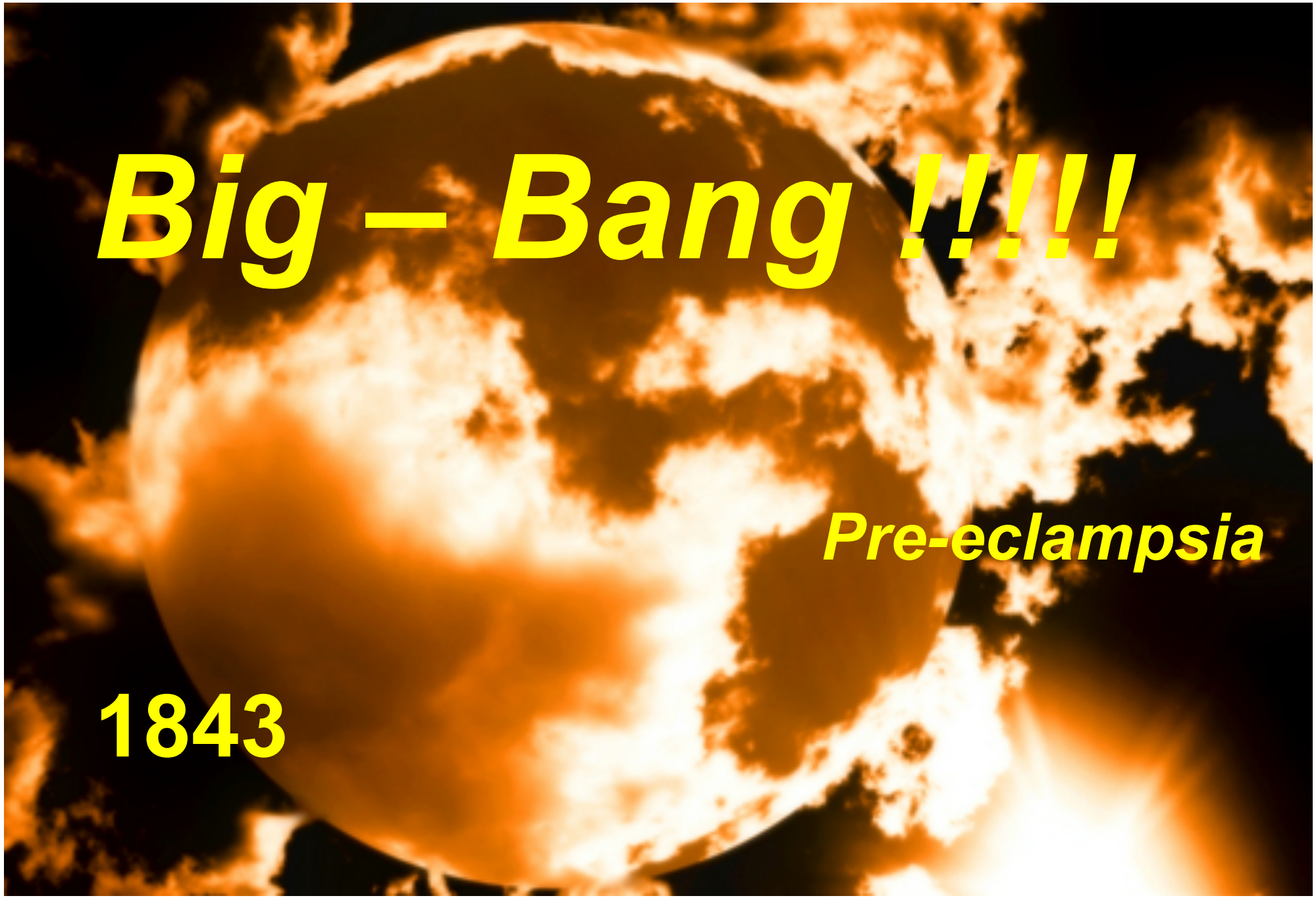
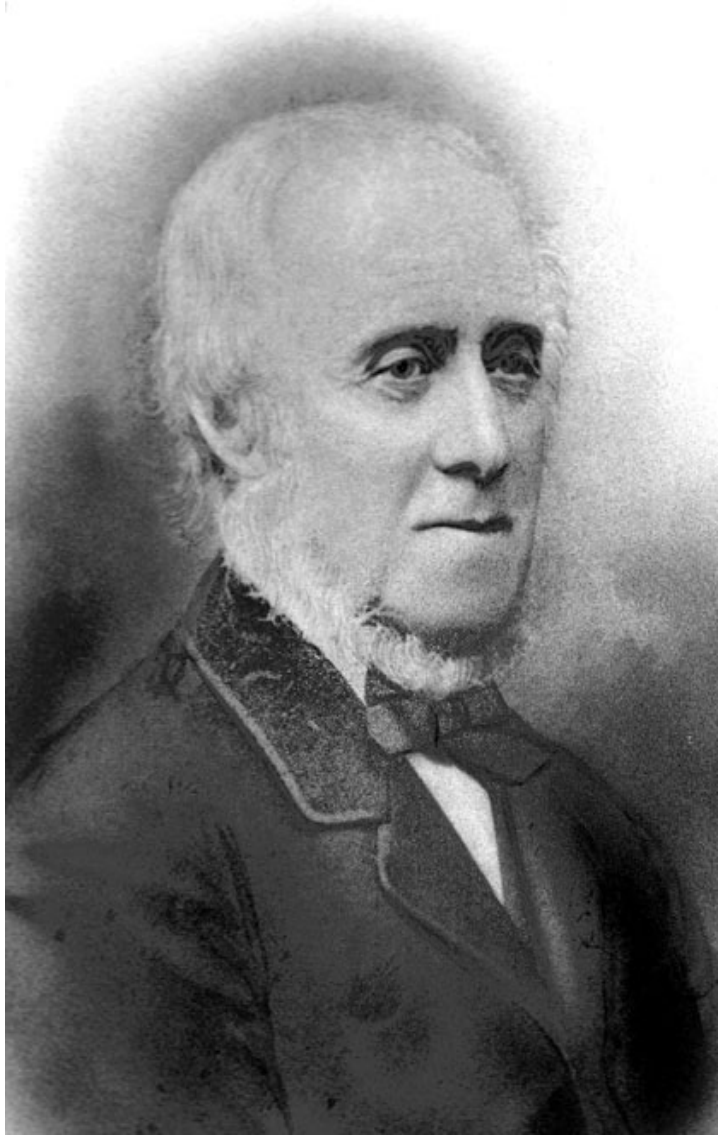
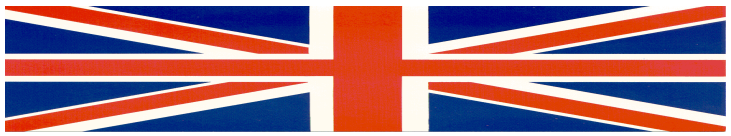
“El riñón durante el episodio crítico de la Pre-eclampsia”

Fernando Lombi - Congreso de la ANBA

Mar del Plata - 2012


Big – Bang !!!!!
Pre-eclampsia
1843





Cuando en plena era victoriana ***Sir John Lever*** en el ***Guy's Hospital*** de Londres hizo la primera descripción a través del descubrimiento de proteinuria en mujeres embarazadas con convulsiones.

	RCOG severe pre-eclampsia (2006)[9]	SOMANZ (2008)[10]	SOGC (2008)[11]	ASH (2008)[12]
Pre-existing or chronic hypertension (blood pressure ≥140/90 mm Hg before 20 weeks' gestation)	NA	Chronic hypertension: essential; secondary; white coat; with or without superimposed pre-eclampsia	Pre-existing hypertension: with or without comorbid conditions; with or without superimposed pre-eclampsia	Chronic hypertension of any cause: with or without superimposed pre-eclampsia
Gestational hypertension (blood pressure ≥140/90 mm Hg after 19 weeks' (+6 days) gestation	NA	Gestational hypertension without significant proteinuria returning to normal within 12 weeks' post partum	Gestational hypertension: with or without comorbid conditions; with or without superimposed pre-eclampsia	Gestational hypertension: transient hypertension; blood pressure returning to normal within 6 weeks' post partum; late post partum hypertension, with blood pressure rise developing weeks' to 6 months' post partum and normalised by 1 year post partum
Pre-eclampsia (clinical definition)	Gestational hypertension (pregnancy-induced hypertension) and significant proteinuria (>0·3 g/24 h)	Gestational hypertension plus one or more of the following: dipstick proteinuria confirmed by either random Pr:Cr ratio ≥30 mg/mmol or 0·3 g/24 h; serum or plasma creatinine >90 µmol/L; oliguria; thrombocytopenia; haemolysis; disseminated intravascular coagulation; raised serum transaminases; severe epigastric or right upper quadrant pain; eclampsia; hypereflexia with sustained clonus; severe headache; persistent visual disturbances; stroke; pulmonary oedema; fetal growth restriction; placental abruption	Pre-existing hypertension and resistant hypertension, new proteinuria, or adverse condition (see severity criteria below) Gestational hypertension and proteinuria (random Pr:Cr ratio ≥30 mg/mmol or 0·3 g/24 h), or adverse condition	Gestational hypertension or chronic hypertension and proteinuria (dipstick ≥1+, random Pr:Cr ratio ≥30 mg/mmol or 0·3 g/24 h)
Pre-eclampsia (research definition)	Not defined	De novo hypertension >20 weeks' gestation, returning to normal post partum with properly documented proteinuria	Not defined	Not defined
Severe hypertension	170/110 mm Hg	170/110 mm Hg	160/110 mm Hg	160/110 mm Hg
Heavy proteinuria	1 g/L	Not defined	3–5 g per day	3 g per day
Severity criteria				
Gestational age at onset	Not included	Not defined	<34 weeks' gestation	<35 weeks' gestation
Maternal symptoms	Severe headache; visual disturbance; epigastric pain or vomiting	Not defined	Persistent or new/unusual headache; visual disturbances; persistent abdominal or right upper quadrant pain; severe nausea or vomiting, chest pain or dyspnoea	Headache; visual disturbances; abdominal pain
Maternal signs of end-organ dysfunction	Eclampsia; severe hypertension; heavy proteinuria; liver tenderness; signs of clonus; papilloedema	Not defined	Eclampsia; severe hypertension; pulmonary oedema; or suspected placental abruption	Severe diastolic hypertension (≥110 mm Hg); heavy proteinuria, oliguria
Abnormal maternal laboratory testing	Platelet count <100×10⁹/L, HELLP syndrome, abnormal liver enzymes (ALT or AST rising to above 70 U/L)	Not defined	Raised serum creatinine; increased AST, ALT, or LDH with symptoms; platelet count <100×10⁹/L; or serum albumin <20 g/L	Raised serum creatinine, decreased glomerular filtration rate, or increased AST or LDH
Fetal morbidity or mortality	Not included	Not defined	Oligohydramnios; intrauterine growth restriction; absent or reversed end-diastolic flow in the umbilical artery by Doppler velocimetry; intrauterine fetal death	Fetal morbidity (non-reassuring fetal testing)

RCOG=Royal College of Obstericians and Gynaecologists. SOMANZ=Society of Obstetric Medicine of Australia and New Zealand. SOGC=Society of Obstetricians and Gynaecologists of Canada. ASH=American Society of Hypertension. NA=not applicable. Pr:Cr=protein-to-creatinine ratio. HELLP= haemolysis, elevated liver enzymes, and low platelet count. ALT=alanine transaminase. AST=aspartate transaminase. LDH=lactate dehydrogenase.

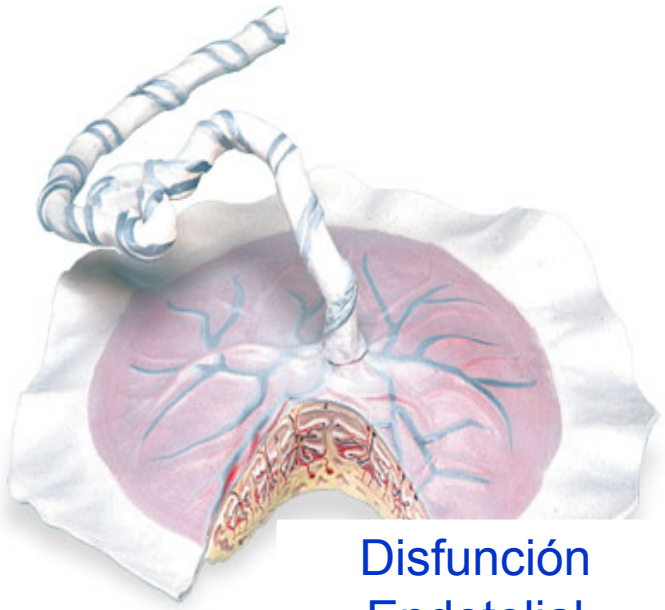
Table 1: **International comparison between recent classification systems**

Eclampsia

Pre-eclampsia

Pre-eclampsia severa

Síndrome HELLP



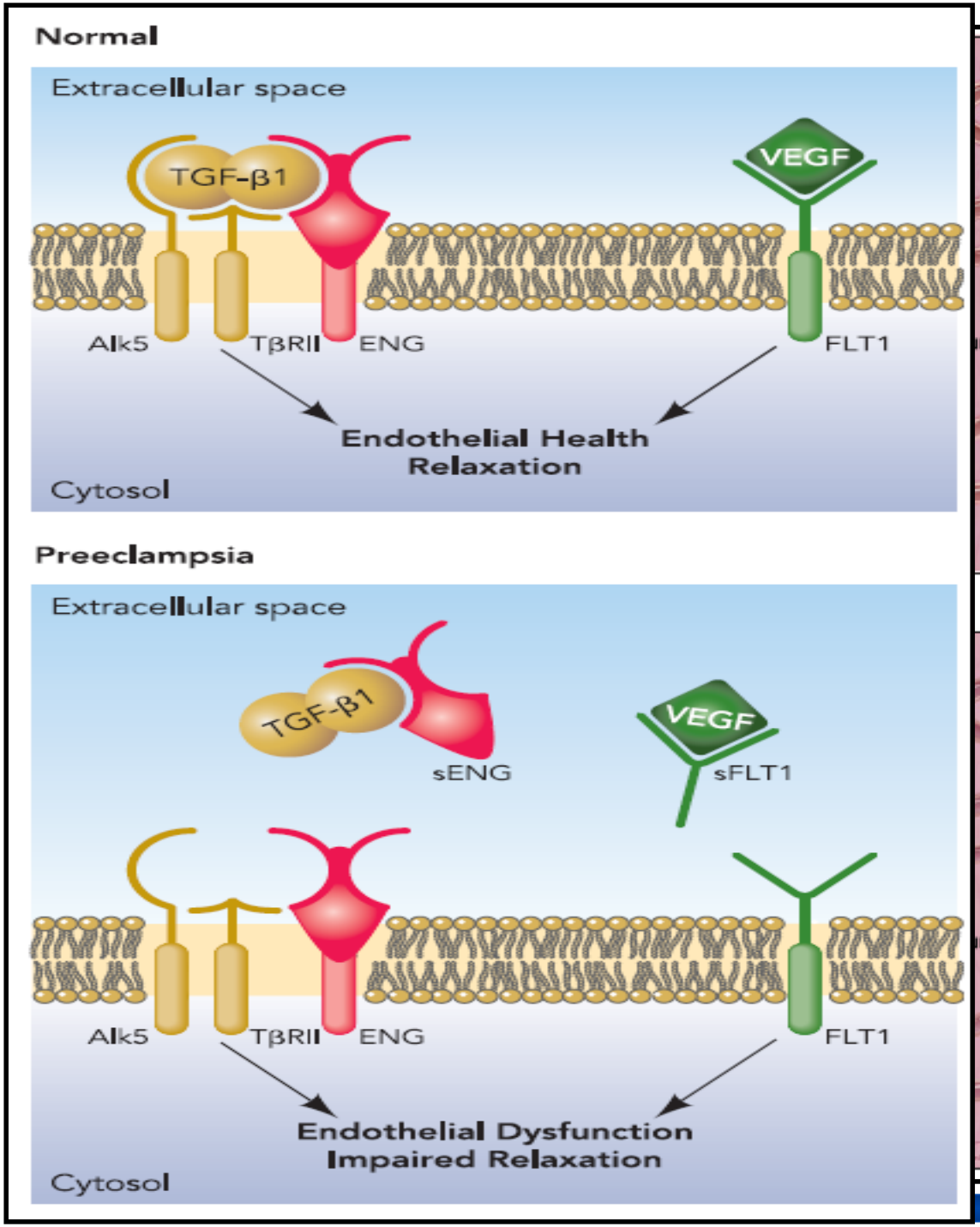
Disfunción Endotelial

Pre-eclampsia sobreimpuesta HTA crónica

HTA gestacional

HTA crónica

Adapted from American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice: ACOG practice bulletin: diagnosis and management of preeclampsia and eclampsia, number 33, January 2002, ***Int J Gynaecol Obstet*** 77:67-75, 2002.



Ocurre sólo en presencia de una placenta anormal, incluso cuando no hay feto (mola hidatiforme) y remite con el alumbramiento

7- 58.

Cambios fisiológicos en el embarazo

Table 2. Central hemodynamic changes in normal pregnancy

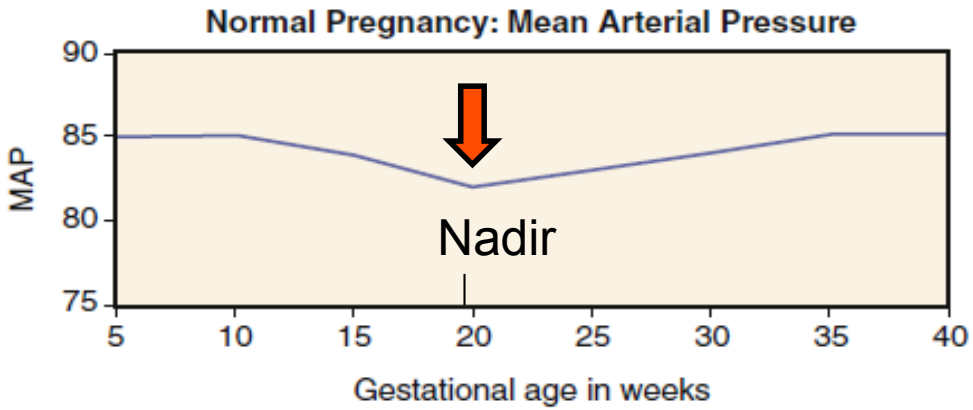
Measurement	Nonpregnant	Pregnant
Cardiac output, L/min	4.3 ± 0.9	6.2 ± 10
Heart rate, beats/min	71 ± 10	83 ± 10
Systemic vascular resistance, dyne · cm · sec^{-5}	1530 ± 520	1210 ± 266
Mean arterial pressure, mm Hg	86.4 ± 7.5	90.3 ± 5.8
Pulmonary artery occlusion pressure, mm Hg	6.3 ± 2.1	7.5 ± 1.8
Central venous pressure, mm Hg	3.7 ± 2.6	3.6 ± 2.5
Colloid oncotic pressure, mm Hg	20.8 ± 1.0	18.0 ± 1.5

Table 1. Normal laboratory variables in pregnancy

Variable	Normal Value in Pregnancy
BUN	9.0 mg/dL (average)
Cr	0.5 mg/dL (average)
GFR	↑ ~40% over baseline
CrCl	↑ ~25% over baseline
P_{CO_2}	↓ ~10 mm Hg below baseline
HCO_3	18–20 mEq/L
Urinary protein	Maximum 300 mg/24 hrs
Plasma osmolality	↓ ~10 mOsm/kg H_2O

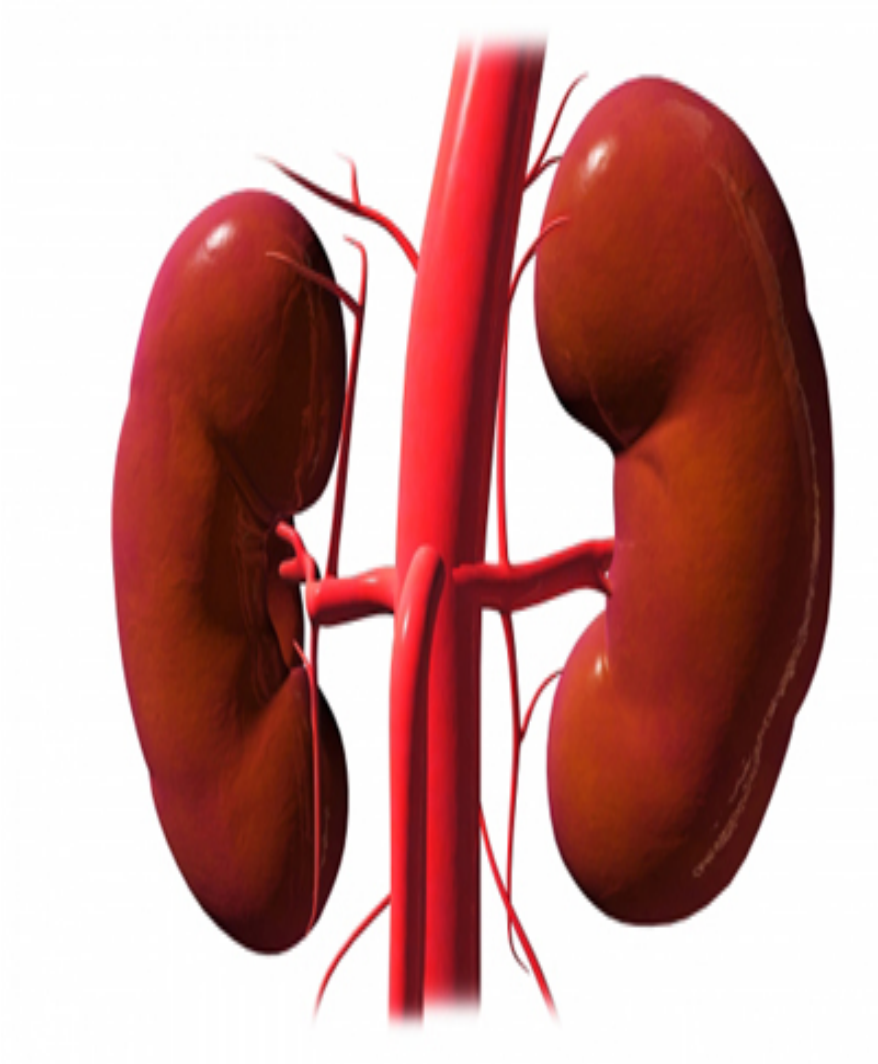
BUN, blood urea nitrogen; Cr, creatinine; GFR, glomerular filtration rate; CrCl, creatinine clearance.

Clark SL, Cotton DB, Lee W, et al: Central hemodynamic assessment of normal term pregnancy. ***Am J Obstet Gynecol*** 1989; 161: 1439–1442



Asrat T, Nageotte M: Acute renal failure in pregnancy. ***In: Obstetric Intensive Care Manual.*** Foley MR, Strong TH, Garite TJ (Eds). New York, McGraw-Hill, 2004, 184–195

Cambios renales inducidos por la preeclampsia



Tensión arterial

HTA

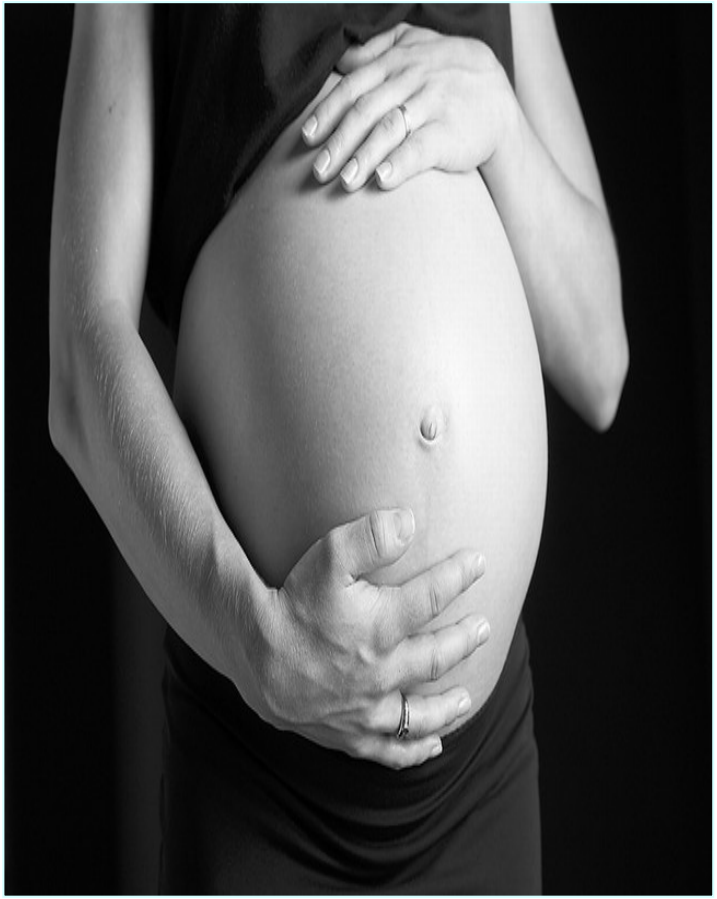
Filtrado Glomerular

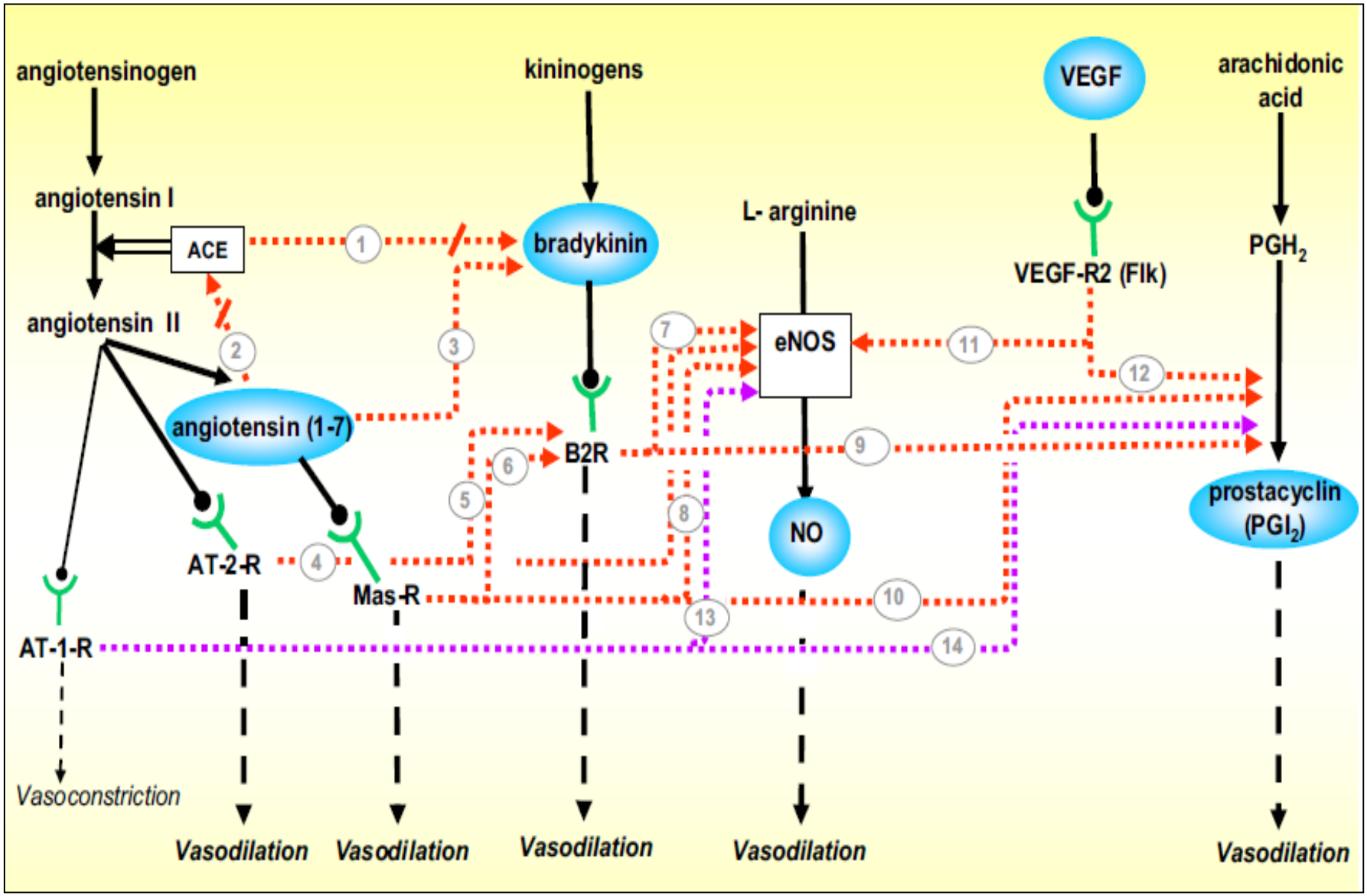
IRA

Proteinuria Fisiológica

Proteinuria

Tensión Arterial en el embarazo

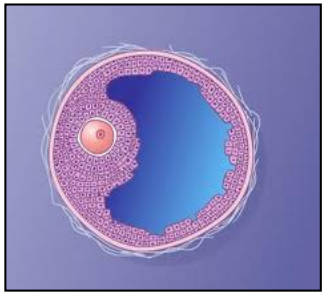


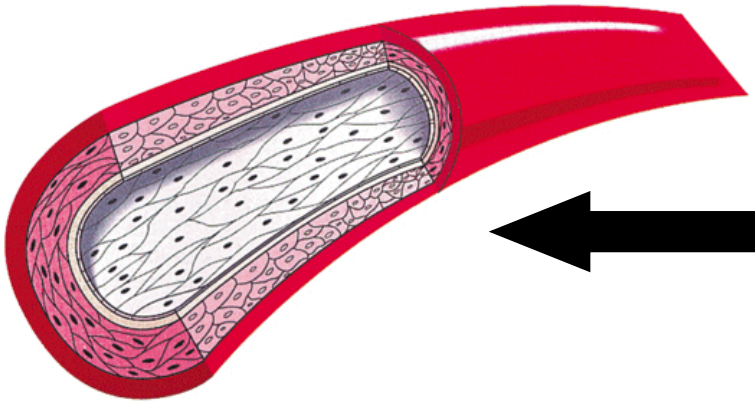


Reproductive Biology and Endocrinology 2009, **7**:79

Oxido Nítrico

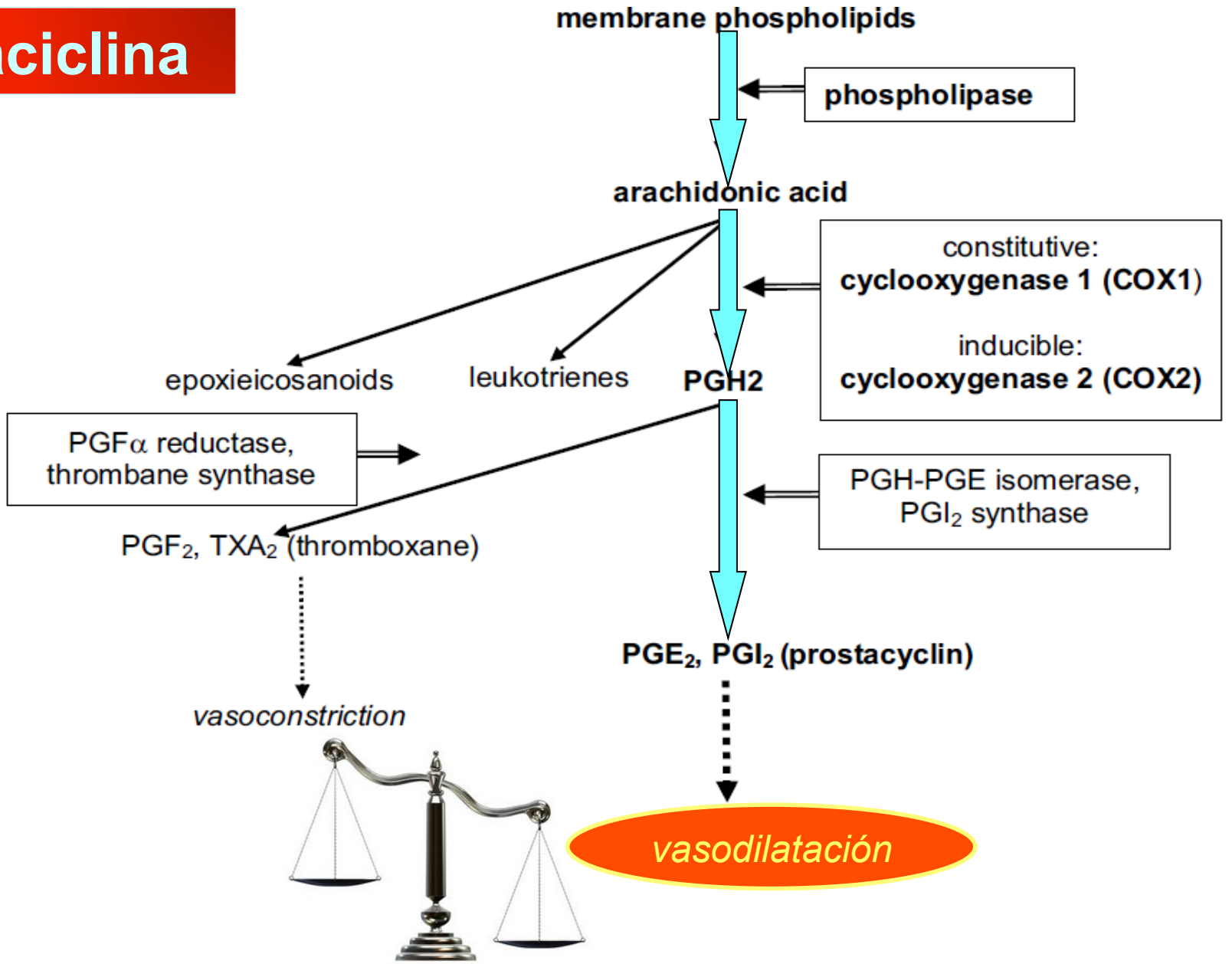
HCG → (+) → Cuerpo Lúteo → Relaxina → (+) Receptor B Endotelina → NO → Vasodilatación → ⬇TA





Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14

Prostaciclina

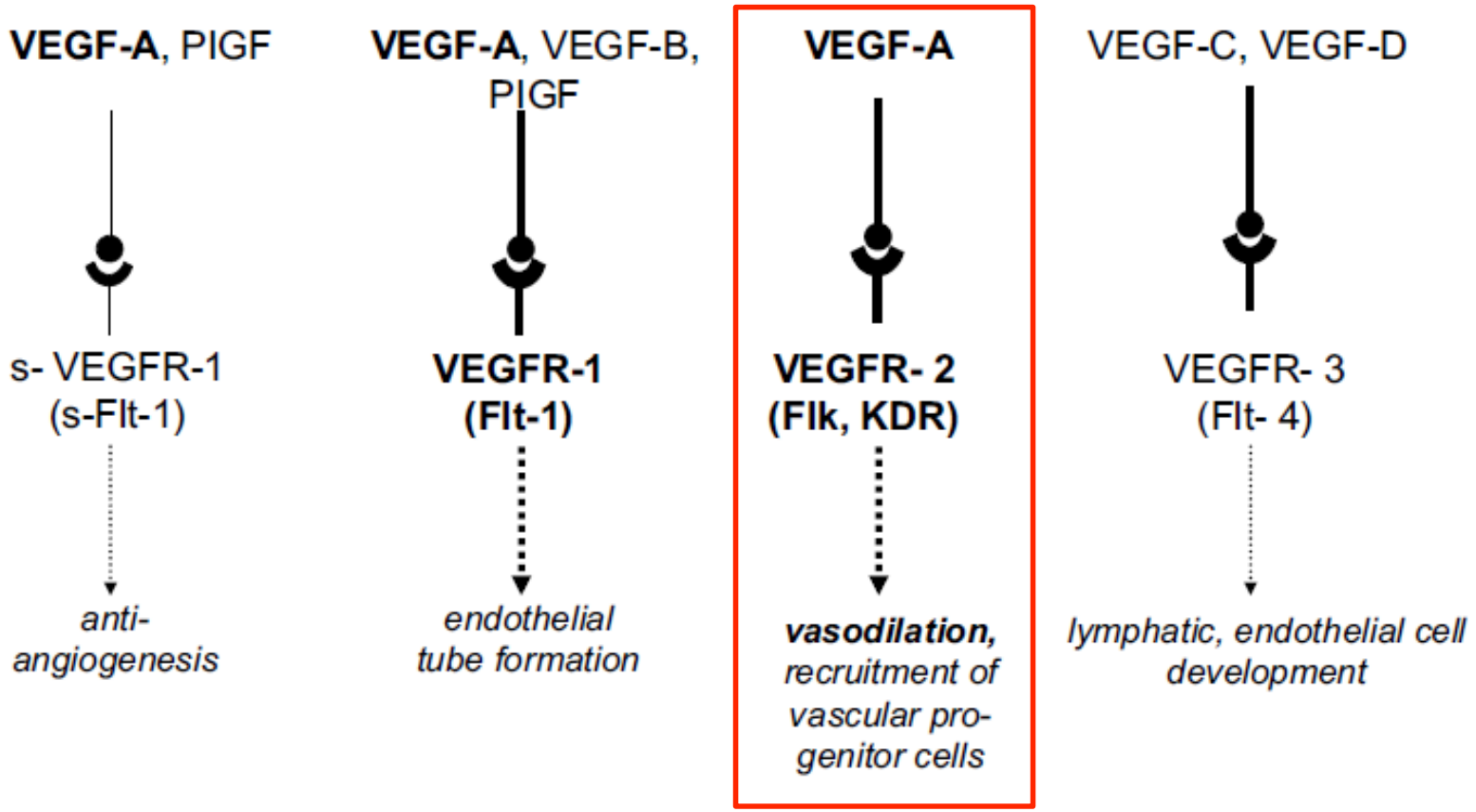


Reproductive Biology and Endocrinology 2009, **7**:79

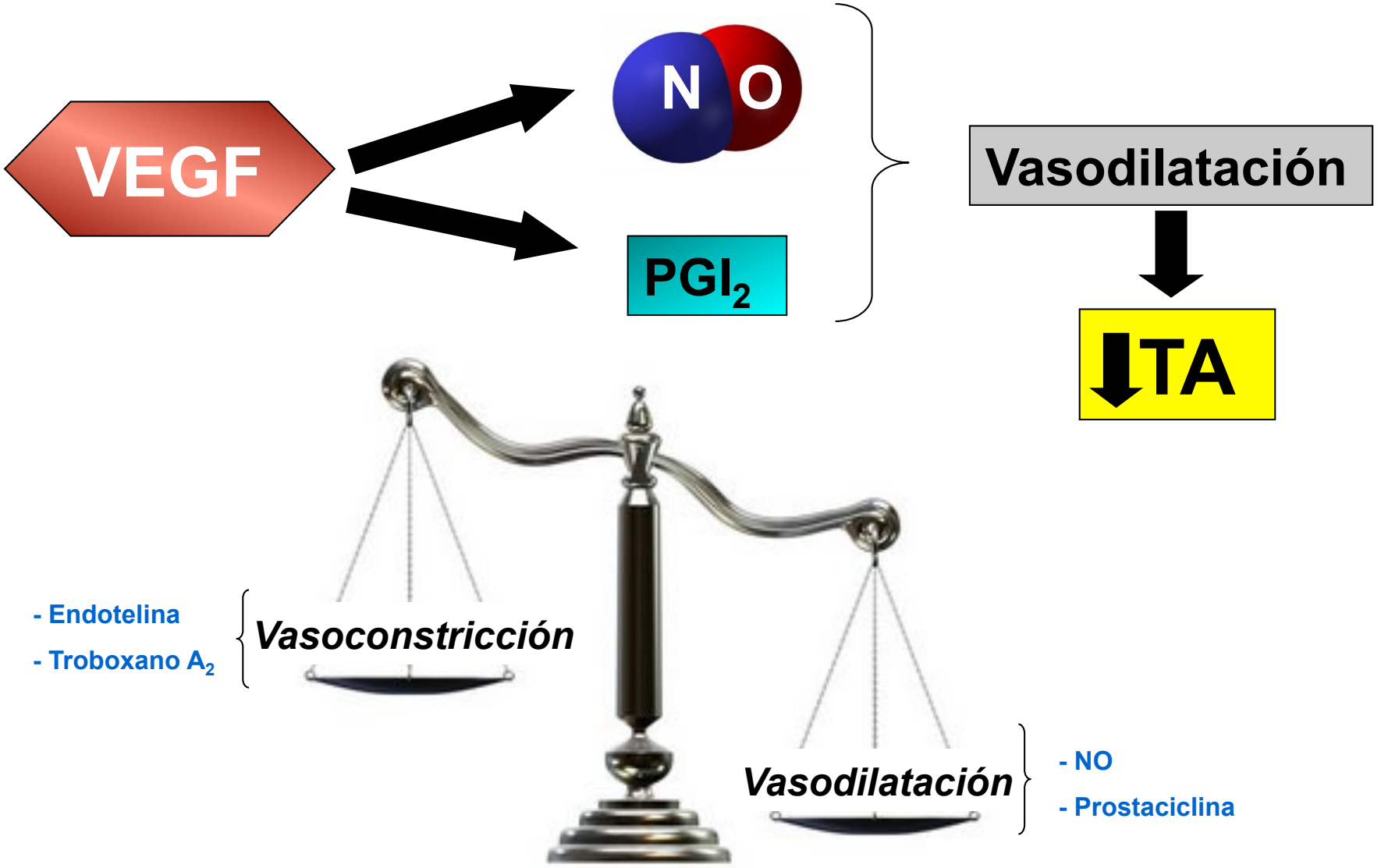
VEGF - A

Vascular endothelial growth factors

(VEGF-A: placenta; VEGF-B: neural tissues; VEGF-C: placenta;
VEGF-D: various organs except placenta and PIGF: placenta and other tissues)



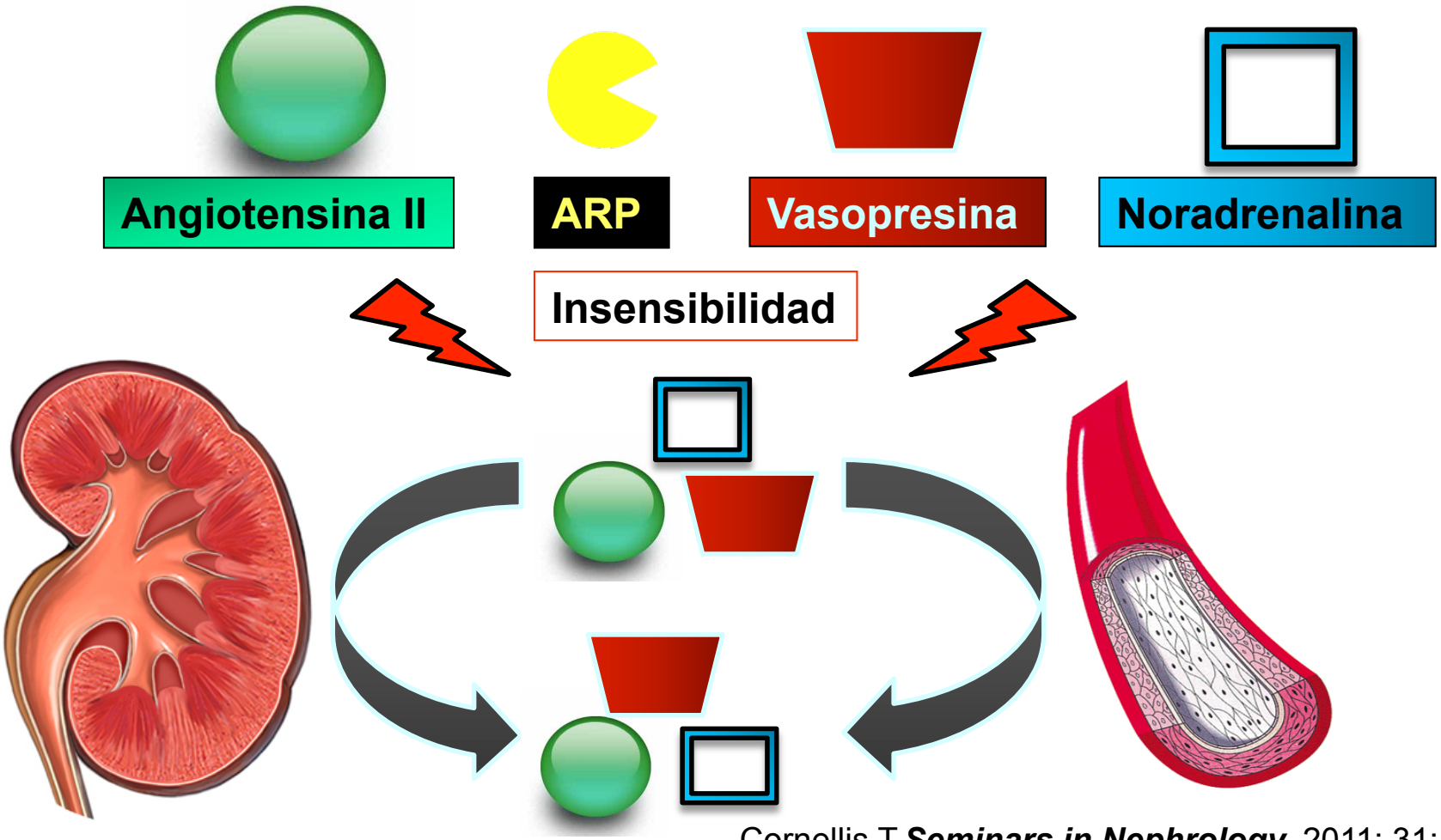
Reproductive Biology and Endocrinology 2009, **7**:79



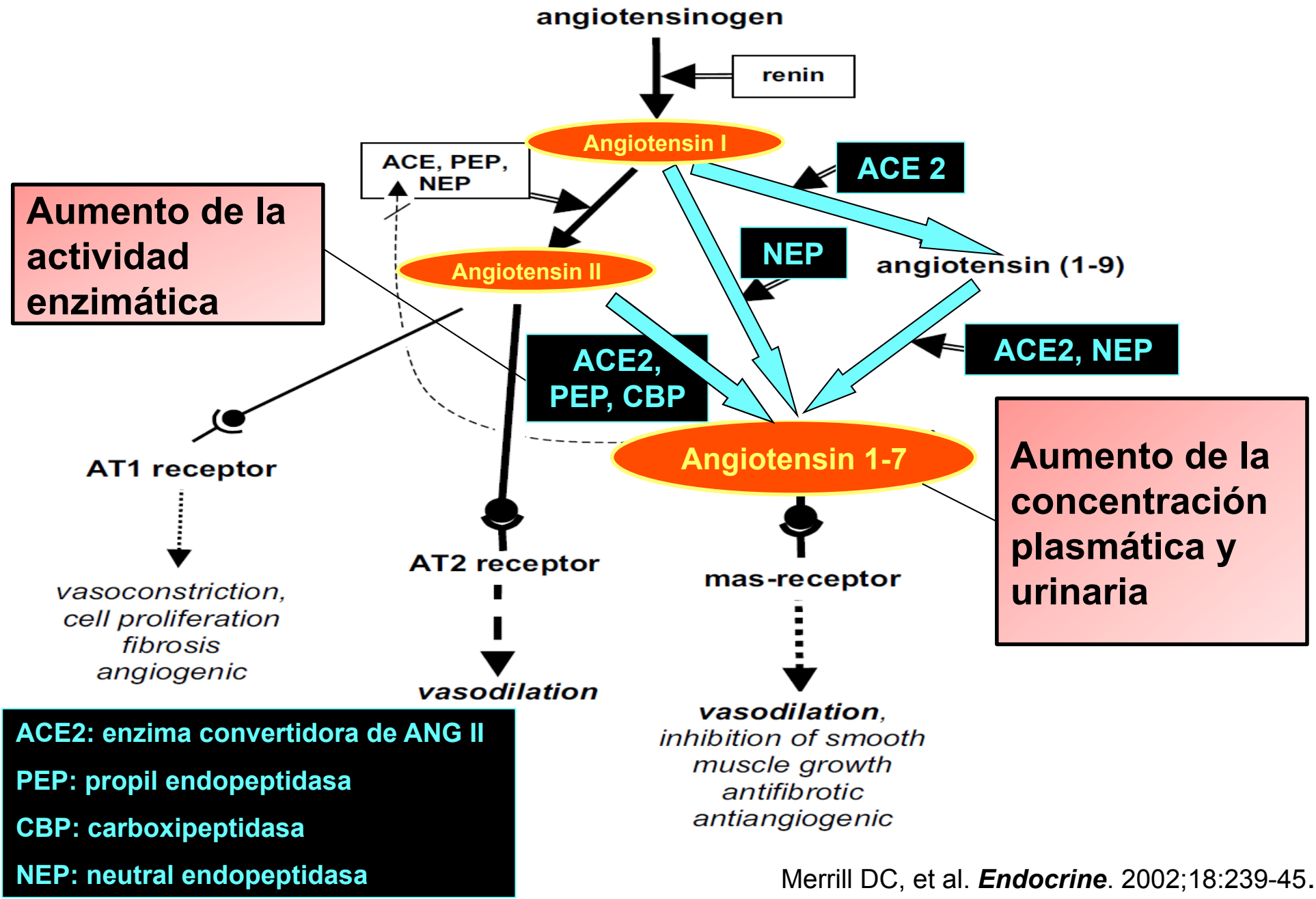
Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14

Angiotensina II

Up – regulation de varios componentes

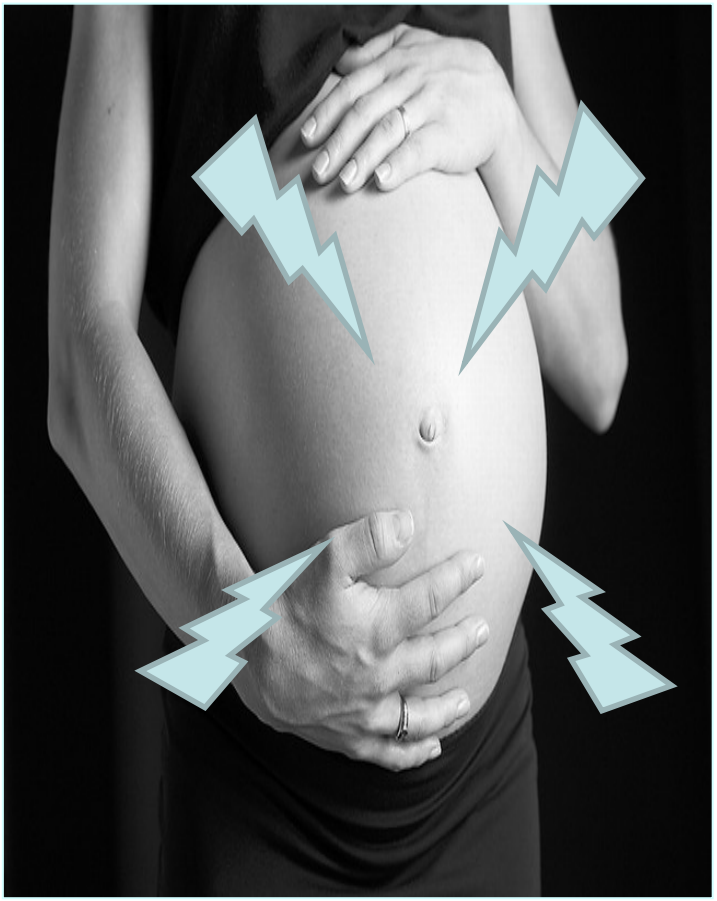


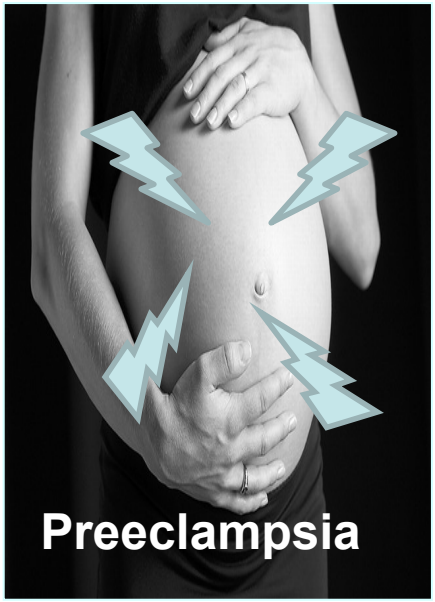
Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14

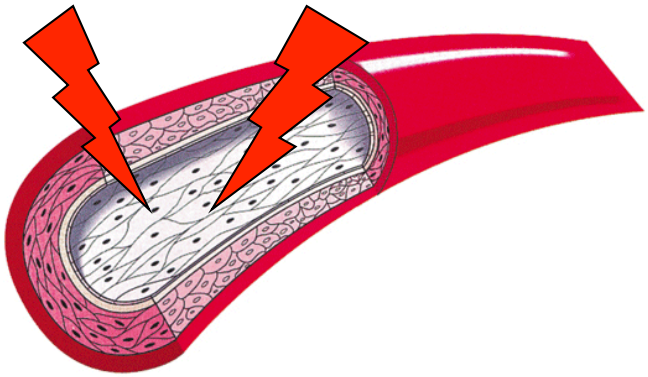


Merrill DC, et al. ***Endocrine***. 2002;18:239-45.

Tensión Arterial en la Preeclampsia

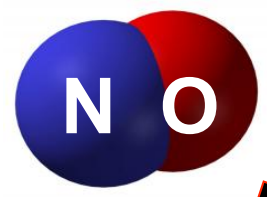






Disfunción Endotelial

eNOS



Vasodilatación

- NO
- Prostaciclina

Vasoconstricción

- Endotelina
- Troboxano A_2

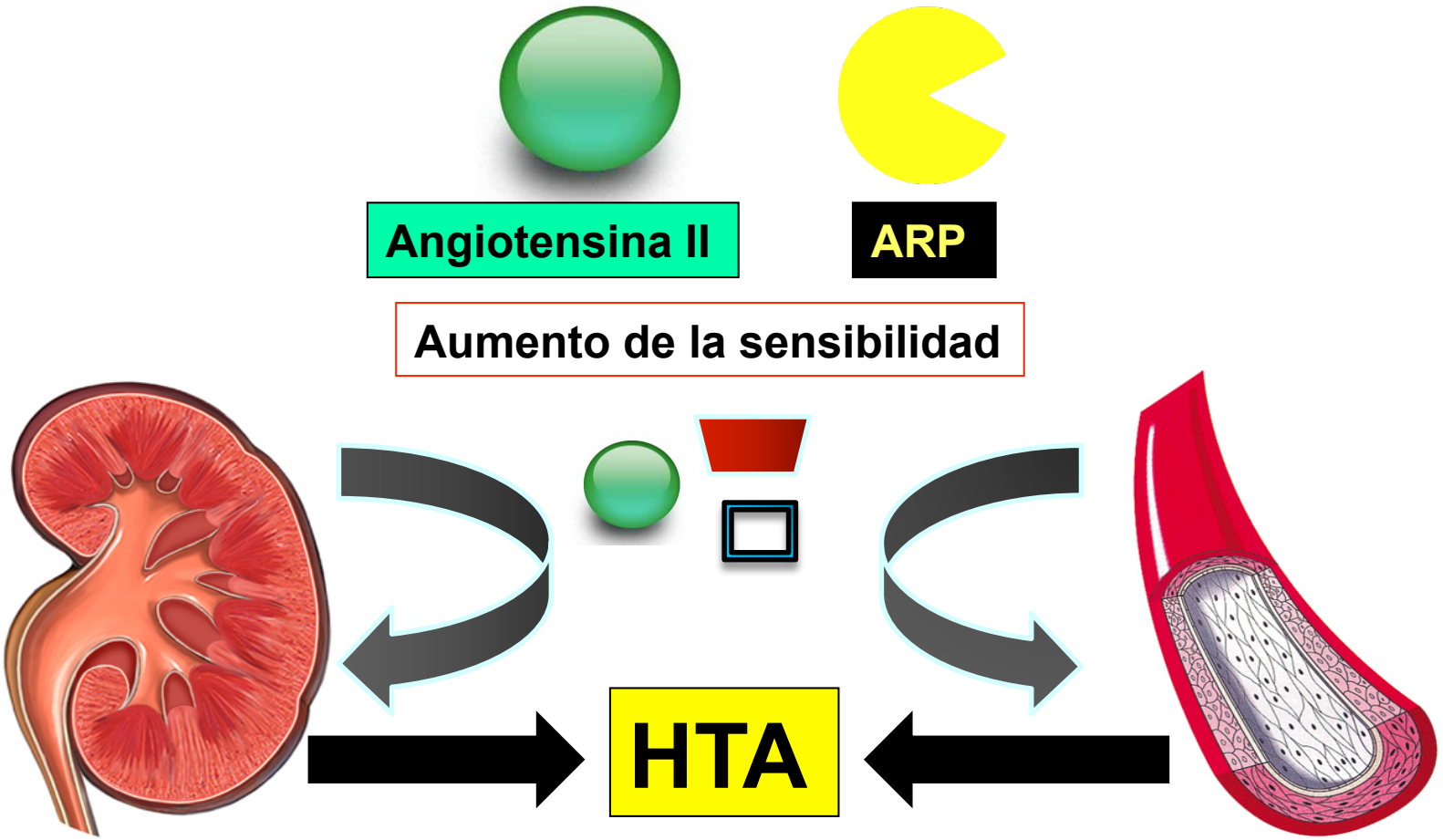
Bradiquinina

HTA

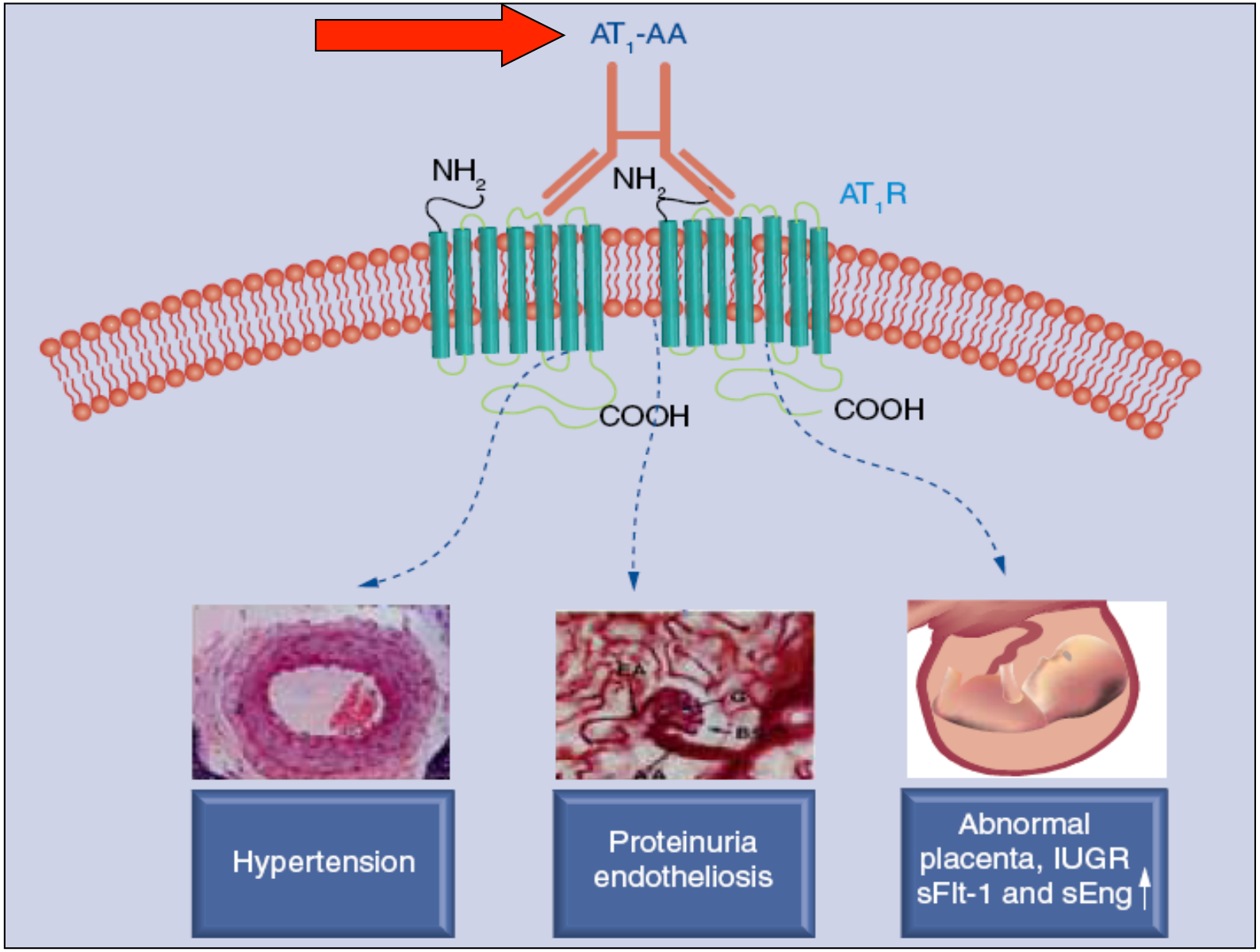
Reproductive Biology and Endocrinology 2009, **7**:79

¿Cuál es el mecanismo HTA en la preeclampsia?

Down – regulation de los componentes del SRAA



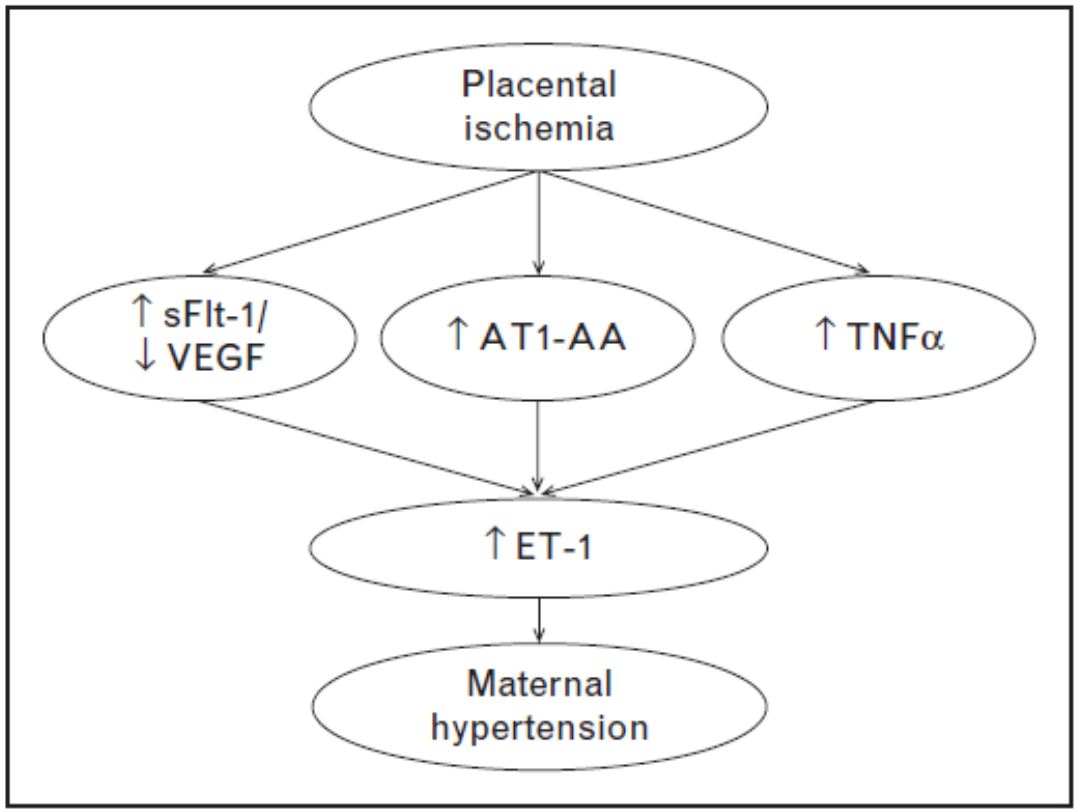
Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14



Yang Xia, Rodney E Kellems. ***Expert Rev. Clin. Immunol***. 7(5), 659–674 (2011)

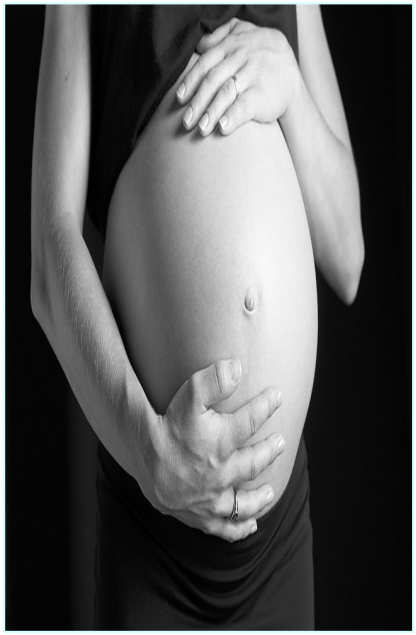
Endothelin as a final common pathway in the pathophysiology of preeclampsia: therapeutic implications

Eric M. George, Ana C. Palei, and Joey P. Granger



Curr Opin Nephrol Hypertens 2012, 21:157–162

Filtrado glomerular en el embarazo normal



↑ TFG

Hiperfiltración:
149 mL/min/1,73 m²

↓ Cr

Creatinina:0,6 ± 10 mg/dL

TFG= (Delta Ph – ↓P oncótica $_{CG}$) x Kf

π CG

Hemodilución → ↓π $_{plasma}$

↑ FPR mayor al 80%

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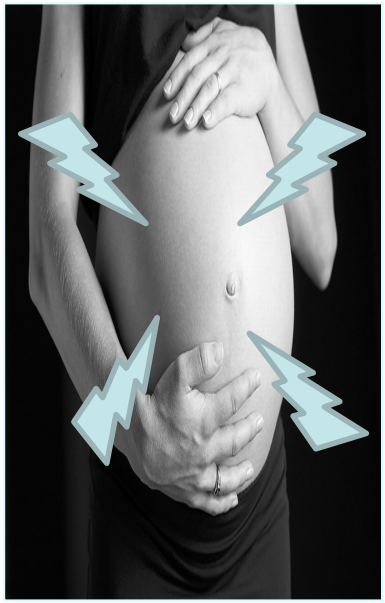
Filtrado glomerular en la preeclampsia



↓TFG

FG: < 91 mL/min/1,73 m^2

↑ Cr

Creatinina: 0,8±10 mg/dL

TFG= (Delta Ph – P oncótica $_{CG}$) x ↓ Kf

Kf = ↓ Permeabilidad hidráulica x ↓ Área de filtración

Permeabilidad hidráulica

- Depósito subendotelial de material fibrinoide
- Injuria de los podocitos

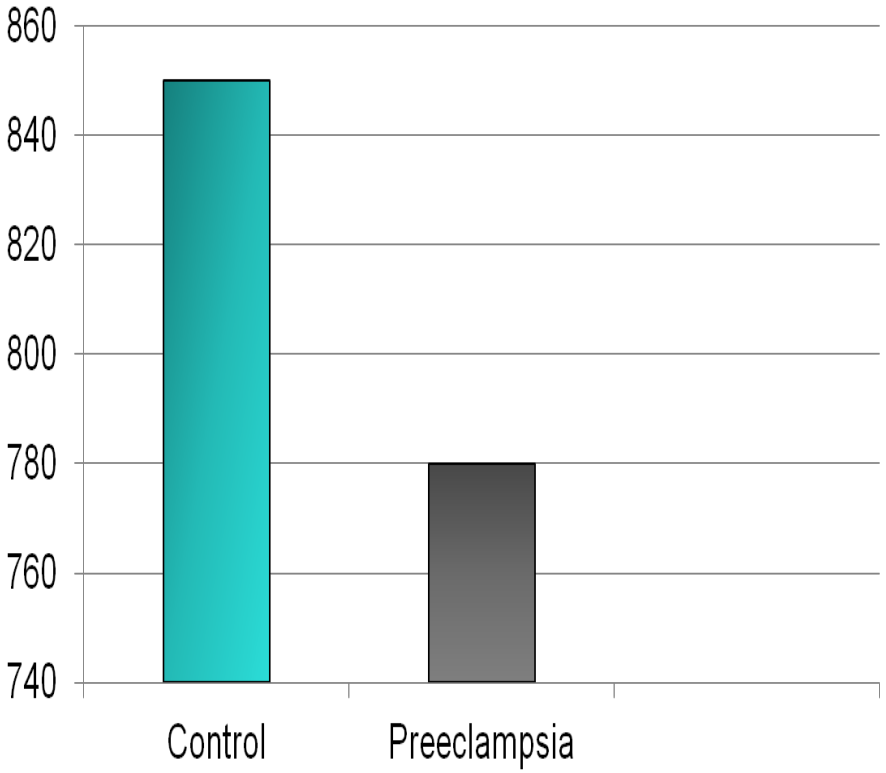
Área de filtración

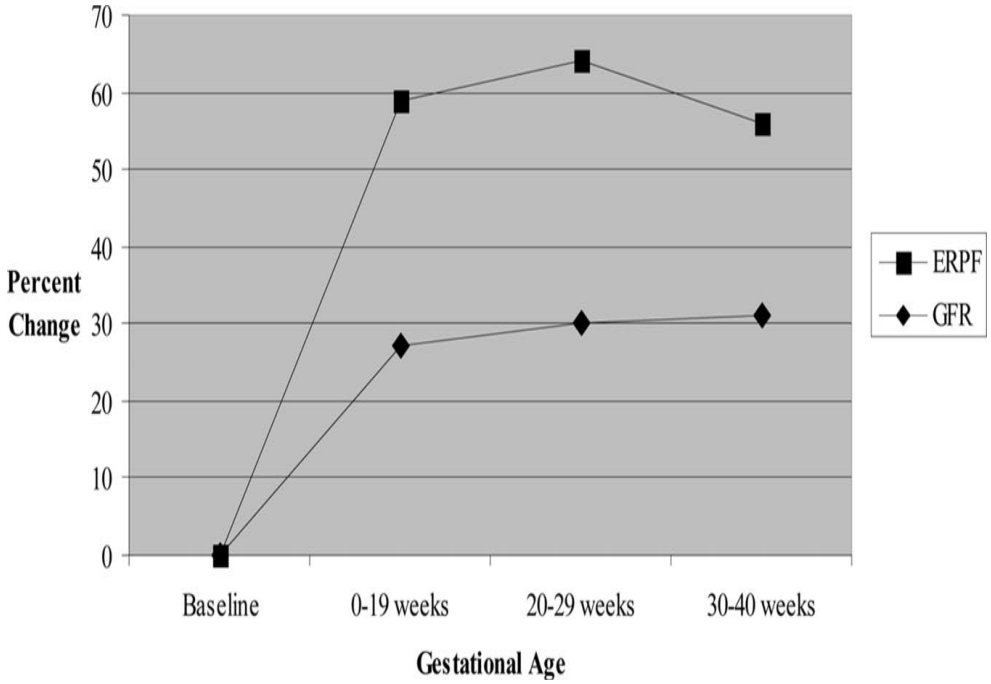
- Interposición de células mesangiales
- Edema células endoteliales capilar glomerular

Lafayette RA, et al. Nature of glomerular dysfunction in pre-eclampsia. ***Kidney Int***. 1998;54:1240-9.

TFG= (Delta Ph – ↑ P oncótica $_{CG}$) x Kf

FPR



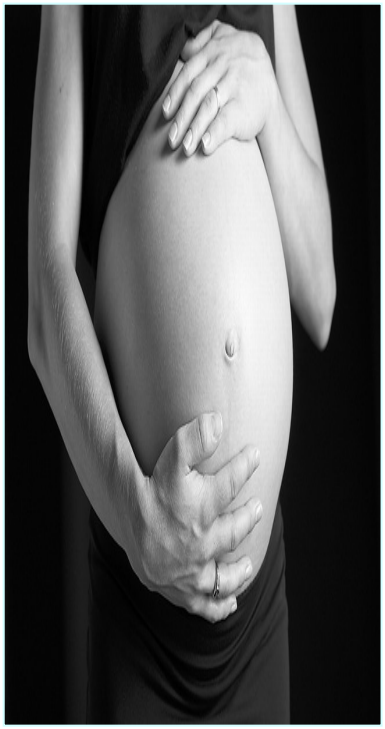


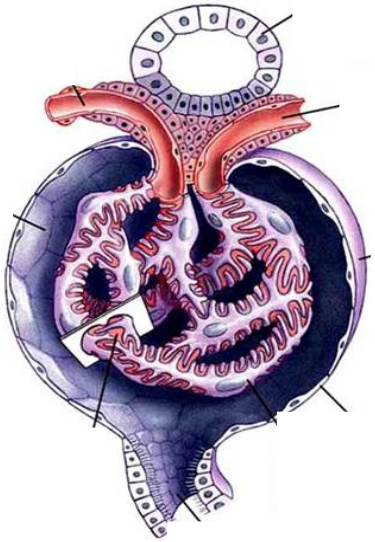
Conrad K,et al. Lindheimer M (Ed). Stamford, CT, Appleton & Lange, 1999, pp 263–326

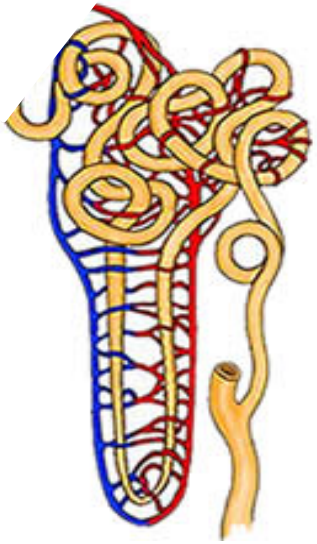
El aumento del FPR mantiene la presión oncótica baja en el flujo axial a través del capilar glomerular.

Moran P, et al. Glomerular ultrafiltration in normal and preeclamptic pregnancy. ***J Am Soc Nephrol***. 2003;14:648-52.

“Proteinuria” en el embarazo







Proteinuria
< 300 mg/24 Hs
< 0,3 $_{p}/_{Cr}$

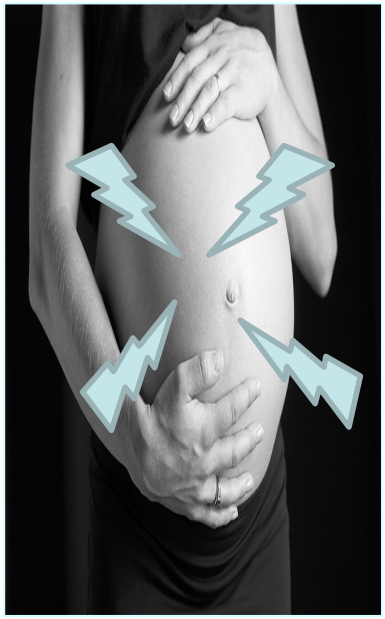
Hiperfiltración

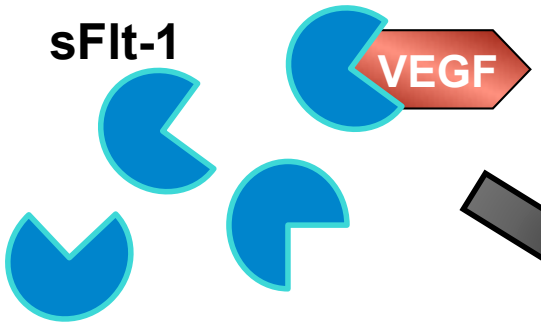
Alteración en la reabsorción tubular de proteínas

Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14

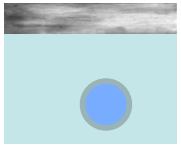
Proteinuria en la pre-eclampsia

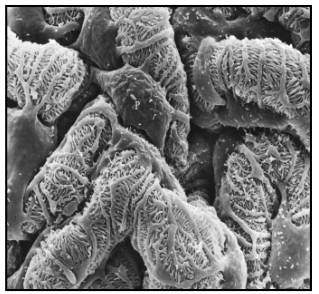
Proteinuria
> 300 mg/24 Hs
> 0,3 p/Cr
NO selectiva





⇧ concentración plasmática sFlt-1

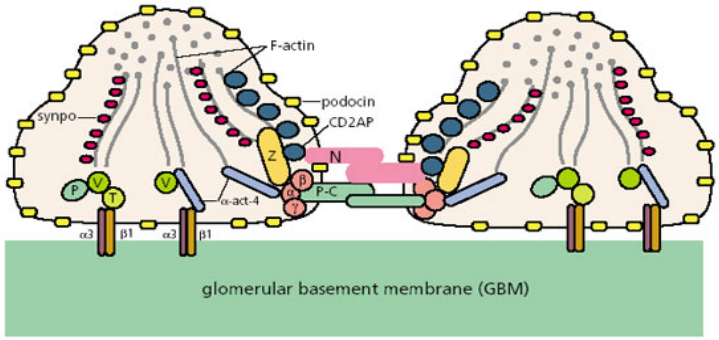




La malformación de la fenestras está asociada a daño del glucocálix

Disminución de la densidad y tamaño de las fenestraciones. Alteraciones en las señales por disfunción endotelial

Satchell SC, et al. ***Am J Physiol Renal Physiol***. 2009; 296:F947-56.



Desprendimiento de la Nefrina de los podocitos por el bloqueo de VEGF inducido por la liberación por parte del endotelio de endotelina-1

Collino F, et al. ***Am J Physiol Renal Physiol***. 2008;294:F1185-94.

Injuria Renal Aguda y Embarazo

1960

2012

1 / 3000

20- 40%

1 / 15000

1 / 20000

2- 10%

Mejoras en la atención y campañas de prevención

Grunfeld J, Pertuiset N: Acute renal failure in pregnancy: 1987. ***Am J Kidney Dis*** 1987; 9:359–362

Stratta P, Canavese C, Dogliani M, et al: Pregnancy-related acute renal failure. ***Clin Nephrol*** 1989; 32:14–20

Turney J, Ellis C, Parsons F: Obstetric acute renal failure 1956 –1987. ***Br J Obstet Gynaecol*** 1989; 96:679–687

INDIA

La incidencia de IRA asociada Embarazo (IRA-E) es del 20% y las tasas de mortalidad permanecen altas llegando al 50%

Chugh K, Singhal P, Sharma B: Acute renal failure of obstetric origin. ***Obstet Gynecol*** 1976; 48:642–646

Prakash J, Tripatti K, Srivastava P: Pregnancy related acute renal failure is still high in India. ***Proceedings of the 11th International Congress of Nephrologists***, 1990:15A

Injuria Renal Aguda y Embarazo

↑ Cr

Creatinina: > 0,8 mg/dL

- **Existe un alto grado de heterogeneidad en las definiciones de diagnóstico de las enfermedades renales en el embarazo y por lo tanto, no existe una definición validada para IRA**

- **RIFLE/AKIN, no está consensuado su uso para este tipo de pacientes y son necesarios más estudios para demostrar su utilidad**

	RIFLE	SCr Criteria	UOP Criteria	AKIN Stage	SCr Criteria	UOP Criteria
Increasing Severity of AKI	R	↑ SCr × 1.5	<0.5 mL/kg/hr × 6 hrs	1	↑ in SCr ≥0.3 mg/dL or ↑ ≥150% to 200% from baseline (1.5- to 2-fold)	<0.5 mL/kg/hr for >8 hrs
	I	↑ SCr × 2	<0.5 mL/kg/hr × 12 hrs	2	↑ in SCr to >200% to 300% from baseline (>2- to 3-fold)	<0.5 mL/kg/hr for >12 hrs
	F	↑ SCr × 3, or SCr ≥4 mg/dL with an acute rise of at least 0.5 mg/dL	<0.5 mL/kg/hr × 24 hrs or anuria × 12 hrs	3	↑ in SCr to >300% (3-fold) from baseline or SCr ≥4 mg/dL with an acute rise of at least 0.5 mg/dL	<0.5 mL/kg/hr × 24 hrs or anuria × 12 hrs
	L	Persistent loss of kidney function for >4 wks				
	E	Persistent loss of kidney function for >3 months				

Bellomo R, et al. ***Crit Care*** *2004; 8:R204–R212*

Mehta RL, et al. ***Crit Care*** *2007; 11:R31*

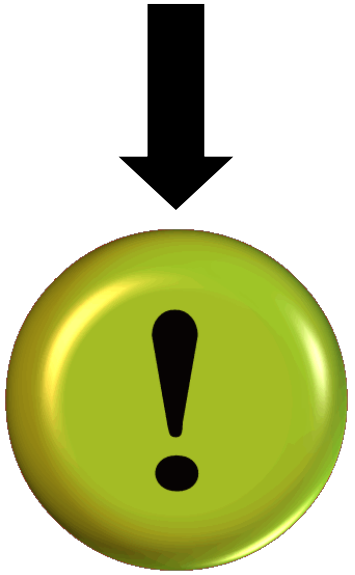
ACUTE KIDNEY INJURY ETIOLOGY IN PREGNANCY

Causes	
Prerenal	Hemorrhage
	Hyperemesis gravidarum
	Congestive heart failure
	Sepsis
Intrarenal	Acute tubular necrosis
	Pyelonephritis
	Renal cortical necrosis
	Thrombotic microangiopathy
	Preeclampsia/HELLP syndrome
	Acute fatty liver of pregnancy
	Glomerulonephritis
	Medications
Postrenal	Obstruction

HELLP = hemolysis, elevated liver enzymes and low platelet count.

Primer Trimestre

Tercer Trimestre



Machado S, et al. ***JNEPHROL*** 2012; 25(01): 19-30.

Preeclampsia severa

IRA → **Incidencia del 1,5 al 2% (existen variaciones de acuerdo a la definición)**

Drakeley AJ, et al. . ***Am J Obstet Gynecol*** 2002; 186:253–256

Sdme. HELLP

Incidencia > al 7 %

Sibai BM, et al. ***Am J Obstet Gynecol*** 1993; 168:1682–1690

Sería una variante de la preeclampsia severa que ocurre entre el 4 a 14 % de los casos

Sibai BM,et al. . ***Am J Obstet Gynecol*** 1986; 155:501–509

Años más tarde, la misma autora sostiene que es una enfermedad distinta, dado que el 20% no tiene antecedentes de hipertensión o proteinuria

Barton JR, Sibai BM. ***Semin Perinatol***. 2009;33(3):179-188.

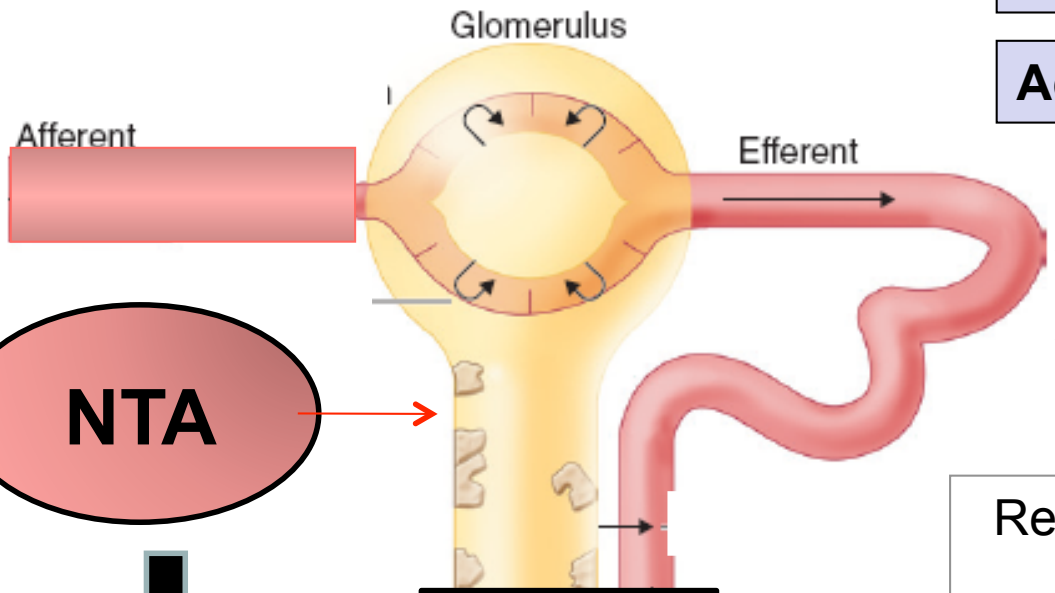
Preeclampsia severa / Sdme. HELLP

Lesiones Primarias → **Glomérulo endoteliosis**

Depleción de volumen intravascular

Vasoconstricción **SIRS**

Activación de la coagulación



NTA → **IRA**

NECROSIS CORTICAL

Reducción Volumen Intravascular

Activación de la coagulación

Abruptio Placentae

Hemorragia postparto

Complicaciones superpuestas

Brown M, et al. *Aust N Z* ***J Obstet Gynaecol*** *1989; 29:230–232*

Imitators of severe pre-eclampsia, HELLP, and eclampsia

- Acute fatty liver of pregnancy
- Thrombotic thrombocytopenic purpura
- Hemolytic uremic syndrome
- Exacerbation of lupus erythematosus
- Immune thrombocytopenic purpura
- Thrombophilias
  - Antiphospholipid syndrome
  - Homozygous FVL or prothrombin gene mutation
- Cholecystitis/pancreatitis
- Systemic viral sepsis (disseminated herpes)
- Systemic inflammatory response syndrome (sepsis)
- Hemorrhagic or hypotensive shock
- Stroke in pregnancy/post partum
  - Hypertensive encephalopathy
  - Intracerebral hemorrhage
  - Cerebral vascular thrombosis/embolism
  - Cerebral vasoconstriction syndrome

Sibai B. Imitators of severe pre-eclampsia/eclampsia. ***Clin Perinatol :*** 31 (2004) 835– 852

Signs and Symptoms	HELLP Syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Hypertension	85	50	20–75	80–90	80 with APA, nephritis
Proteinuria	90–95	30–50	With hematuria	80–90	100 with nephritis
Fever	Absent	25–32	20–50	NR	Common during flare
Jaundice	5–10	40–90	Rare	Rare	Absent
Nausea and vomiting	40	50–80	Common	Common	Only with APA
Abdominal pain	60–80	35–50	Common	Common	Only with APA
Central nervous system	40–60	30–40	60–70	NR	50 with APA

Diferencias

Baha M. Sibai. . ***Obstetrics & Gynecology***. Vol 109; 4: 2007

Laboratory Findings	HELLP Syndrome	AFLP	TTP	HUS	Exacerbation of SLE
Thrombocytopenia (less than 100,000/mm³)	More than 20,000	More than 50,000	20,000 or less	More than 20,000	More than 20,000
Hemolysis (%)	50–100	15–20	100	100	14–23 with APA
Anemia (%)	Less than 50	Absent	100	100	14–23 with APA
DIC (%)	Less than 20	50–100	Rare	Rare	Rare
Hypoglycemia (%)	Absent	50–100	Absent	Absent	Absent
VW factor multimers (%)	Absent	Absent	80–90	80	Less than 10
ADAMTS13 less than 5% (%)	Absent	Absent	33–100	Rare	Rare
Impaired renal function (%)	50	90–100	30	100	40–80
LDH (IU/L)	600 or more	Variable	More than 1,000	More than 1,000	With APA
Elevated ammonia (%)	Rare	50	Absent	Absent	Absent
Elevated bilirubin (%)	50–60	100	100	NA	Less than 10
Elevated transaminases (%)	100	100	Usually mild*	Usually mild*	With APA

Manejo de la Preeclampsia severa/ Sme. HELLP

THE MANAGEMENT OF PRE-ECLAMPSIA*

occurred among our prenatal cases. Approximately four-fifths of the patients were primi-

562 EASTMAN AND STEPTOE: PRE-ECLAMPSIA [Canad. M. A. J. June 1945, vol. 52

THE MANAGEMENT OF PRE-ECLAMPSIA*

By Nicholson J. Eastman, M.D. and Philip P. Steptoe, M.D.

Baltimore, Maryland

IF a case of pre-eclampsia is to be managed with complete success, a number of objectives must be attained. Among these are: (1) Prevention of convulsions. (2) Prevention of residual hypertension. (3) Delivery with minimum trauma yet in a manner which will not handicap patient in future pregnancies (Cæsarean section). (4) Delivery of a child which survives.

In certain cases of pre-eclampsia, especially in patients near term, all four of these objectives may be served equally well by the same treatment, namely, prompt induction of labour; and no question of conflict between any two of them arises. In other instances, however, the attainment of certain of these desiderata may so conflict with the realization of another as to make it virtually impossible to gain all four objectives. For instance, if a patient develops severe pre-eclampsia two or three months before her expected date of confinement, prompt termination of pregnancy may seem indicated if objectives Nos. 1 and 2 are to be realized, but this course may well result in the delivery of a non-viable premature infant and consequent failure to attain objective No. 4. Again, when pre-eclampsia develops at such an early date, a long

From the Department of Obstetrics, the Johns Hopkins University and Hospital.

occurred among our prenatal cases. Approximately four-fifths of the patients were primigravidæ. The criterion used for the diagnosis of pre-eclampsia was the development, after the 28th week of pregnancy, of a systolic blood pressure of 140 mm. Hg. and/or a diastolic pressure of 90 mm. Hg., the hypertension to be maintained on at least two occasions, six hours or more apart. As may be seen in Table I,

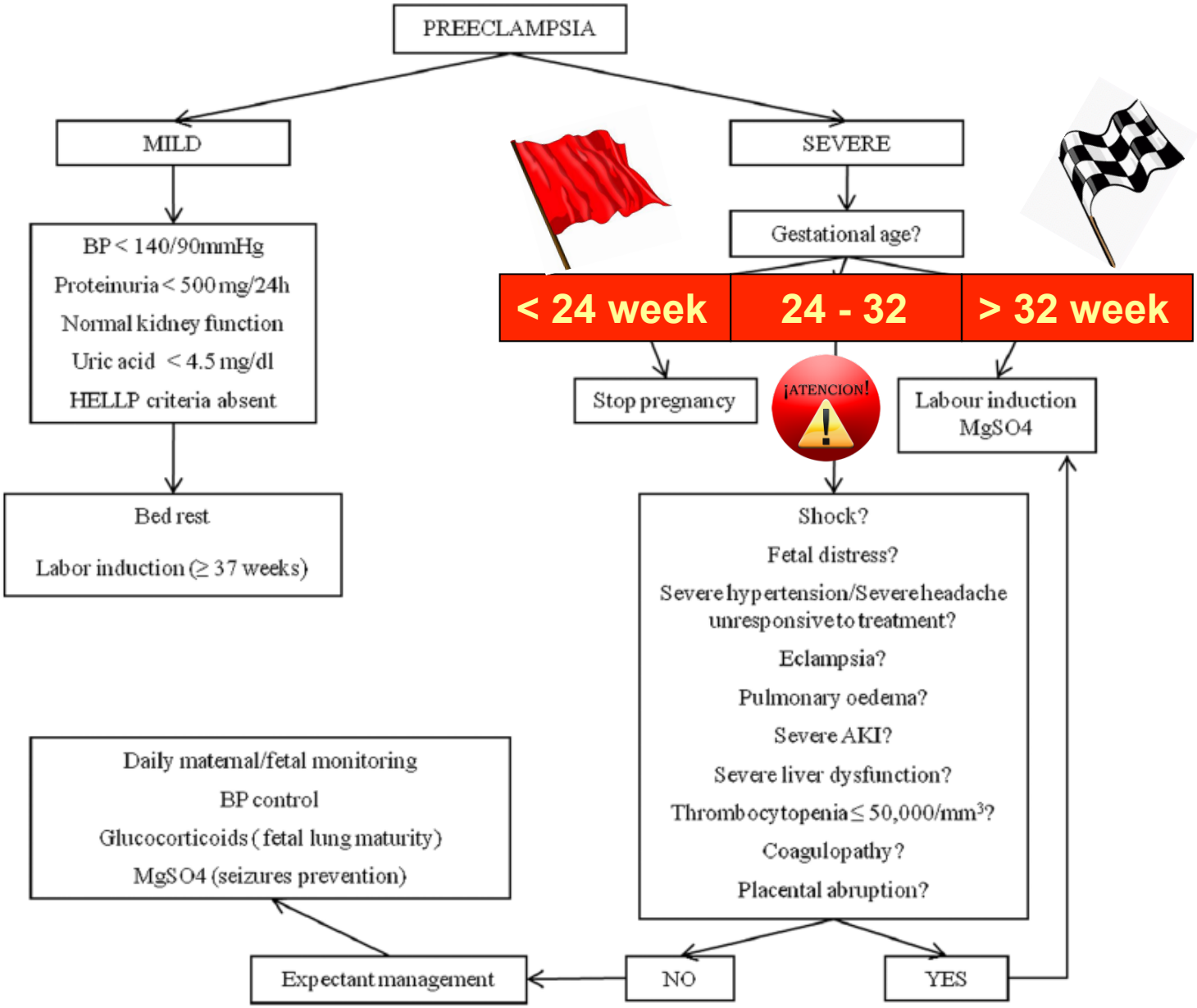
TABLE I.

Incidence of eclampsia developing in cases of pre-eclampsia, and mortality rates in eclamptic and non-eclamptic groups. J.H.H., January 1, 1924 to December 31, 1943.

Total cases of pre-eclampsia—2,418	
Developed eclampsia 92 (3.8%)	Did *not* develop eclampsia 2,326 (96.2%)
Maternal mortality, 7 (7.6%)	Maternal mortality, 4 (0.2%)
Total infant mortality, 20 (21.7%)	Total infant mortality, 158 (6.8%)
Total number of convulsions 398 (Av. 4.3)	

among these 2,418 cases of pre-eclampsia under our surveillance, 92 instances of eclampsia developed, an incidence of 3.8%. These 92 eclamptic cases represent failures to attain the first objective in the management of pre-eclampsia, namely, prevention of convulsions. Although the great majority of these patients suffered only one to three convulsions, the gravity of these failures in general is made plain by the fact that 7 of the 92 mothers and 20 of the infants died, a maternal and fetal mortality rate of

to inquire into the causes of our failure to prevent this costly complication in the 92 cases.



Susana Machado, et al. Acute kidney injury in pregnancy: a clinical challenge. ***JNEPHROL*** 2012; 25(01): 19-30

Manejo de la Preeclampsia severa/ Sme. HELLP

Management of Preeclampsia	
Clinical Problem	**Management**
Assess indications for delivery	Always review whether an indication for delivery is present by clinical and laboratory monitoring
Control blood pressure (BP)	Acute treatment if BP ≥170/110 mmHg Chronic treatment if BP ≥140/90 mmHg
Eclampsia prophylaxis or treatment	Diazepam 10–20 mg IV to terminate convulsions Magnesium sulfate for persistent neurologic signs (also an indication for delivery): 4 g IV over 20 min, then 1.5 g/h for 48 h
Supportive therapies (sometimes required)	Platelet infusion if count < 20–40 $\times 10^9$/l Fresh-frozen plasma for microangiopathy or for reduced clotting factors Dialysis for established acute kidney injury
Progressive decline in renal, hepatic, or clotting function or of fetal growth	Delivery

Floege J, et al. ***Comprehensive Clinical Nephrology***. 4th 2010; 511

Evolución Preeclampsia severa/ Sme. HELLP

- **Tanto la HTA como la *proteinuria* generados por la preeclampsia usualmente desaparecen a los pocos días o semanas del parto**
- **En casos excepcionales se puede extender hasta los 6 meses**
- **En caso de persistir más allá de los 6 meses es necesario efectuar una Punción Biopsia Renal**

Floege J, et al. ***Comprehensive Clinical Nephrology***. 4th 2010; 511

Conclusiones

- Preeclampsia severa cursa con caída de la TFG, HTA, proteinuria

- La IRA en los cuadros de Preeclampsia severa son raros a excepción que cursen con cuadros concomitantes que disminuyan FPRE

- Tener en cuenta los imitadores de preeclampsia tales como ***Microangiopatía trombótica***, ***Hígado graso del embarazo***, ***LES***

- La ***Endotelina*** parecería ser un target racional para el tratamiento de sostén

- La interrupción del embarazo sigue siendo el tratamiento efectivo

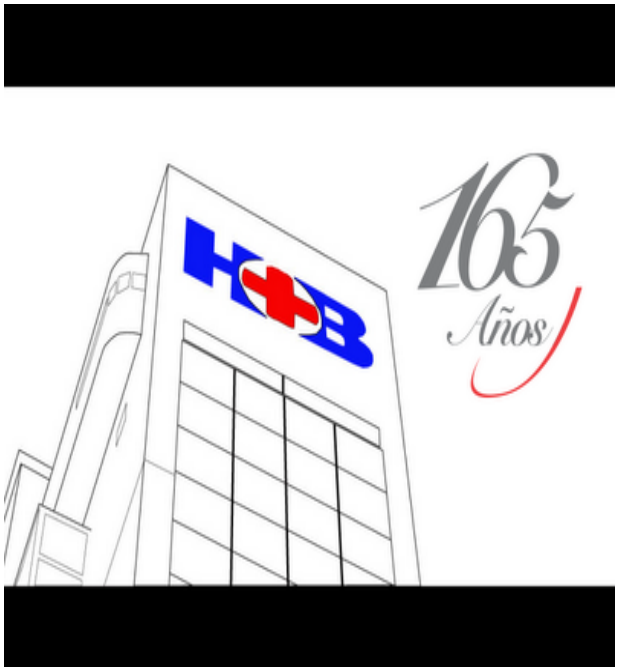
Estudio Argentino Multicéntrico Prospectivo de Pacientes Obstétricas Críticas (ProPOC)

Email del estudio: propoc@gmail.com

En la utopía de ayer, se incubó la realidad de hoy, así como en la utopía de hoy se palpitarán las realidades del mañana.

José Ingenieros 1877-1925

Gracias por su atención…!!!!!



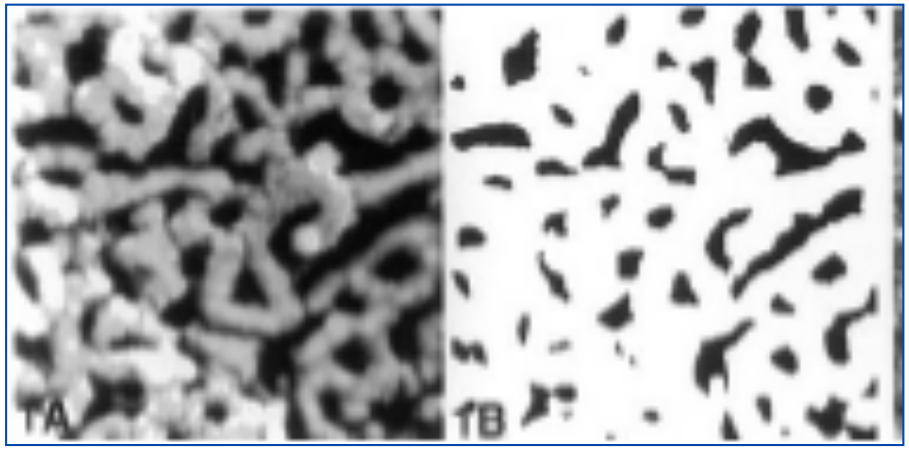
Servicio de Nefrología

Hospital Británico de Bs. As.

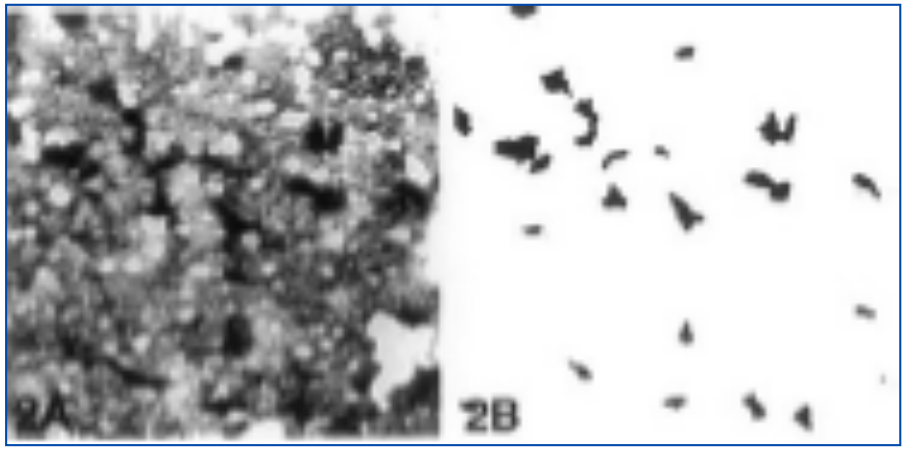
www.nefrohospbritanico.org.ar

Scanning electron microscopy and digitized of fenestrae

Control



Preeclampsia



Lafayette RA, et al. Nature of glomerular dysfunction in pre-eclampsia. ***Kidney Int***. 1998;54:1240-9.

Manejo de la falla renal aguda en la Preeclmapsia

	1er Perfil	2do Perfil	3er Perfil
Wedge	↓	↑ ⊥	↑
VM	↑	↑ ⊥	↓
RSP	↑	⊥	↑

Clark SL, et al. ***Am J Obstet Gynecol*** 1986; 154:490–494

Table 3. Potential indications for hemodynamic monitoring in obstetric patients

Cardiac indications
- Severe valvular heart disease (aortic stenosis or mitral stenosis associated with pulmonary hypertension)
- Cardiomyopathy with ejection fraction <15–20%
- Sudden cardiovascular collapse (suspected amniotic fluid embolism or pulmonary embolism)

Pulmonary indications
- Adult respiratory distress syndrome with positive end-expiratory pressure >15 mm Hg
- Severe pulmonary disease with secondary pulmonary hypertension
- Pulmonary edema associated with severe preeclampsia

Renal indications
- Persistent oliguria despite fluid resuscitation (e.g., severe preeclampsia) ←

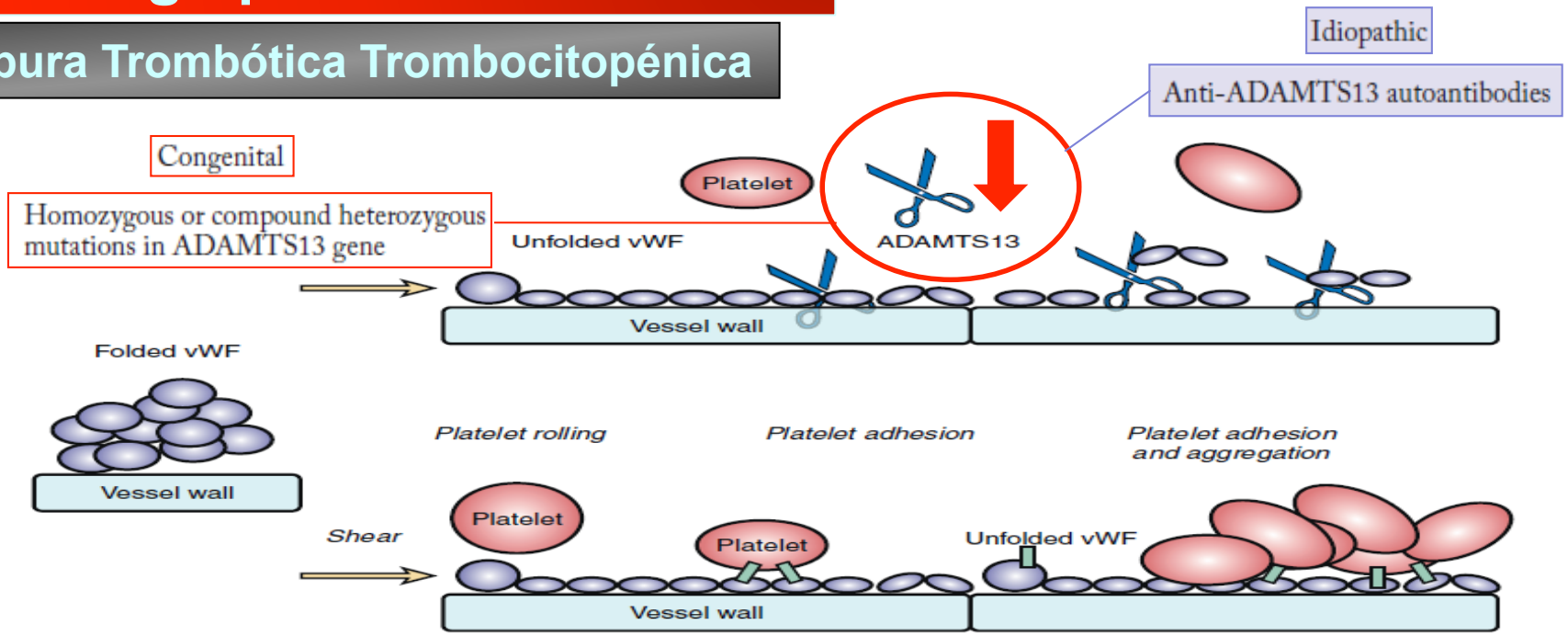
Miscellaneous
- Septic shock refractory to fluid resuscitation and vasopressor therapy

La falla renal fue la indicación más frecuente de monitoreo hemodinámico invasivo

Gilbert WM,, et al. . ***Am J Obstet Gynecol*** 2000; 182: 1397–1403

Microangiopatías trombóticas

Púrpura Trombótica Trombocitopénica



- **El embarazo puede precipitar la recaída en mujeres con antecedentes de PTT**

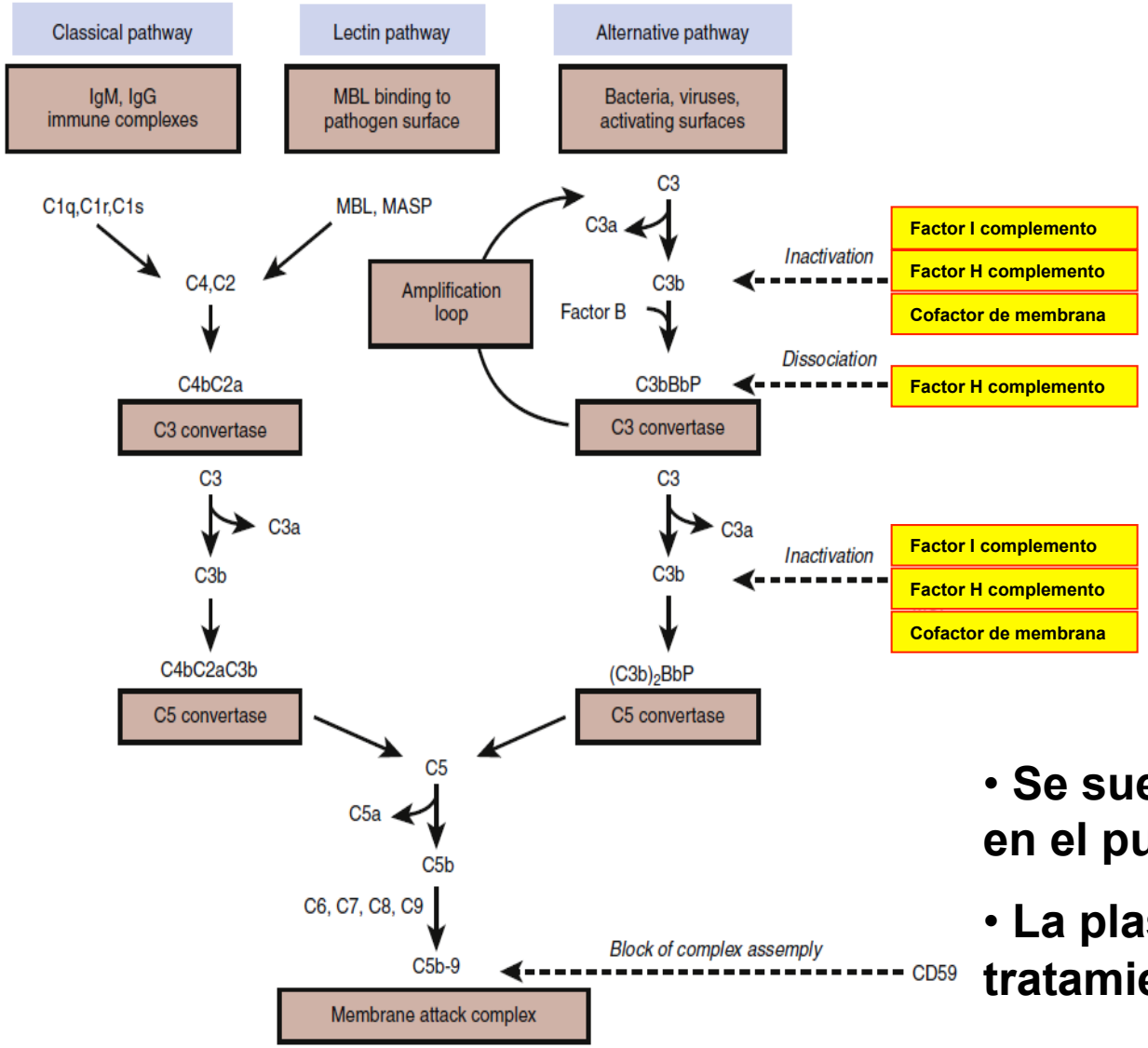
- **Los niveles funcionales de ADAMTS13 disminuyen durante el segundo y tercer trimestre, lo que podría contribuir a la aumento de la incidencia de PTT**

- **La interrupción del embarazo no cambia el curso de la enfermedad**

- **La plasmaferesis constituye el tratamiento**

Microangiopatías trombóticas

Síndrome Urémico Hemolítico



Idiopathic

Mutations: CFH (15%-20%); CFI (3%-6%); C3 (4%-6%); membrane cofactor protein (6%-10%); THBD (2%); CFB (2 cases) Anti-CFH autoantibodies (6%-10%)

Pregnancy-associated

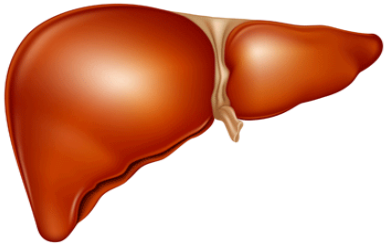
Mutations: CFH (20%); CFI (15%)

HELLP syndrome

Mutations: CFH (10%); CFI (20%); membrane cofactor protein (10%)

- **Se suele presentar en 3 trimestre o en el puerperio**
- **La plasmaféresis constituye el tratamiento**

Higado graso del embarazo



- **Se da en 1/12500 nacimientos. Potencialmente fatal.**
- **Un 15-20% cursa asintomático. Se presenta como un cuadro de malestar general, anorexia, náuseas, vómitos y dolor hipocondrio derecho 1 a 2 semanas de evolución.**
- **Es frecuente encontrar alteración del hepatograma, hipoglucemia, hiperamonemia, bajo fibrinógeno, baja concentración antitrombina III y tiempo protrombina alterado. Ecografía hepática muestra incremento de la ecogenicidad.**
- **Se da por la acumulación de microvesiculas de grasa en el hígado.**

Complicaciones

- **Sepsis 10%**
- **EAP/SDRA 25%**
- **IRA ⟷ 44%**
- **CID, hipoglucemia, pancreatitis 15%**

Baha M. Sibai. Imitators of Severe Pre-eclampsia. ***Semin Perinatol*** 33:196-205, 2009

LES Exacerbación

- **Enfermedad multiorgánica caracterizada por el deposito de inmunocomplejos en capilares sanguíneos y a nivel tisular.**
- **En general el *Flaire* grave aparece en un 25-30% y puede presentarse por primera vez en el embarazo o periodo post-parto.**

Cortes-Hernandez J,et al. ***Rheumatology (Oxford)*** 2002; 41:643–50.

Hallazgos durante el *Flair:*

-Lesiones cutáneas
-Dolores articulares
-Fiebre
-HTA
-Proteinuria
-Hematuria

Laboratorio durante el *Flair:*

-Pancitopenia
-Ac Anti ADN
-C_3 C_4

Preeclampsia severa / Sdme HELLP

LES

Ac Antifosfolipido en mujeres con LES

Ac Antifosfolipidos

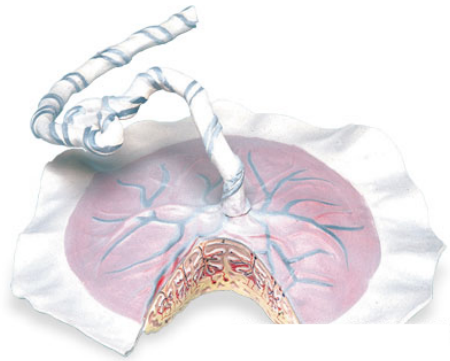
- **Anticoagulante lúpico**
- **Ac Anticardiolipina**

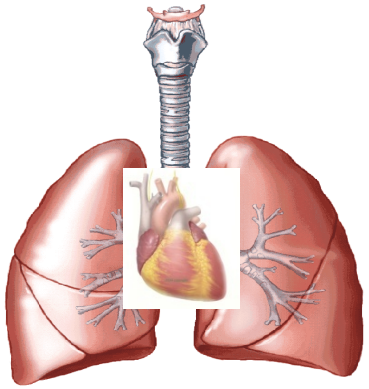
30% LES

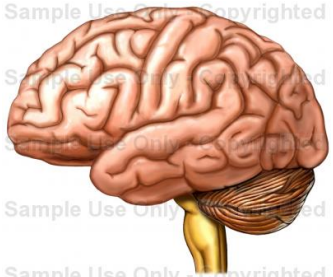
Riesgo

ISQUEMIA

Eventos tromboembólicos ⟷ **Microangiopatía Trombótica**







Sde. Antifosfolípido catastrófico aparece en < 1% de LES con AC Antifosfolípido

Baha M. Sibai. Imitators of Severe Preeclampsia. ***Obstetrics & Gynecology***. Vol 109; 4: 2007

Pre-eclmapsia sobreimpuesta HTA crónica

Sin proteinuria antes de las semana 20 de gestación:

- Aparición de proteinuria en mujeres con hipertensión crónica

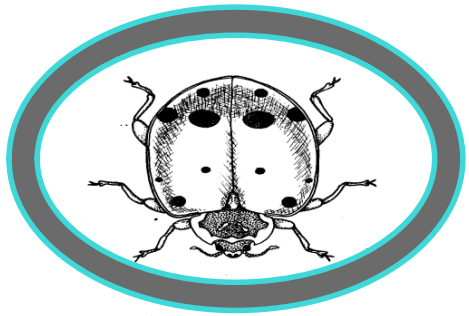
Con proteinuria antes de las semana 20 de gestación:

- Aumento súbito de la proteinuria
- Aumento súbito en la hipertensión arterial
- Trombocitopenia (< 100000 plaq/mm^3)
- Aumento de las enzimas hepáticas

Eclampsia

Aparición súbita de convulsiones tónico clónicas durante el embarazo o hasta 4 semanas después del parto en mujeres preeclámpticas.

Adapted from American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice: ACOG practice bulletin: diagnosis and management of preeclampsia and eclampsia, number 33, January 2002, ***Int J Gynaecol Obstet*** 77:67-75, 2002.



Auto Anticuerpo Receptor Angiotensina -1

Receptor Angiotensina -1

Heterodimerización del Receptor Ag-1/Receptor Bradikinina 2

HTA

AbdAlla S, et al.. ***Nat Med***. 2001;7:1003-9.

Síndrome HELLP

Sibal, et al.

- Hemólisis en frotis de sangre periférica, LDH > 600 U/L o Bilirrubina 1,2 mg/dL.
- GOT > 70 U/L
- Plaquetas < 100000 cel/mm^3

Martin, et al.

- LDH > 600 U/L
- GOT > 40 U/L
- Plaquetas < 150000 cel/mm^3

Sibai BM, et al. ***Am J Obstet Gynecol*** 1993;169:1000-6.

Martin JN Jr,et al . ***Am J Obstet Gynecol*** 1991;164:1500-9.

HTA gestacional

Aparición de HTA sin proteinuria después de la semana 20

HTA crónica

HTA documentada antes de la semana 20

Adapted from American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice: ACOG practice bulletin: diagnosis and management of preeclampsia and eclampsia, number 33, January 2002, ***Int J Gynaecol Obstet*** 77:67-75, 2002.

Pre-eclampsia

HTA: PAS > 140 mmHg PAD > 90 mmHg en paciente previamente normales , objetivadas en 2 tomas separadas por 2 horas, luego de la semana 20.
Proteinuria: > 300 mg/24 Hs o > 0.3 mg/mg

Pre-eclampsia severa

Idem preeclampsia + 1 o más de los siguientes criterios:

- TAS ≥160 mm Hg o TAD ≥110 mm Hg en 2 tomas separadas por 6 hs en reposo
- Proteinuria >5 g/24 hs o proteinuria dipstick ≥3 gr/dL (≥300 mg/dL) en 2 muestras al azar separadas por 4 hs.
- Oliguria (<500 ml/24 hr)
- Cefalea severa, cambios del sensorio o escotomas visuales
- Edema agudo de pulmón o cianosis
- Epigastralgia o dolor en hipocondrio derecho
- Injuria hepatocelular (elevación de las transaminasas x 2)
- Trombocitopenia (<100,000 plts/mm^3)
- Retraso del crecimiento intrauterino
- Accidente cerebrovascular

Pre-eclmapsia sobreimpuesta HTA crónica

Sin proteinuria antes de las semana 20 de gestación:

- Aparición de proteinuria en mujeres con hipertensión crónica

Con proteinuria antes de las semana 20 de gestación:

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Medición FG: Embarazo normal y pre-eclampsia

- ***Clearence de inulina*** es el gold standard se reserva para los estudios de investigación.

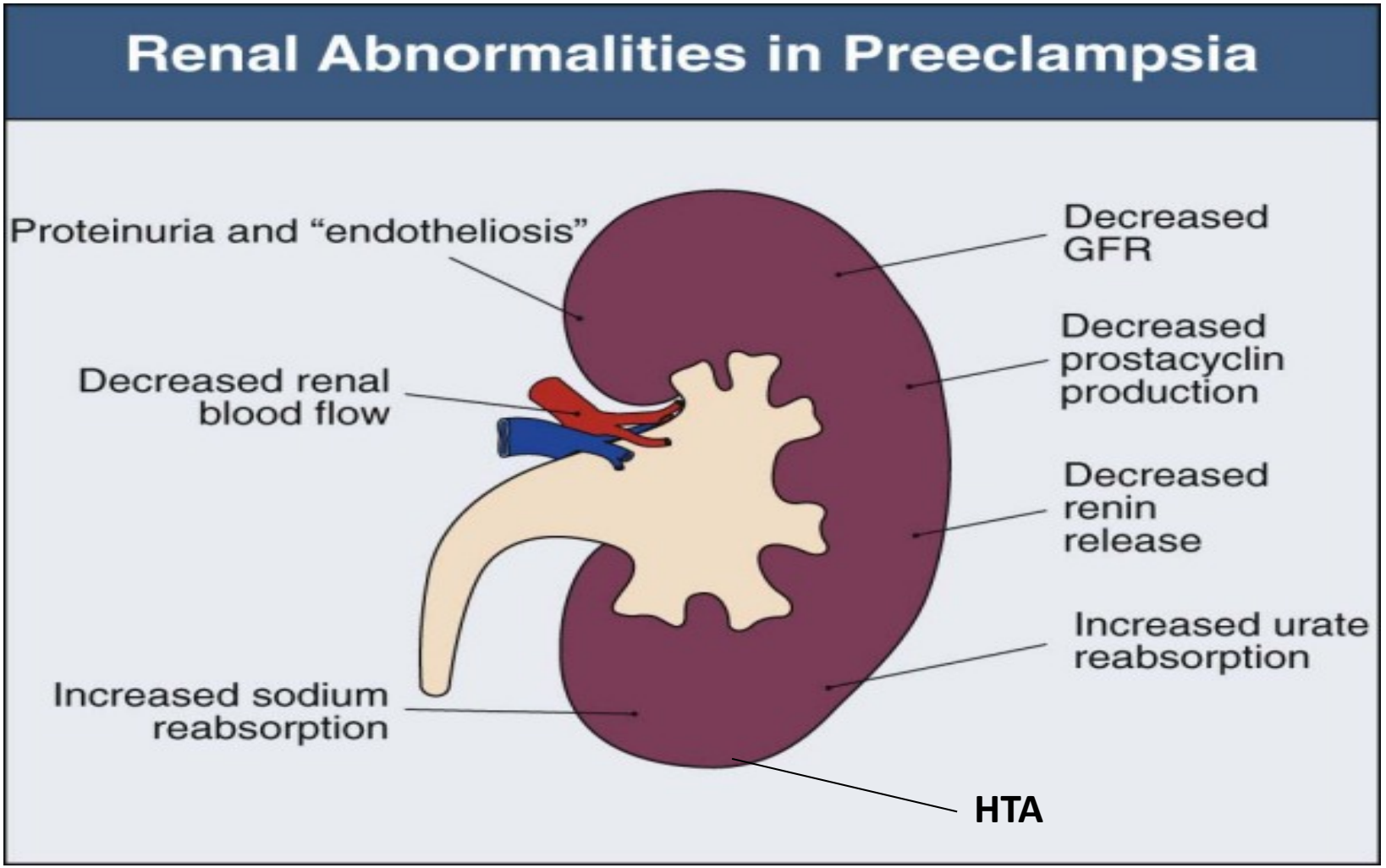
- ***Clearence de Cr $_{24}$*** se dificulta su recolección por la dilatación dela vía urinaria y la retención urinaria.

- Ecuaciones como ***Crockcroft-Gault*** sobreestiman el FG y ***MDRD*** infraestima el FG.

- ***Creatinina sérica*** los niveles se hacen evidente con caídas del 50% del FG.

Cornellis T.***Seminars in Nephrology.*** 2011; 31: 4-14

Cambios renales inducidos por la preeclampsia



Floege J, et al. ***Comprehensive Clinical Nephrology***. 4th 2010; 511

• ***Cistatina C*** es un marcador potencial para evidenciar los cambios en la TFG.

• Hasta el momento no existen trabajos que comparen en los tres trimestres los niveles de Cistatina C y el Gold Standard.

• Hay trabajos que sugieren que la Cistatina C se encuentra incrementada en contexto de la isquemia placentaria.

• Lo cual complicaría la lectura de los niveles de Cistatina C como marcadores de TFG.

Kristensen K, et al. ***Mol Hum Reprod***. 2007;13:189-95.

• Interferir con la producción o señalización de sFlt1 puede mejorar la disfunción endotelial de la preeclampsia, ensayos fase I con VEGF recombinante estan en marcha-121 en el manejo de la preeclampsia severa están siendo programadas.

• Las estatinas también se han propuesto como un potencial agente terapéutico para la preeclampsia a través de sus efectos sobre la actividad de hemo oxigenasa-1 (HO1) y la disminución en la producción de sFlt1, se han visto en estudios animales.219

• Por su seguridad y eficacia, se esta estudiando la relaxina como tratamiento en la preeclampsia.220

Las principales diferencias radican en:
(1) la inclusión o exclusión de la HTA complicada sin proteinuria como pre-eclampsia
(2) diferencia entre las definiciones clinicas y de investigación en la guía de Australasia,
(3) el uso de preclampsia de aparición temprana como un criterio de gravedad en Canadá (menores de 34 semanas) y EE.UU (<35 semanas)
(4) importancia clínica de la evaluación de hipertensión de bata blanca
(5) definición de la hipertensión severa

Biopsia renal y embarazo

• En la población general la tasa de complicaciones graves en la biopsia renal es < 1 %[1], mientras que en las embarazadas es de 1,6% a 4,4%.[2]

• La utilidad principal de la biopsia renal en el embarazo es la identificación de otras etiologías diferentes a la preeclampsia.

• Packham y Fairley[3], incluyeron las siguientes indicaciones: inicio brusco de ***hematuria, proteinuria o insuficiencia renal***, en el primer o segundo trimestre. Encontraron en el 80% de las biopsiadas Glomerulonefritis.

• Lindheimer y Davidson[4], la indicación de la biopsia debe ser limitada a "cuando se produce un **repentino deterioro de la función renal** antes de la semana 32 de gestación y no existe una causa obvia".

1. Parrish A. *Clin Nephrol 1992; 38:135–141*
2. Dennis E, *Clin Obstet Gynecol 1968;* 11:473–486
3. Packham D. *Br J Obstet Gynaecol 1987; 94:935–939*
4. Lindheimer MD. *Br J Obstet Gynaecol 1987; 94:932–934*