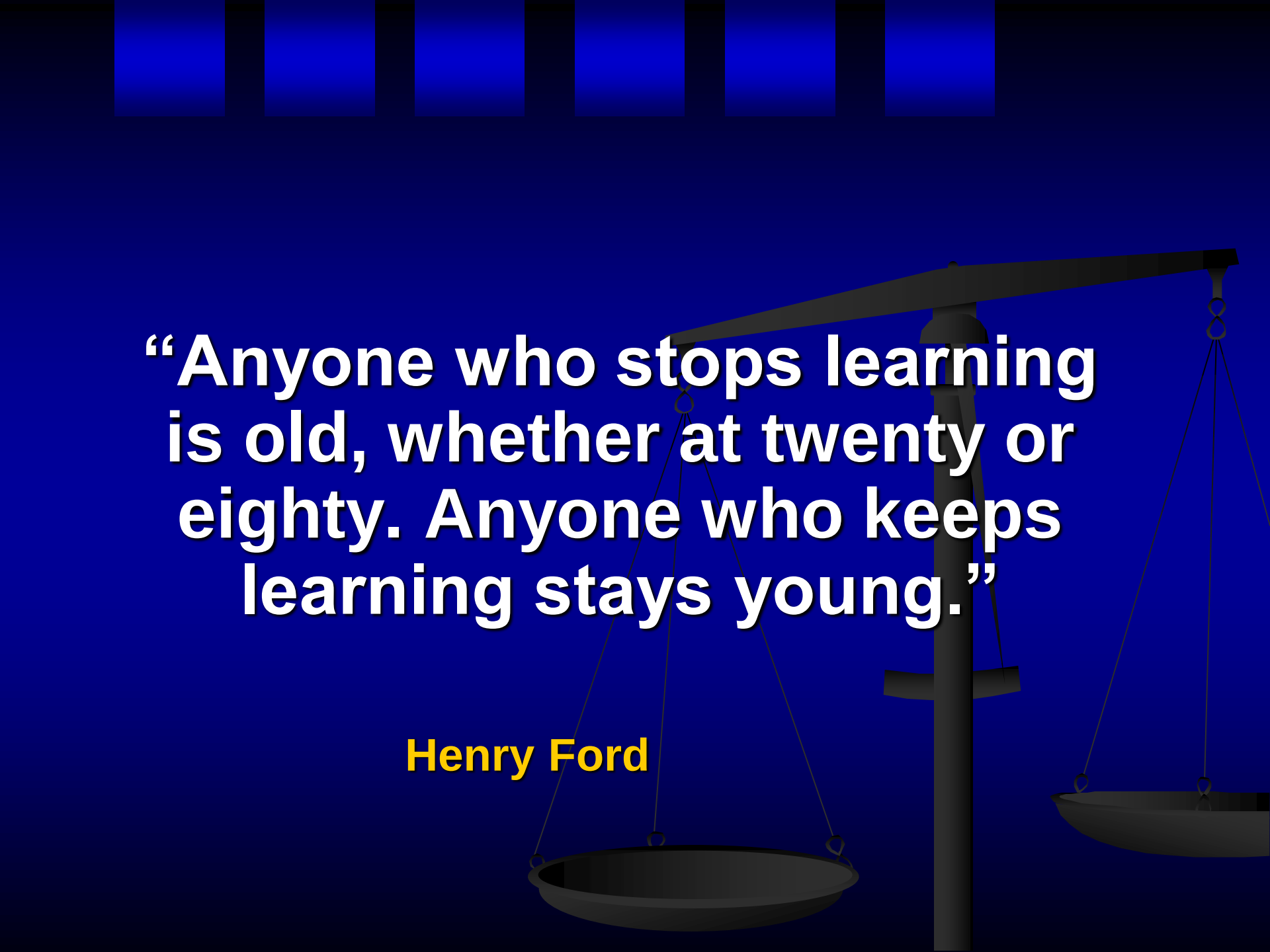
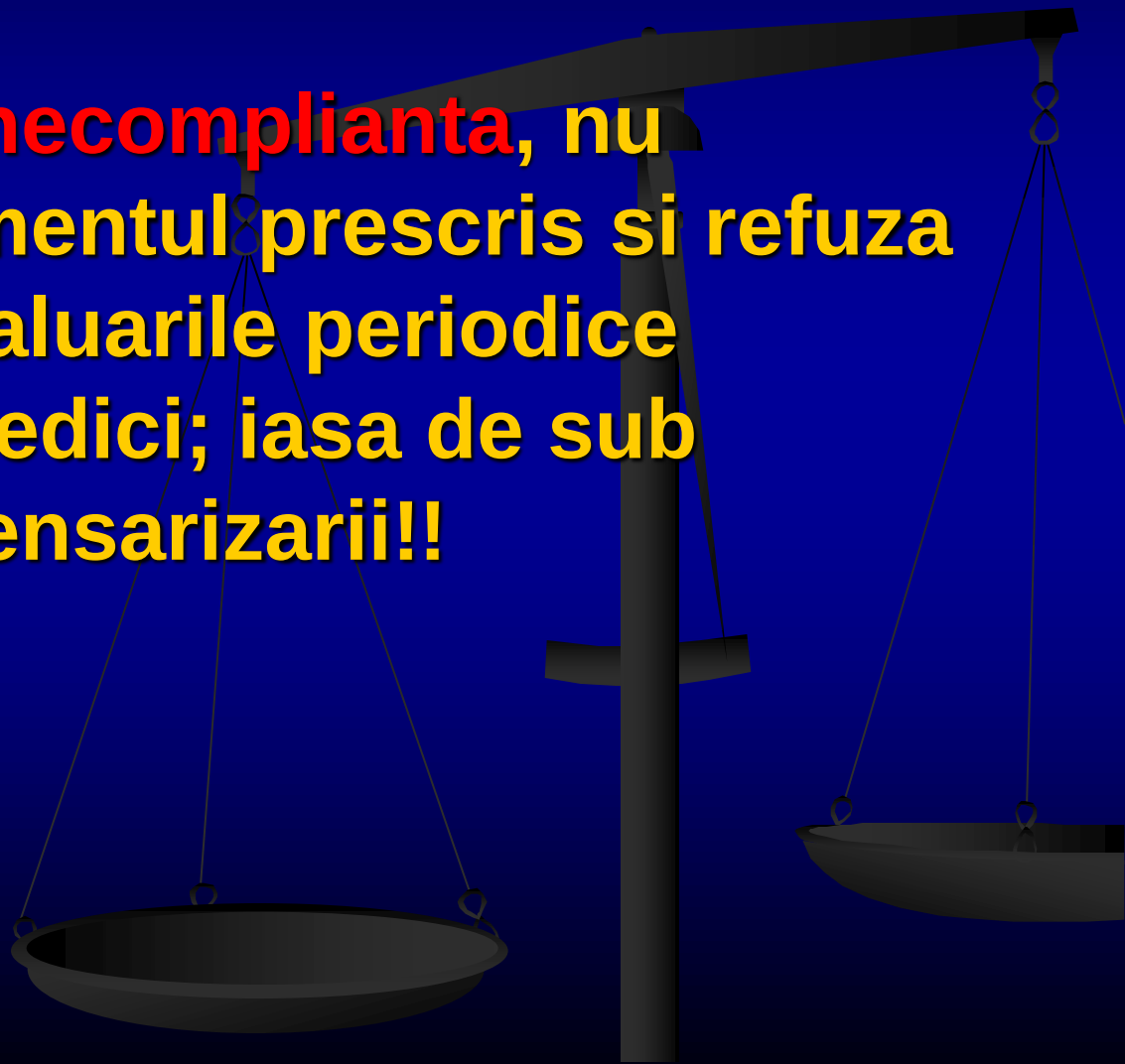

“Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young.”
Henry Ford

Motivele prezentarii

- F.A., 41 de ani din mediul urban
- In 2011 acuza: cefalee, tulburari ale acuitatii vizuale; este evaluata de mai multi medici si in final se efectueaza RMN cerebral care evidentiaza modificari suggestive de vasculita cerebrala
- Se dozeaza anticorpii antifosfolipidici care sunt pozitivi

- Se efectueaza punctie-biopsie cerebrala insa rezultatul obtinut este neconcludent
- Pacienta este necomplianta, nu urmeaza tratamentul prescris si refuza sa revina la evaluarile periodice solicitate de medici; iasa de sub incidenta dispensarizarii!!



28.01.2020

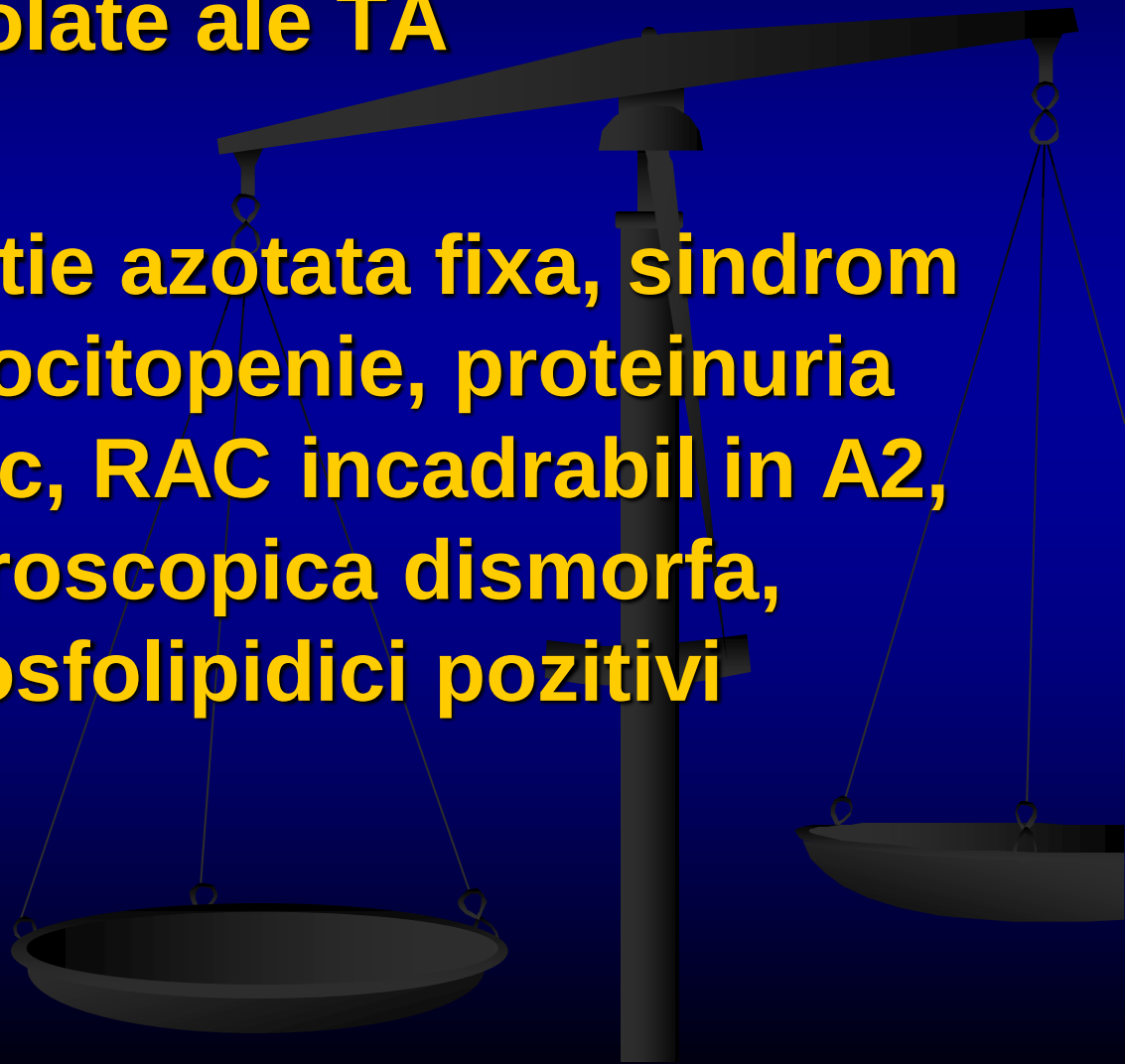
- Pacienta se prezinta in serviciul UPU SCJUT cu aceleasi acuze mentionate si la prezentarile anterioare: cefalee, afectarea acuitatii vizuale, la care se adauga si vertijul!
- La examenul clinic facut in UPU: valori necontrolate ale TA (220/120 mmHg)
- Ecografic se deceleaza: poliserozita (pleurezie mica bazal dreapta, pericardita mica, lichid de ascita in cantitate medie)

- **Biologic:**

	Val. normale	2011	05-06.2019
Creatinina serica	0,5 – 1 mg/dl	Valori normale	3.1 – 2.6
Ureea serica	6-20 mg/dl	Valori normale	70 - 136
Hemoglobina serica	12 g/dl	Valori normale	9.5 – 7.8
Nr Trombocite	15-40*10^4/mm3	Valori normale	114000 - 147000
Proteinurie/24h	<150 mg/24h	-	3
RAC	<30 mg/g	-	51
Sediment ADDIS	Hematii 0/min	-	15300, dismorfe
Profil ANA val C3	Negativ 0.9-1.8 g/l	-	Ac antinucleozomi 0.73
Ac antifosfolipidici	negativi	pozitivi	pozitivi

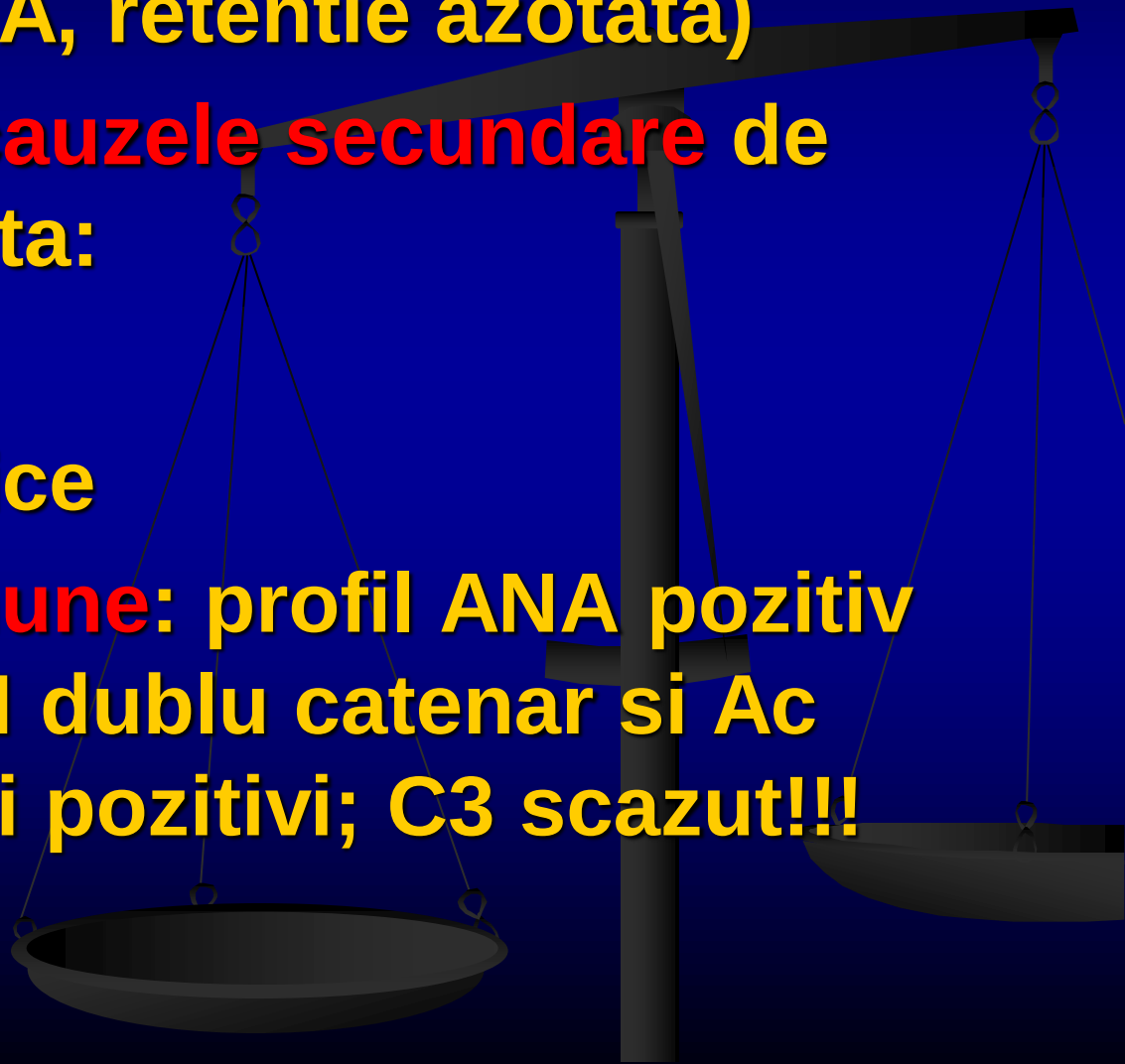
Ce date avem pana in prezent?

- Manifestari neurologice
- Valori necontrolate ale TA
- Poliserozita
- Biologic: retentie azotata fixa, sindrom anemic, trombocitopenie, proteinuria de rang nefrotic, RAC incadrabil in A2, hematuria microscopica dismorfa, anticorpi antifosfolipidici pozitivi



Orientare diagnostica

- Pacienta cu sindrom nefrotic impur (hematurie, HTA, retentie azotata)
- Se evalueaza cauzele secundare de glomerulonefrita:
- 1. neoplazii
- 2. Infectii cronice
- 3. boli autominune: profil ANA pozitiv cu Ac anti ADN dublu catenar si Ac antinucleozomi pozitivi; C3 scazut!!!

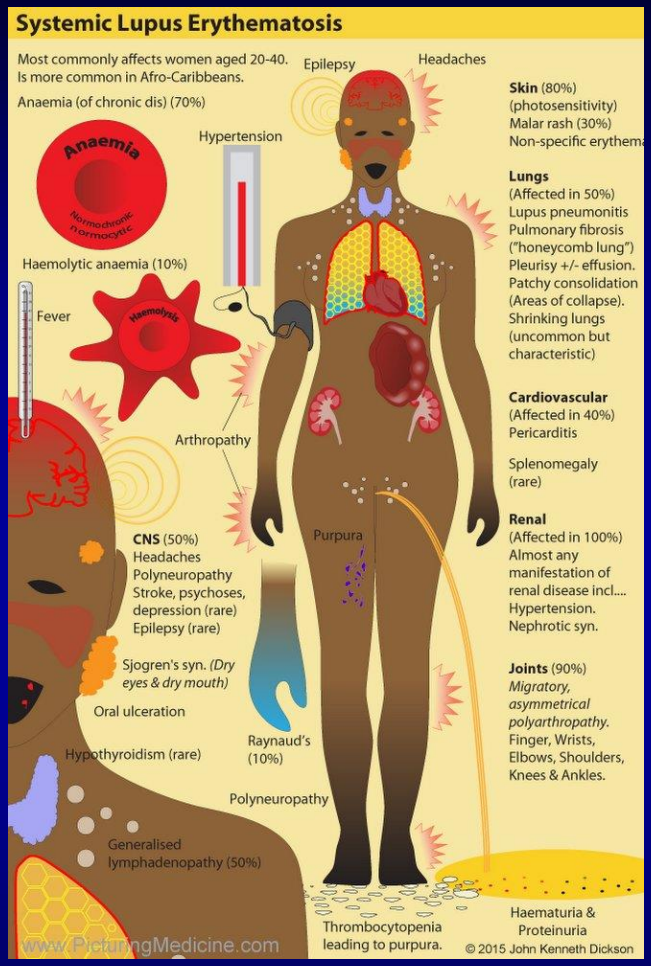


Diagnostic de etapa

- **Suspiciune majora**

LUPUS ERITEMATOS SISTEMIC

- Se evalueaza criteriile de diagnostic ale bolii in vederea stabilirii diagnosticului final



SLICC† Classification Criteria for Systemic Lupus Erythematosus

RheumTutor.com

Requirements: ≥ 4 criteria (at least 1 clinical and 1 laboratory criteria)
OR biopsy-proven lupus nephritis with positive ANA or Anti-DNA

Clinical Criteria

1. Acute Cutaneous Lupus*
2. Chronic Cutaneous Lupus*
3. Oral or nasal ulcers *
4. Non-scarring alopecia
5. Arthritis *
6. **Serositis***
7. **Renal***
8. **Neurologic***
9. Hemolytic anemia
10. Leukopenia *
11. Thrombocytopenia (<100,000/mm^3)

Immunologic Criteria

1. **ANA**
2. Anti-DNA
3. Anti-Sm
4. **Antiphospholipid Ab***
5. **Low complement (C3, C4, CH50)**
6. Direct Coombs' test (do not count in the presence of hemolytic anemia)

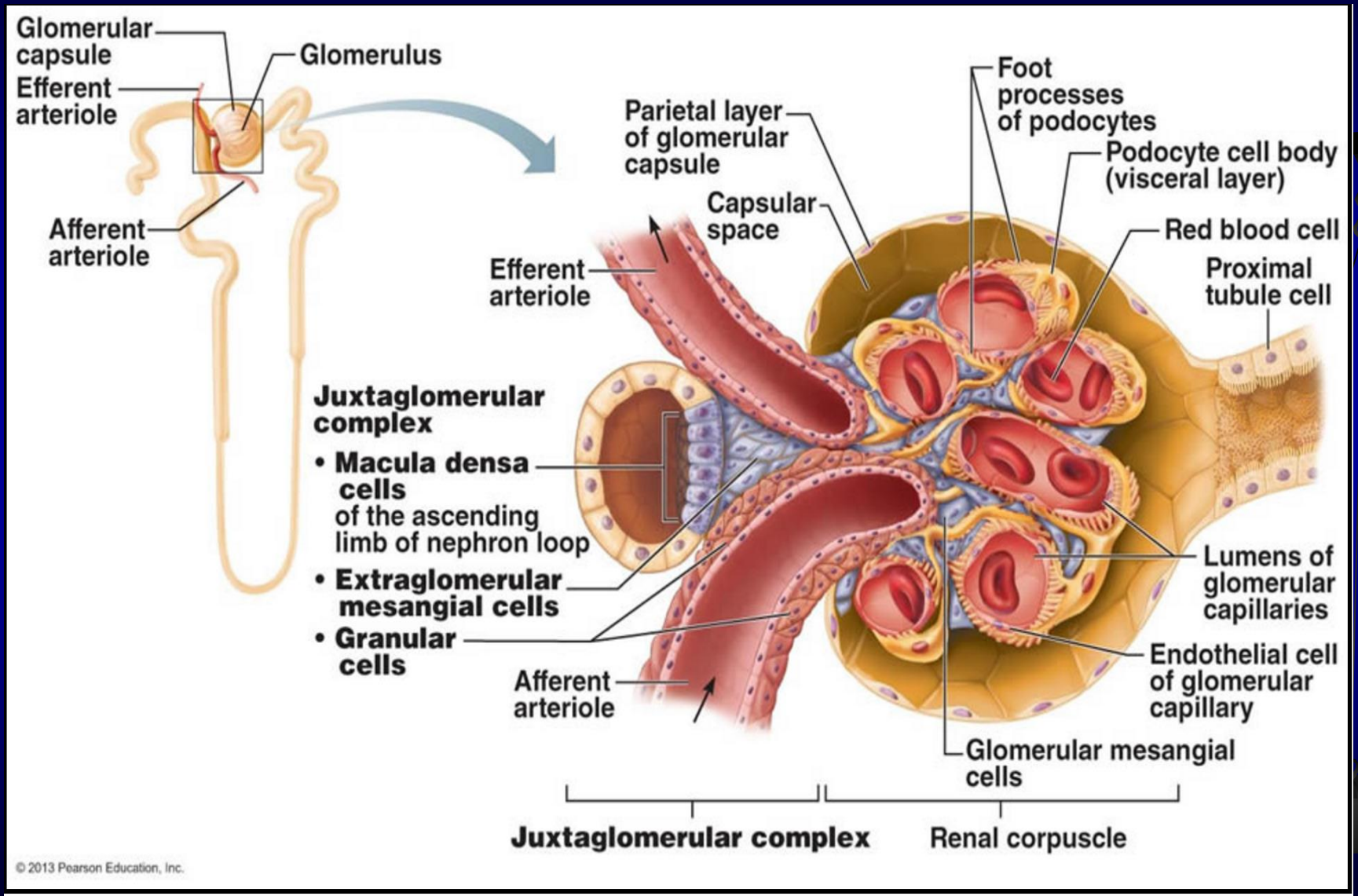
†SLICC: Systemic Lupus International Collaborating Clinics
* See notes for criteria details

Petri M, et al. Arthritis and Rheumatism. Aug 2012

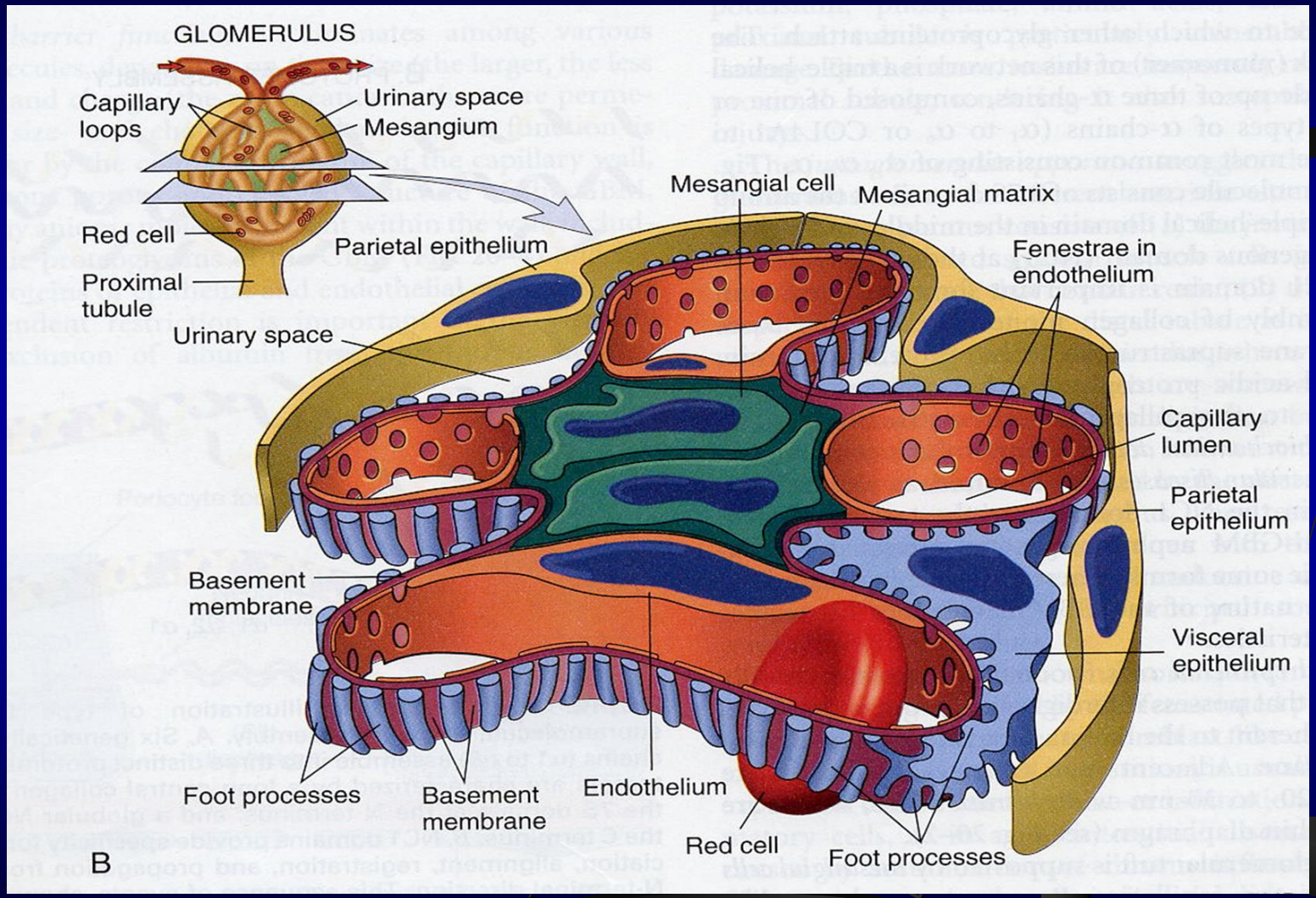
Punctie – Biopsie renala (02.02.2020)

- 20 de corpusculi renali:
- 6 cu scleroza glomerulara avansata segmentara si totala
- restul hipercelulari, 2 cu aspect de necroza fibrinoida, infiltrat celular leucocitar si semilune fibroase; simfize parieto-capilare si aspect de scleroza segmentara
- La nivel tubulo-interstitial: fibroza usoara zonala cu infiltrat celular mononuclear, zonal tubi atrofici.
- Concluzie: Leziuni de glomerulonefrita lupica proliferativ activa, asociind glomeruloscleroza (clasa III/A LES)

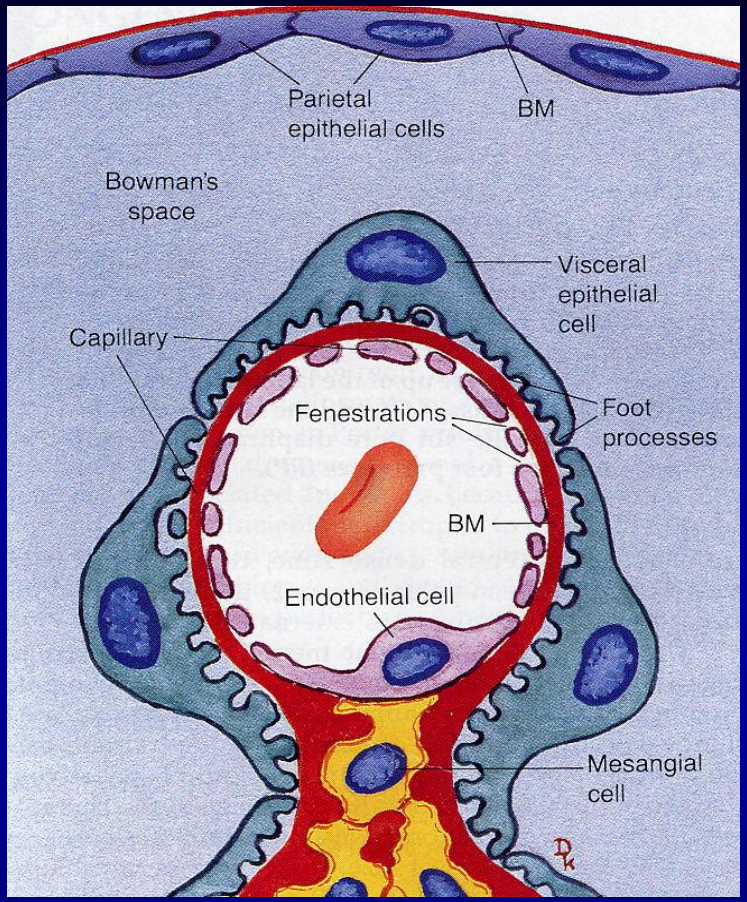
Aspect histologic normal

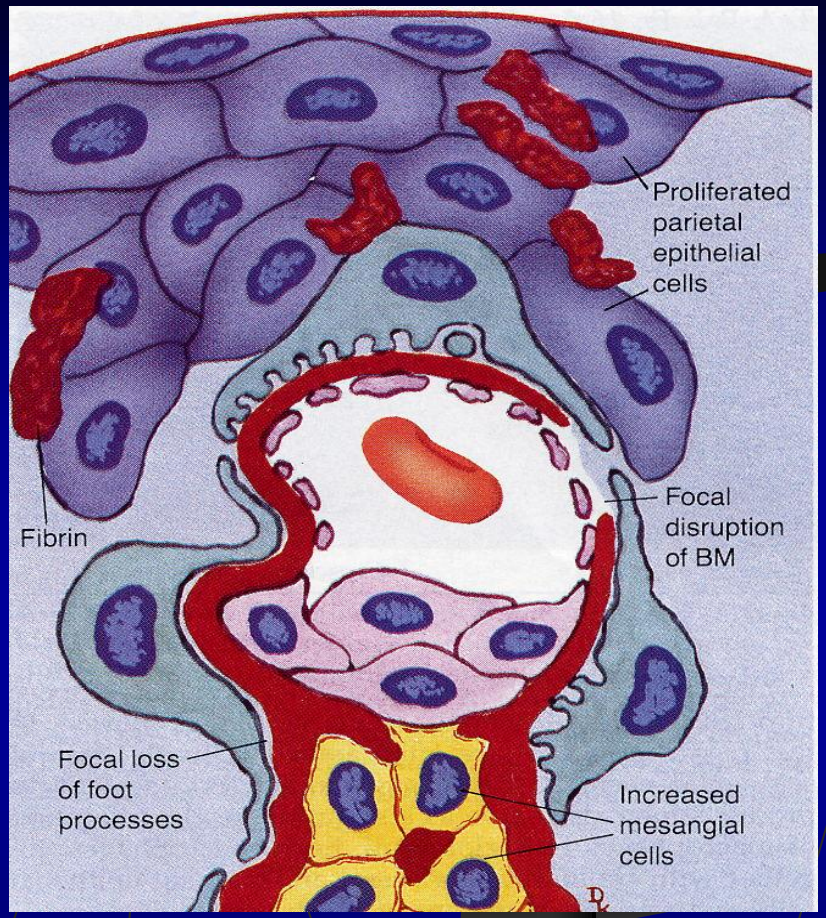


Aspect histologic normal



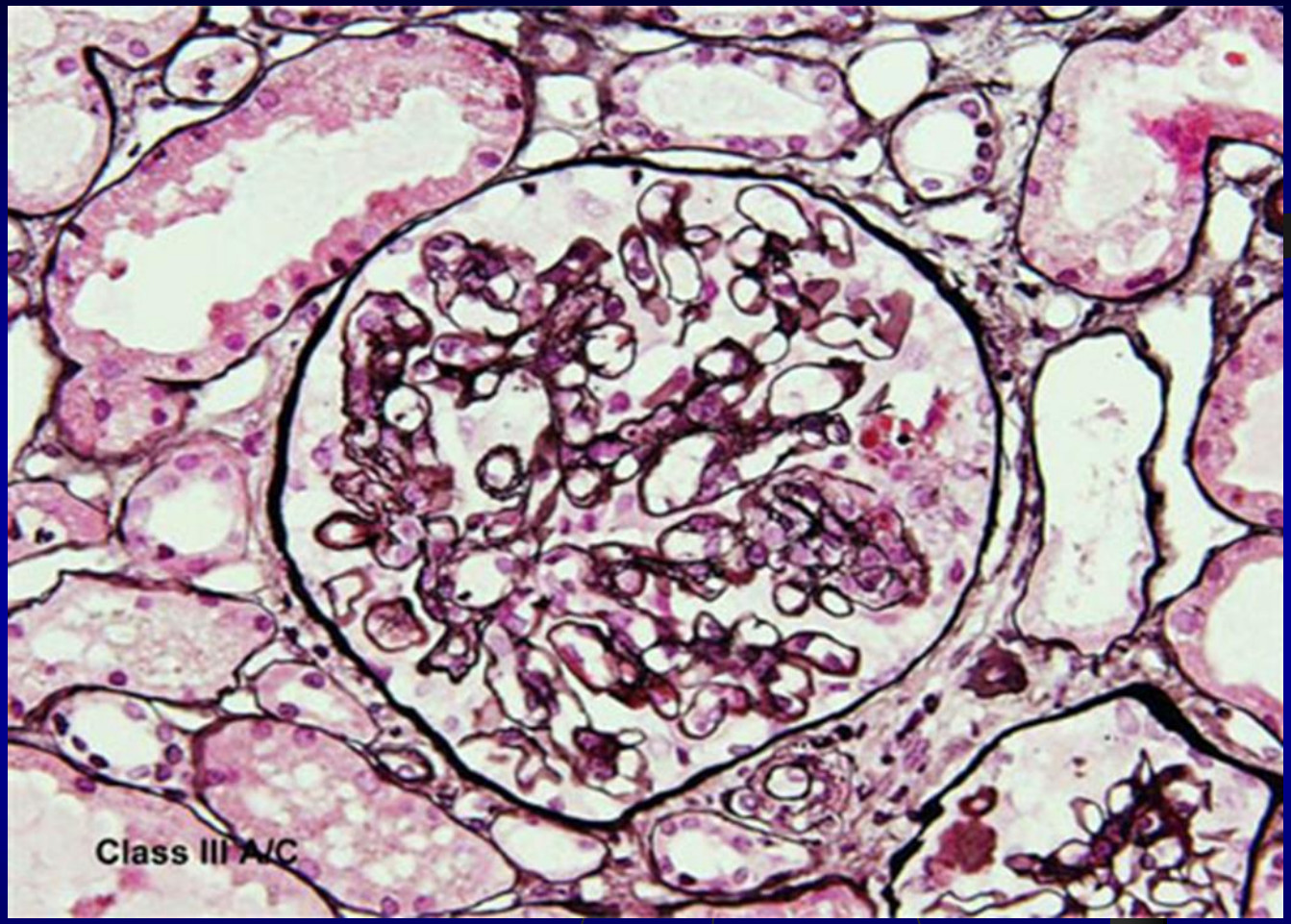
Formarea semilunelor epiteliale



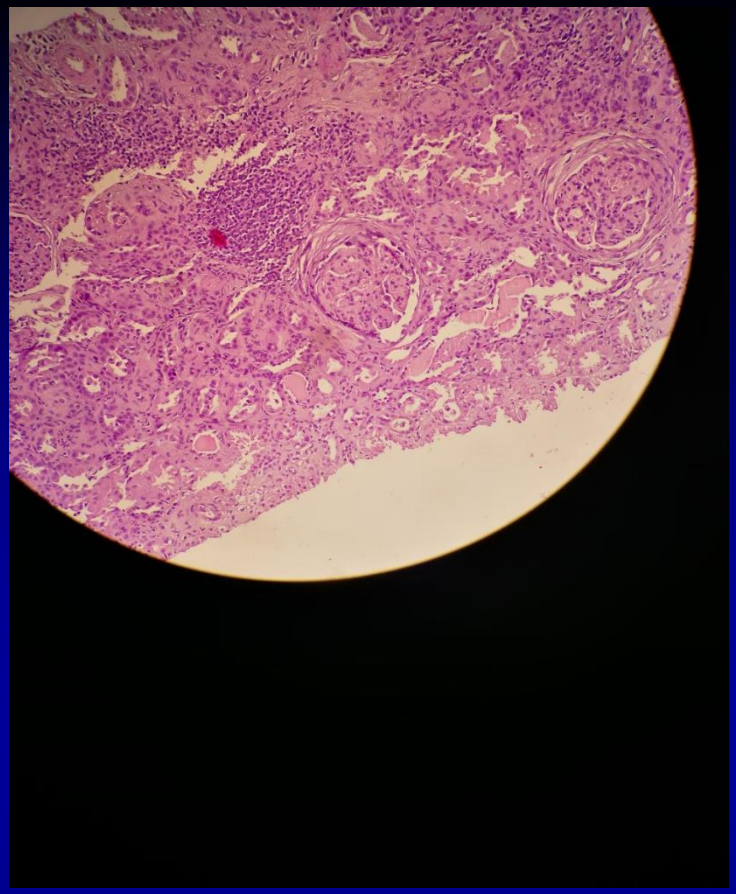


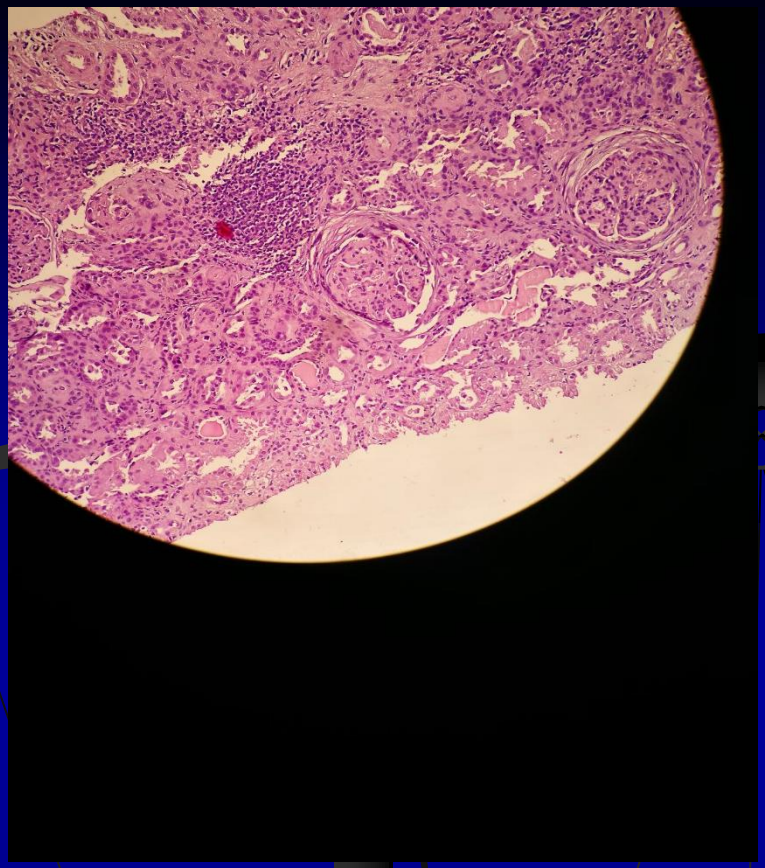
Formarea semilunelor este declansata de trecerea hematiilor si fibrinei in spatiul de filtrare ca urmare a cresterii permeabilitatii membranei bazale glomerulare. Fibrina determina proliferarea celulelor epiteliale ale capsulei Bowman si aflux de monocite si PMN-uri in spatiul Bowman. Cresterea rapida si fibroza semilunelor comprima ansele capilare glomerulare si ocuparea in intregime a spatiului de filtrare, ducind la instalarea rapida a BCR. In interstitiu poate exista infiltrat inflamator cronic.

Modificari histopatologice in LES clasa III A/C



Focal segmental glomerulonephritis with active necrotizing and sclerosing lesions





Proliferative LN is caused by the deposition of IC in the subendothelial space of the glomerular capillaries, which triggers local inflammation and endocapillary hypercellularity. The criteria for activity are: endocapillary hypercellularity; glomerular neutrophils; fibrinoid necrosis; wire loop lesions and/or hyaline thrombi in the glomeruli; cellular and/or fibrocellular crescents; and interstitial inflammation. The criteria for chronicity include: total score of segmental or global glomerulosclerosis; fibrous crescents; tubular atrophy and interstitial fibrosis.

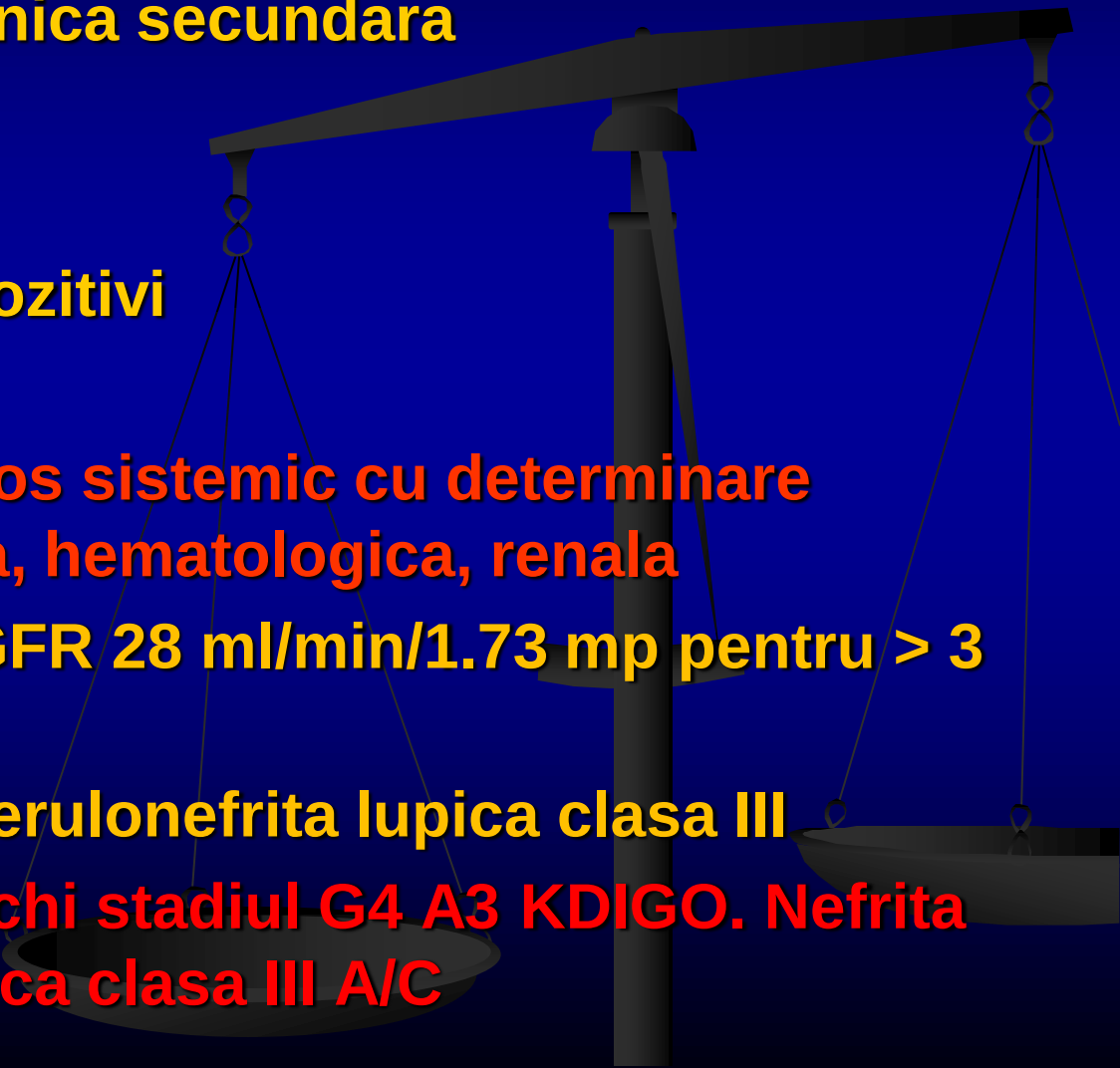
Diagnostic pozitiv

- Poliserozita (pericardita, pleurezie, ascita)
- Vasculita cerebrala
- Glomerulonefrita cronica secundara
- Sindrom anemic
- Profil ANA pozitiv
- Ac antifosfolipidici pozitivi
- C3 scazut

Lupus eritematos sistemic cu determinare neurologica, hematologica, renala

- Retentie azotata cu GFR 28 ml/min/1.73 mp pentru > 3 luni
- Biopsie renala: glomerulonefrita lupica clasa III

Boala cronica de rinichi stadiul G4 A3 KDIGO. Nefrita lupica clasa III A/C



Diagnostic diferential

- Glomerulonefrite primitive: mezangio-capilara,SGFS, membranoasa

- Glomerulonefrite secundare: asociate diabetului zaharat, mielomului, amiloidozei, paraneoplazice

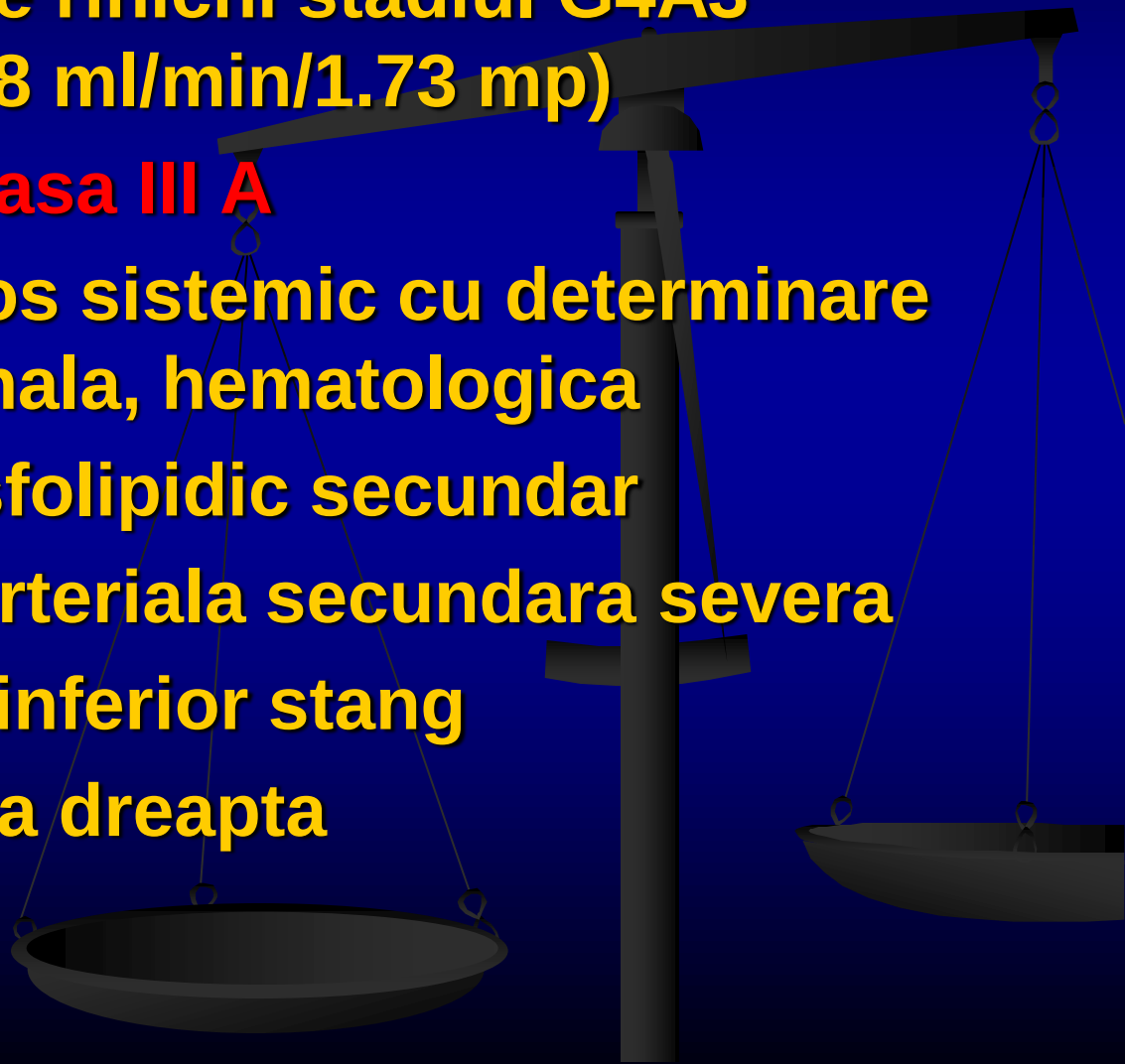
- Glomerulonefrite rapid progresive: vasculite sistemice ANCA pozitive, sindromul Goodpasture

20.02.2020

- Dispnee, junghi toracic, fatigabilitate
- Investigatii de laborator constante fata de determinarile de la spitalizarea anterioara
- Persista ascita in cantitate medie: evaluare biochimica, sediment, cultura
- RX torace: pneumonie lob inferior stang
- Ecografie abdominala: formatiune tumorala ovariana dreapta
- Evaluare ginecologica: tumora ovariana dreapta 44.7/28 mm
- Scor ROMA: 96,7% (risc crescut de cancer ovarian)

Diagnostic pozitiv

1. Boala cronica de rinichi stadiul G4A3 KDIGO (RFG= 28 ml/min/1.73 mp)
2. Nefrita lupica clasa III A
3. Lupus eritematos sistemic cu determinare neurologica, renala, hematologica
4. Sindrom antifosfolipidic secundar
5. Hipertensiune arteriala secundara severa
6. Pneumonie lob inferior stang
7. Tumora ovariana dreapta



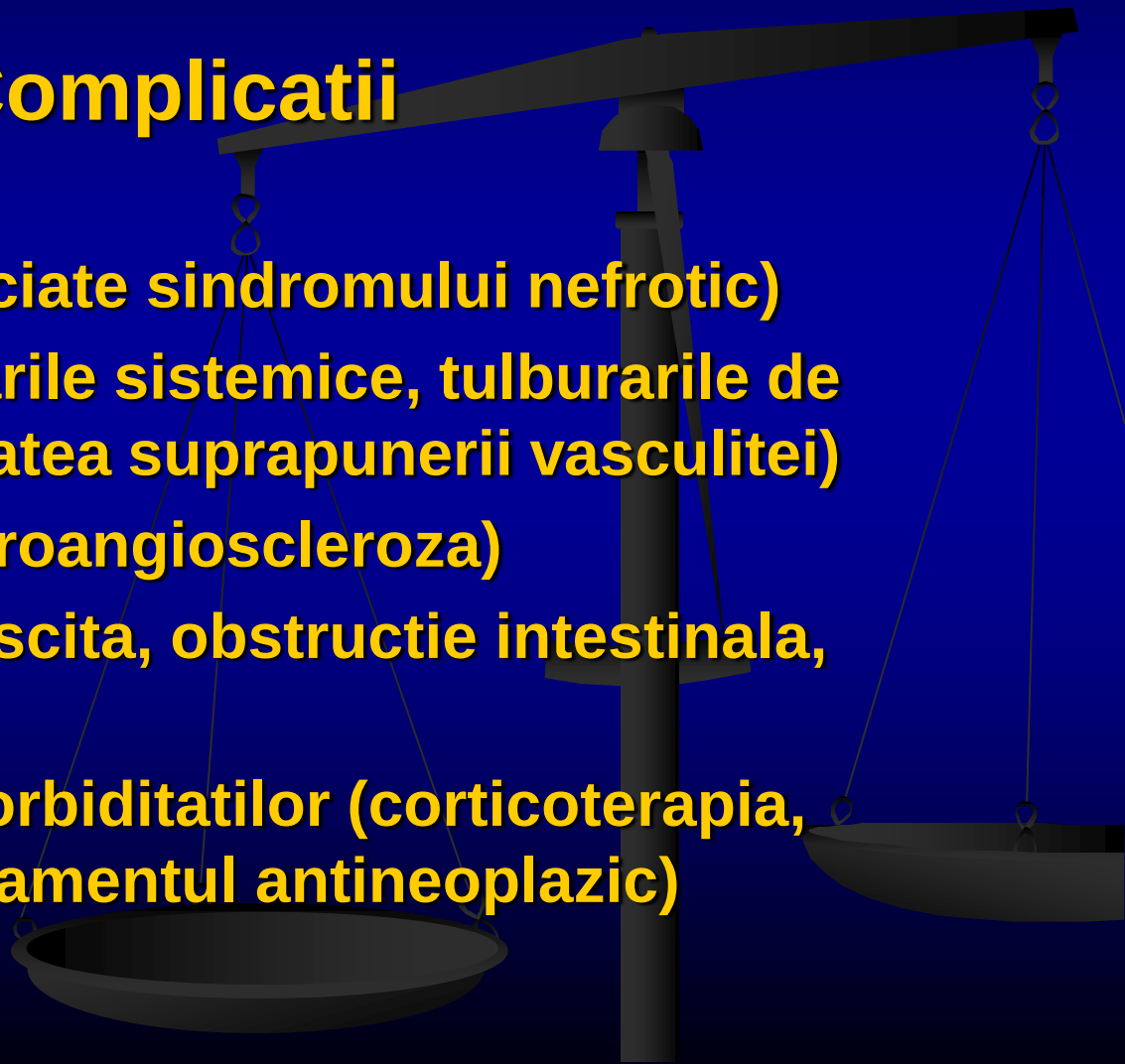
Evolutie

Grevata de:

- **Complicatii**
- **Stadiile BCR**

Complicatii

- **BCR (anemie, TMO)**
- **nefrita lupica (associate sindromului nefrotic)**
- **LES (prin manifestarile sistemice, tulburarile de coagulare, posibilitatea suprapunerii vasculitei)**
- **HTA (AVC, IMA, nefroangioscleroza)**
- **Tumorii ovariane (ascita, obstructie intestinala, obstructie vezicala)**
- **Tratamentelor comorbiditatilor (corticoterapia, imunosupresia, tratamentul antineoplazic)**

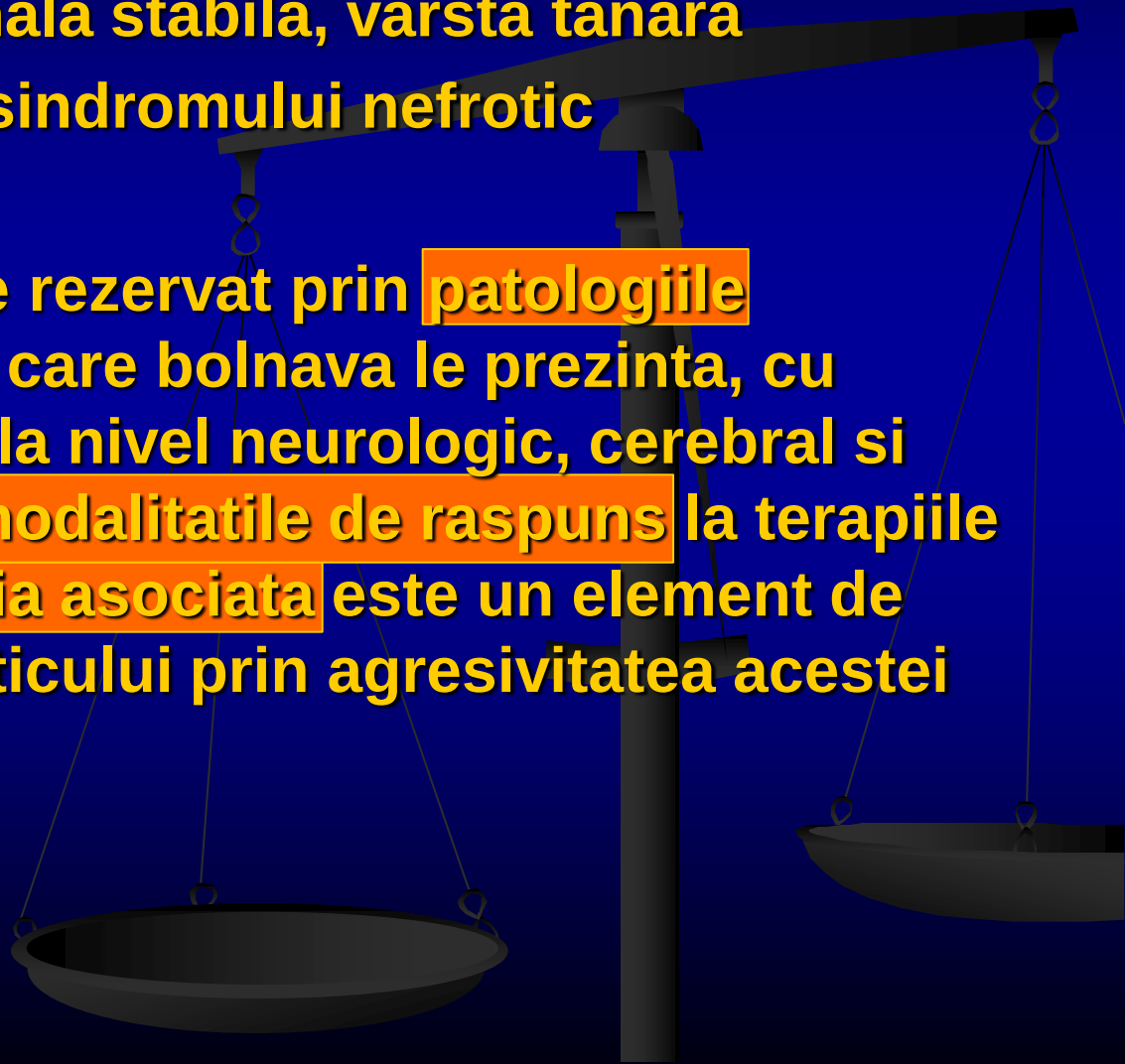


Prognostic

Pe termen scurt este dictat de elementele prognostice:

- **pozitive: functia renala stabila, varsta tanara**
- **negative: prezenta sindromului nefrotic**

Pe termen lung devine rezervat prin patologiile complexe asociate pe care bolnava le prezinta, cu manifestari sistemice la nivel neurologic, cerebral si renal precum si prin modalitatile de raspuns la terapiile administrate. Neoplazia asociata este un element de inrautatire al prognosticului prin agresivitatea acestei forme de neoplazie.



Tratament

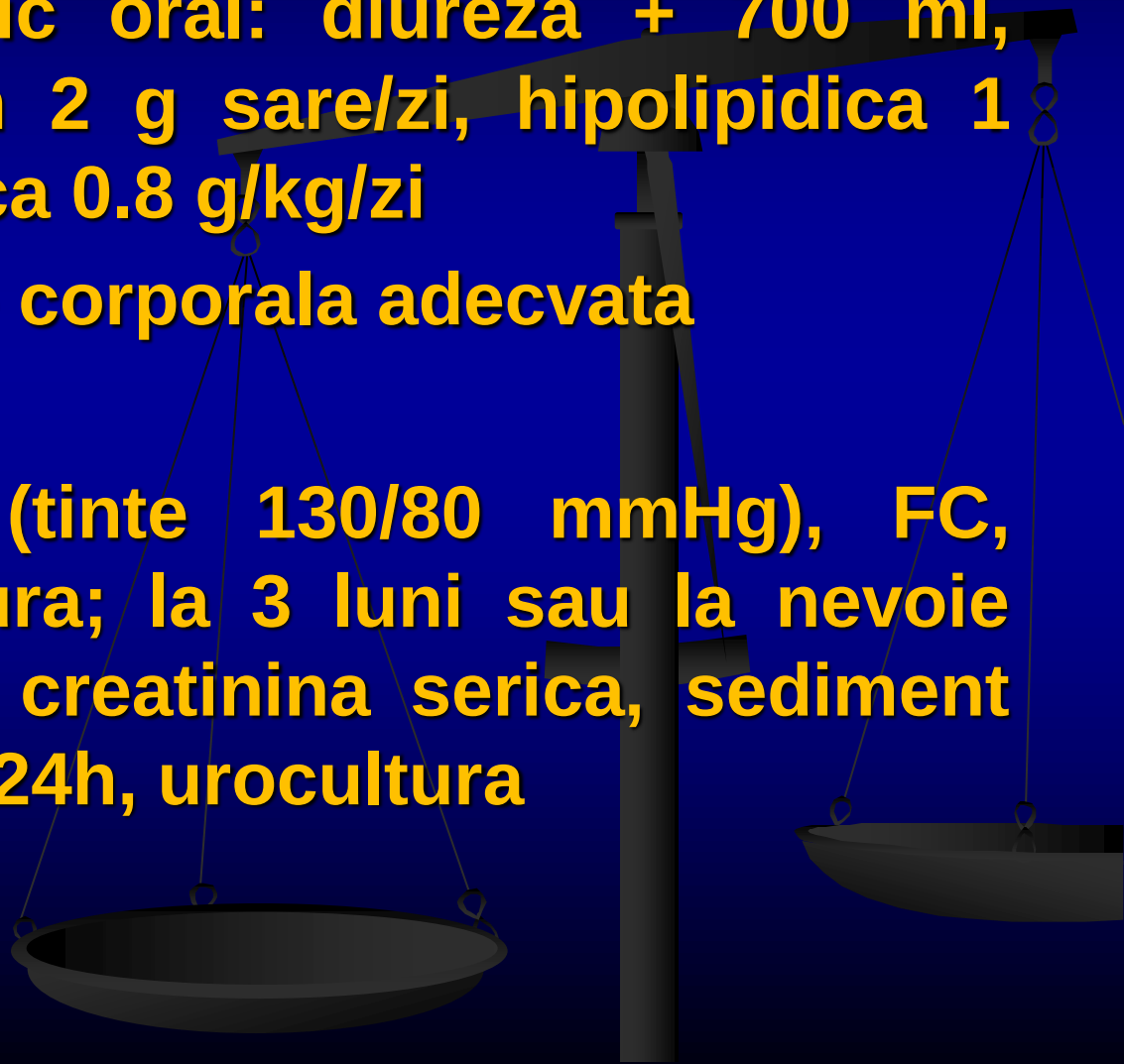
1. Schimbarea stilului de viata:

Dieta: aport hidric oral: diureza + 700 ml, hiposodata maxim 2 g sare/zi, hipolipidica 1 g/kg/zi, hipoproteica 0.8 g/kg/zi

Mentinere greutate corporala adecvata

Efort fizic adecvat

Monitorizare TA (tinte 130/80 mmHg), FC, diureza, temperatura; la 3 luni sau la nevoie HLG, uree serica, creatinina serica, sediment Addis, proteinuria/24h, urocultura



Tratament

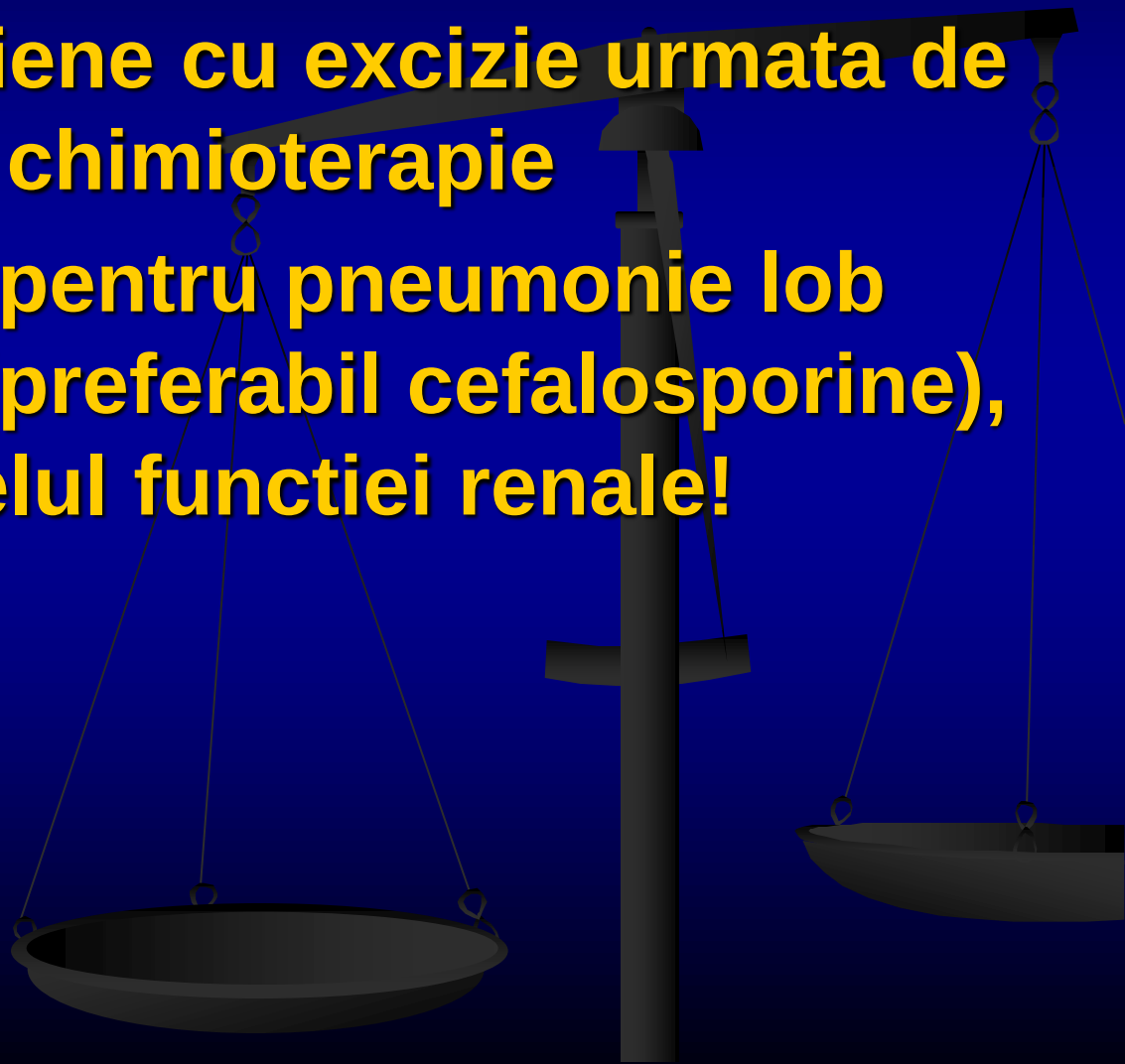
- **Medicamentos:**

- **Etiologic al pneumoniei cu carbapeneme: Meropenem 3x1 gr/zi**
- **Simptomatic al HTA cu betablocante (Carvedilol 12.5 mg 2/1 cp/zi) si Blocante ale canalelor de calciu (Leridip 10 mg 1 cp/zi)**
- **Simptomatic antitusiv cu ACC 600 mg/zi si antalgic cu Algocalmin 1 cp la nevoie**
- **Patogenic al nefritei lupice: din 07.06.2019 – Medrol 44 mg/zi cu reducerea progresiva a dozei**
- **Tratament asociat sindromului antifosfolipidic: anticoagulare sistemica orala cu Acenocumarol doza ajustata in functie de INR**

Tratament

2. Etiologic:

- al tumorii ovariene cu excizie urmata de radioterapie si chimioterapie
- Antibioterapie pentru pneumonie lob inferior stang (preferabil cefalosporine), ajustate la nivelul functiei renale!



Tratament

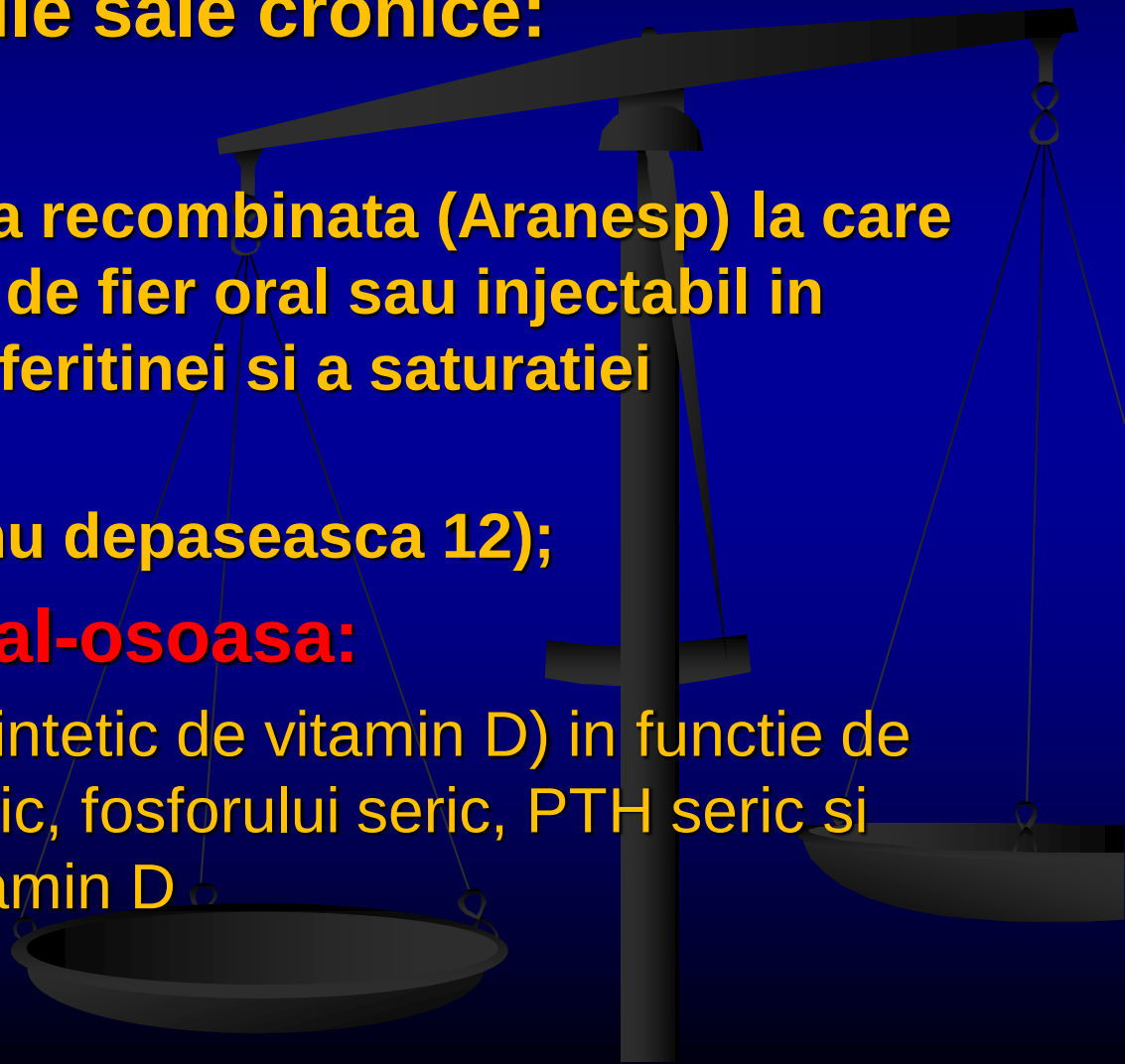
3. Simptomatic:

BCR cu complicatiile sale cronice:

- **anemia:**
- **Eritropoetina umana recombinata (Aranesp) la care se adauga preparat de fier oral sau injectabil in functie de valoarea feritinei si a saturatiei transferinei**

tinta Hb 11.5 g/dl (sa nu depaseasca 12);

- **tulburarea mineral-osoasa:**
- Paricalcitol (analog sintetic de vitamin D) in functie de valoarea calciului seric, fosforului seric, PTH seric si dozare 25 hidroxi vitamin D

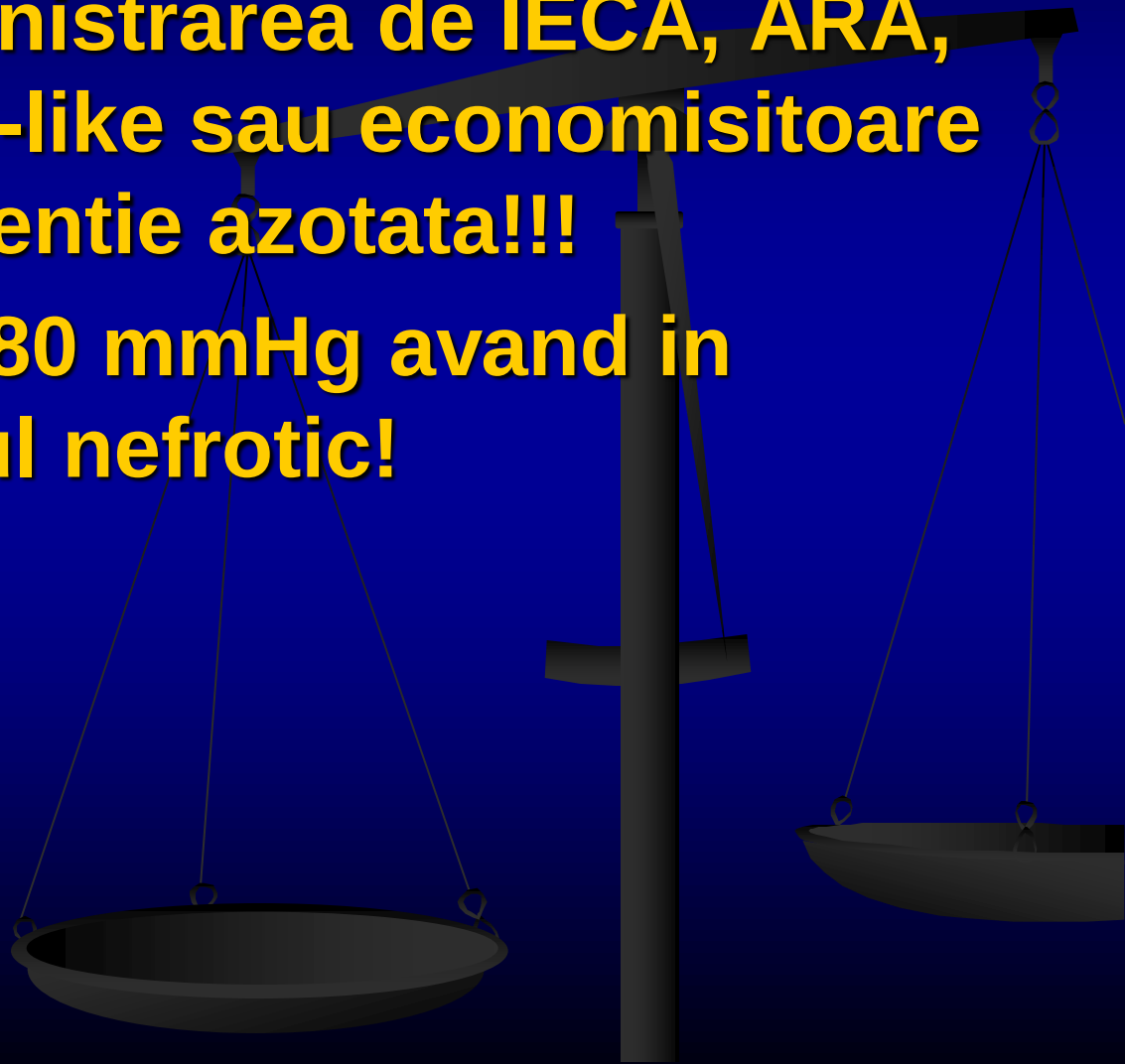


Tratament

- **HTA:**

- atentie la administrarea de IECA, ARA, diuretice tiazidic-like sau economisitoare de potasiu in retentie azotata!!!

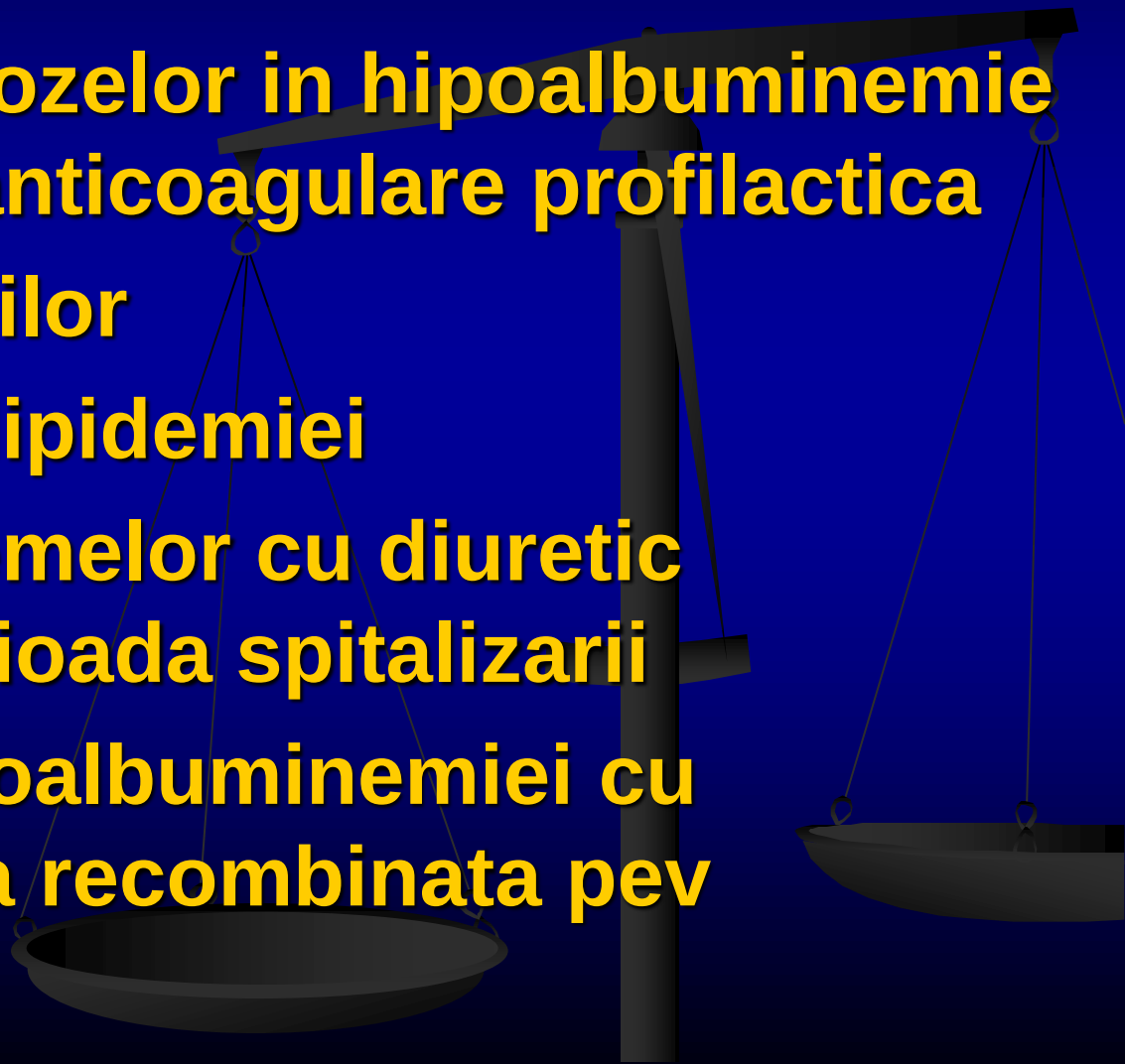
- Tinta TA < 130/80 mmHg avand in vedere sindromul nefrotic!



Tratament

- **Sindromul nefrotic:**

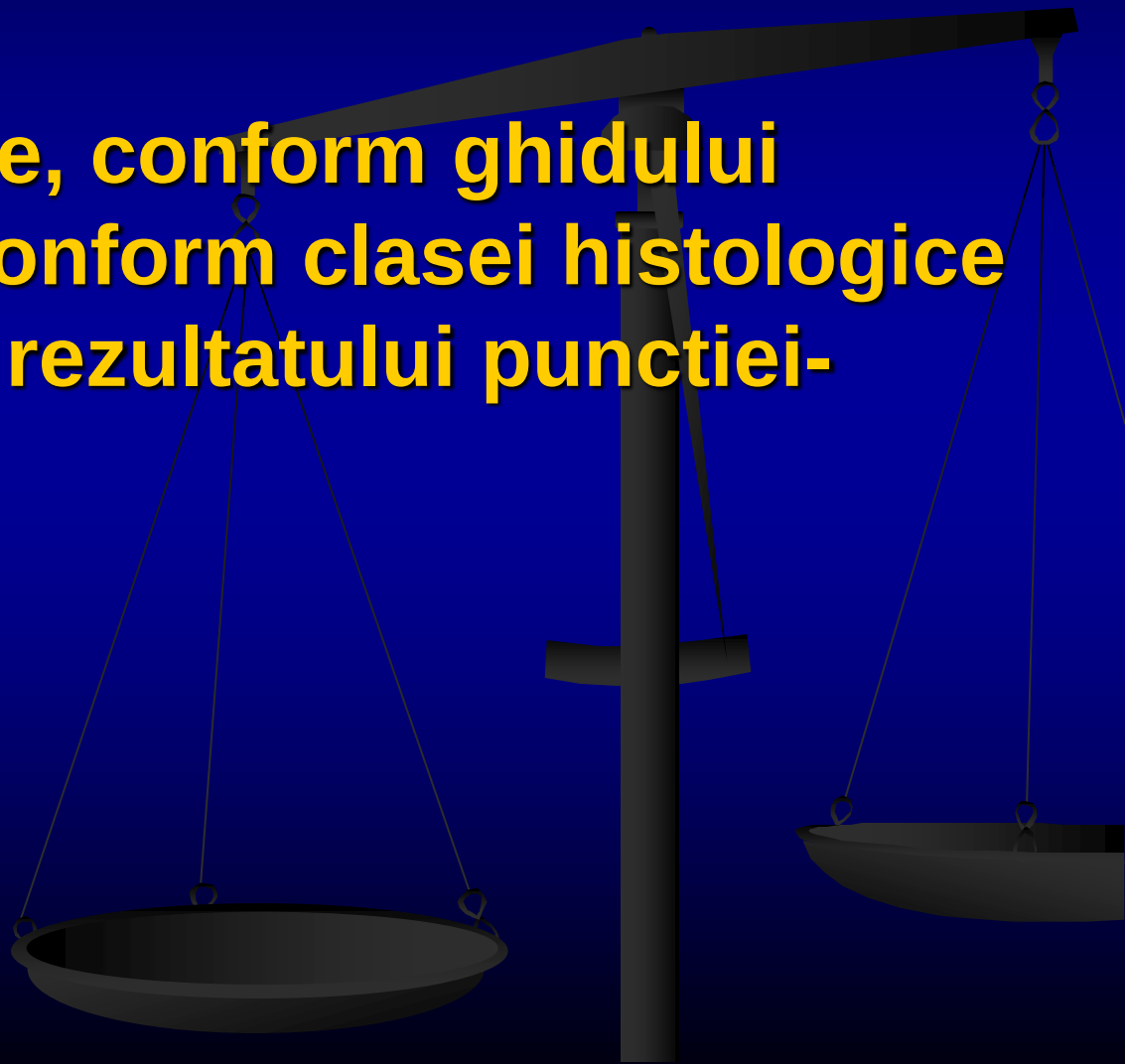
- preventia trombozelor in hipoalbuminemie < 2-2,5 g/dl, cu anticoagulare profilactica
- preventia infectiilor
- Tratamentul dislipidemiei
- Tratamentul edemelor cu diuretic injectabil pe perioada spitalizarii
- Tratamentul hipoalbuminemiei cu albumina umana recombinata pev



Tratament

- **4. Patogenic**

- Al nefritei lupice, conform ghidului KDIGO 2012 si conform clasei histologice relevata in urma rezultatului punctiei-biopsie renala



KDIGO 2012

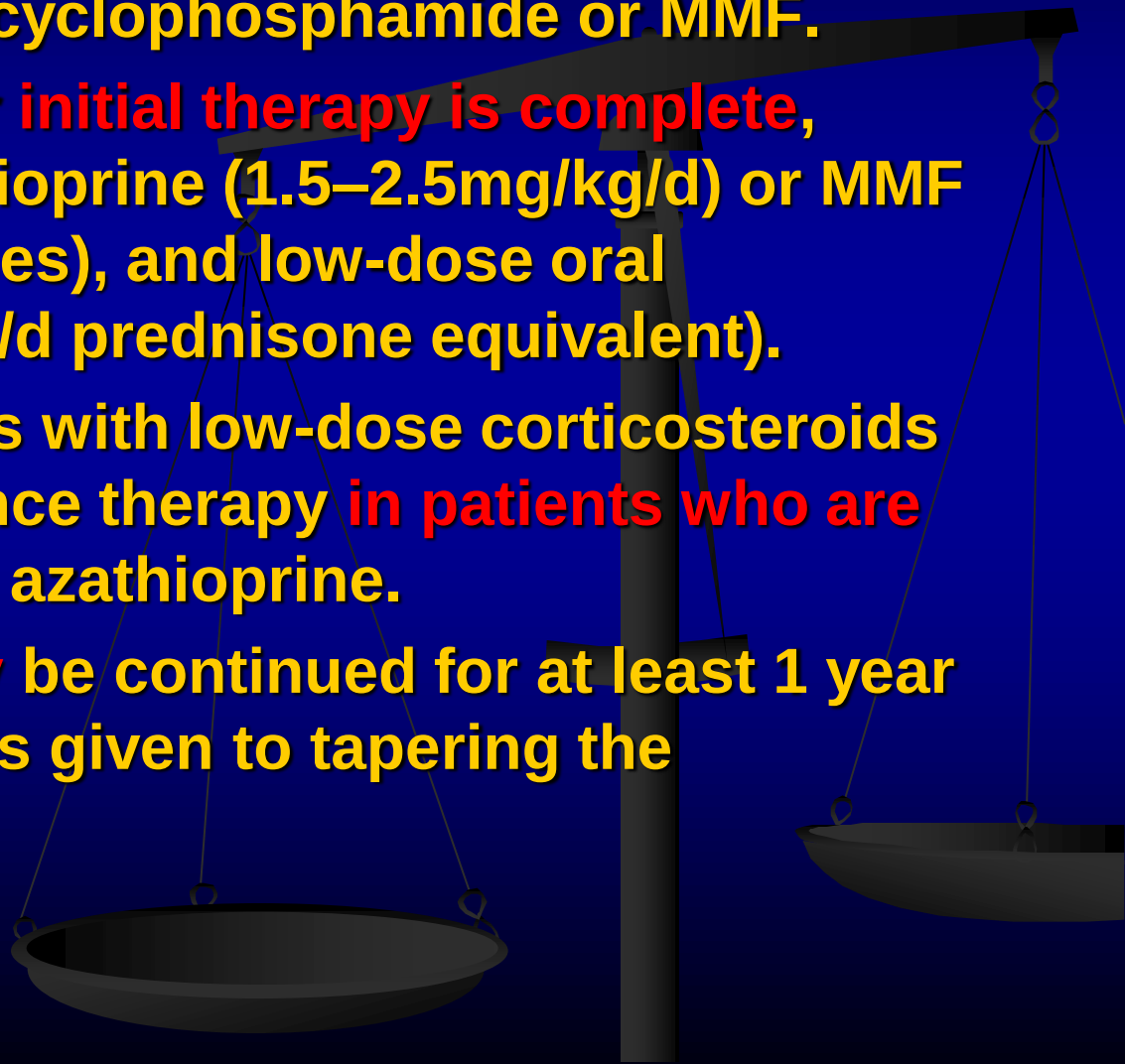
Class III LN (focal LN) and class IV LN (diffuse LN)

- We recommend initial therapy with corticosteroids, combined with either cyclophosphamide or MMF.

- We recommend after initial therapy is complete, patients receive azathioprine (1.5–2.5mg/kg/d) or MMF (1–2g/d in divided doses), and low-dose oral corticosteroids (10mg/d prednisone equivalent).

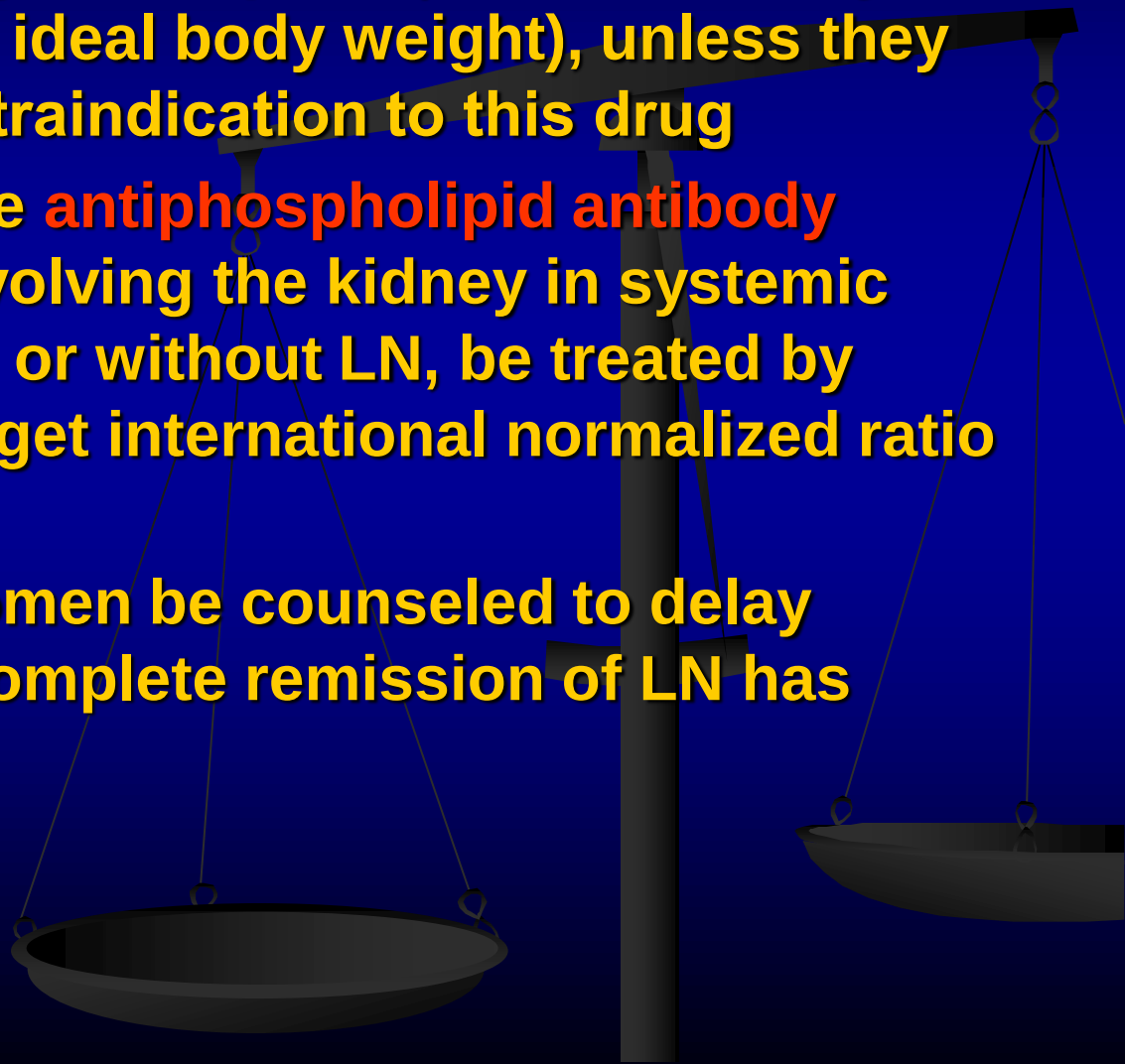
- We suggest that CNIs with low-dose corticosteroids be used for maintenance therapy in patients who are intolerant of MMF and azathioprine.

- Maintenance therapy be continued for at least 1 year before consideration is given to tapering the immunosuppression.



KDIGO 2012

- We suggest that all patients with LN of any class are treated with hydroxychloroquine (maximum daily dose of 6–6.5mg/kg ideal body weight), unless they have a specific contraindication to this drug
- We suggest that the antiphospholipid antibody syndrome (APS) involving the kidney in systemic lupus patients, with or without LN, be treated by anticoagulation (target international normalized ratio [INR] 2–3).
- We suggest that women be counseled to delay pregnancy until a complete remission of LN has been achieved

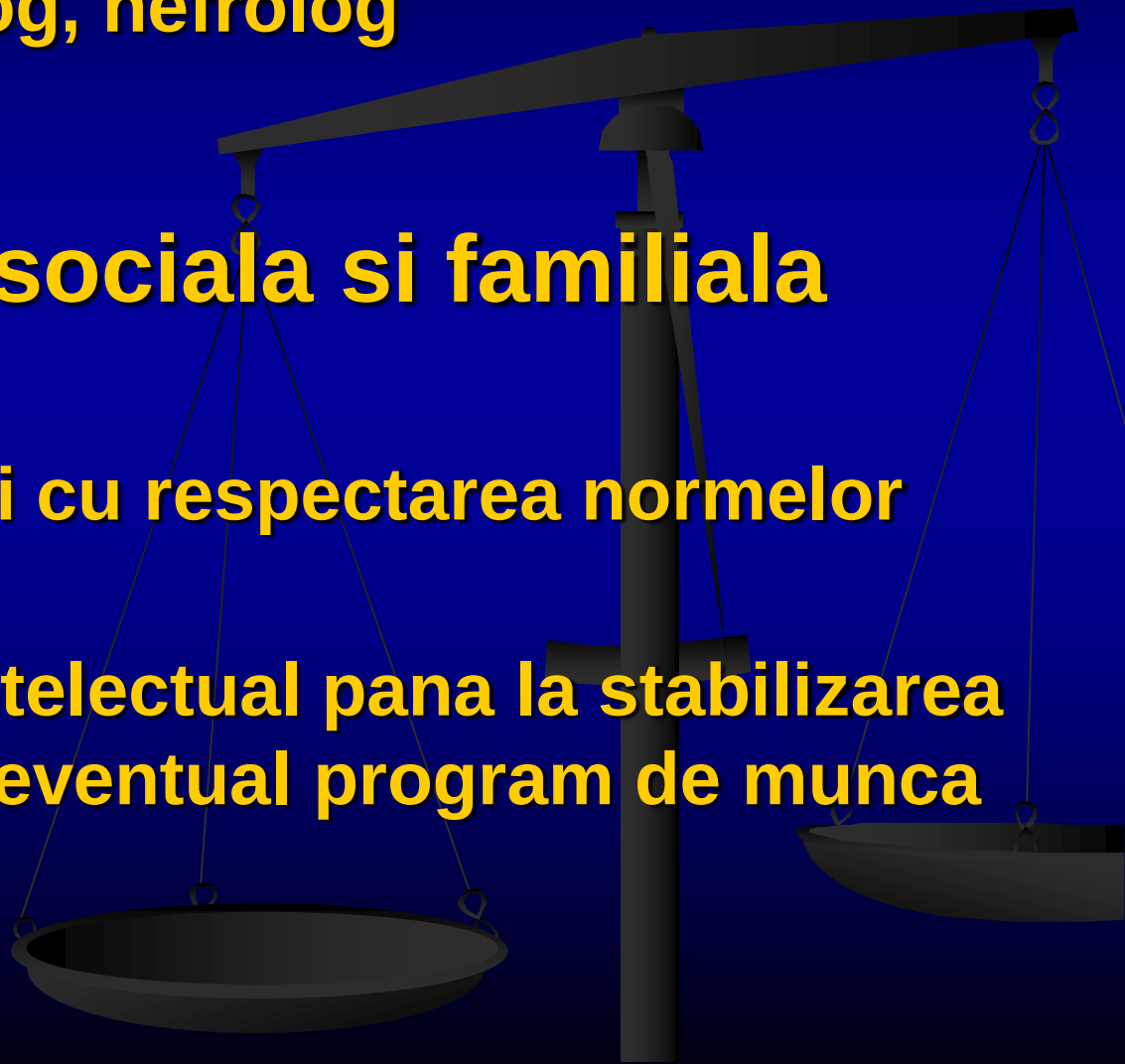


Dispensarizare

- **Pluridisciplinara: medic de familie, neurolog, cardiolog, oncolog, nefrolog**

Reinsertie sociala si familiala

- **Suport familial**
- **Ambient linistit si cu respectarea normelor de igiena**
- **Repaus fizic si intelectual pana la stabilizarea afectiunilor apoi eventual program de munca redus**

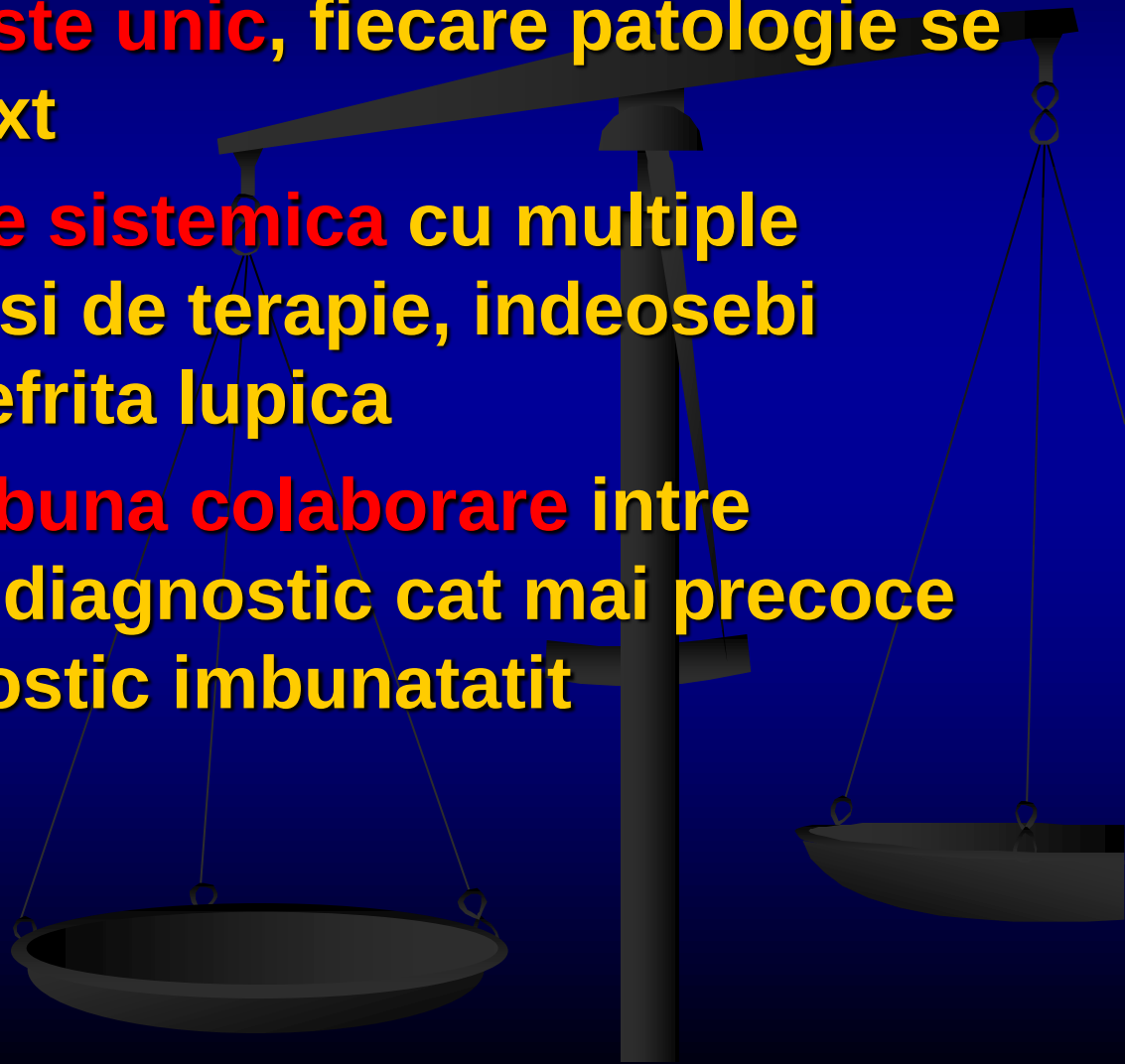


Particularitatea cazului

- **Debut cu manifestari neurologice care au durat o perioada de cativa ani pana la aparitia altor manifestari**
- **Asocierea tumorii de ovar cu evolutie agresiva si prognostic agravant**
- **Necesitatea unei ajustari terapeutice avand in vedere complexitatea patologiilor**

Take-Home Messages

- **Fiecare bolnav este unic, fiecare patologie se trateaza in context**
- **LES – o patologie sistemica cu multiple implicatii clinice si de terapie, indeosebi cand asociaza nefrita lupica**
- **Este necesara o buna colaborare intre specialitati si un diagnostic cat mai precoce pentru un prognostic imbunatatit**




Va multumesc!