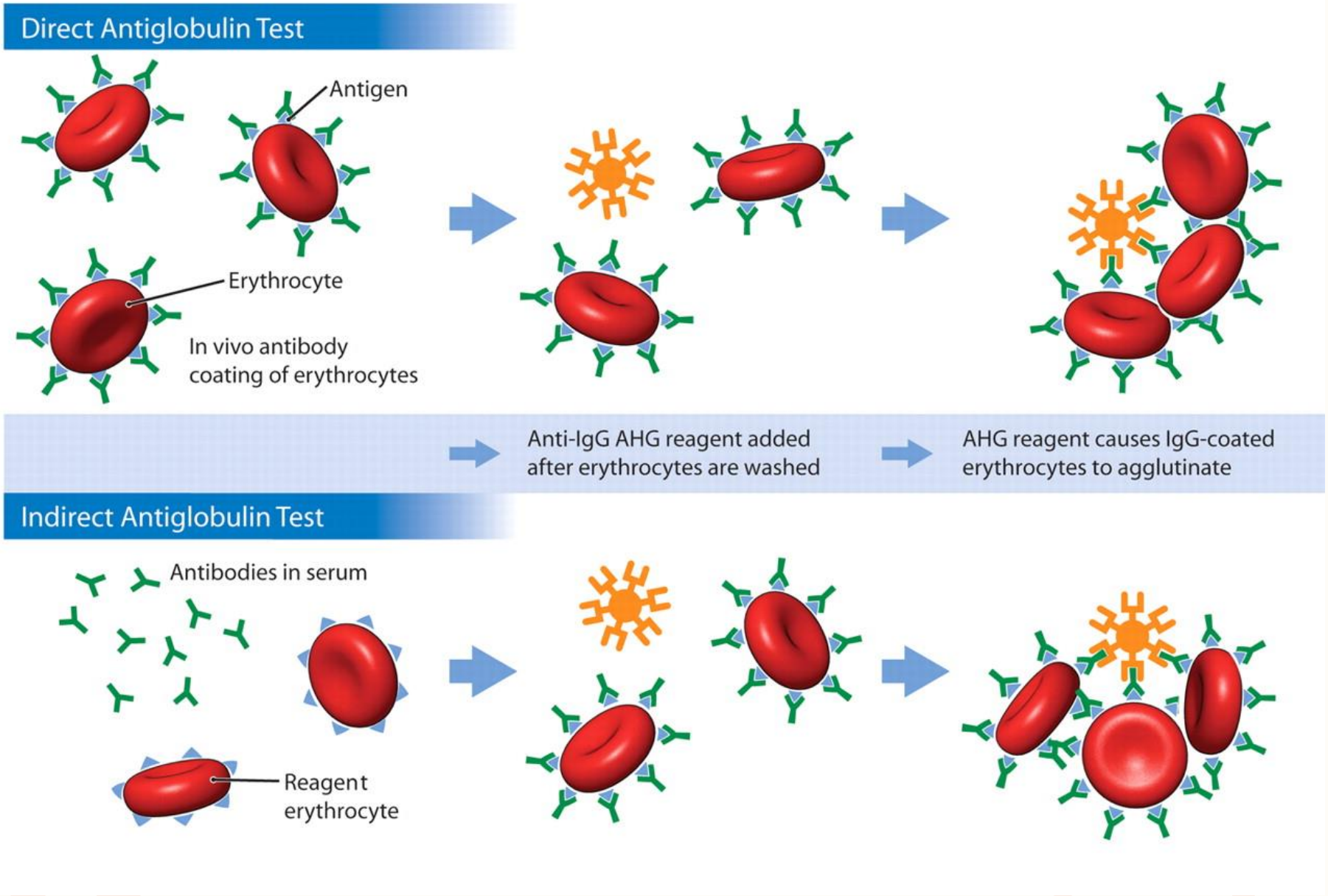


MINISTERIO DE SALUD Normativa — 109. Guía de intervenciones basada en evidencias que reducen morbilidad y mortalidad perinatal y neonatal , Nov 2014.. Tratado de cuidados criticos y Emergencia

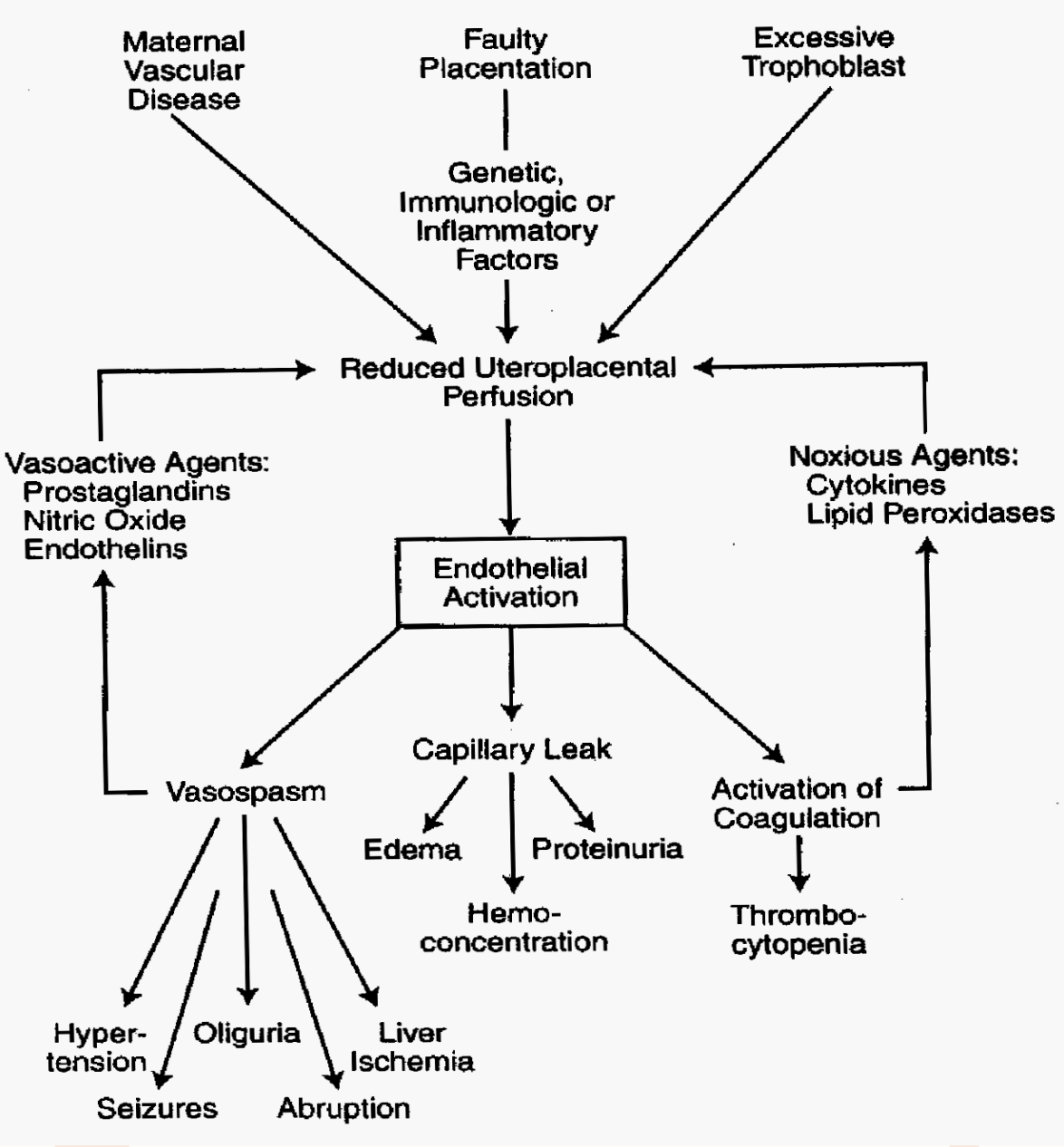
Preeclampsia – Pathology (2)

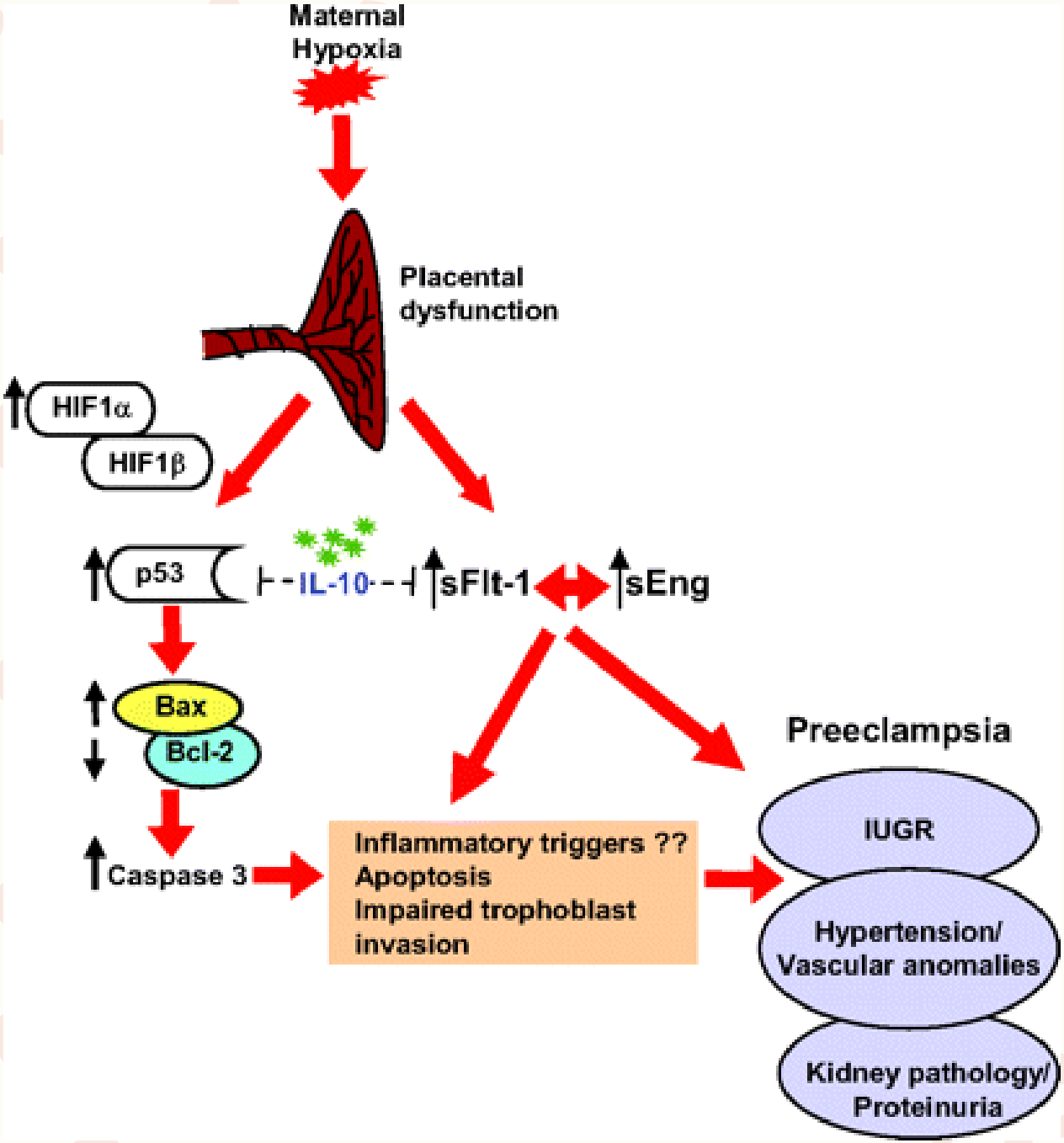
- Alloimmune Theory
  - Sperm exposure
  - → mucous alloimmunization
  - → cascade (≈ classical inflammatory response)
  - → inhibition of placentation

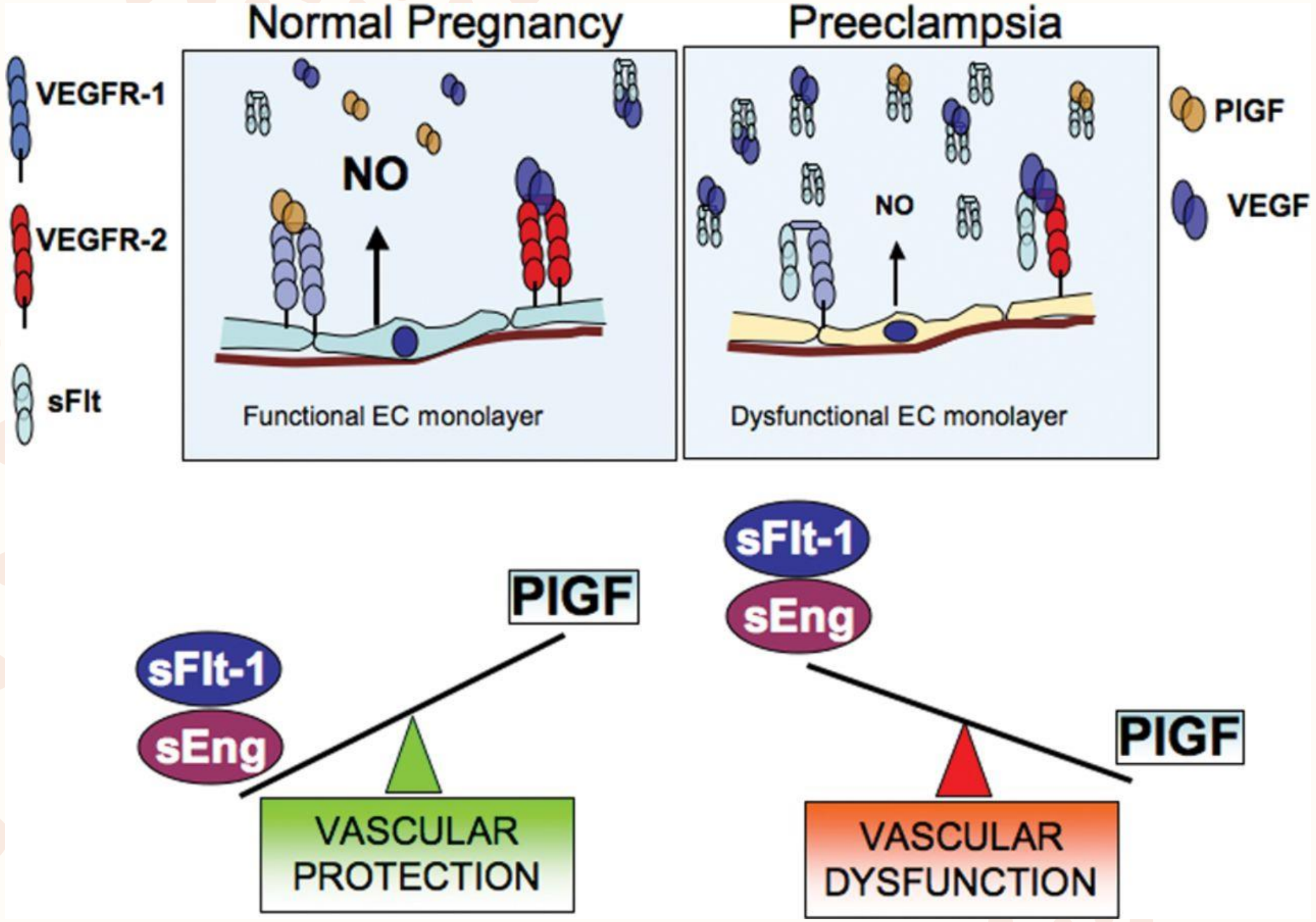


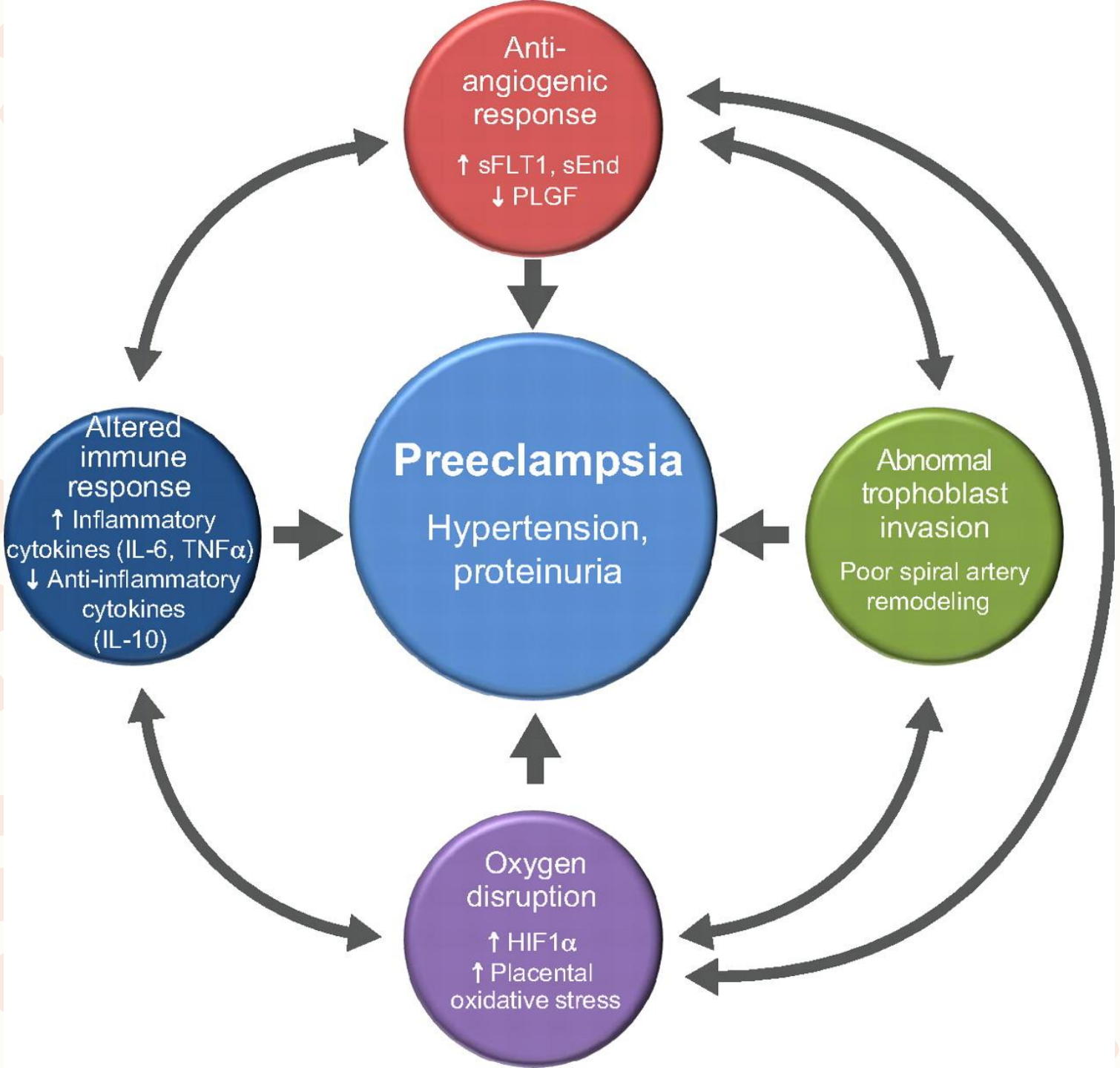

Direct Antiglobulin Test
Antigen
Erythrocyte
In vivo antibody coating of erythrocytes
Anti-IgG AHG reagent added after erythrocytes are washed
AHG reagent causes IgG-coated erythrocytes to agglutinate
Indirect Antiglobulin Test
Antibodies in serum
Reagent erythrocyte

Possible mechanisms in Preeclampsia




Maternal
Hypoxia
Placental
dysfunction
HIF1α
HIF1β
p53
IL-10
sFlt-1
sEng
Bax
Bcl-2
Caspase 3
Inflammatory triggers ??
Apoptosis
Impaired trophoblast
invasion
Preeclampsia
IUGR
Hypertension/
Vascular anomalies
Kidney pathology/
Proteinuria


Normal Pregnancy
Preeclampsia
VEGFR-1
VEGFR-2
sFlt
PIGF
VEGF
NO
NO
Functional EC monolayer
Dysfunctional EC monolayer
sFlt-1
sEng
PIGF
VASCULAR PROTECTION
sFlt-1
sEng
PIGF
VASCULAR DYSFUNCTION


Anti-angiogenic response
↑ sFLT1, sEnd
↓ PLGF
Altered immune response
↑ Inflammatory cytokines (IL-6, TNFα)
↓ Anti-inflammatory cytokines (IL-10)
Preeclampsia
Hypertension, proteinuria
Abnormal trophoblast invasion
Poor spiral artery remodeling
Oxygen disruption
↑ HIF1α
↑ Placental oxidative stress

Risk Factors for Hypertension in Pregnancy

- Nulliparity
- Preeclampsia in a previous pregnancy
- Age >40 years or <18 years
- Family history of pregnancy-induced hypertension
- Chronic hypertension
- Chronic renal disease
- Antiphospholipid antibody syndrome or inherited thrombophilia
- Vascular or connective tissue disease
- Diabetes mellitus (pregestational and gestational)
- Multifetal gestation
- High body mass index
- Male partner whose previous partner had preeclampsia
- Hydrops fetalis
- Unexplained fetal growth restriction

Preeclampsia – Risk Factors

- Nulliparous
- Previous preeclampsia
- Multiple Gestation
- Abnormal Placentation

Immunogenic Related

- Chronic HTN
- Chronic Renal Disease
- Collagen Vascular Disease
- Pregestational DM

Disease Related

- African American
- Obesity
- 35 < Age < 20
- New paternity
- Cohabiliation < 1 year

Maternal Related

- Relatives
- Mother-in-Law

Family History

Aetiology of preeclampsia:-

(Genetic predisposition)

↓

(Abnormal immunological response)

↓

(Deficient trophoblast invasion)

↓

(Hypoperfused placenta)

↓

(Circulating factors)

↓

(Vascular endothelial cell activation)

↓

(Clinical manifestations of the disease)

Preeclampsia - Complications

Maternal

CNS
- Seizures
- Cerebral Edema
- Cerebral Hemorrhage
- Strokes (thrombosis)

Hepatic
- Hepatic Failure
- Hepatic Rupture
- Subcapsular Hemorrhage

Heamatological
- DIC
- HELLP

Renal
- Renal Failure
- Oliguria
- Proteinuria >> Hypoproteinemia (Glomerular Injury)

Lungs
- Pulmonary Edema

Fetal

Preterm Delivery

Stillbirth (IUFD)
Intrapartum Fetal Distress

Placental Abruption

Uteroplacental Insufficency
- Hypoxic Neurological Injury
- IUGR
- Oligohydraminos

Complications

Eclampsia

CVA

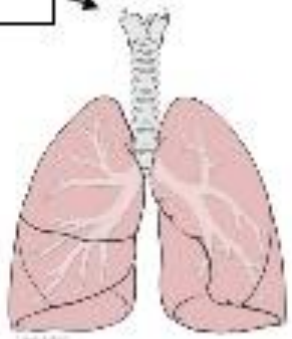
DIC

HELLP

Renal Failure

Pre-eclampsia: a placental disease

Pulmonary oedema

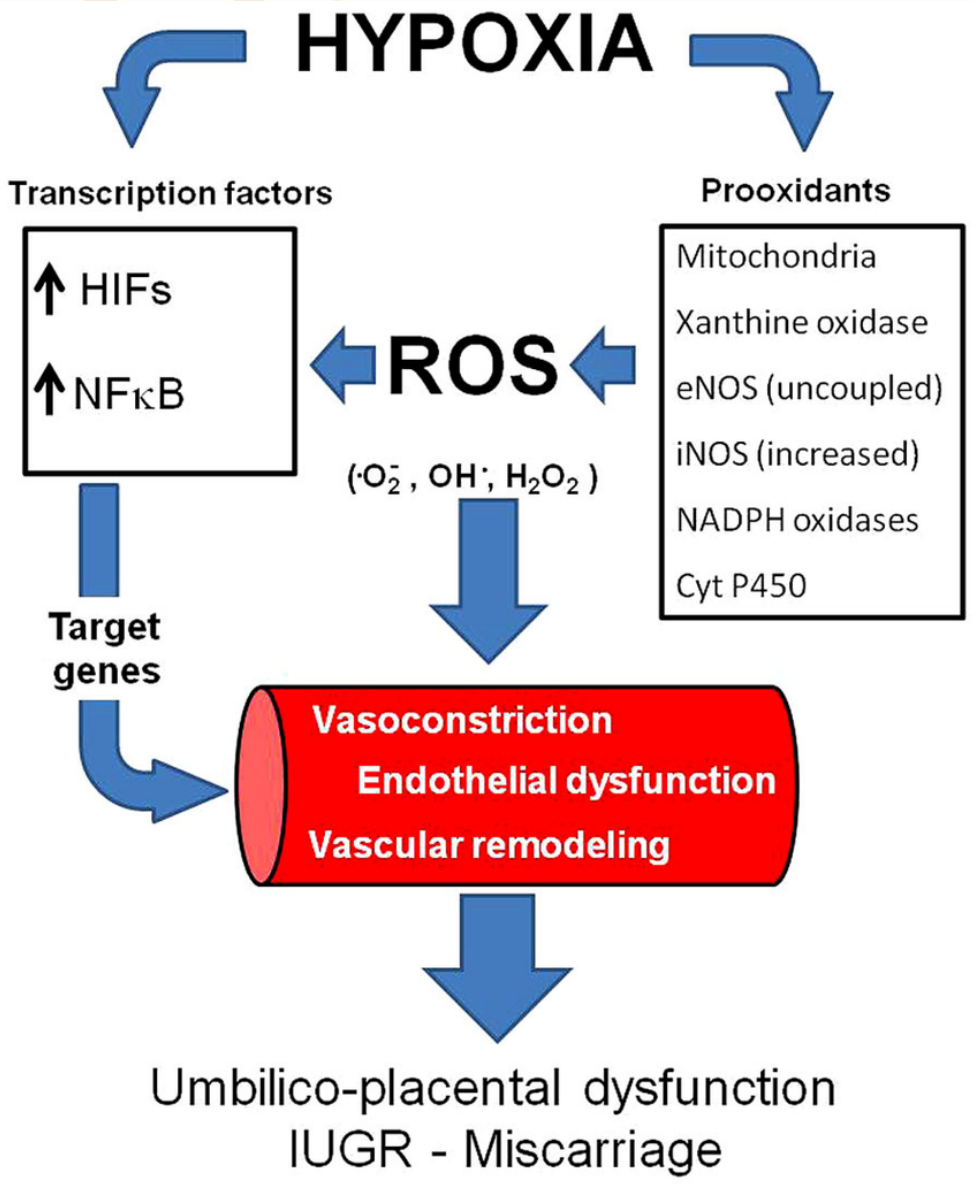


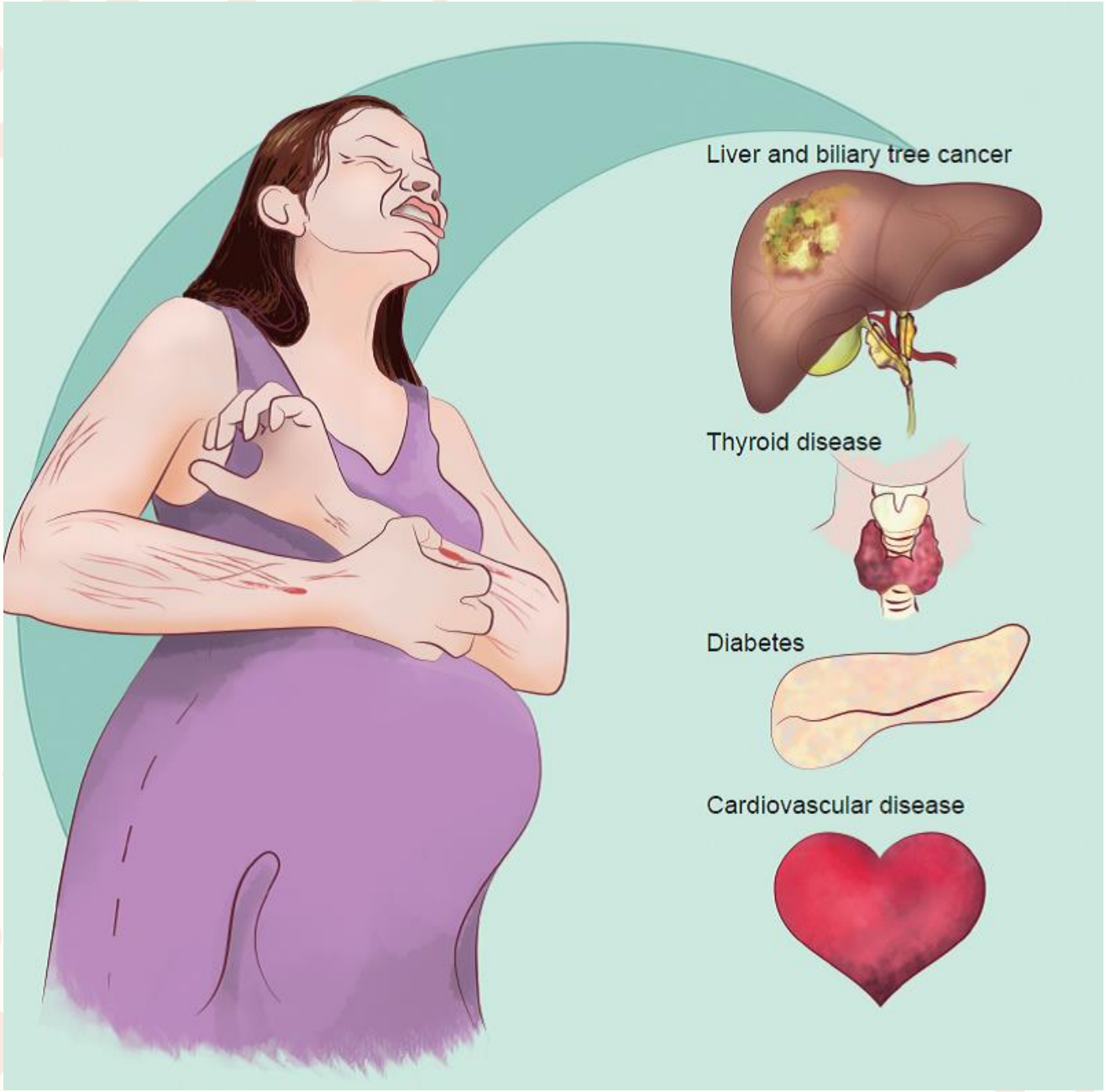
IUGR

Placental abruption

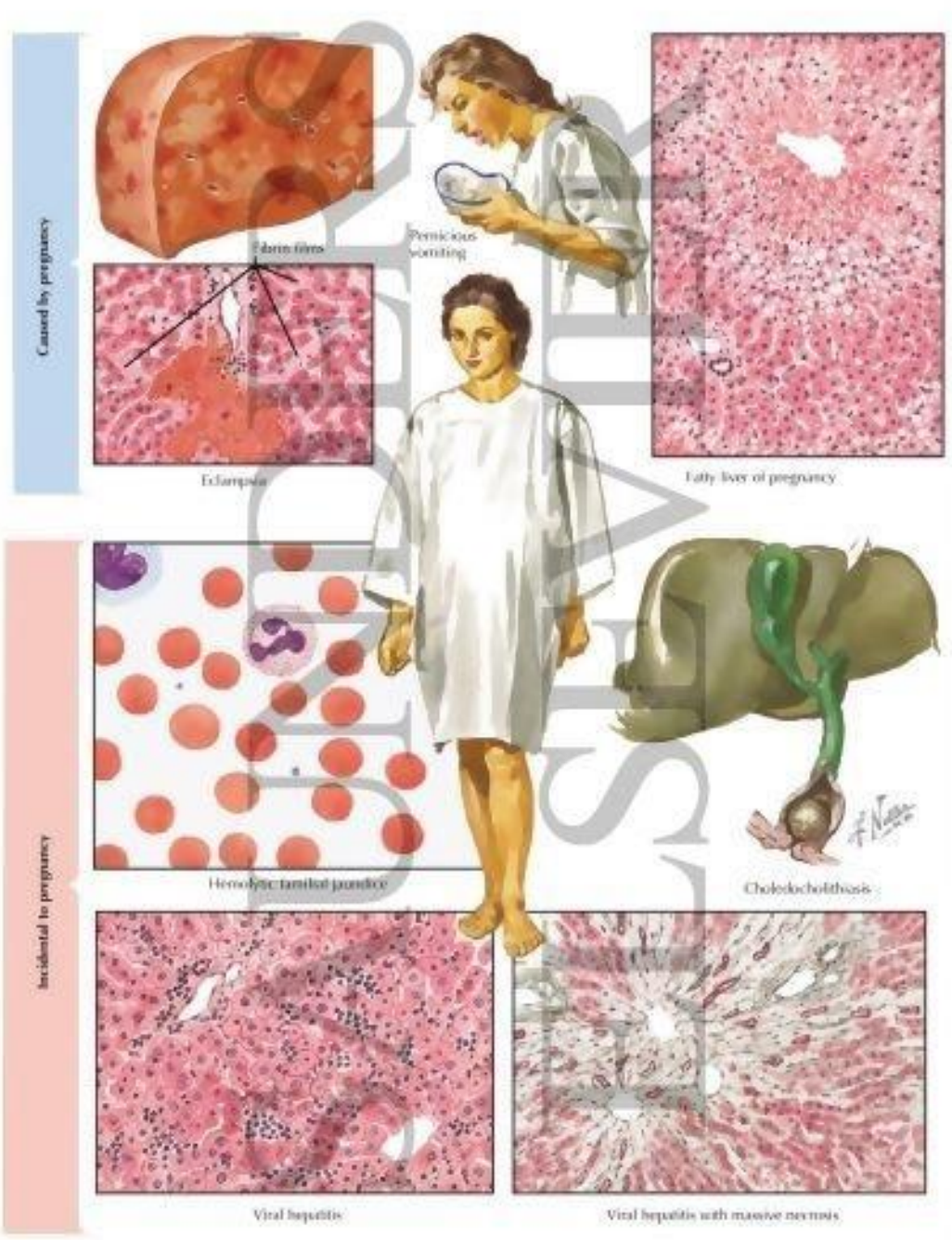
Increased mortality/morbidity

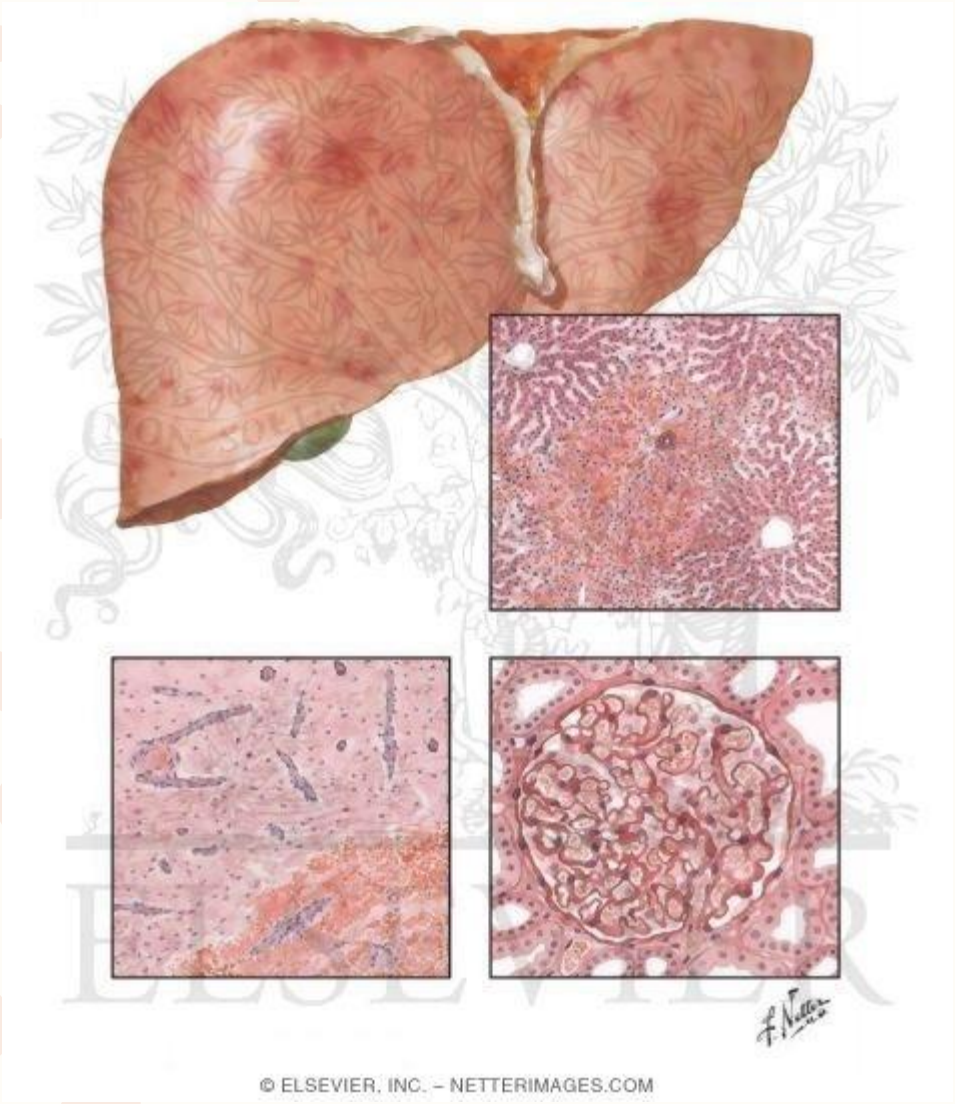
Liver complications

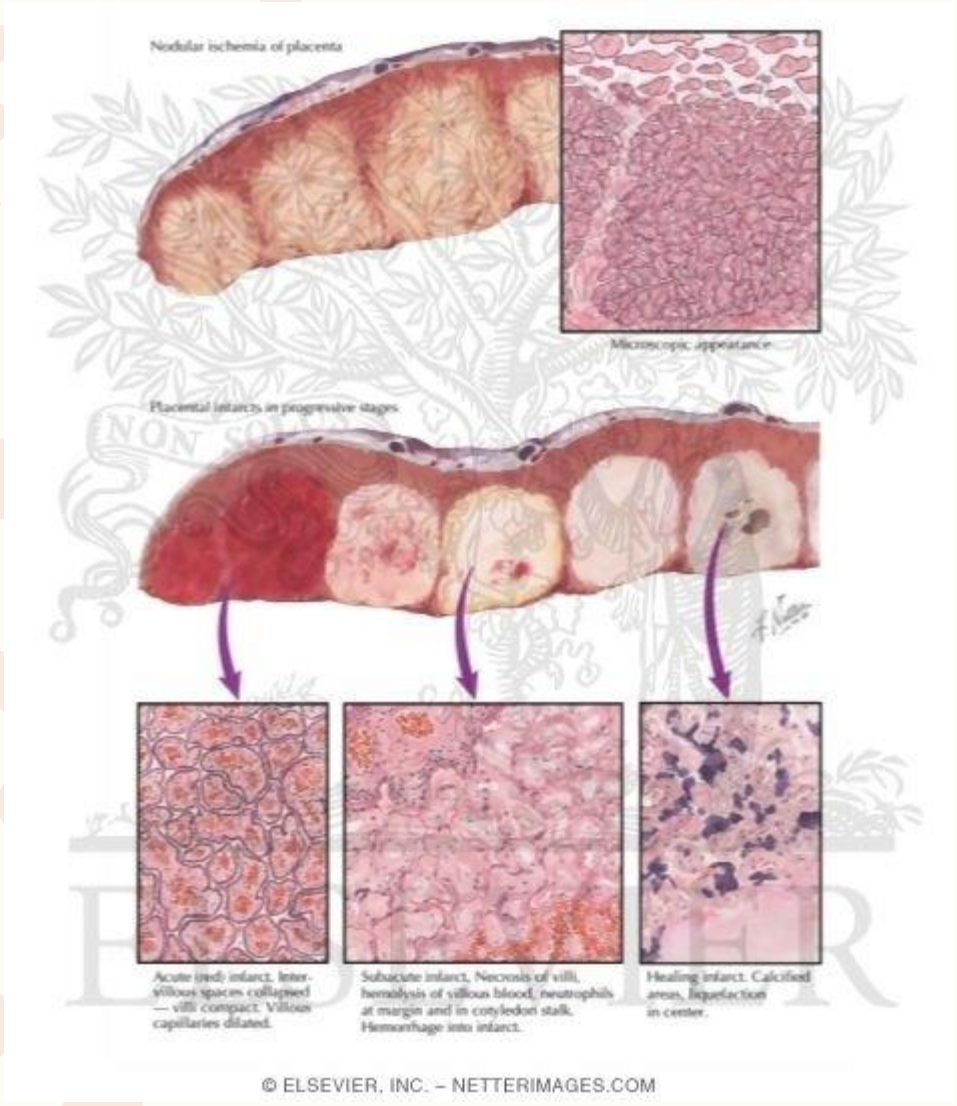

HYPOXIA
Transcription factors
Prooxidants
↑ HIFs
↑ NFκB
ROS
(·O2-, OH·, H2O2)
Mitochondria
Xanthine oxidase
eNOS (uncoupled)
iNOS (increased)
NADPH oxidases
Cyt P450
Target genes
Vasoconstriction
Endothelial dysfunction
Vascular remodeling
Umbilico-placental dysfunction
IUGR - Miscarriage

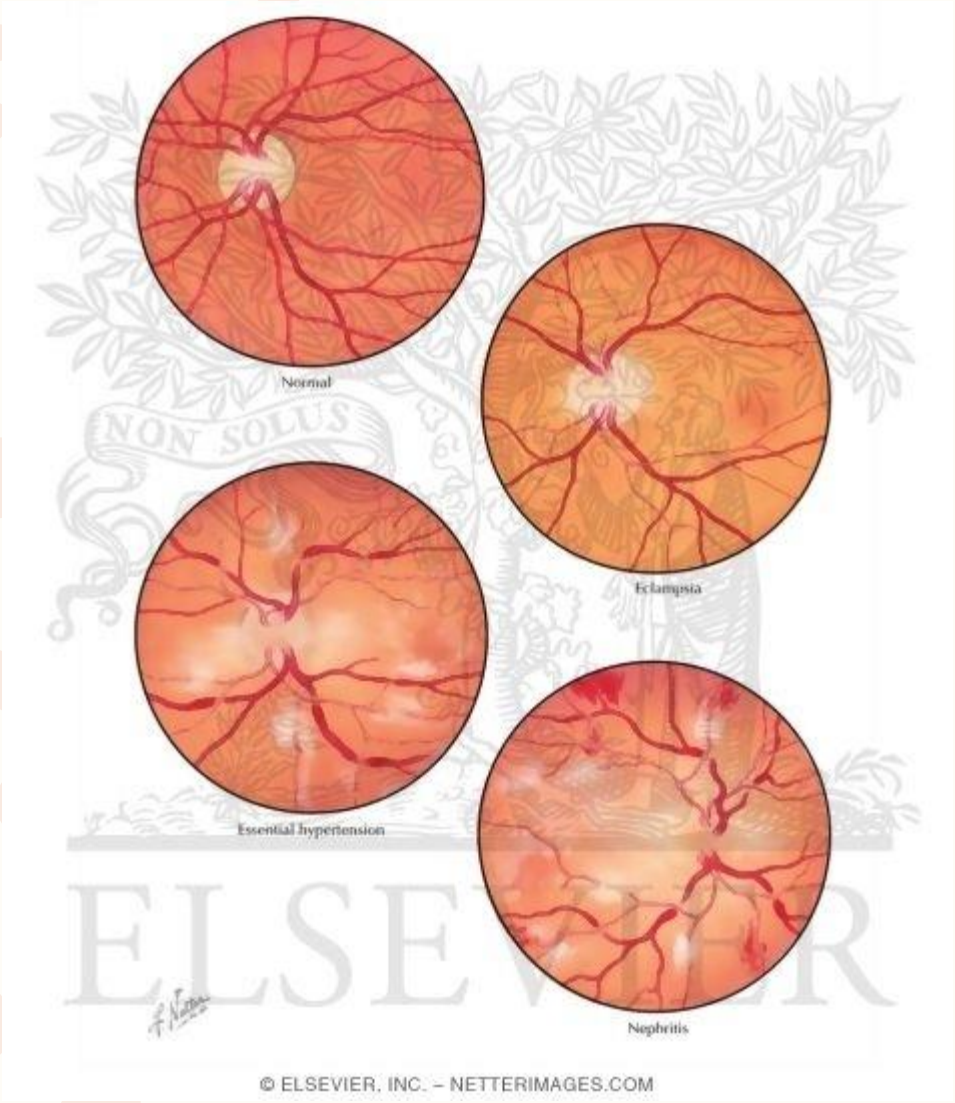

Liver and biliary tree cancer
Thyroid disease
Diabetes
Cardiovascular disease

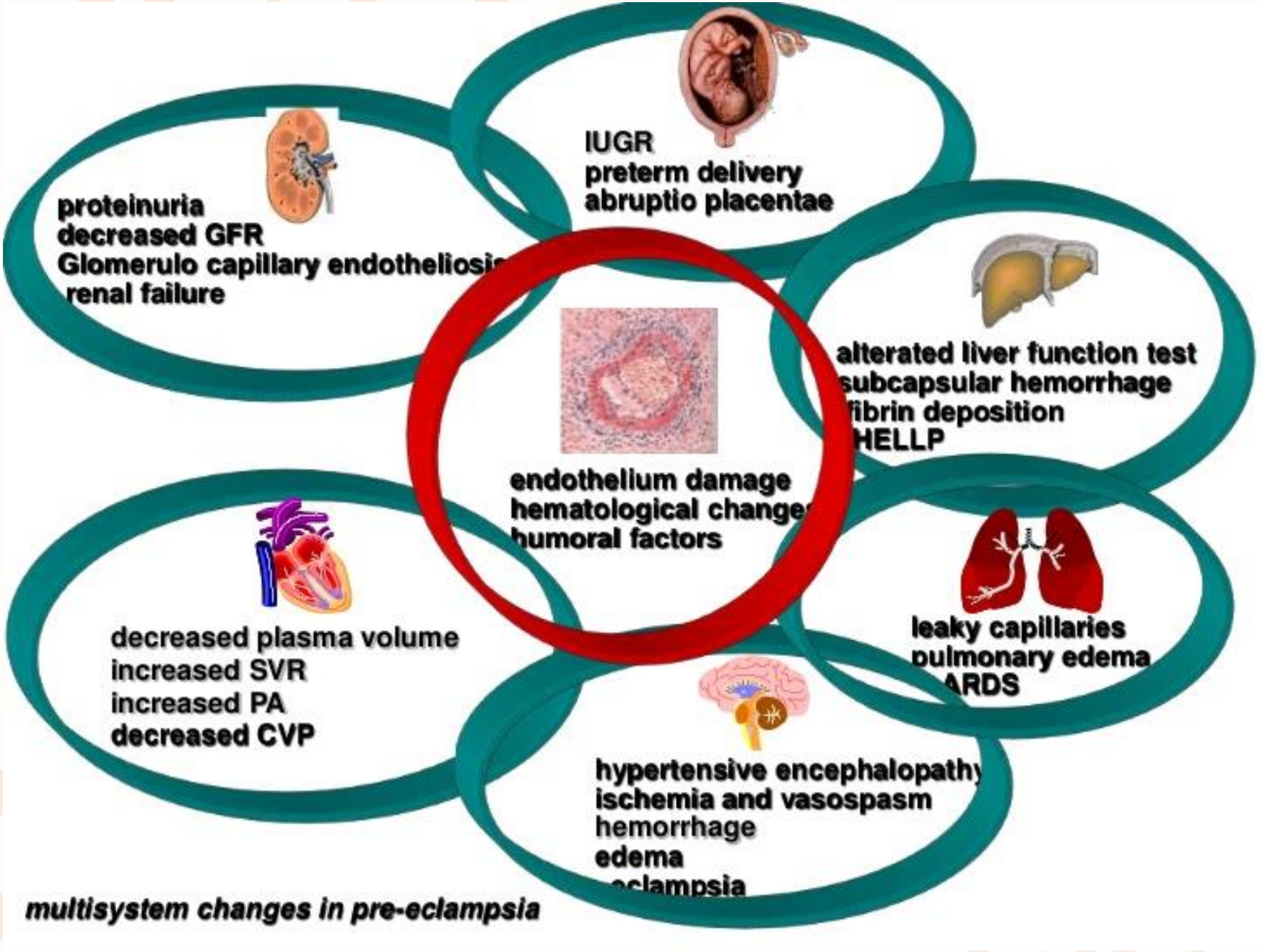
Hepatic Disease in Pregnancy



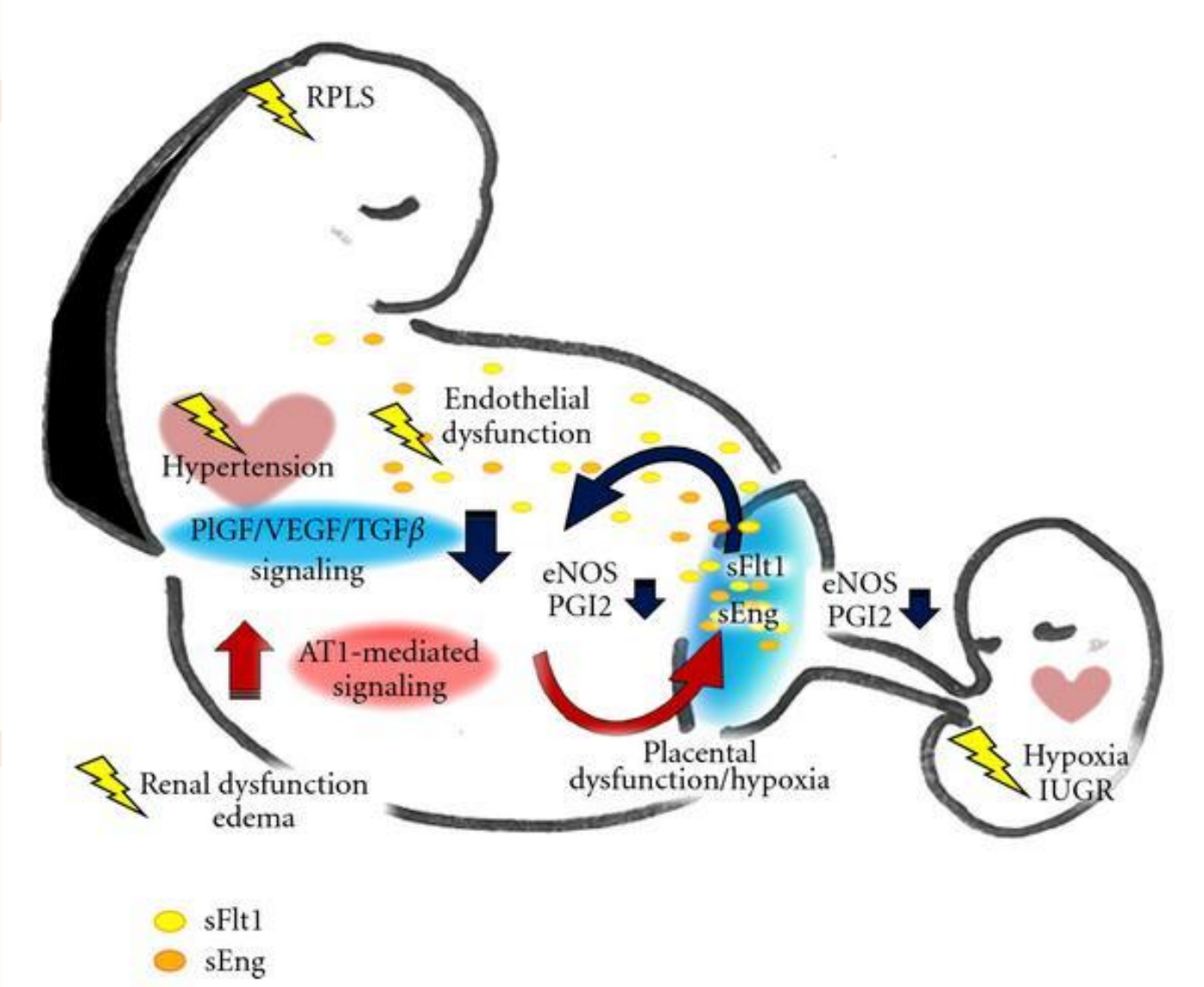


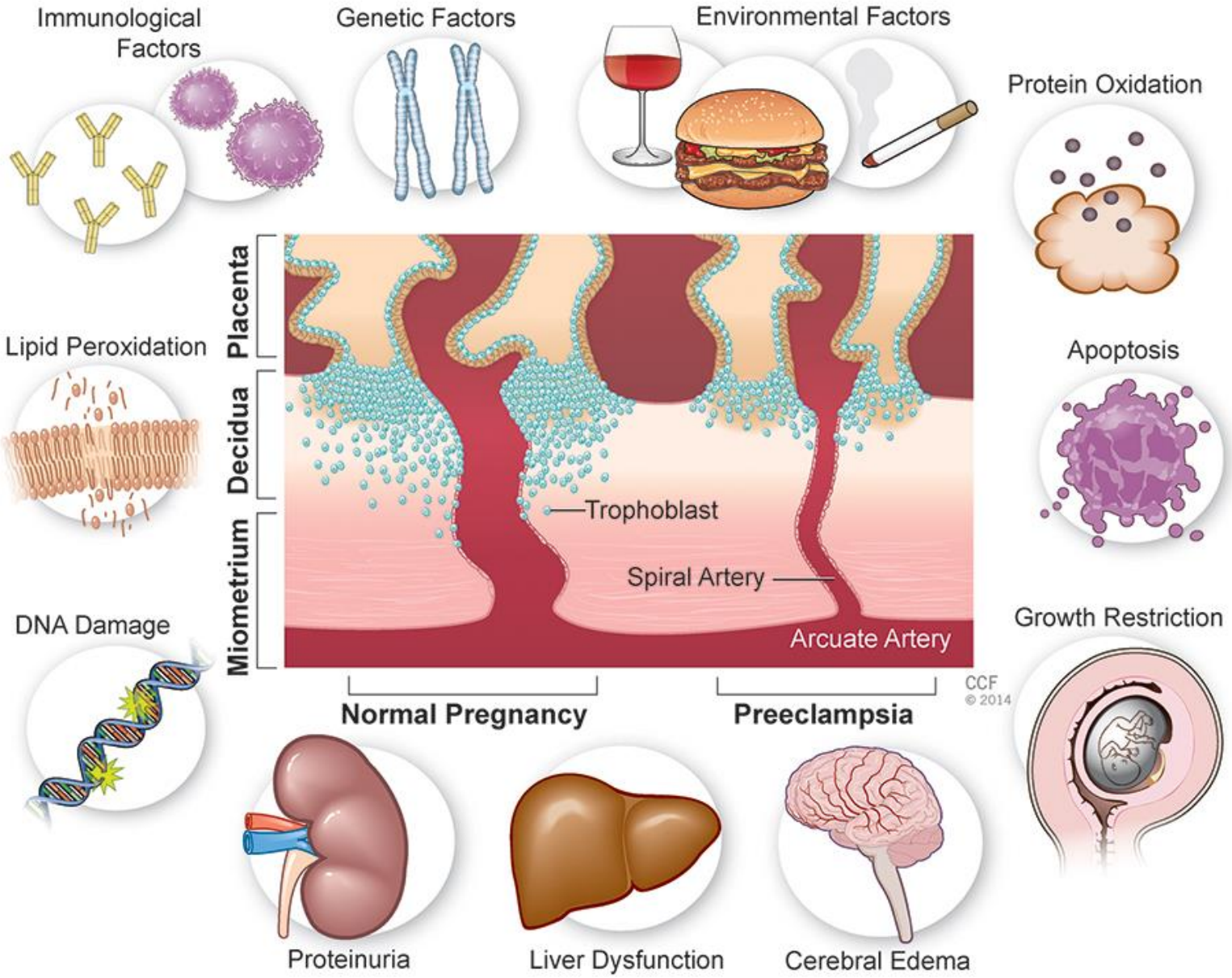


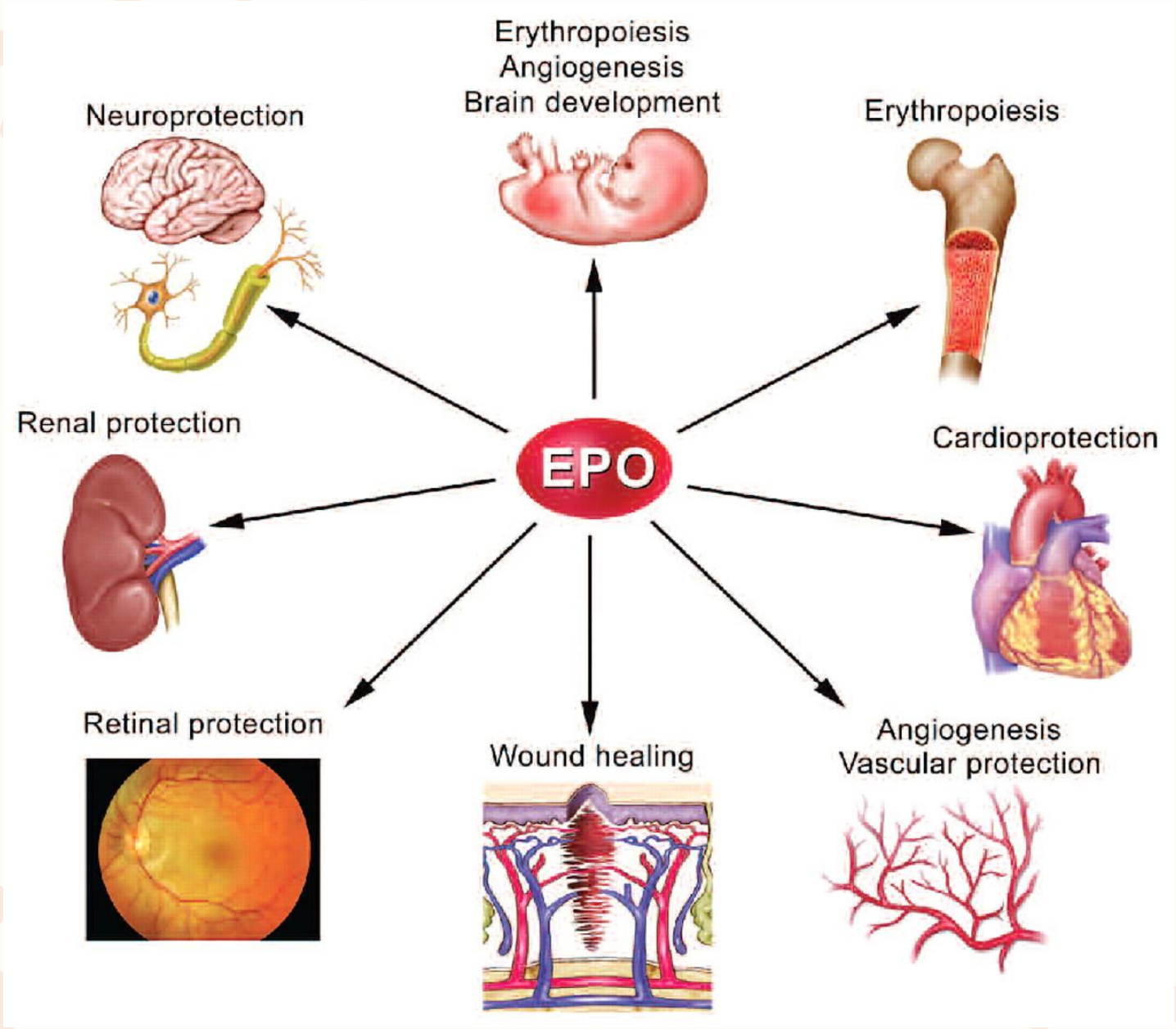




multisystem changes in pre-eclampsia

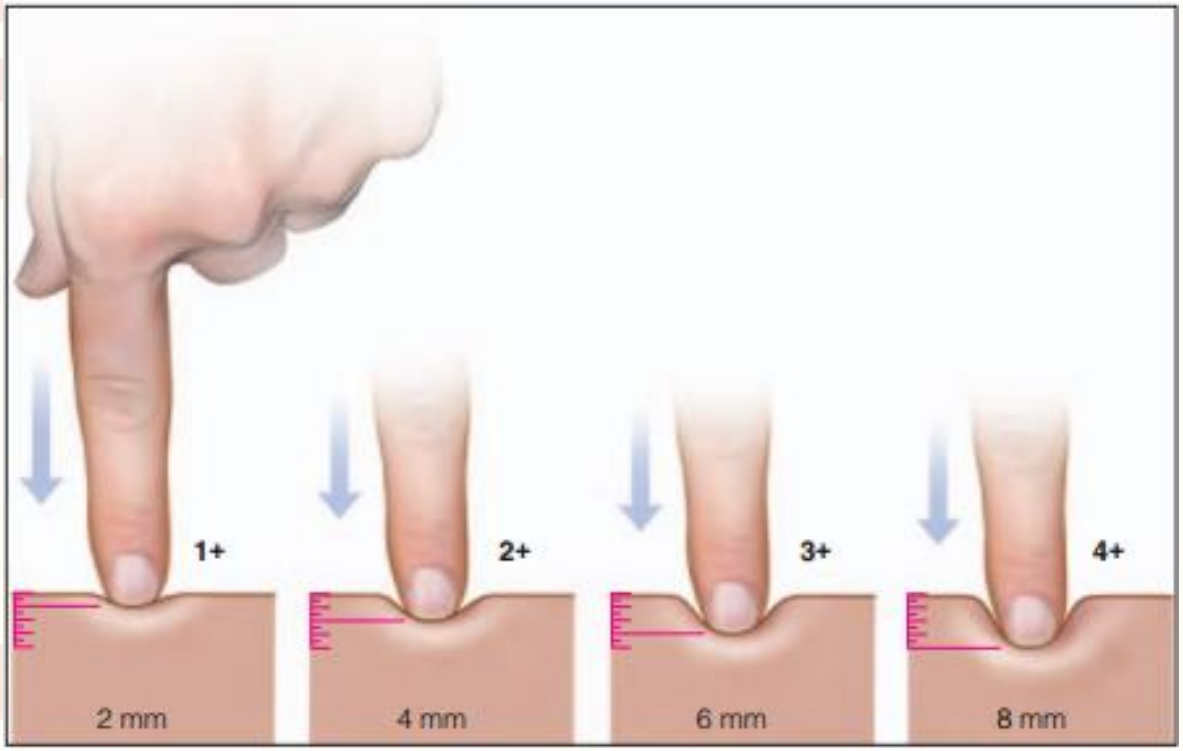

RPLS
Endothelial dysfunction
Hypertension
PlGF/VEGF/TGFβ signaling
eNOS PGI2
sFlt1 sEng
eNOS PGI2
AT1-mediated signaling
Renal dysfunction edema
Placental dysfunction/hypoxia
Hypoxia IUGR
sFlt1
sEng

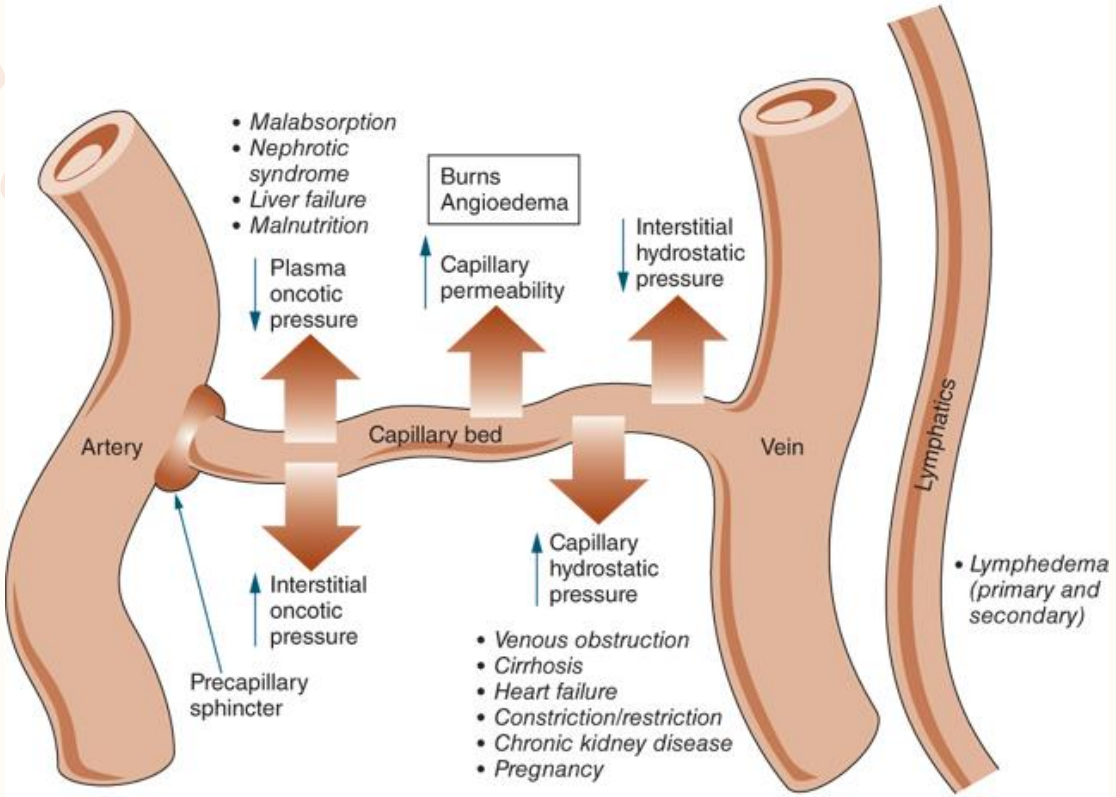

Immunological Factors
Genetic Factors
Environmental Factors
Protein Oxidation
Lipid Peroxidation
Apoptosis
DNA Damage
Growth Restriction
Placenta
Decidua
Miometrium
Trophoblast
Spiral Artery
Arcuate Artery
Normal Pregnancy
Preeclampsia
CCF © 2014
Proteinuria
Liver Dysfunction
Cerebral Edema

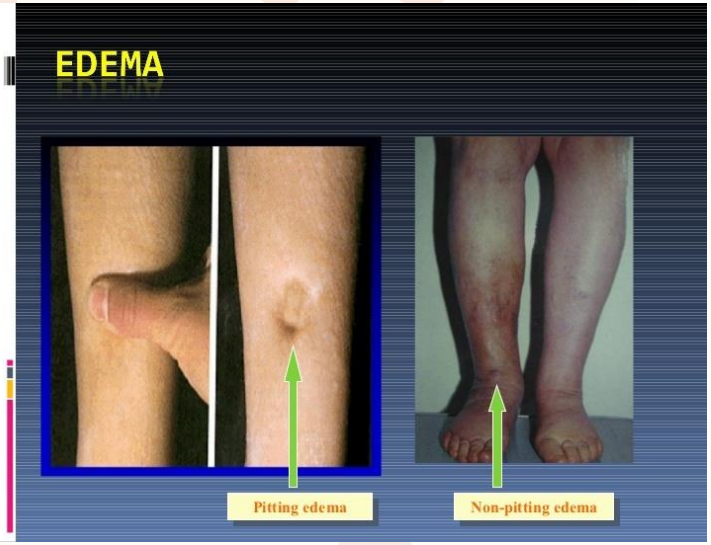

Erythropoiesis
Angiogenesis
Brain development
Neuroprotection
Erythropoiesis
Renal protection
EPO
Cardioprotection
Retinal protection
Wound healing
Angiogenesis
Vascular protection

Preeclampsia - Diagnosis

- Upon antenatal visits
  - First visit
    - Identify risk (Hx, PEx)
    - BP + Urine protein test
  - Following visits
    - 28/52 : Monthly BP + Urine protein test
    - After 28/52 : More frequent BP + Urine protein tests
    - 2nd trimester : Uterine Artery Doppler (not sensitive)


1+
2+
3+
4+
2 mm
4 mm
6 mm
8 mm


• Malabsorption
• Nephrotic syndrome
• Liver failure
• Malnutrition
Plasma oncotic pressure
Burns
Angioedema
Capillary permeability
Interstitial hydrostatic pressure
Artery
Capillary bed
Vein
Lymphatics
Interstitial oncotic pressure
Capillary hydrostatic pressure
• Lymphedema (primary and secondary)
Precapillary sphincter
• Venous obstruction
• Cirrhosis
• Heart failure
• Constriction/restriction
• Chronic kidney disease
• Pregnancy


EDEMA
Pitting edema
Non-pitting edema

Evaluation of Hypertension in Pregnancy

- **Laboratory Tests**
  - ***CBC (Hgb, Plts)***
  - ***Renal Function (Cr, UA, Albumin)***
  - ***Liver Function (AST, ALT, ALP, LD)***
  - ***Coagulation (PT, PTT, INR, Fibrinogen)***
  - ***Urine Protein (Dipstick, 24 hour)***

Evaluation of Hypertension in Pregnancy

- **History**
  - *ID and Complaint*
  - *HPI (S/S of Preeclampsia)*
  - *Past Medical Hx, Past Family Hx*
  - *Past Obstetrical Hx, Past Gyne Hx*
  - *Social Hx*
  - *Medications, Allergies*
  - *Prenatal serology, blood work*
  - *Assess for Hypertension in Pregnancy risk factors*

- **Physical**
  - *Vitals*
  - *HEENT = Vision*
  - *Cardiovascular*
  - *Respiratory*
  - *Abdominal = Epigastric pain, RUQ pain*
  - *Neuromuscular and Extremities = Reflex, Clonus, Edema*
  - *Fetus = Leopold's, FM, NST*

Treatment of Preeclampsia

- Definitive Treatment = Delivery
- Major indication for antihypertensive therapy is prevention of stroke.
  - Diastolic pressure ≥105-110 mmHg or systolic pressure ≥160 mmHg
- Choice of drug therapy:
  - Acute – IV labetalol, IV hydralazine, SR Nifedipine
  - Long-term – Oral methyldopa or labetalol

Preeclampsia - Management

Admission
- Close monitoring required

IV Line
- Bloods
- Infusions

Urinary Catheter
- Monitoring urine output and ease of 24h urine collection

Severity Assessment
- Maternal
  - PEx
  - BP :15m, 30, 4qh
  - 24/24 Urinary Collection
  - 2qw: FBC, Coag. Profile, LFT, serum(Cr), Uric Acid

Severity Assessment
- Fetal: 2qw
- CTG
- US
- US Doppler: Umbilical + Cerebral
- Liquor Assessment

Stabilize Patient

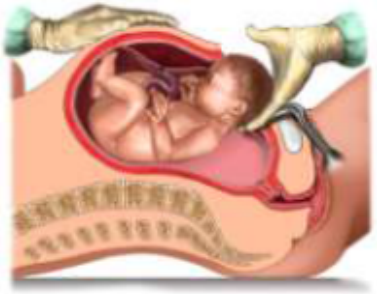
Therapy
- Fluid Restriction (80ml/h)
- Decision based on severity + gestational age
  - Mother is concern

Delivery
- Decision on date required

Preeclampsia – Delivery Indications

- Mild Preeclampsia
  - Expectant
    - Stable
    - Preterm
  - Deliver
    - Term
    - Unstable preterm
    - Fetal compromise
      - GR/OH/abnormal Umbilical Doppler

Induced delivery (PG, Oxytocin, Amniotomy) unle obstetric indication



- Severe Preeclampsia
  - Expectant (Betamethasone + $MgSO_4$)
    - GA 24-32/52
  - Deliver
    - GA > 32/52
    - Patient presenting with
      - Uncontrollable BP
      - Symptoms
        - Headache, RUQ, Visual
      - Hyperreflexia
      - Complications
        - HELLP or LP
        - Renal Failure
        - Hepatic Injury
        - Pulmonary Edema
        - DIC

Preeclampsia – Therapy (2)

- $MgSO_4$
  - Monitor
    - Ox Stat
    - Respiratory Rate
      - Replace Ca Gluconate 1g infusion
    - Deep tendon reflexes
    - Urine Output
      - Halt if less than 20 ml/h
  - Recurrent Seizures
    - $MgSO_4$: 2g bolus (RCOG: increase infusion to 2g/h)
- Antihypertensive
  - Monitor
    - BP
      - ≥ 130/80
  - Only improves morbidity
- Aspirin
  - Inhibits thromboxane A2 synthesis
  - → re-altering TXA2/Prostacyclin balance

Preeclampsia – Treatment

- Curative Therapy: Delivery
  - Balance maternal and fetal status

Mild Preeclampsia	Severe Preeclampsia	Seizure	Follow-Up (44% PP → 1/12)

•Expectant
•Admission
•Betamethasone
•MgSo4 4g.2g/h
•RCOG: 1g/h
	• Admission
	• $MgSO_4$
	  • Intrapartum
	  • Postpartum 24h
	• IV Labetalol / IV Hydralizine / Nifedipine
	• Decide on delivery
		• A,B,C
		• Ox Stat
		• Oxygen
		• $MgSO_4$ 4g.2g/h
		  • 2g bolus
		• Left Lateral Position
		• Prepare for delivery
			• Reassess. Discharge when stable → 6/52
			• $MgSO_4$ 1d postpartum/post last seizure
			• PO Labetalol / PO Methyldopa / Nifedipine: CHTN
			• Low dose Aspirin / LMWH
			• Monitor HELLP (LP: corticosteroids)

SO

Management of Hypertension in Pregnancy

- Depends on severity of hypertension and gestational age!!!!

- **Observational Management**
  - *Restricted activity*
  - *Close Maternal and Fetal Monitoring*
    - BP Monitoring
    - S/S of preeclampsia
    - Fetal growth and well being (NST, and U/S)
  - *Routine weekly or biweekly blood work*

Management of Hypertension in Pregnancy

- **Medical Management**
  - *Acute Therapy = IV Labetalol, IV Hydralazine, SR Nifedipine*
  - *Expectant Therapy = Oral Labetalol, Methyldopa, Nifedipine*
  - *Eclampsia prevention = MgSO4*
- **Contraindicated antihypertensive drugs**
  - ***ACE inhibitors***
  - ***Angiotensin receptor antagonists***

Management of Hypertension in Pregnancy

- **Proceed with Delivery**
  - *Vaginal Delivery VS Cesarean Section*
  - *Depends on severity of hypertension!*
  - *May need to administer antenatal corticosteroids depending on gestation!*

–Only cure is DELIVERY!!!