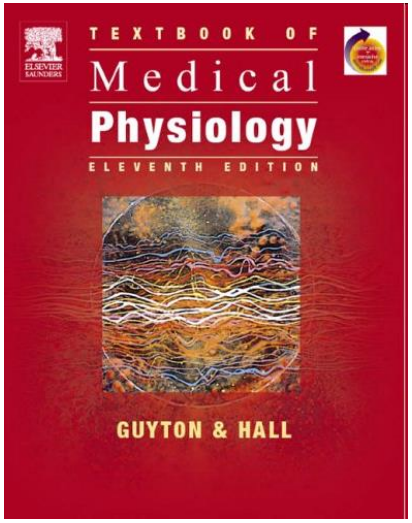
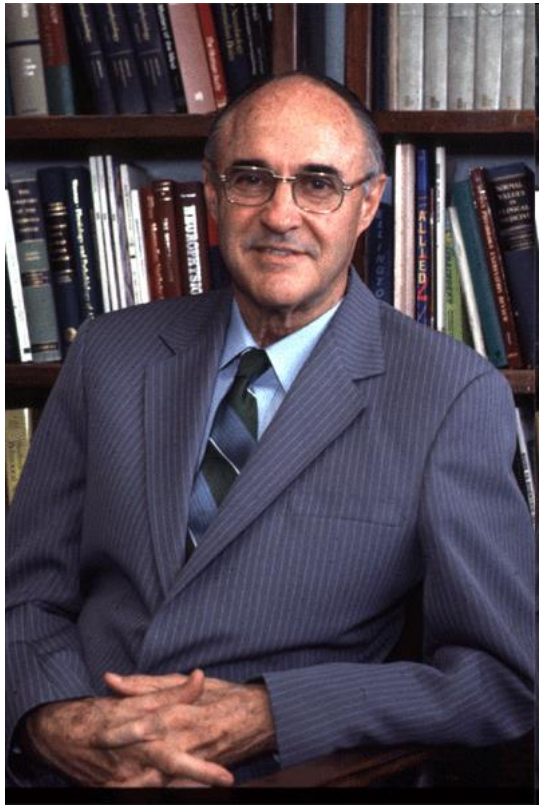
HIPERTENSIUNEA ARTERIALA SI RINICHIUL

- **NEFRO(ANGIO)SCLEROZA BENIGNA SI MALIGNA**
- **HIPERTENSIUNEA IN CURSUL SARCINII**
- **HIPERTENSIUNEA RENOVASCULARA**

HTA



„The kidney is involved in the genesis of any type of hypertension“



Arthur C. Guyton
1919 - 2003

HTA R

HT is associated with increased risk of ESKD and the risk of ESKD increases with the increase of BP

Kaiser Permanente of Northern California – Multiphasic Health Testing Service Program between 1964 and 1985

Table 2. Age-Adjusted Rates of ESRD and Multivariable Risk of ESRD for Each Category of Blood Pressure*

Blood Pressure Category	No. of Persons	Mean Systolic/ Diastolic Blood Pressure, mm Hg	No. of ESRD Events	Age-Adjusted Rate per 100 000 Person-Years (95% CI)	RR (95% CI)	
					Multivariable Risk†	Adjusted Further for Serum Creatinine
Optimal	89 774	109/66	106	4.5 (3.6-5.8)	1.00	1.00
Normal, not optimal	72 192	122/73	182	9.3 (7.5-11.5)	1.61 (1.27-2.05)	1.62 (1.27-2.07)
High normal	56 078	132/77	192	12.9 (10.3-16.0)	1.97 (1.54-2.51)	1.98 (1.55-2.52)
Hypertension						
Stage 1	69 083	143/83	379	19.5 (15.8-24.1)	2.57 (2.06-3.22)	2.59 (2.07-3.25)
Stage 2	21 340	161/92	199	31.7 (24.6-41.0)	3.82 (2.97-4.92)	3.86 (3.00-4.96)
Stage 3	6626	177/101	70	34.5 (24.7-48.0)	3.88 (2.82-5.33)	3.88 (2.82-5.34)
Stage 4	1582	189/122	21	43.7 (26.9-71.1)	4.18 (2.59-6.76)	4.25 (2.63-6.86)
Total	**316 675**		**1149**			

669 out of 98631 HT patients (0.67%) developed ESKD

Hsu, McCulloch, *Arch Intern Med.* 2005;165:923-928

EFECTELE CARDIOVASCULARE ALE HTA

CORD

REMODELARE CARDIACA HIPERTENSIVA

HVS

CARDIOPATIE HIPERTENSIVA

ARTERE

ATEROSCLEROZA (factor favorizant)

ISCHEMIE

REMODELARE VASCULARA HIPERTENSIVA

- **DISFUCTIE ENDOTELIALA**
- **HIPERTROFIA FMN**
- **RIGIDITATE VASCULARA**

Hypertension and Prehypertension and Prediction of Development of Decreased Estimated GFR in the General Population: A Meta-analysis of Cohort Studies

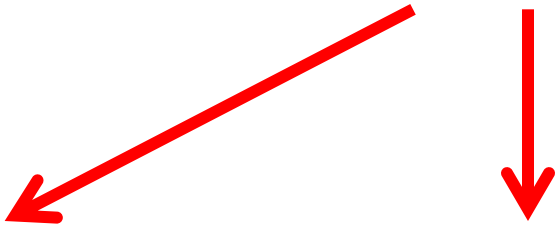
Hypertension - BP > 140/90 mm Hg ,
Prehypertension - Systolic BP of 120-139 and/or diastolic BP of 80-89 mm Hg),

Data from **16 cohorts (315,321 participants)**
All studies had a Newcastle-Ottawa score in the range of 6 to 8
During a mean follow-up of 6.5 years, decreased eGFR occurred in 6.6% of participants.

- **Prehypertension increased renal risk -** 1.19 [95% CI, 1.07 1.33; I^2 = 23.8%]
- **Hypertension increased renal risk -** 1.76 [95% CI, 1.58-1.97; I^2 = 37.7%].
- **Every 10–mm Hg increase in systolic and diastolic BPs** associated with higher risk for decreased eGFR (RRs of 1.08 [95% CI, 1.04-

Garofalo C AJKD vol67, 1 2016 89-97

Renal effects of HT



ATHEROSCLEROSIS

Renal artery stenosis

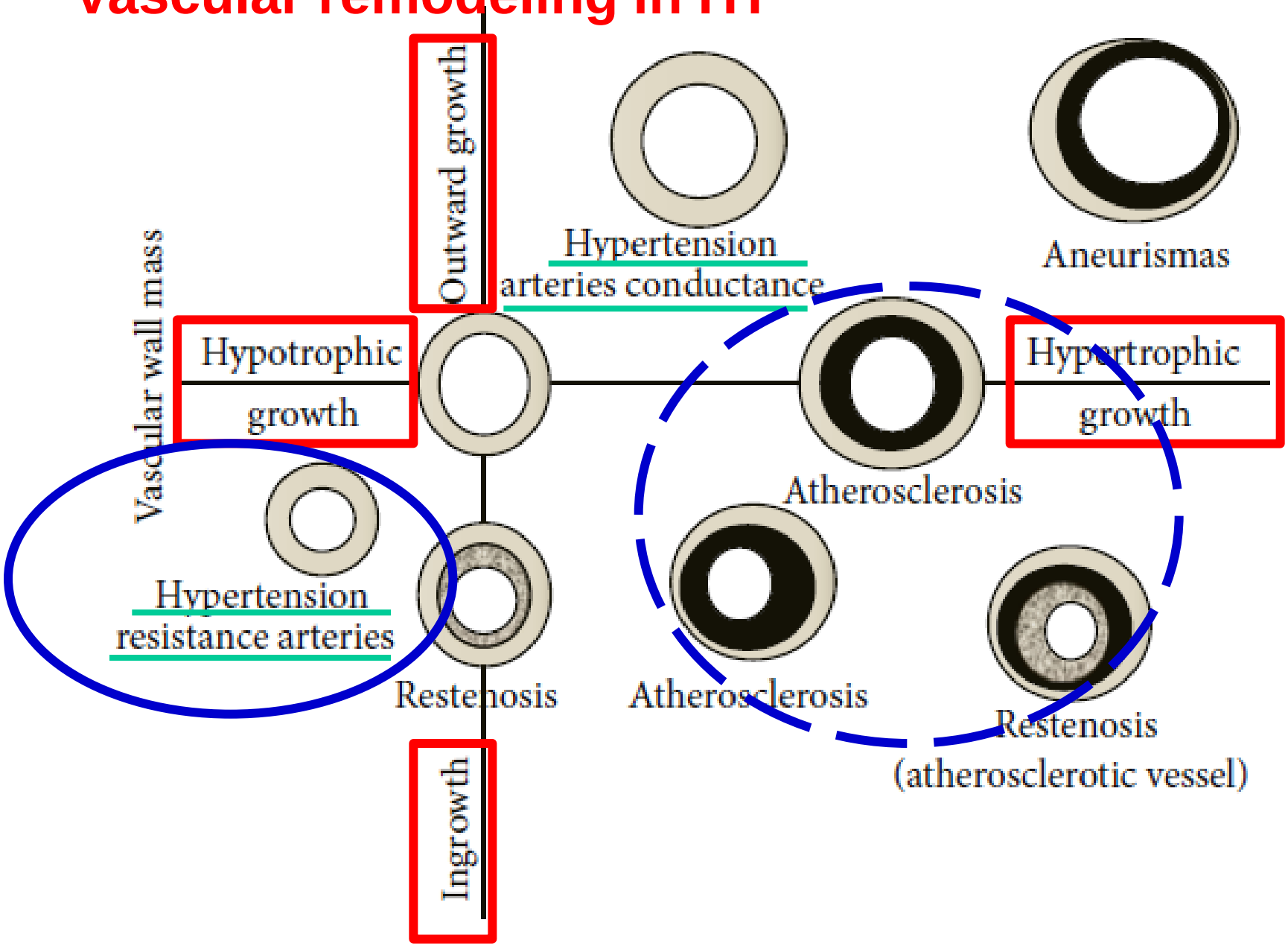
REMODELING OF RESISTANCE VESELS

Hypertensive nephroangiosclerosis

Intraglomerular HT

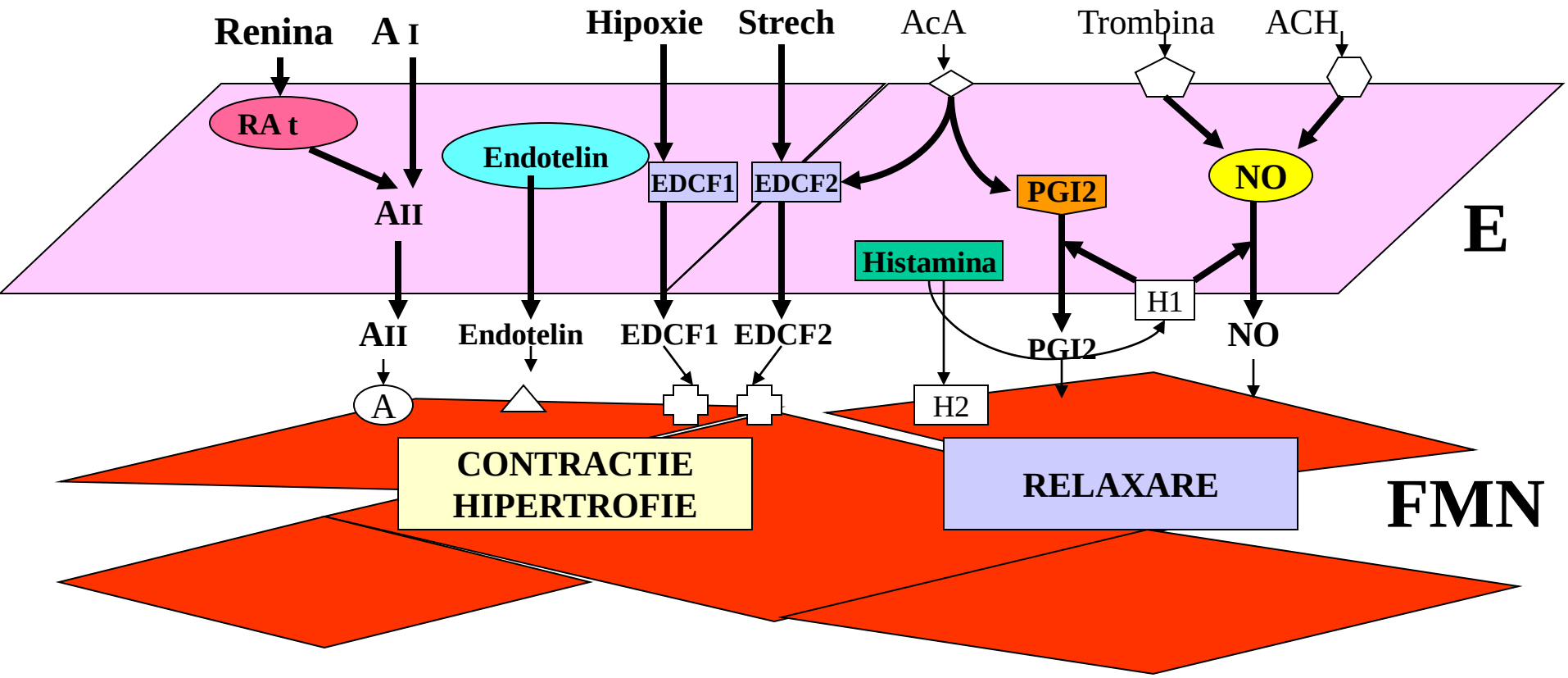
Glomerular sclerosis

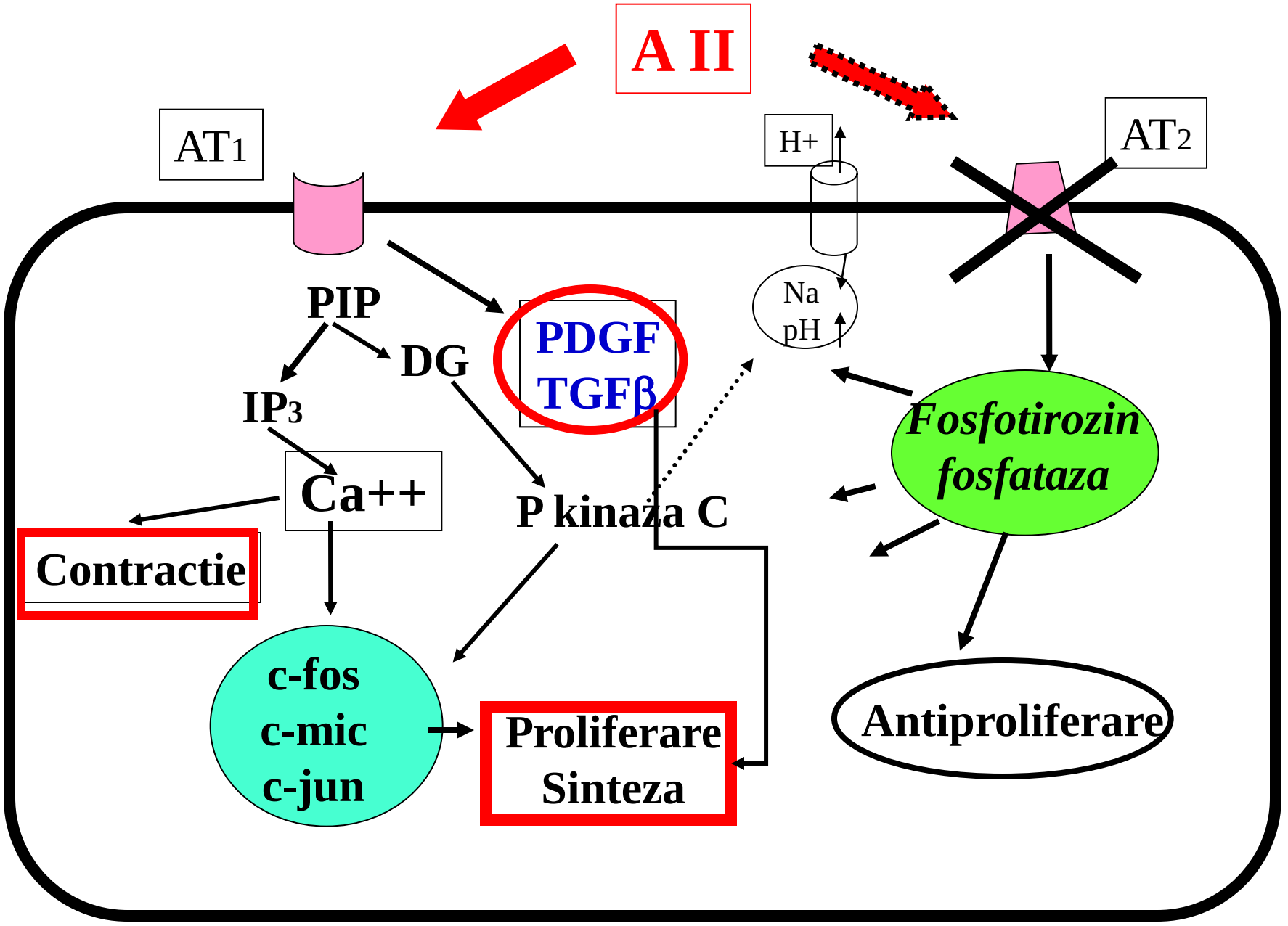
Vascular remodeling in HT



Renna NF et al *Int J of Hypertension* http://dx.doi.org/10.1155/2013/808353 2014

DISFUNCTIE ENDOTELIALA - REMODELARE




A II
AT1
AT2
H+
Na
pH
PIP
DG
IP3
PDGF
TGFβ
Ca++
P kinaza C
Contractie
c-fos
c-mic
c-jun
Proliferare
Sinteza
Fosfotirozin
fosfataza
Antiproliferare

EFECTELE RENALE ALE HTA

ATEROSCLEROZA

Stenoza de artera renala si ramuri intrarenale

REMODELARE VASCULARA HIPERTENSIVA

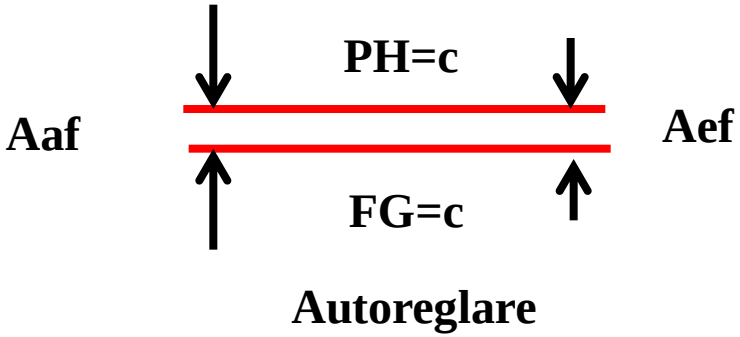
Nefro(angio)scleroza benigna si maligna

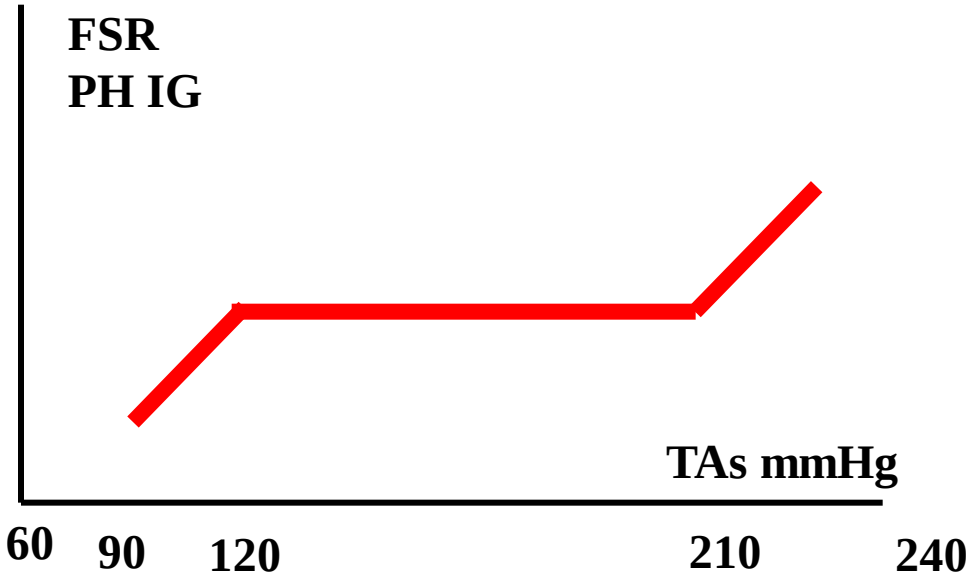
HIPERTENSIUNE GLOMERULARA

Scleroza glomerulara

NEFRO(ANGIO)SCLEROZA HIPERTENSIVA

HTA

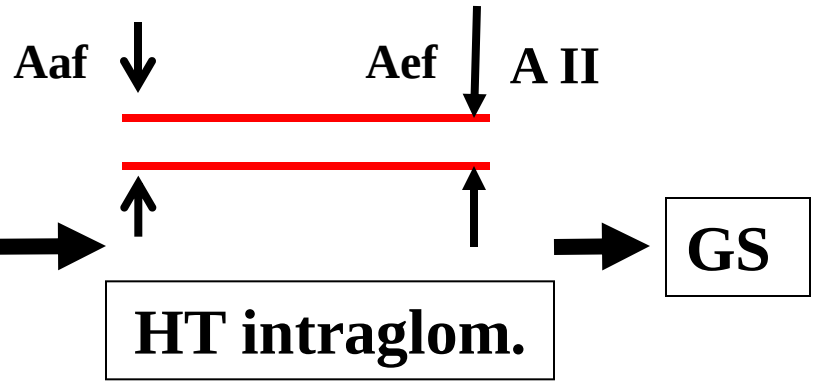


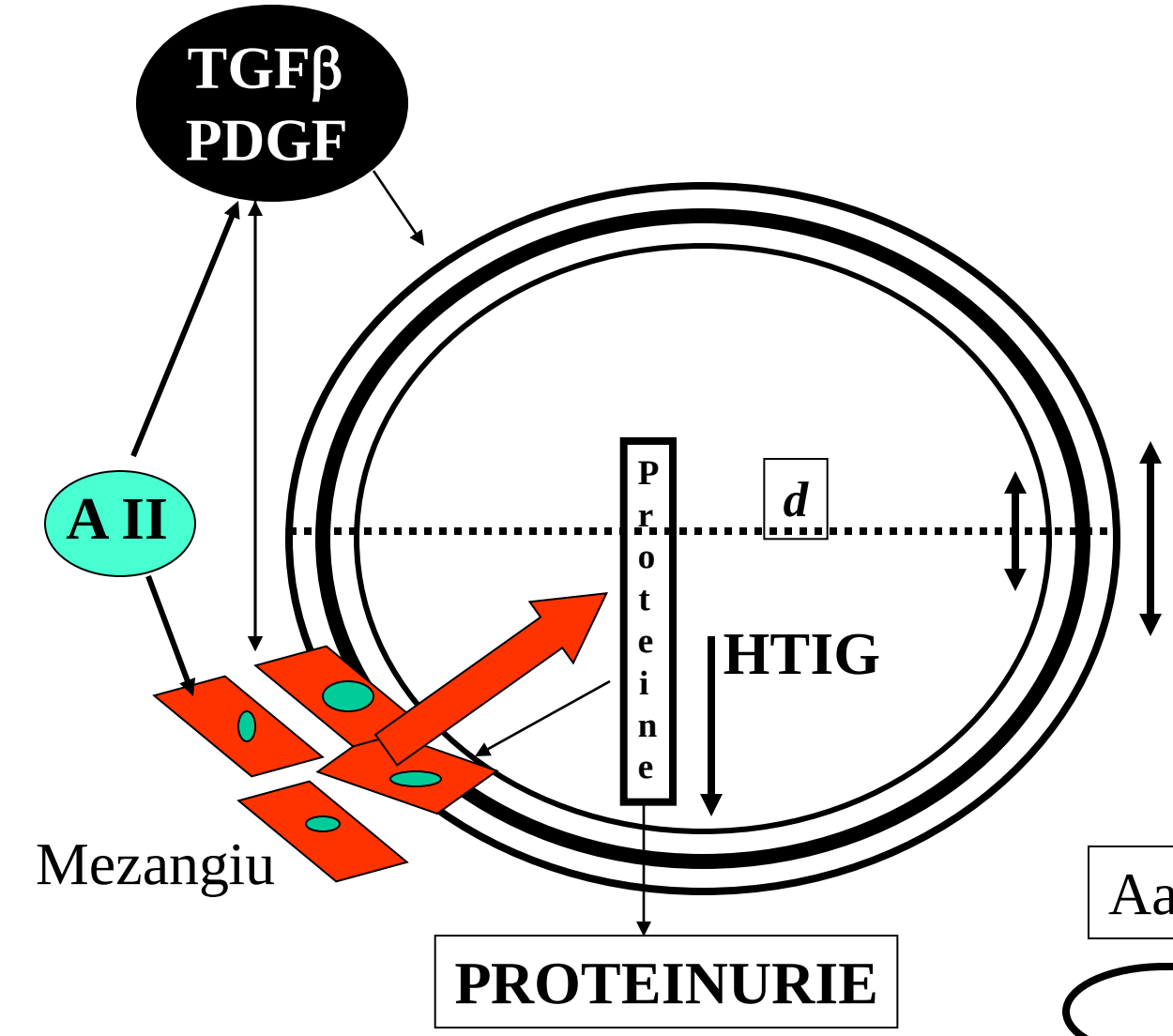


Leziuni ale arterelor interlobare arcuate si arteriolelor aferente

- Hipertrofie miointimala
- Hialinizare

Glomeruli ischemici → **RAA** → **Glomeruli normali**



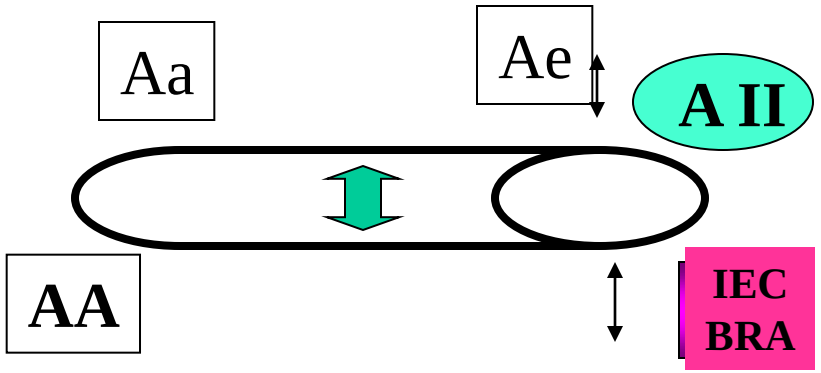


HT glomerulara

- A II
- AA
- Diametru capilarului
- TA sistemica

Factori de crestere

Proteinurie

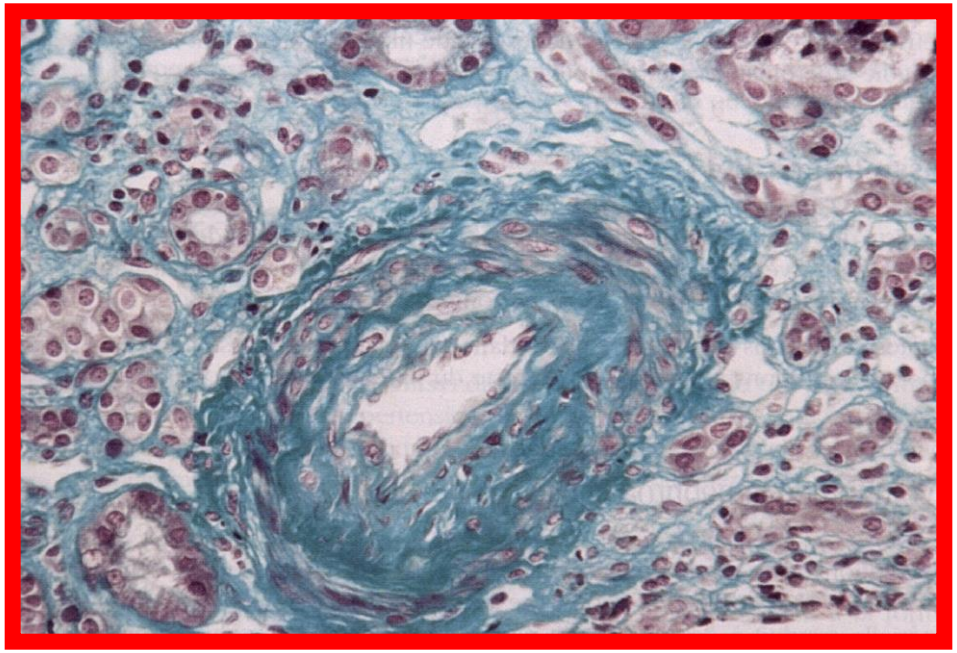


MORFOPATOLOGIE

- **artere interlobare si arteriolele aferente**
  - **hialinizare segmentala a mediei - lipide, proteine plasmatice, material din MB, colagen**
  - **hipertrofie miointimala**
  - **in hipertensiunile secundare renale - leziuni proprii bolii de baza**
- **scleroze glomerulare**

Depozite arteriolare subendoteliale : clare si hialine

Endarterita fibroasa cu duplicarea laminei elastice, fibroza interstitiala, atrofii tubulare



DIAGNOSTIC POZITIV

ANAMNEZA

- **Antecedente heredocolaterale hipertensive**
- **Factori de risc cardio-vascular**
- **HTAE benigna cu evolutie > 10 ani**
- **Absenta unei boli renale**

CLINIC

- **cord - HVS**

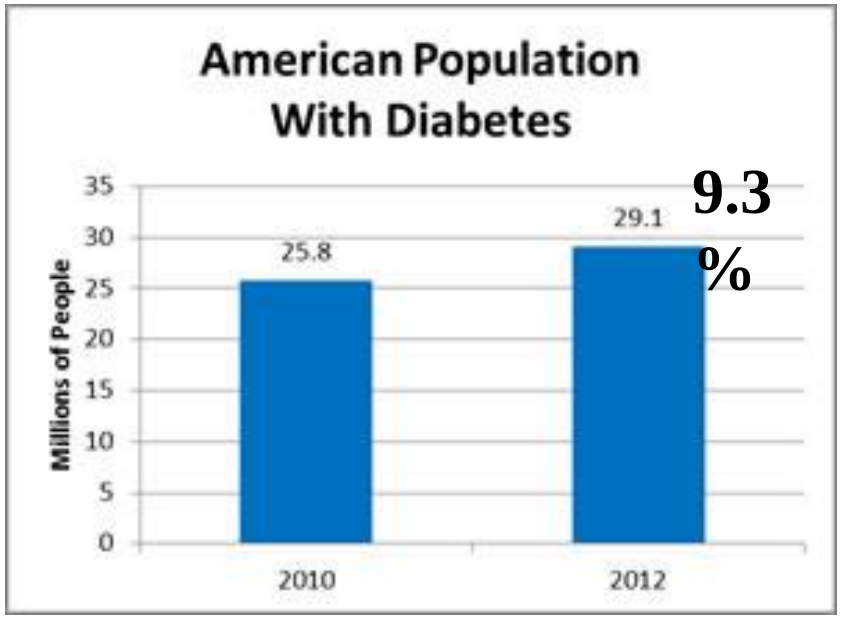
BIOLOGIC

- **Albuminurie patologica**
- **Retentie azotata (RFG scazut)**

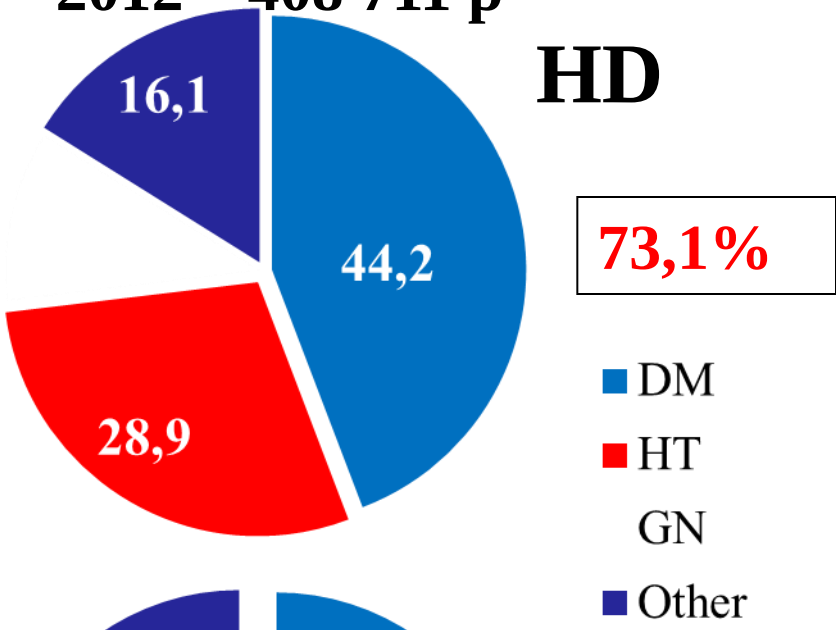
IMAGISTICA

- **rinichi mici , egali**

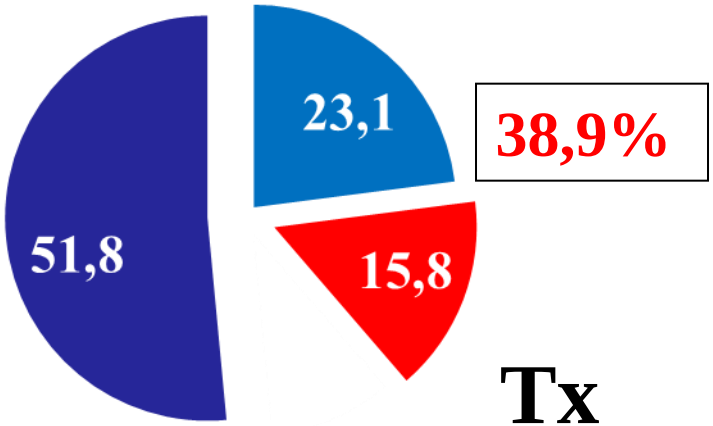
Etiology of ESKD on RRT - USRDS 2014



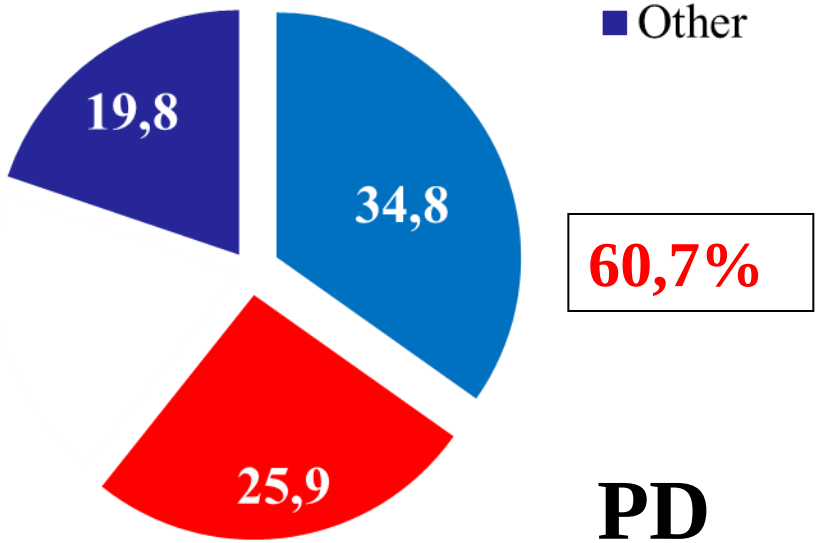
HD – 2012 – 408 711 p



All ESKD – 2012 – 636 905 p



Tx – 2012 – 186 303 p



PD – 2012 – 40 631 p

USRDS Annual Data Report 2012 – 2014

http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf

RISCUL DZ de a dezvolta BCRT SUA

- **DZ 9,1 % din populatie - 29 100 000 diabetici**
- **Pe EER din cauza DZ – 180 600 HD + 14 100 PD + 44 300 Tx = 245 000 BCRT de cauza DZ = 0,8% din DZ**

RISCUL HTA de a dezvolta BCRT SUA

- **HTA 29% din populatia generala – 70 000 000 hipertensivi**
- **BCRT de cauza HTA – 118 100 HD + 10 500 PD + 29 400 Tx = 158 000 BCRT de cauza HTA – 0,2% din HTA**

Prevalenta HTA este de aprox 3 x mai mare decat prevalenta DZ pe cand pe EER ajung de 4 X mai putini hipertensivi decat diabetici din grupurile respective

DA, DAR…

Prevalenta reala NAB este semnificativ mai mica decat cea diagnosticata

Diagnosis	No. of patients
Analgesic nephropathy	1
Unsuspected IgA nephropathy	1
Immunotactoid nephropathy	1
Light-chain deposition disease without free light chains in the plasma and urine	1
Unclassified	7
Atheromatous vascular disease	19
True hypertensive nephrosclerosis	26

53.5% din NAB diagnosticat clinic se dovedeste a fi altceva decat NAB la PBR

P. Zucchelli NDT (1995) 10 [Suppl. 6]: 2-5

TRATAMENT

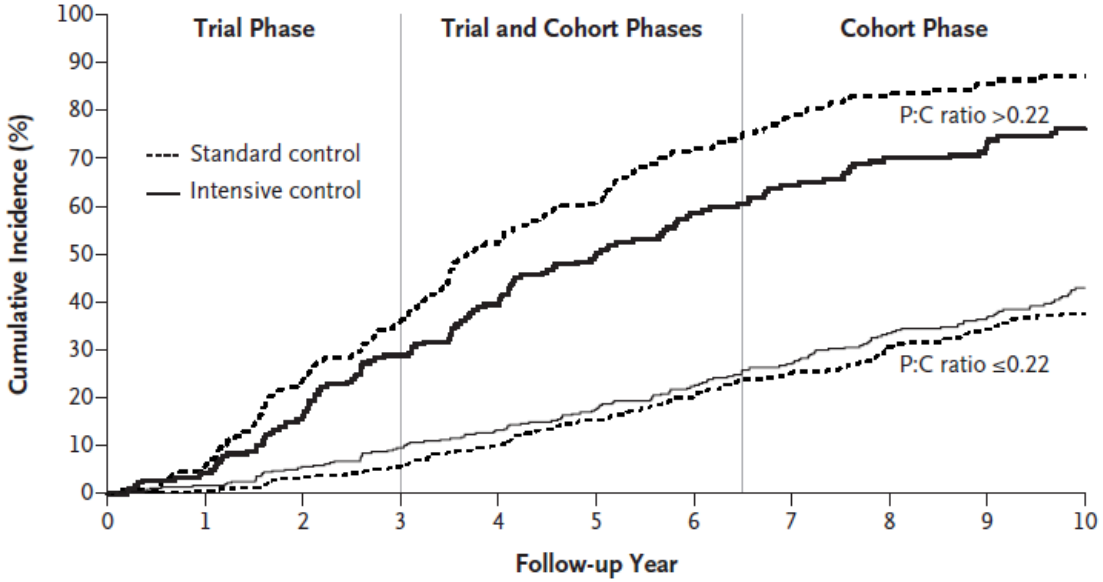
KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease

	CKD no DM		CKD & DM	
Albuminuria	**Target BP** (mmHg)	**Drugs**	**Target BP** (mmHg)	**Drugs**
< 30 mg/dl	< 140 / 90	Any class	< 140 / 90	Any class
30-300 mg/dl	< 130 / 80	**ACEI/ ARB**	< 130 / 80	**ACEI/ ARB**
> 300 mg/dl	< 130 / 80	**ACEI/ ARB**	< 130 / 80	**ACEI/ ARB**

: : KDIGO *Kidney International Supplements* (2012) 2, 405–414

In absenta proteinuriei controlul tensional intensiv nu scade rata progresiei BCR

The AASK population african-americans, No DM, 10 years FU



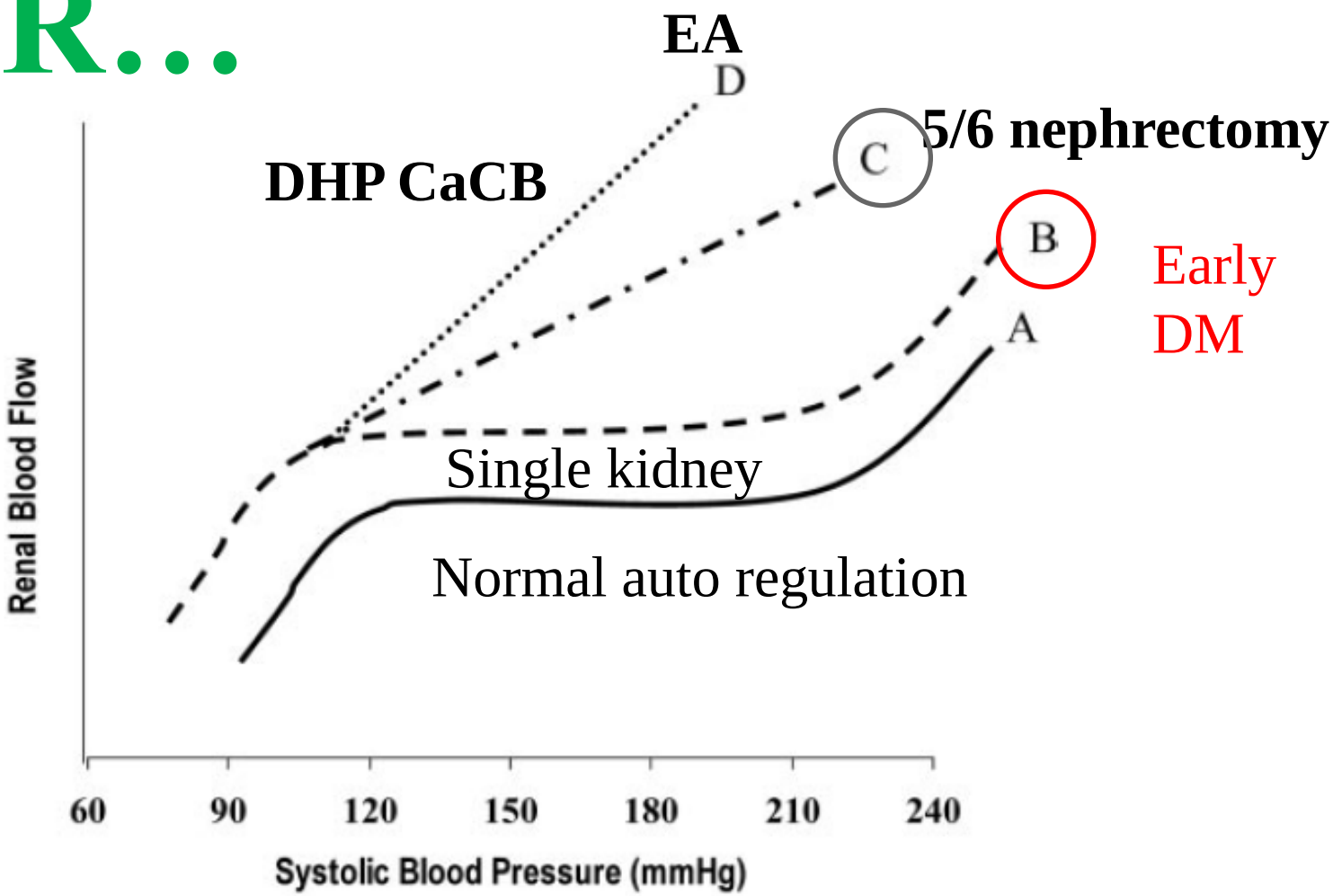
P:C Ratio >0.22											
Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25
P:C Ratio ≤0.22											
Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

Appel J.L *N Engl J Med* 363;10 sept 2, 2010

Scop
Reducerea riscului cardiovascular
Reducerea ratei de degradare a functiei renale
Reducerea albuminuriei

- IEC sau BRA
- BCCa – Amlodipin, Lecarnidipin
- Diuretice – Indapamid sau ansa
- Alte hipotensoare

DA, DAR…



Bidani AK, Griffin KA *Hypertension. 2004;44:595-601*

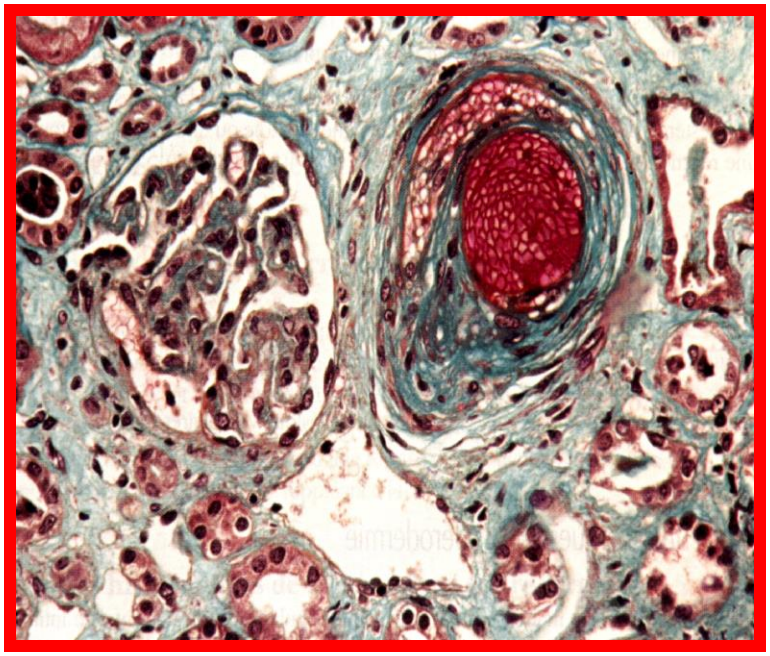
NEFRO(ANGIO)SCLEROZA HIPERTENSIVA MALIGNA

PATOGENIE

- **Fenomenele de proliferare si hipertrofie predomina → necroza fibrinoida → activarea RAA → vasoconstrictie**
- **Natriureza crescuta sub influenta HTA si FNA → hipovolemie activarea SNS → se accentueaza vasoconstrictia**

HISTOPATOLOGIE

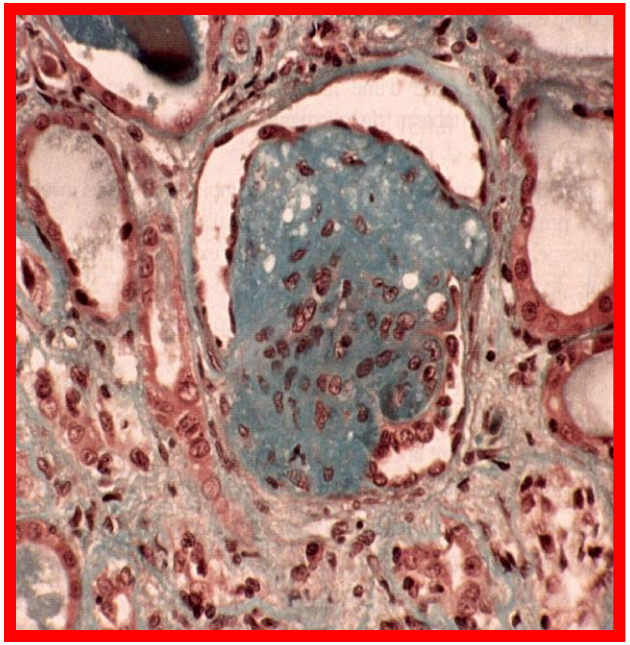
- **Necroza fibrinoida a arteriolelor aferente**
- **Proliferari FMN din medie → aspect in bulb de ceapa – endartrita proliferativa**
- **Ischemie si scleroza glomerulara**
- **Atrofii tubulare, infiltrat LP**



Ischemie glomerulara,

leziuni arteriolare

Leziuni glomerulare mai avansate cu fibroza a ghemului de capilare



DIAGNOSTIC POZITIV

- **TAD >140mmHg**
- **FO - retinopatie hipertensiva st IV**
- **encefalopatie hipertensiva**
- **cardiomegalie, insuficienta cardiaca**
- **nicturie, poliurie, retentie azotata**
- **+/- anemie hemolitica microangiopatica, CID, schizocitoza**
- **hiperreninemie cu hiperaldosteronism secundar**
- **PBR - aspectul histologic anterior**

TRATAMENT

- **De urgenta - Nitroprusiat de Na, Minoxidil, Labetalol, Nifedipin**
- **De intretinere - TA tinta 160/100-140/95**
  - **IEC, BRA**
  - **BCCa**
  - **Betablocante**
  - **Alfa Blocante Periferice**
  - **Nu se recomanda diuretice**

HIPERTENSIUNEA ARTERIALA DIN CURSUL SARCINII

DEFINITII SI CLASIFICARE

- **TAS > 140mmHg sau TAD > 90 mmHg**

HTA din cursul sarcinii (Clasificarea ACOG 2014)

1. Preeclampsie / eclampsie
2. Hipertensiune cronica cu preeclampsie supraadaugata
3. Hipertensiune cronica (de orice cauza)
4. Hipertensiune gestationala

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

PREECLAMPSIE

Hipertensiune specifica sarcinii cu manifestari multisistemice definit prin :

- **Debut** uzual **dupa saptamana 20** de sarcina
- **TA ≥140 mmHg** si /sau **≥ 90 Hg la 2 determinari dupa 4 h** interval (in hipertensiuni severe confirmarea in minute)
- **Proteinurie ≥300mg/24h** sau Proteine/Creatinina ≥ 3 (mg/dl) / (mg/dl)
- **In absenta proteinuriei**
  - **Trombocitopenie < 100000** si/sau
  - **GOT, sau GPT >2x valoarea normala** si /sau
  - **IRA - creatinina ser > 1,1mg/dl sau dublarea Cr ser** de baza (in absenta altei boli renale) si/sau
  - **edem pulmonar acut** si /sau
  - **debutul unor tulburari cerebrale sau vizuale**

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

Clasificarea preeclampsiei

1. **Fara manifestari clinice severe**
2. **Preeclampsie cu manifestari clinice severe** (oricare din urmatoarele):
   - **TAs ≥ 160 si/sau TAd ≥ 110mmHg** 2 det la 4 ore , repaus la pat (daca hipotensoarele nu sunt administrate pana la determinare
   - **Trombocitopenie** <100000/µl
   - **Epigastralgie severa** sau **durere severa in HCD** ce nu cedeaza la medicatie, **si/sau cresterea enzimelor hepatice > 2x valoarea normala**
   - **Insuficienta renala progresiva** (>1,1mg/dl)sau de> 2x valoarea bazala
   - **Edem pulmonar**
   - Aparitia unor **manifestari cerebrale** sau tulburari de vedere

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

ECLAMPSIE

- Convulsii tonico-clonice ce apar in timpul unei preeclampsii precedate uneori de o “aura” – cefalee violenta, hiperreflectivitate.
- Este expresia clinica cea mai grava a preeclampsiei. Poate apare inainte in timpul sau dupa nastere

HIPERTENSIUNE CRONICA

HTA indiferent de etiologie, prezenta inaintea sarcinii sau depistata in cursul sarcinii **inainte de saptamana 20** de gestatie.

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

HIPERTENSIUNE CRONICA CU PREECLAMPSIE SUPRAADAUGATA

Preeclampsie supraadaugata oricarei forme de HTA (incidenta PE creste de 4x).

Diagnosticul este mai probabil daca:

1. **Femeie hipertensiva in primele saptamani de sarcina care dezvolta proteinurie dupa 20 sapt de sarcina**
2. **Femeie cu HTA si proteinurie inainte de 20 de saptamani** care
   - **Exacerbeaza HTA** – creste nevoia de hipotensoare
   - **Creste brusc proteinuria**
   - **Manifesta brusc alte semne de preeclampsie cu severitate crescuta**

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

HIPERTENSIUNE GESTATIONALA

Hipertensiune tranzitorie care apare dupa 20 saptamani de sarcina (sau inainte de nastere) fara proteinurie sau alte semne de preeclampsie.
Poate fi un semn de dezvoltare ulterioara a unei HTA esentiale.

HIPERTENSIUNE POSTPARTUM

Nu este inclusa in clasificare
HTA usoara care se dezvolta intre 2 sapt si 6 luni postpartum

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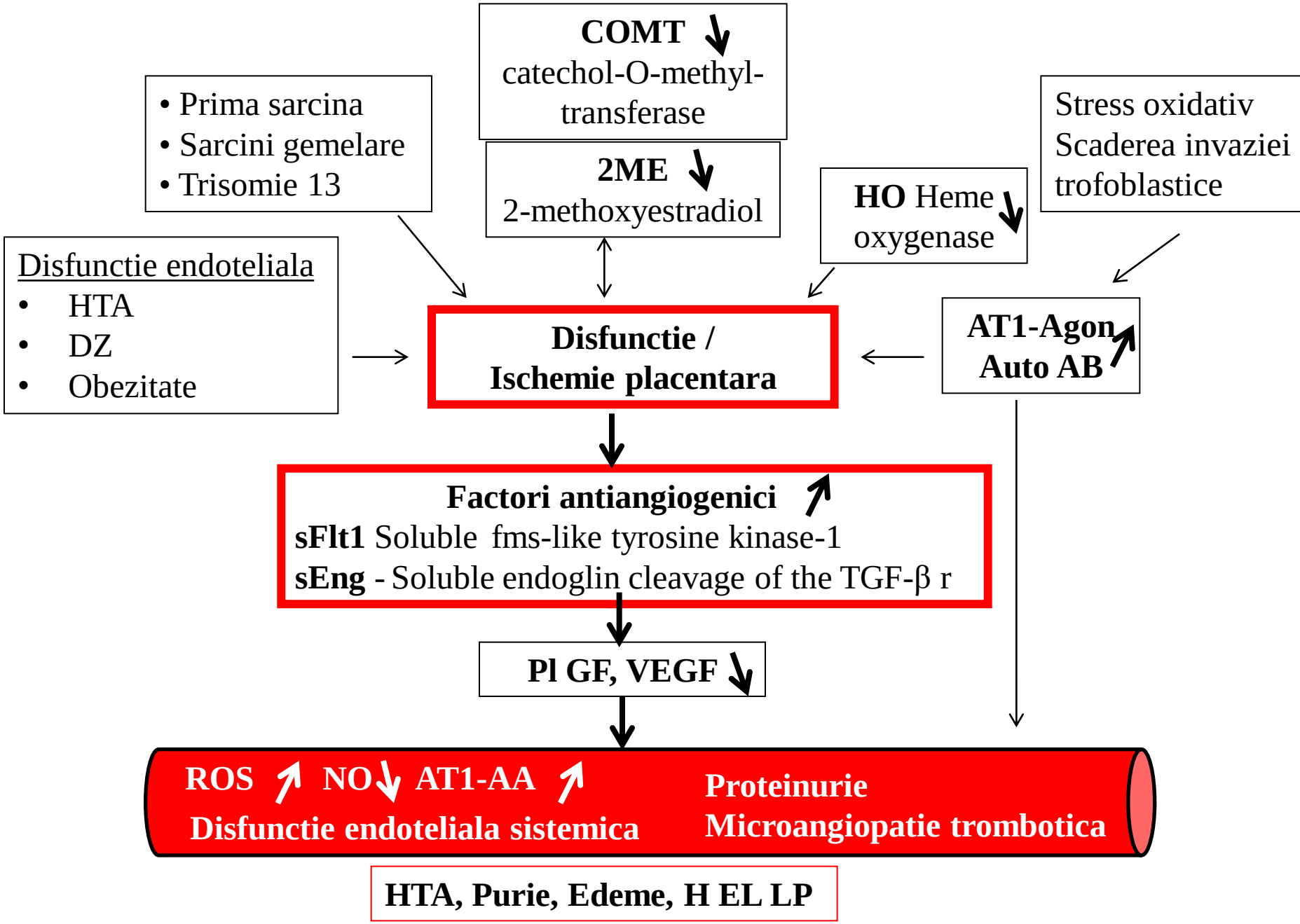
PREECLAMPSIA

- **Hipertensiune dobandita dupa 20 de saptamani caracterizata clinic prin: HTA, +/- edem, +/- proteinurie, +/- tulburari de coagulare si afectarea functiei hepatice**
- **5-10% din sarcini**
- **apare mai frecvent la primipare**
- **se instaleaza dupa saptamana 20 de sarcina**



Maynard *SE J Am Soc Nephrol* 20: 14-22, 2009

Factori de risc ai preeclampsiei

1. Primiparitate
2. Sarcina cu preeclampsie in antecedente
3. HTA cronica
4. Boala Cronica de Rinichi
5. Istoric de trombofilie
6. Sarcina multifetala
7. Fertilizare in vitro
8. Istoric familial de preeclampsie
9. Diabet zaharat (tip I sau II)
10. Obezitate
11. LES
12. Varsta materna avansata (> 40 de ani)

A.C.O.G. Task Force on Hypertension in Pregnancy 2013

Screening pentru preeclampsie

- Scaderea PI GF **Phosphatidylinositol-glycan biosynthesis class F protein** – primul trimestru de sarcina
- Cresterea sFlt1 si sEng – a II a jumatate a trimestrului II
- Eco doppler de artera uterina
- PP-13 – proteina placentara 13 – scazuta in preeclampsie dar si in scaderea cresterii fetale intrauterine

Eco doppler de artera uterina

Creste rezistenta la curgerea prin artera uterina ceea ce genereaza o forma patologica de unda uni sau bilaterala.

- Valoare de predictibilitate scazuta.
- La cei la care a avut rol de predictibilitate precoce nu s-au obtinut rezultate favorabile de terapie la aparitia preeclampsiei

Maynard *SE J Am Soc Nephrol* 20: 14-22, 2009
A.C.O.G. Task Force on Hypertension in Pregnancy 2013

Preventie

- **Aspirina** – amelioreaza echilibrul prostacicline / tromboxani
  - 2 Meta A mari – efect mic dar semnificativ la femeile cu risc crescut

- **Antioxidanti** – Vit C si Vit E – 3 RCT mari – fara efect

- **Ca si Acid folic** – studii observationale cu rezultate promitatoare – deocamdata nu sunt date din RCT uri mari.

- **Terrapii angiogenice**
  - VEGF 121 recombinat – studii pilot cu rezultate promitatoare
  - PI GF
  - MAB anti s Flt1
- **Arginina** – cu scopul cresterii NO – rezultate promitatoare
- **Restrictia de Na** – nu previne aparitia preeclampsiei

Maynard *SE J Am Soc Nephrol* 20: 14-22, 2009

ECLAMPSIA

- **ENCEFALOPATIE HIPERTENSIVA CU CONVULSII TONICO-CLONICE SECUNDARA UNEI PREECLAMPSII**
- **Poate apare : inaintea nasterii, in cursul nasterii, mai rar in cursul lehuziei**
- **SEMNE CLINICE**
  - **Semnele preeclampsiei preced debutul eclampsiei**
  - **Sindrom prodromal:** cefalee, agitatie, epigastralgie, tulburari vizuale
  - **Convulsii tonico-clonice, HTA severa, proteinurie, oligurie, coma**
  - **+/- hemoragii cerebrale, hemoragii meningiale, EPA, IRA, soc**

MANAGEMENT

Hipertensiune gestationala usoara sau preeclampsie fara fenomene clinice severe

≥ 37 saptamani de gestatie
sau
≥ 34 saptamani de gestatie cu:
- **Travaliu sau membrane rupte**
- **Rezultate materno fetale anormale**
- **Greutate fetala < 5 percentile (ECO)**
- **Suspect abruptio placente**

DA → **NASTERE**

NU ↓

< 37 saptamani de gestatie
In spital sau domiciliu
- **Evaluare materna 2 x / sapt**
- **Evaluare fetala**
  - **Preeclampsie 2x/sapt test nonstress (TNS)**
  - **HTA gestational saptamanal TNS**

→

≥ 37 saptamani de gestatie
- **Conditii materne sau fetale ce se inrautatesc**
- **Travaliu sau ruptura prematura de membrane**

↑ **NASTERE**

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• Pentru femeile cu **Hipertensiune gestationala usoara sau preeclampsie fara fenomene clinice severe < 37 saptamani** de sarcina se recomanda atitudine expectativa cu monitorizarea mamei si fatului

• Pentru femeile cu Hipertensiune gestationala usoara sau preeclampsie fara fenomene clinice severe **> 37 saptamani** de sarcina se recomanda nastere si nu continuarea monitorizarii

•**Profilaxia cu Sulfat de Magneziu** este recomandata femeilor cu **Hipertensiune gestationala usoara sau preeclampsie fara fenomene clinice severe numai daca apar semne clinice de severitate**: cefalee, altarari ale statusului mental, tulburarea vederii, scotoame, clonus sau dureri in hipocondrul drept

• **Tratamentul hipotensor** este indicat gravidelor cu preeclampsie si **valori tensionale > 160/110mmHg** cu scopul prevenirii complicatiilor hipertensiunii: cardiovasculare (insuficienta cardiaca, ischemie miocardica), renale (LAR), cerebrovasculare (atac cerebral ischemic sau hemoragic).
• Preparatele indicate de ACOG sunt : Hidralazina, Labetalol si Nifedipina

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Preeclampsie cu fenomene clinice severe

Se contraindica continuarea trat. conservator daca:

- Eclampsie
- EPA
- CID
- HTA severa necontrolabila
- Fat neviabil
- Rezultatele testelor fetale anormale
- Abruptio placente
- Moarte fetala intrauterina

DA →

Nastere dupa stabilizarea mamei

↓

Complicatii aditionale ale gravidei

Sarcina > 33,5 saptamani

- Simptome persistente
- HELLP sau HELLP partial
- Intarzierea dezvoltarii fatului (sub 5 percentile)
- Oligohidroamnios sever
- Inversarea fluxului Doppler end-diastolic in a. ombilicala
- Travaliu sau ruptura prematura de membrane
- Disfunctie renala semnificativa

DA →

- Corticosteroizi pentru maturare fetala
- Nastere dupa 48h

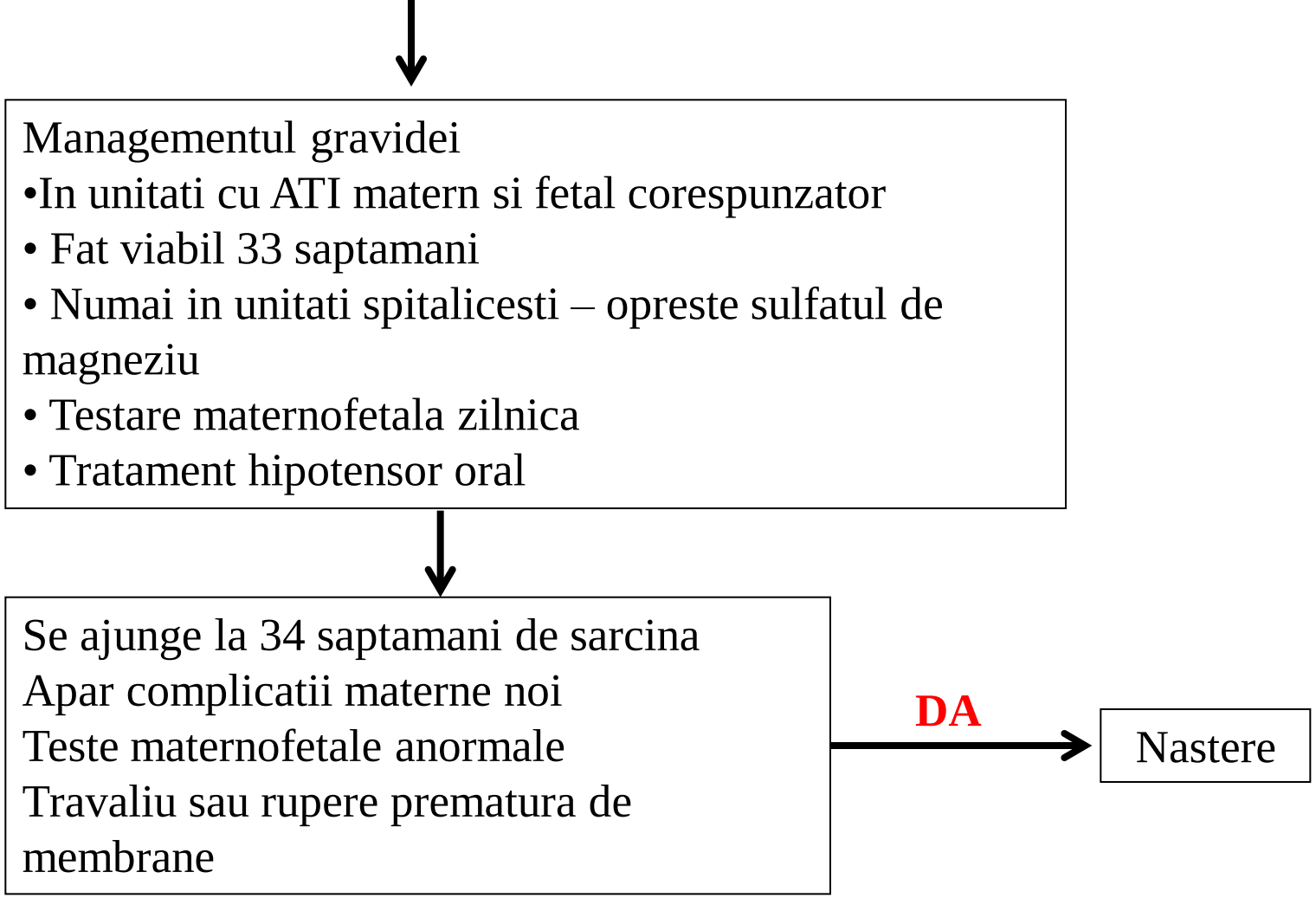

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TABLE 7-1. Antihypertensive Agents Used for Urgent Blood Pressure Control in Pregnancy ⇦

Drug	Dose	Comments
Labetalol	10–20 mg IV, then 20–80 mg every 20–30 min to a maximum dose of 300 mg or Constant infusion 1–2 mg/min IV	Considered a first-line agent Tachycardia is less common and fewer adverse effects Contraindicated in patients with asthma, heart disease, or congestive heart failure
Hydralazine	5 mg IV or IM, then 5–10 mg IV every 20–40 min or Constant infusion 0.5–10 mg/h	Higher or frequent dosage associated with maternal hypotension, headaches, and fetal distress—may be more common than other agents
Nifedipine	10–20 mg orally, repeat in 30 minutes if needed; then 10–20 mg every 2–6 hours	May observe reflex tachycardia and headaches

Abbreviations: IM, intramuscularly; IV, intravenously.

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TABLE 7-2. Common Oral Antihypertensive Agents in Pregnancy

Drug	Dosage	Comments
Labetalol	200–2,400 mg/d orally in two to three divided doses	Well tolerated Potential bronchoconstrictive effects Avoid in patients with asthma and congestive heart failure
Nifedipine	30–120 mg/d orally of a slow-release preparation	Do not use sublingual form
Methyldopa	0.5–3 g/d orally in two to three divided doses	Childhood safety data up to 7 years of age May not be as effective in control of severe hypertension
Thiazide diuretics	Depends on agent	Second-line agent
Angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers		Associated with fetal anomalies Contraindicated in pregnancy and preconception period

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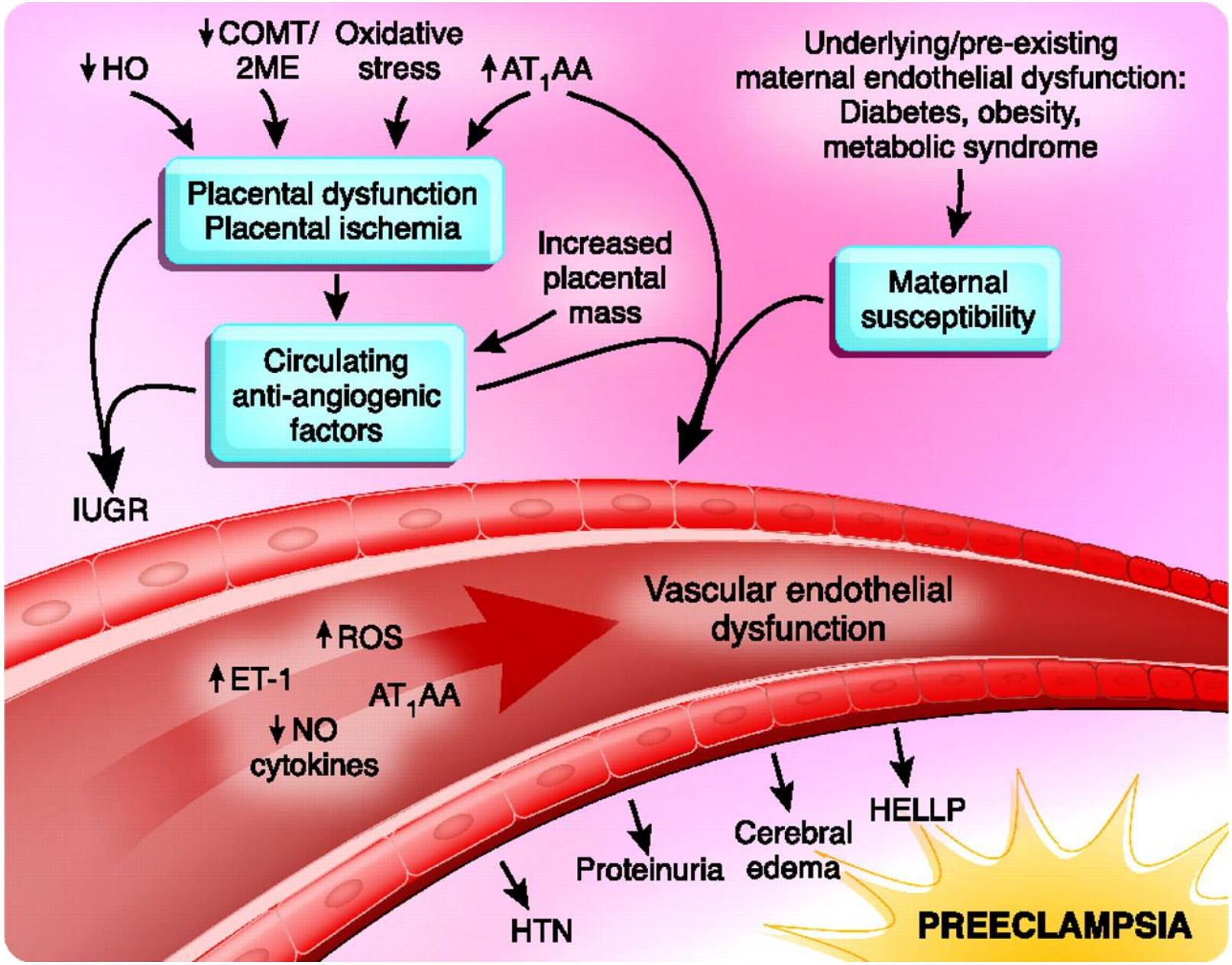

Sharon E. Maynard, and Ravi Thadhani JASN 2009;20:14-22