

GLOMERULONEFRITE SECUNDARE

Afectare glomerulara secundara in cadrul unor boli bine definite

1. BOLI MULTISISTEMICE

- **LES**
- **Purpura HS**
- **Sindrom Goodpasture**
- **Vasculite sistemice**
- **altele**

3. BOLI CRONICE DE FICAT

- **Hepatita cu VHB**
- **Hepatita VHC**
- **Ciroza hepatica**

2. DIS si PARAPROTEINEMII

- **Crioglobulinemie**
- **Macroglobulinemie Waldenstrom**
- **Gamapati monoclonala benigna**
- **Mielomul**
- **Boala lanturilor usoare**
- **Amiloidoza**
- **Glomerulonefrita fibrilara**

4. BOLI INFECTIOASE

- **GNA poststreptococica**
- **Endocardita bacteriana**
- **Nefrita de shunt**
- **Abcese viscerale**
- **Alte infectii bacteriene**
- **Protozoare, alti paraziti**
- **Virale (inclusiv HIV)**

5. BOLI EREDO-FAMILIARE

- **Diabetul zaharat**
- **Sindromul Alport**
- **Boa la Fabri**
- **Osteo-onicodisplazia**
- **Sindromul nefrotic congenital**
- **Siclemia**
- **Lipodistrofia partiala sau totala**

6. BOLI NEOPLAZICE

7. GN IMUNALERGICE

(medicamente, vaccinuri alergeni)

8. ALTELE

NEFROPATIA LUPICA

LES - boala autoimuna cu etiologie neprecizata si afectare renala frecventa

INCIDENTA

- **NL prezent de la depistarea LES - 5% din cazuri**
- **NL se instaleaza in cursul afectiunii la 75% din bolnavi**
- **Afectare renala silentioasa in cadrul LES - frecventa**

PATOGENIE

- modificari ale structurii antigenice - virusi
- modificari ale raspunsului imun - transmisa genetic HLA DR2, , DR3, B12,



- stimularea limfocitelor B
- deficit de limfocite T totale cu - exces de T helper si deficit de T supresor
- implicarea caii alterne si clasice a complementului
- modificari ale functiei receptorilor Fc in sistemul micro-macrofagic al splinei





- **sinteza de autoanticorpi impotriva propriilor structuri**
 - **anticorpi antinucleari**
 - **anticorpi anti ADN dublu si monocatenar**
 - **anticorpi anti Sm - fibra musculara neteda**
 - **anticorpi anti Ro, anti La**
 - **anticorpi anti cardiolipina**
 - **anticorpi anti eritrocitari, anti limfocitari, antiplachetari**
 - **anticorpi anti neuronali**



- **leziuni glomerulare induse de CI (circulante si plantate}**

CLASIFICARE

Clasificarea ISN/RPS al NL (2004)

Clasa I - **NL cu leziuni minime** [optic normali, IF (+)]

Clasa II - **NL proliferativ mezangiala** – hipercelularitate mezangiala cu depozite mezangiale in MO

Clasa III - **NL focala** : leziuni focale si segmentale sau globale, < 50% din glo.

A – activa – focala proliferativa

A/S –activa si sclerozanta – leziuni proliferative si sclerozante

S - focala sclerozanta

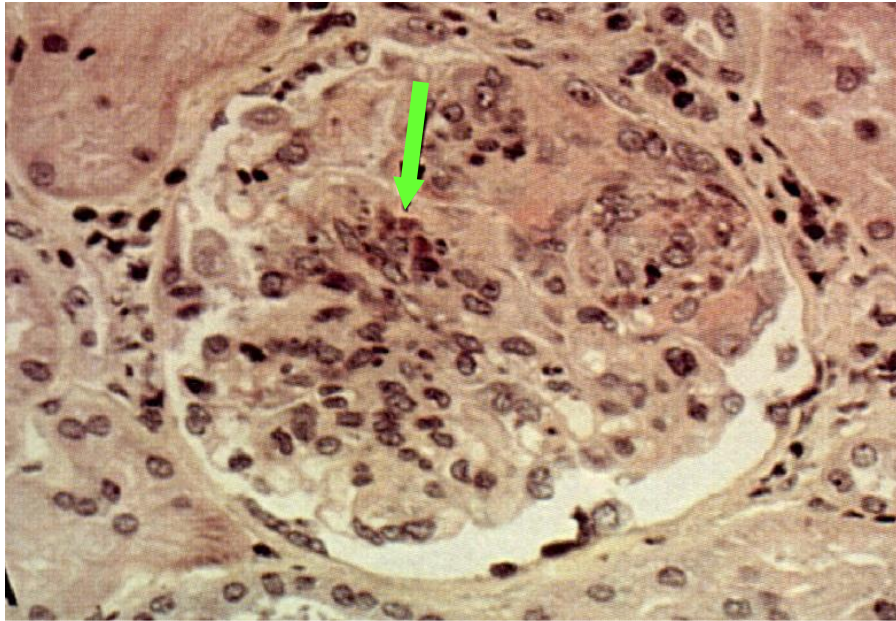
Clasa IV - **NL difuza** – leziuni active sau sclerozante segmentale (S) sau globale (G), endo sau extracapi;are >50% din glomeruli

S sau G (A), S sau G (A/S), S sau G (S)

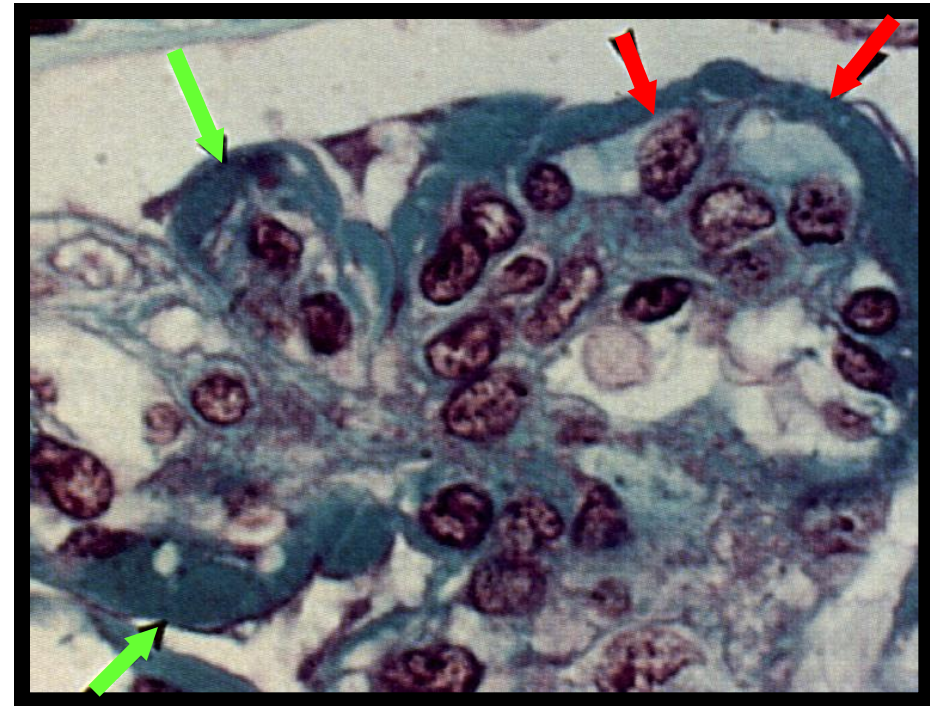
Clasa V – **NL membranoasa**

Clasa VI - **NL cu scleroze avansate**

+/- Leziuni tubulo-interstitiale si vasculare

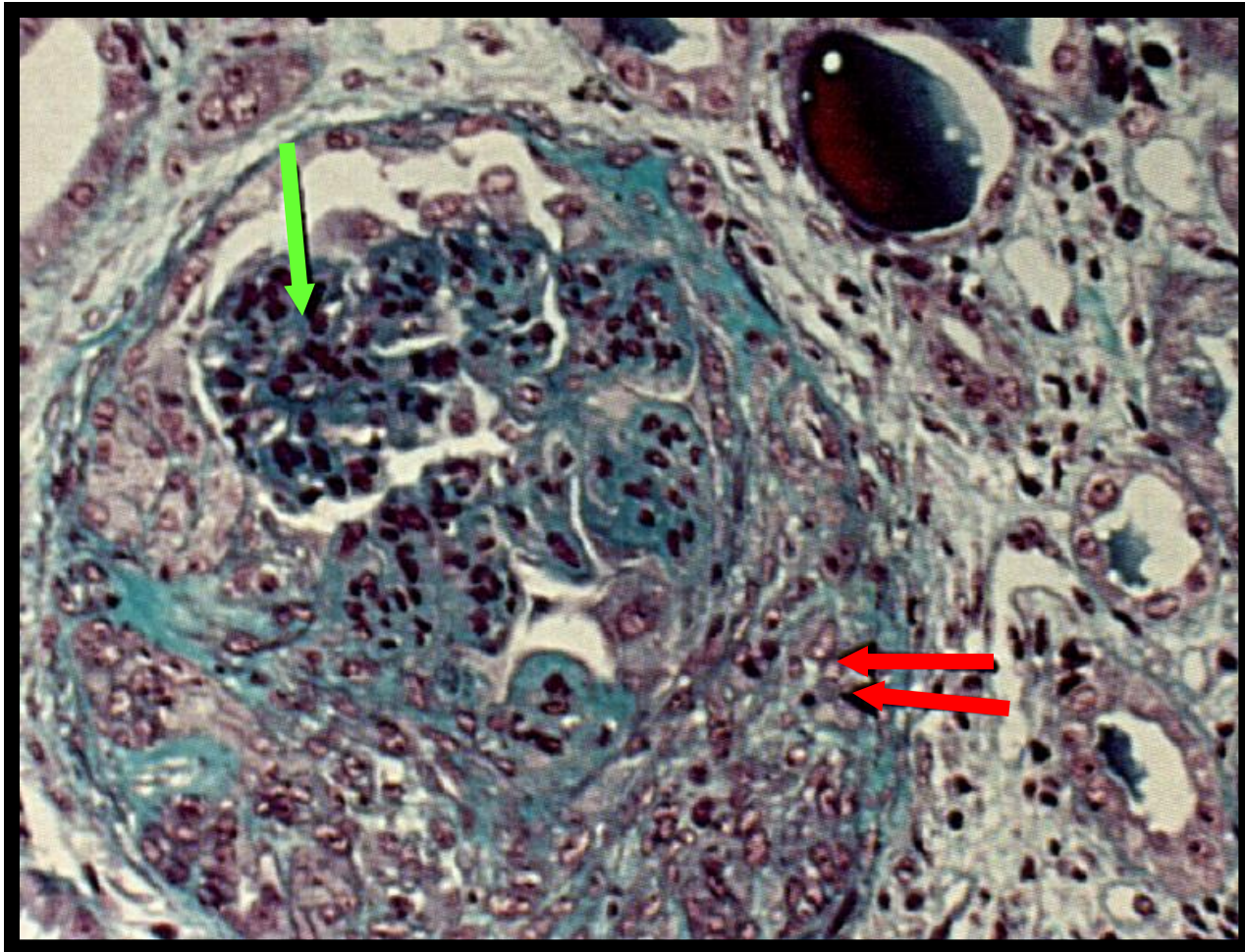


**Proliferare mezangiala, corpi
hematoxilini**

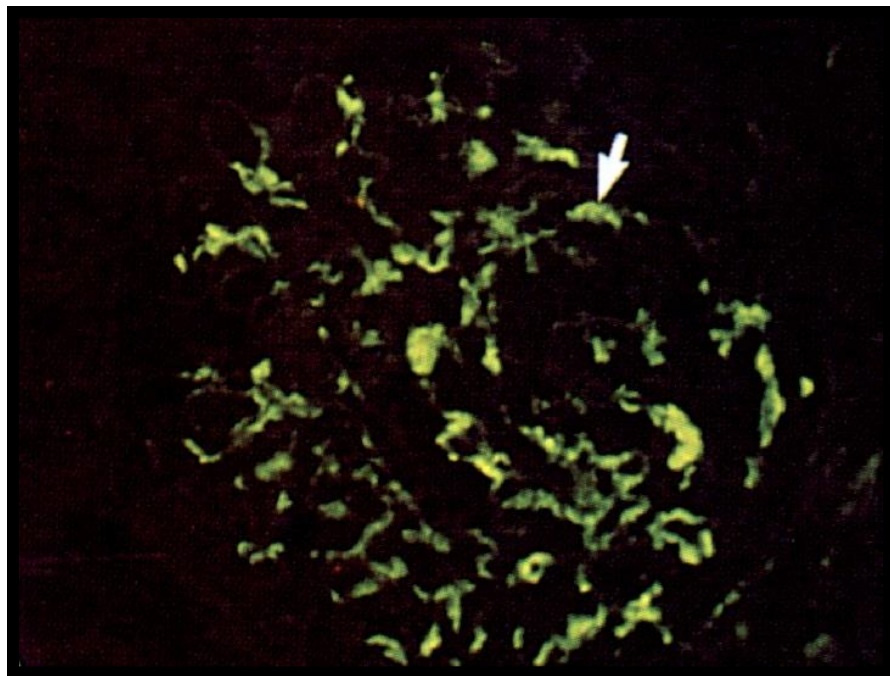


**Priliferare endocapilara, depozite
endomembranoase cu aspect de wire loops**

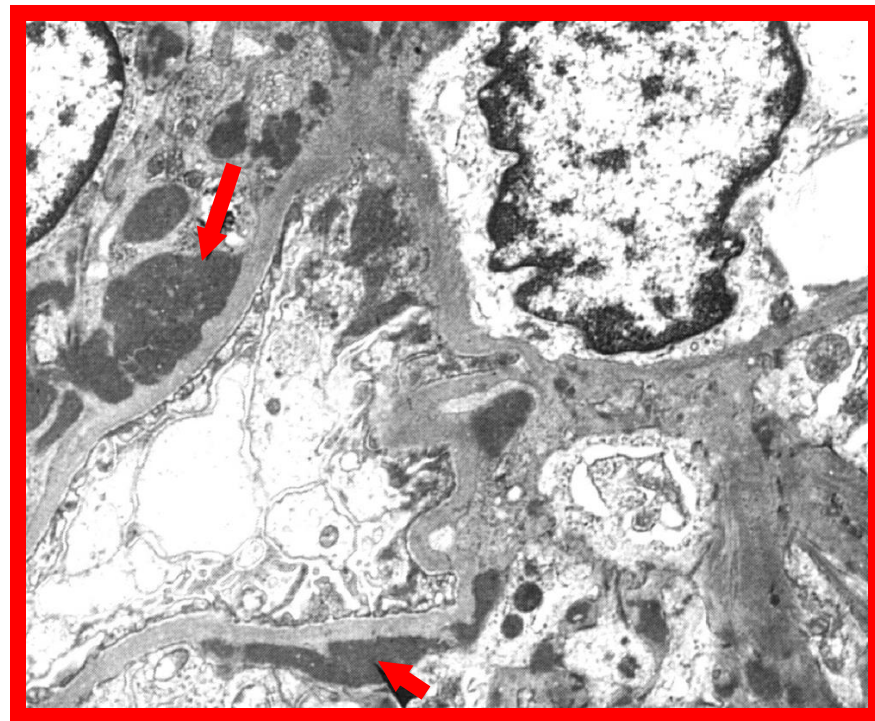
Proliferare endo si extracapilara



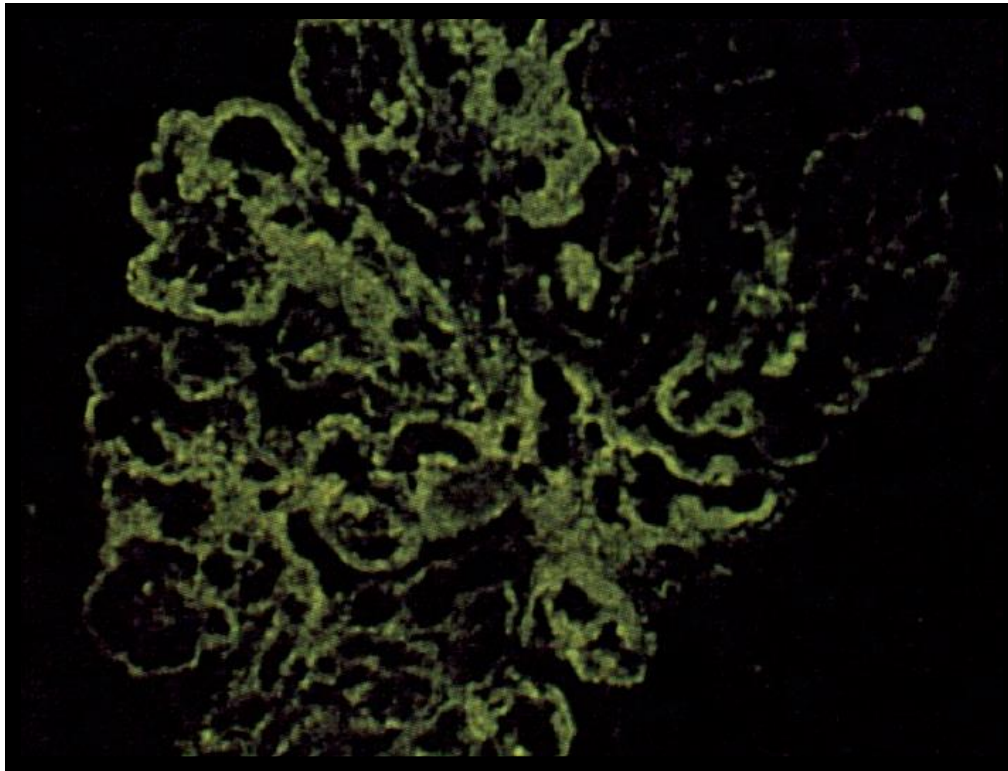
Depozite mezangiale de IgG



I.F.

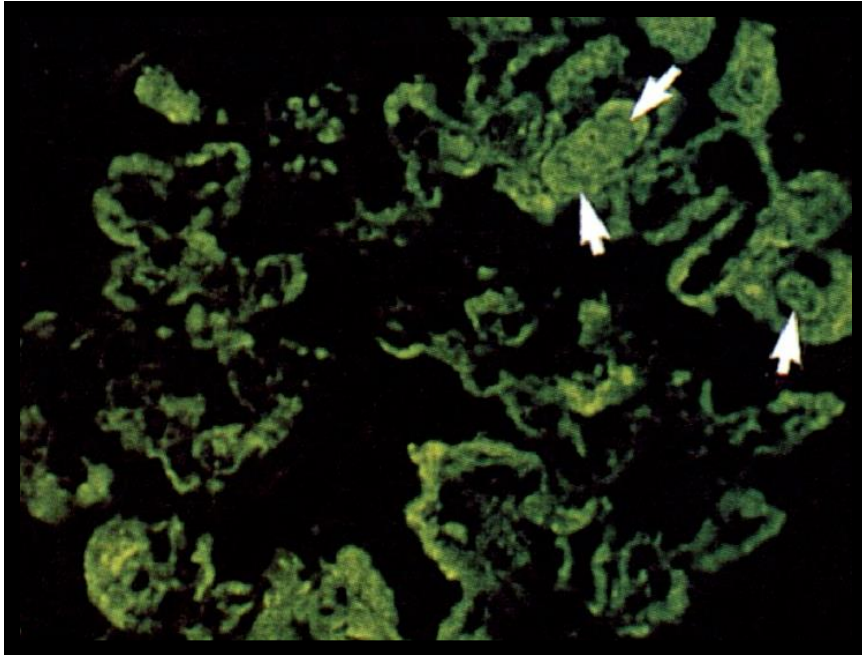


M.E.

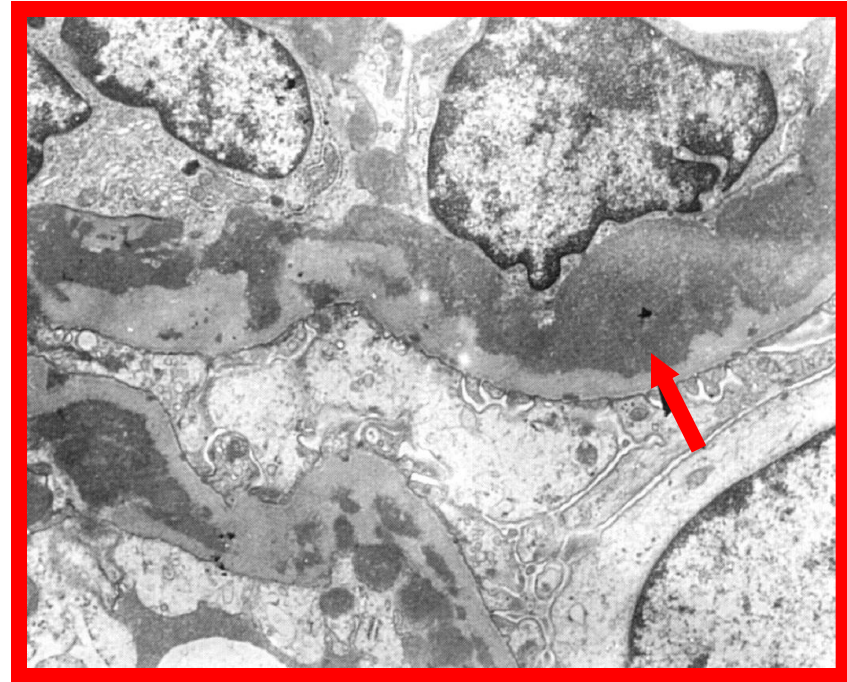


**Depozite mezangiale
si parietale de C1q**

**Depozite
endomembranoase
voluminoase de IgM**

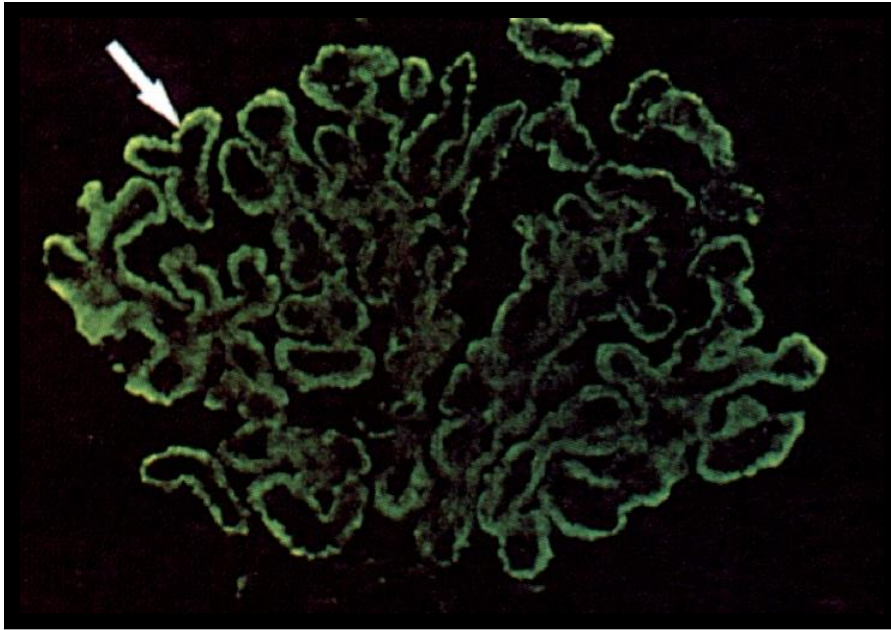


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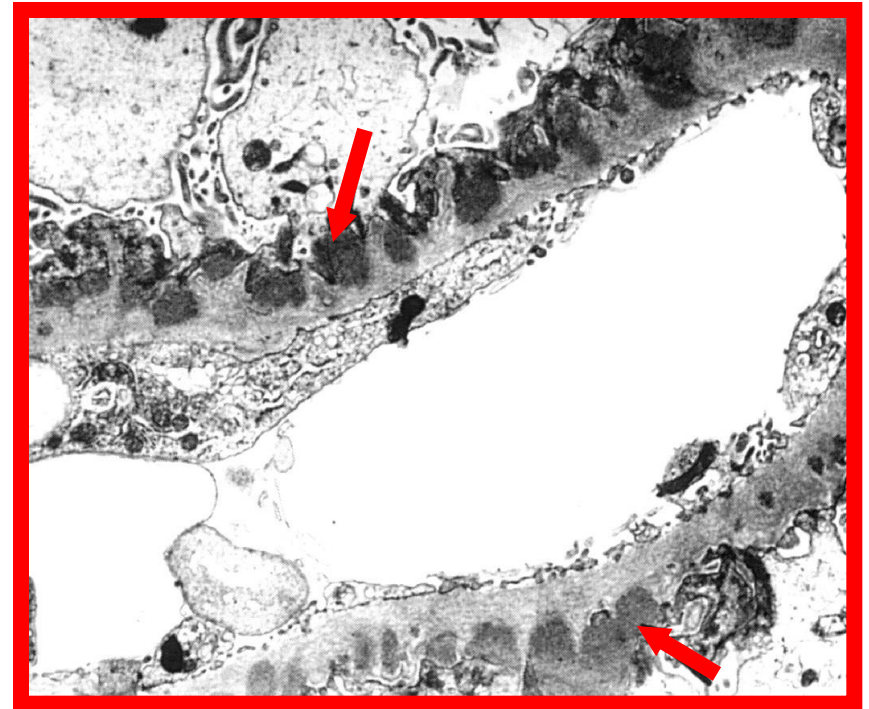


M.E.

**Depozite
extramembranoase
difuze de IgG**

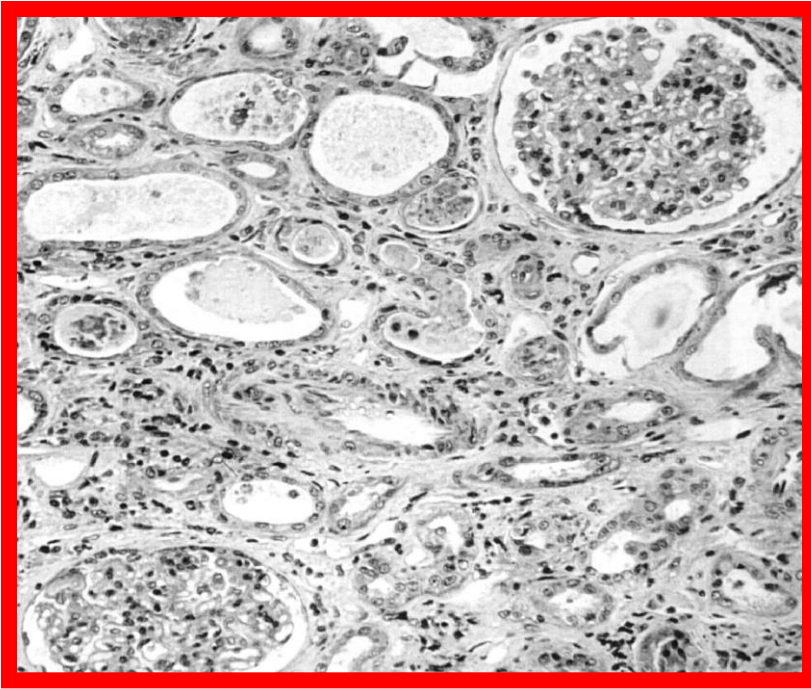


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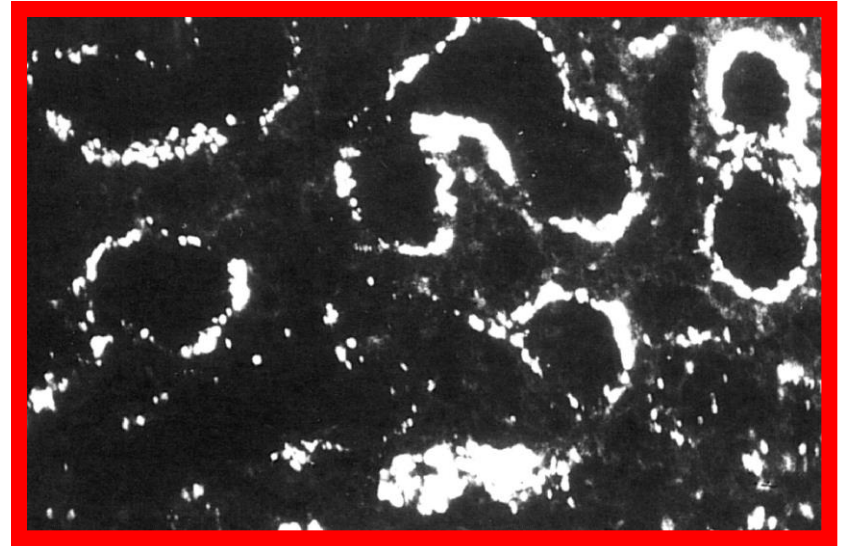


M.E

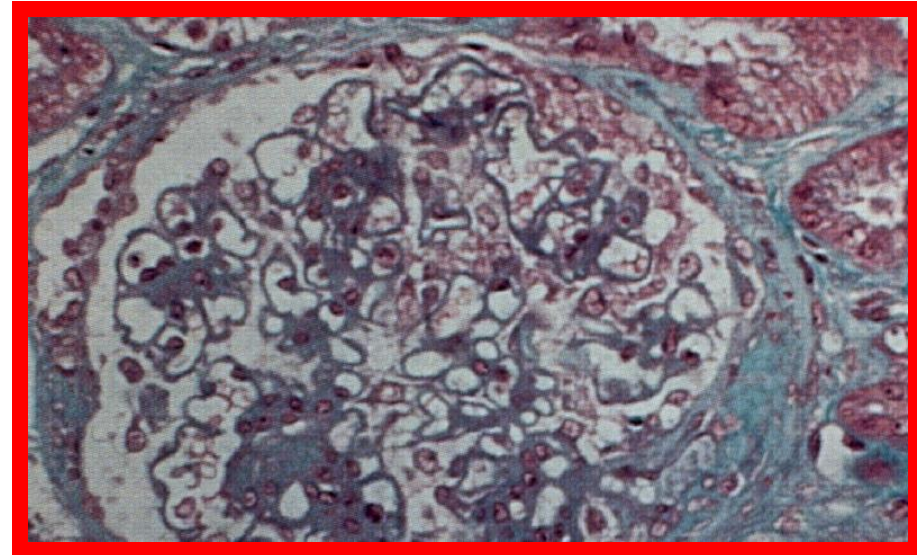
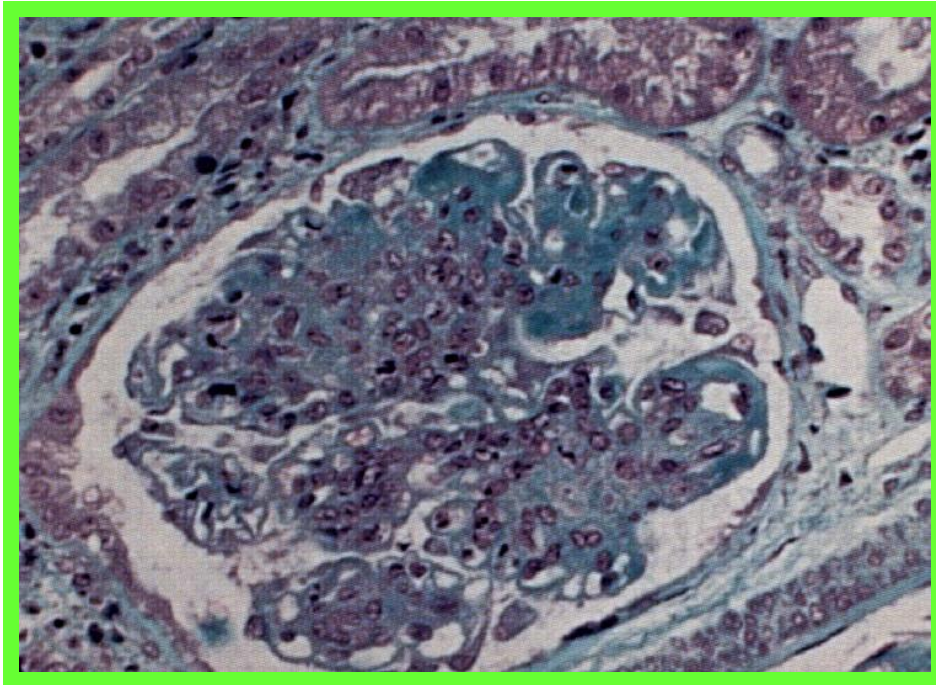
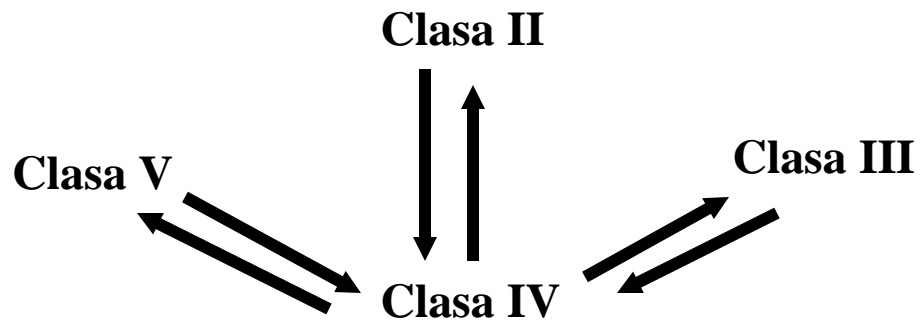
Leziuni tubulare



**Edem si infiltrat celular interstitial,
necroze de epiteliu tubular**



**Depozite de C1q dispuse in jurul MBT
si interstitial**



Leziunile glomerulare pot evolua spontan si sub tratament (din proliferativ mezangial - sub terapie - reducerea proliferarii si depozite extramembranoase)

TABLOU CLINIC

SEMNE CLINICE DE AFECTARE RENALA

- HTA**
- Sindrom nefritic acut**
- Sindrom nefrotic**
- IRA sau IRC**
- acidoza tubulara**

DIAGNOSTIC POZITIV

Criteriile ARA

1. Eritem facial
2. Lupus discoid
3. Fenomen Raynaud
4. Alopecie
5. Fotosensibilitate
6. Ulceratii bucale si naso-faringiene
7. Artrita fara deformari
8. Celule LE
- 9 Reactii fals (+) pentru Lues cu durata > 6 luni
10. Una din : pleurita, pericardita
11. Una sau ambele: psihoza, convulsii
12. Deseuri celulare
13. Proteinurie
14. Una sau mai multe din : anemie hemolitica, leucopenie <4000/mm³, trombocitopenie < 100000

• 4 criterii (+) = LES

+ Semne clinice si biologice

- Sindrom nefritic
- Sindrom nefrotic
- Hematurie sau proteinurie izolata

COMPLICATII

- **RENALE**

- **IRA**
- **IRC**
- **Acidoza tubulara distala**

- **EXTRARENAL**

- **Infectioase - virale si bacteriene variate**
- **Neoplazice - limfoame maligne**
- **Tromboze venoase**

EVOLUTIE PROGNOSTIC

- **Evolutia si prognosticul pot fi discutate din 2 puncte de vedere**
 - **al LES**
 - **al nefropatiei lupice**
- **Prognosticul nefropatiei lupice**
 - **Evolutie favorabila sub terapie GNLM**
 - **Formele proliferative - evolutie si prognostic mai rezervate**

TRATAMENT

Clasa I – tratamentul lupusului extrarenal

Clasa II –proteinurie < 1g/zi – ca mai sus

- proteinurie > 3g/zi – ca si GNLM primitiva – cortizon sau ciclosporina

Clasa III si IV

- Inductie - Corticoterapie + Ciclofosfamida sau MMF pana la remisiune
- Intretinere – Azatioprin 1,5-2,5mg/kg/zi sau MMF 1-2g/zi + Prednison < 10mg/zi – 1an

Clasa V

- Functie ren normala proteinurie < 3,5 – IEC sau BRA + trat imuno necesar lupusului extrarenal
- Proteinurie nefrotica – Cortizon + Ciclofosfamida sau, Ciclosporina sau Azatioprina

Clasa VI – cortico sau imuno dupa indicatiile lupusului extrarenal

VASCULITE SISTEMICE

CLASIFICAREA VASCULITELOR

2011-2012 International Chapel Hill Consensus Conference

Large Vessel Vasculitis (LVV)

- Takayasu Arteritis (TAK)
- Giant Cell Arteritis (GCA)

Medium Vessel Vasculitis (MVV)

- Polyarteritis Nodosa (PAN)
- Kawasaki Disease (KD)

Small Vessel Vasculitis (SVV)

ANCA-Associated Vasculitis (AAV)

- Microscopic Polyangiitis (MPA)
- Granulomatosis with Polyangiitis (Wegener's) (GPA)
- Eosinophilic Granulomatosis with Polyangiitis (Churg Strauss) (EGPA)

Immune Complex SVV

- Anti-GBM Disease
- Cryoglobulinemic Vasculitis (CV)
- IgA Vasculitis (Henoch-Schönlein)(IgAV)
- Hypocomplementemic Urticarial Vasculitis (Anti-C1q Vasculitis)

Variable Vessel Vasculitis (VVV)

- Behçet's Disease (BD)
- Cogan's Syndrome (CS)

Single Organ Vasculitis (SOV)

- Cutaneous Leukocytoclastic Angiitis
- Cutaneous Arteritis
- Primary CNS Vasculitis
- Isolated Aortitis
- Others

Vasculitis Associated with Systemic Disease

- Lupus Vasculitis
- Rheumatoid Vasculitis
- Sarcoid Vasculitis
- Others

Vasculitis Associated with Probable Etiology

- Hepatitis C Virus-Associated Cryoglobulinemic Vasculitis
- Hepatitis B Virus-Associated Vasculitis
- Syphilis-Associated Aortitis
- Drug-Associated Immune Complex Vasculitis
- Drug-Associated ANCA-Associated Vasculitis
- Cancer-Associated Vasculitis
- Others

POLIARTERITA NODOASA (Periarterita nodoasa)

- arterita care afecteaza vasele de calibru mediu

Manifestari clinice

- extrarenale - febra, artralгии, leziuni cutanate variate, greturi varsaturi , colici abdominale, nevrita periferica
- renale - HTA severa, proteinurie , insuficienta renala

Tablou biologic

- leucocitoza cu eozinofilie, VSH accelerat, CIC crescute, CRP crescute, +/- HBs (+), C3 scazut
- Uneori ANCA (+)

PBR

- GN necrotizanta cu proliferare extracapilara (frecvent)
- mai rar GN proliferativa difuza sau segmentara
- necroza fibrinoida a vaselor medii interlobare si arcuate

Arteriografie

- microanevrisme

VASCULITA IgA (HENOCH-SCHONLEIN)

= vasculita a vaselor mici ale pielii, tractului digestiv, rinichiului si articulatiilor

ETIOLOGIE

- neprecizata - mai frecvent se asociaza cu : infectie streptococica, alergii alimentare, unele boli infectioase si medicamente**
- apare mai frecvent la copii, si la persoane HLA BW35**

PATOGENIE

- Vasculita a vaselor mici mediate de CIC IgA anti α -galactozil care pot implica si complementul**

TABLOU CLINIC - debut clinic precedat de episod infectios

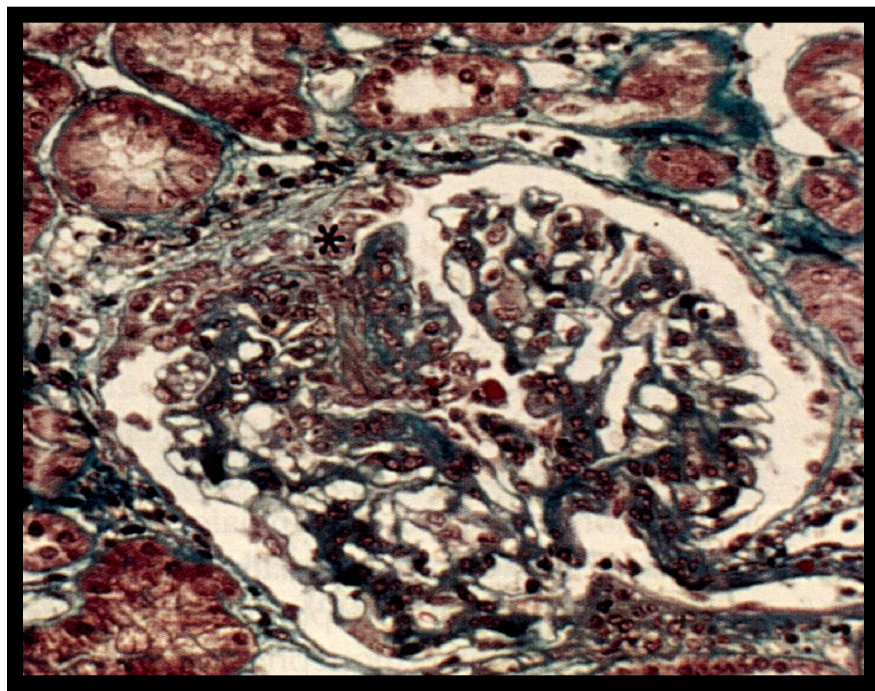
- Sindrom hemoragipar**
- Dureri articulare - artrite ale articulatiilor mari**
- Colici abdominale cu greturi si varsaturi**
- hematurie, HTA, SN, IRA, IR rapid progresiva, IRC**

TABLOU BIOLOGIC

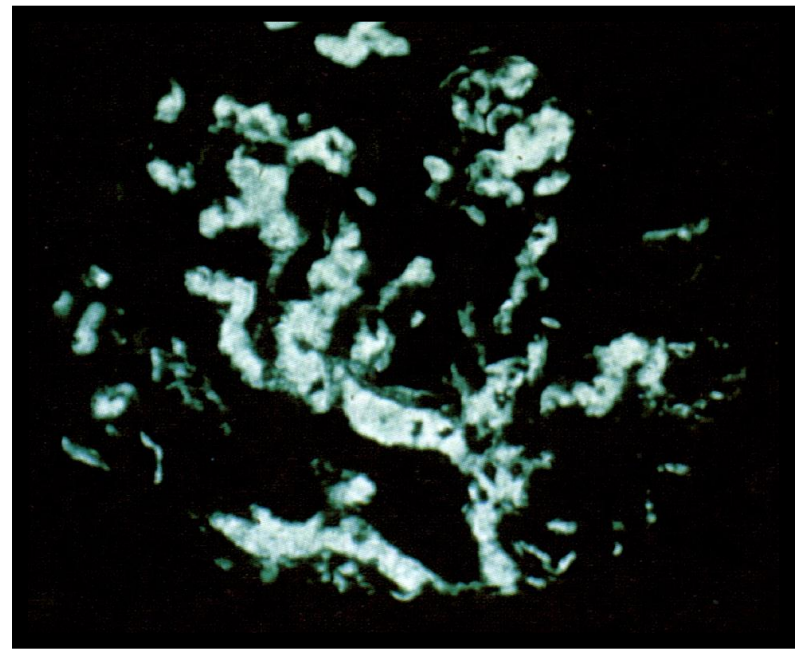
- VSH accelerat, CIC crescut, IgA seric crescut**
- Inconstant - ASLO crescut, C3 scazut, ANCA, FR prezent**
- crioglobuline crescute,**

PBR - GNPM +/- proliferare extracapilara

- depozite mezangiale si subendoteliale cu IgA +/- IgG si C3**



Proliferare mezangiala



Depozite mezangiale de IgA

TRATAMENT

- Corticoterapie - Prednison - 1mg/kg/zi +/- azatioprin 2-3mg/kg/zi**
- in caz de GNRP - plasmafereze, pulsterapie**
- IRA, IRC - hemodializa**

NEOPLAZIILE

Afectarea renala imbraca aspectul maladiei de complexe imune

- **ATG - tumorale, fetale reprimare, autologe netumorale, virale**
- **CI - circulante sau plantate**

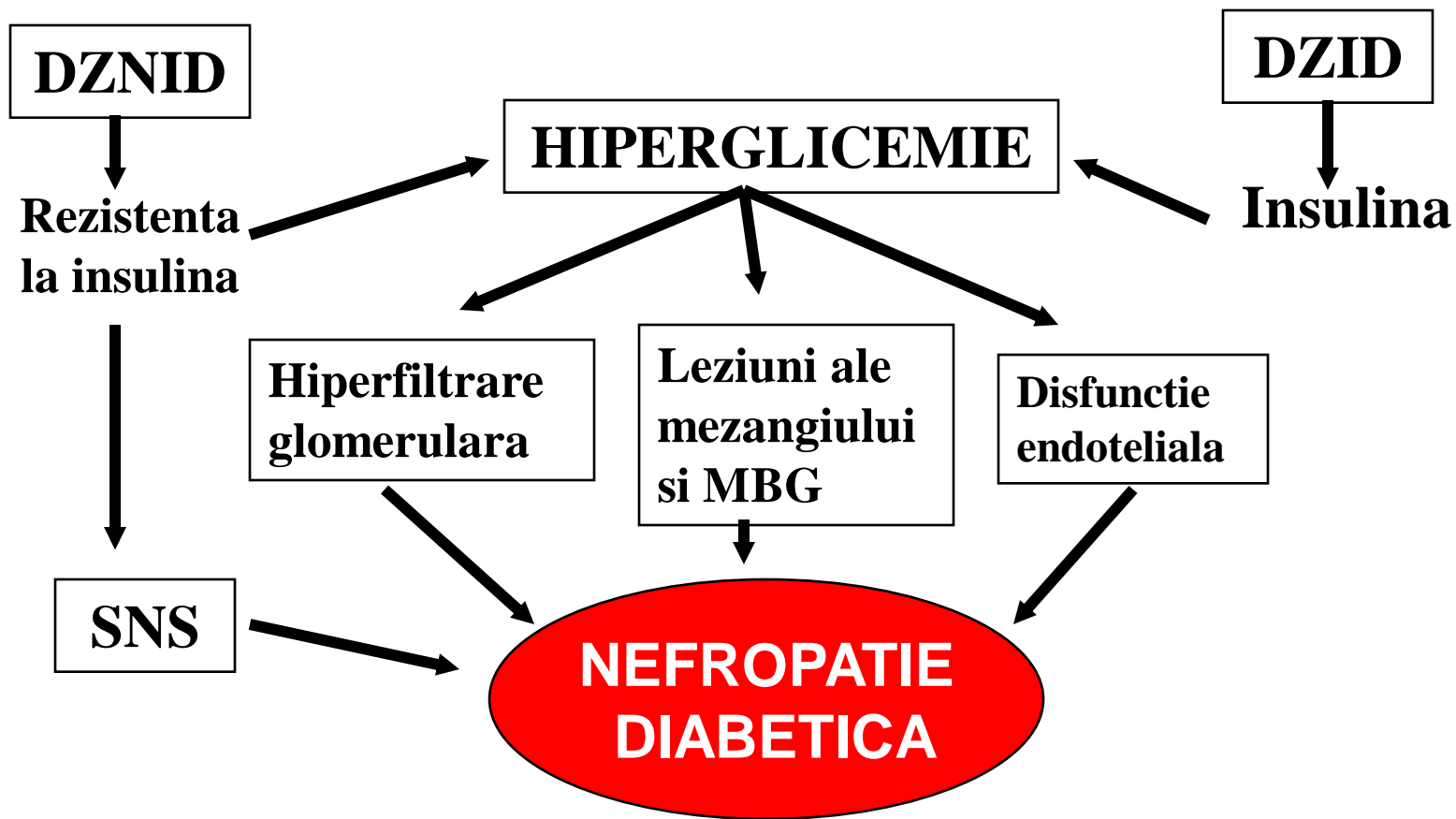
Clinic - proteinurie, microhematurie, frecvent SN

Morfologic - GNM, GNLM, foarte rar GN proliferativ extracapilar

Strategie de diagnostic

- toate SN ale adultului varstnic se vor investiga in directia unei neoplazii
- SN poate precede, poate debuta clinic concomitent sau poate succeda debutului neoplaziei

BCR ASOCIATA DZ si NEFROPATIA DIABETICA



**Prognosis of CKD by GFR
and Albuminuria Categories:
KDIGO 2012**

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/ 1.73 m ²) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Glomeruloscleroza diabetica difuza



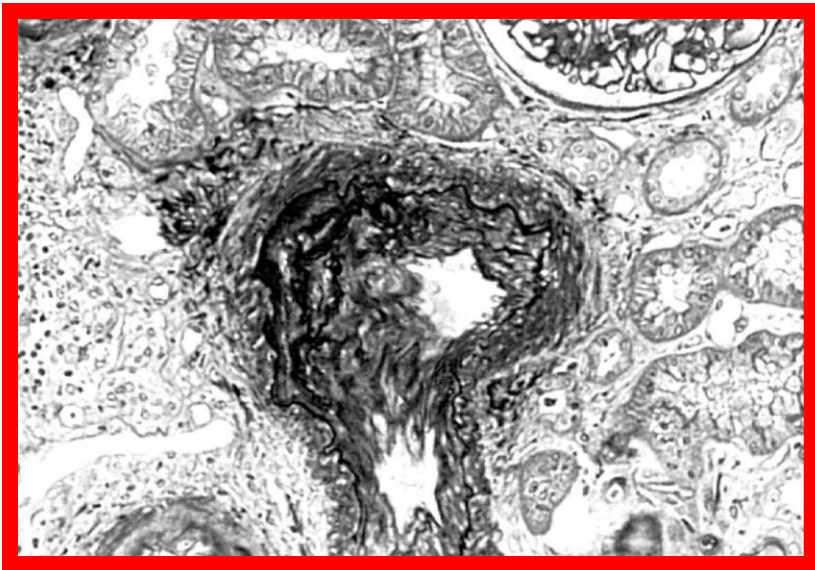
**Cresterea difuza a matricei
mezangiale**

Glomeruloscleroza diabetica nodulara (noduli Kimmelstiel - Wilson)

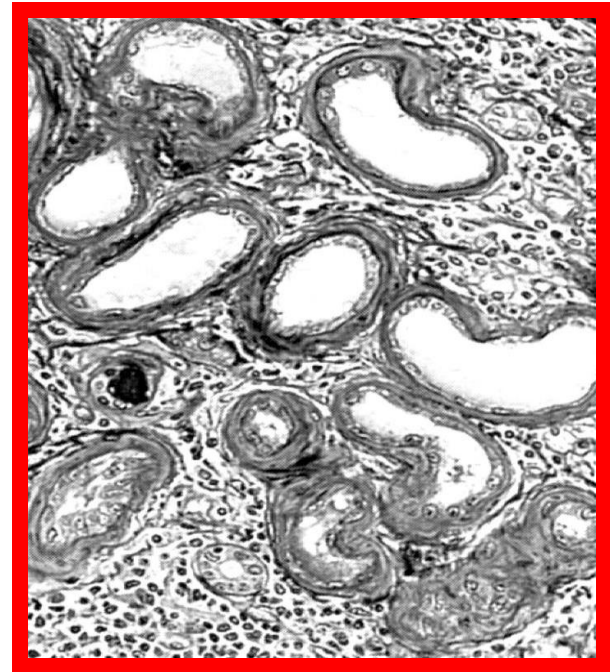


**Noduli mezangiali acelulari,
PAS (+), argirofili**

Leziuni vasculare si tubulo-interstitiale



**Arteriole interlobulare cu
semne de arterioscleroza**



**Atrofii tubulare,
infiltrat LP**

TRATAMENT

Control glicemic intensiv – HbA1c < 7%

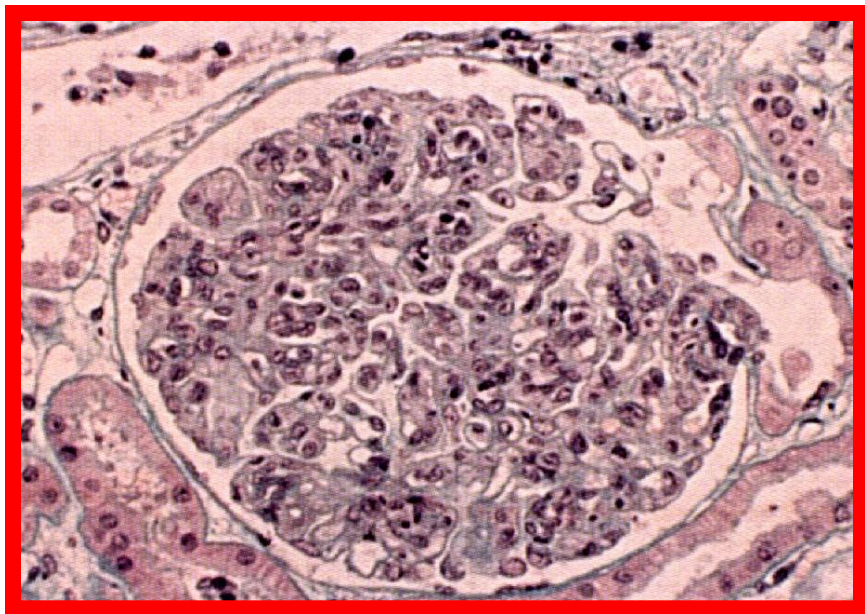
Control tensional

- **albuminurie < 30mg/zi -< 140/90 mmHg – orice hipotensor**
- **albuminurie > 30mg/zi < 130/80 mmHg – IEC sau BRA**

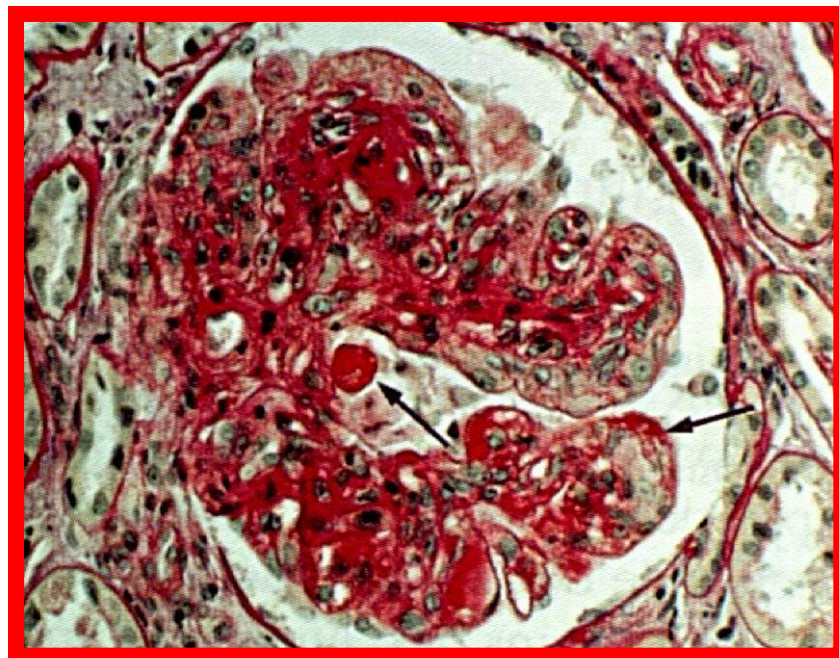
Tratamentul dislipidemiilor

CRIOGLOBULINEMIA MIXTA

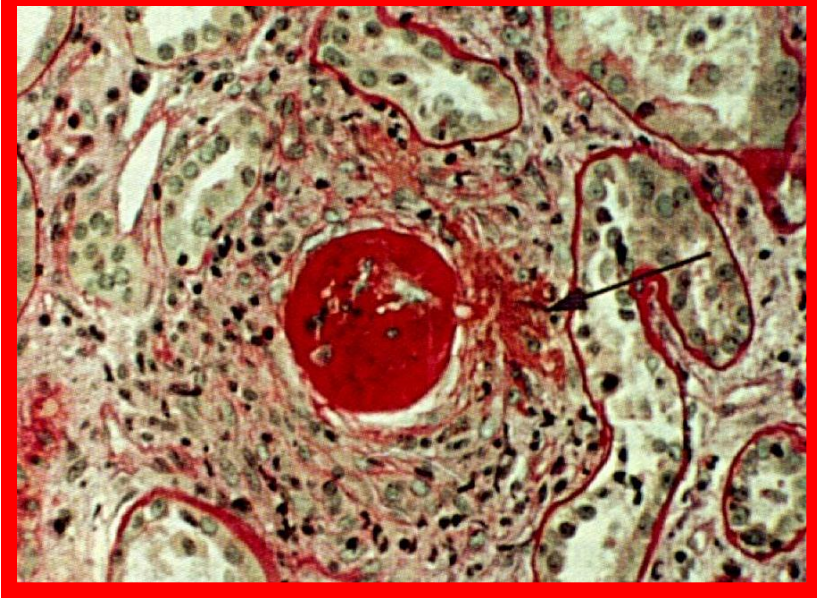
- **Crioglobulinemie in care lipsesc semnele clinice ale altor boli**
- **Crioglobulinele = CIC formate din IgG si IgM anti IgG care precipita la 4°C**
- **Tablou clinic - purpura, artralгии, leziuni necrotice cutanate, sindrom Raynaud, febra (manifestari de vasculita)**
 - **Manifestari renale - acuta - SN +/- IRA - GNPM, GNP endo si extracapilara**
 - **cronica - GNMC**
- **Tablou biologic - VSH, CIC, Crio crescute, 50-75% VHC(+)**



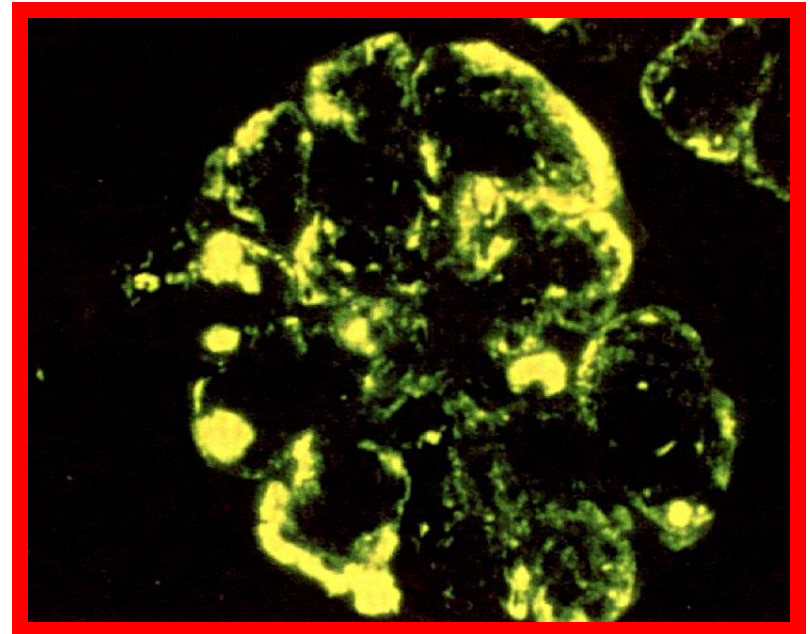
Glomerulonefrita proliferativa



Glomerulonefrita mezangiocapilara



**Necroze fibrinoide a arteriolelor
renale**

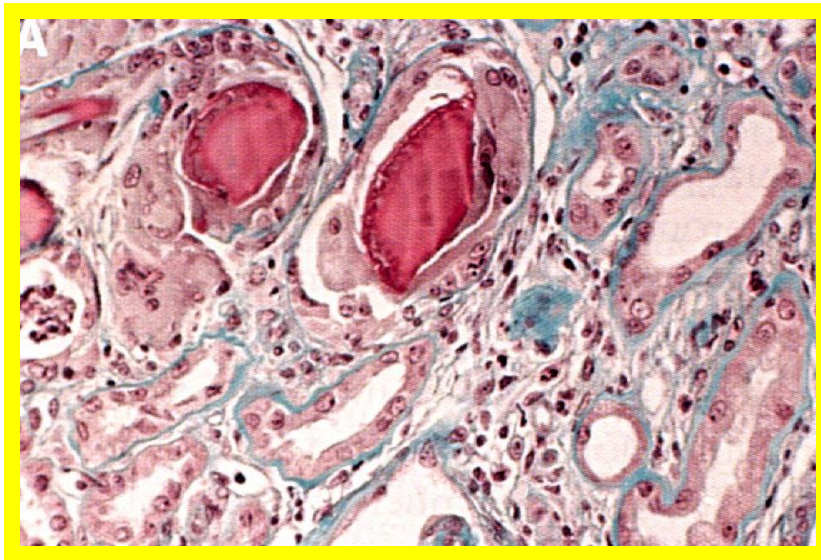


**Depozite endomembranoase
segmentare de IgM**

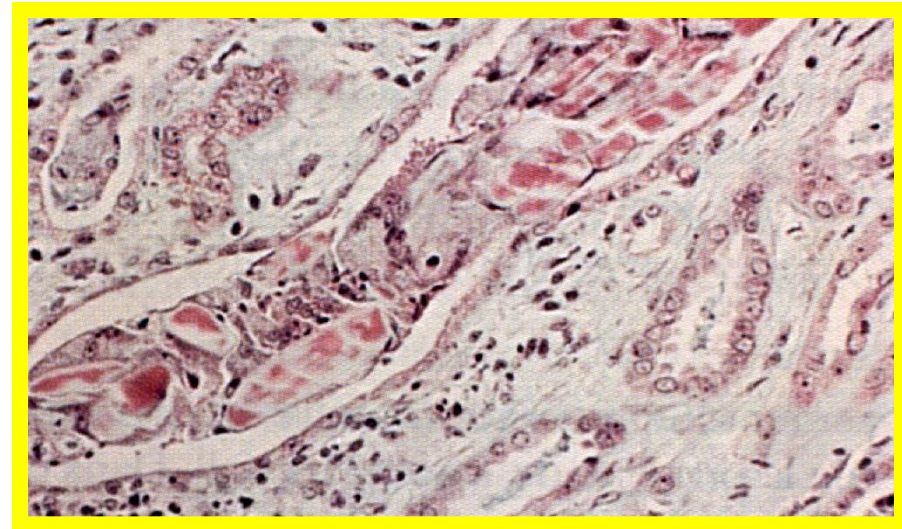
MIELOMUL MULTIPLU

- 50% - din bolnavii cu mielom dezvoltă complicații renale**
- Leziuni renale - 10-15% amiloidoză renală, leziuni tubulo-interstițiale**
- Manifestări clinice generale - proprii bolii**
- Manifestări renale - proteinurie cu lanțuri ușoare, SN, IRA sau IRC, sindrom Fanconi, nefropatie urică, nefrocalcinoză**
- Tratament: chimioterapie antitumorală, tratamentul hiperuricemiei, plasmafereza**

Tubulopatie mielomatoasa

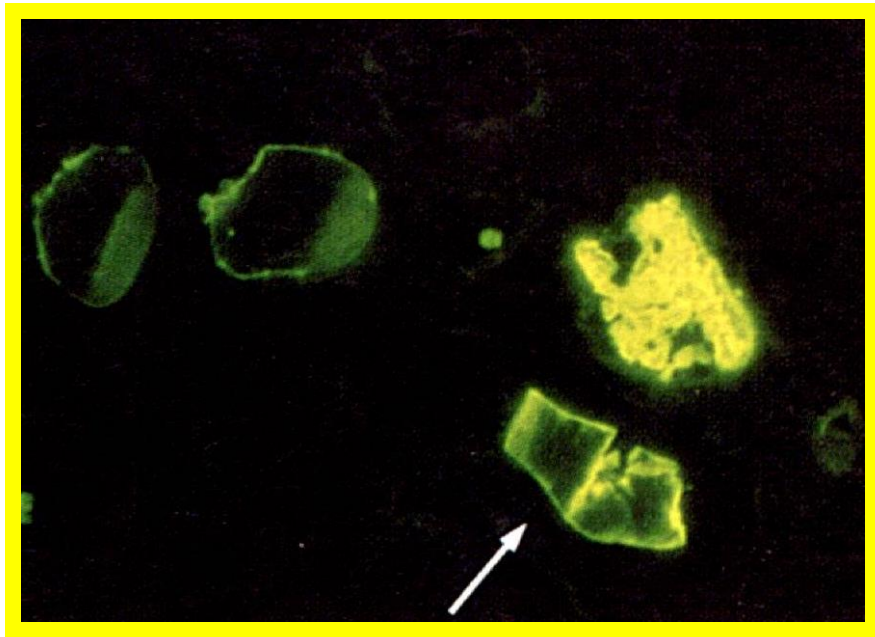


Cilindri mielomatosi inconjurati de celule gigante

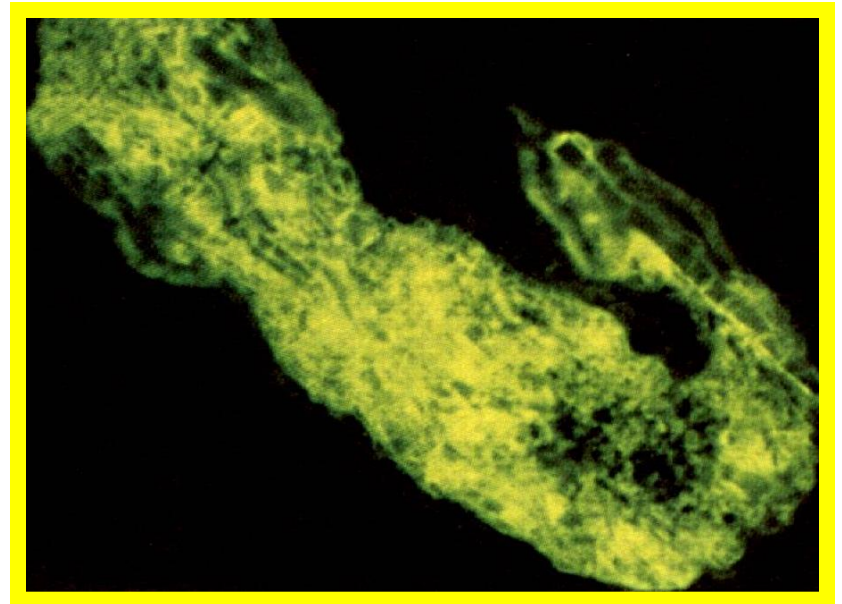


Cilindri granulomatosi cu elemente angulate inconjurati de macrofage

Tubulopatie mielomatoasa

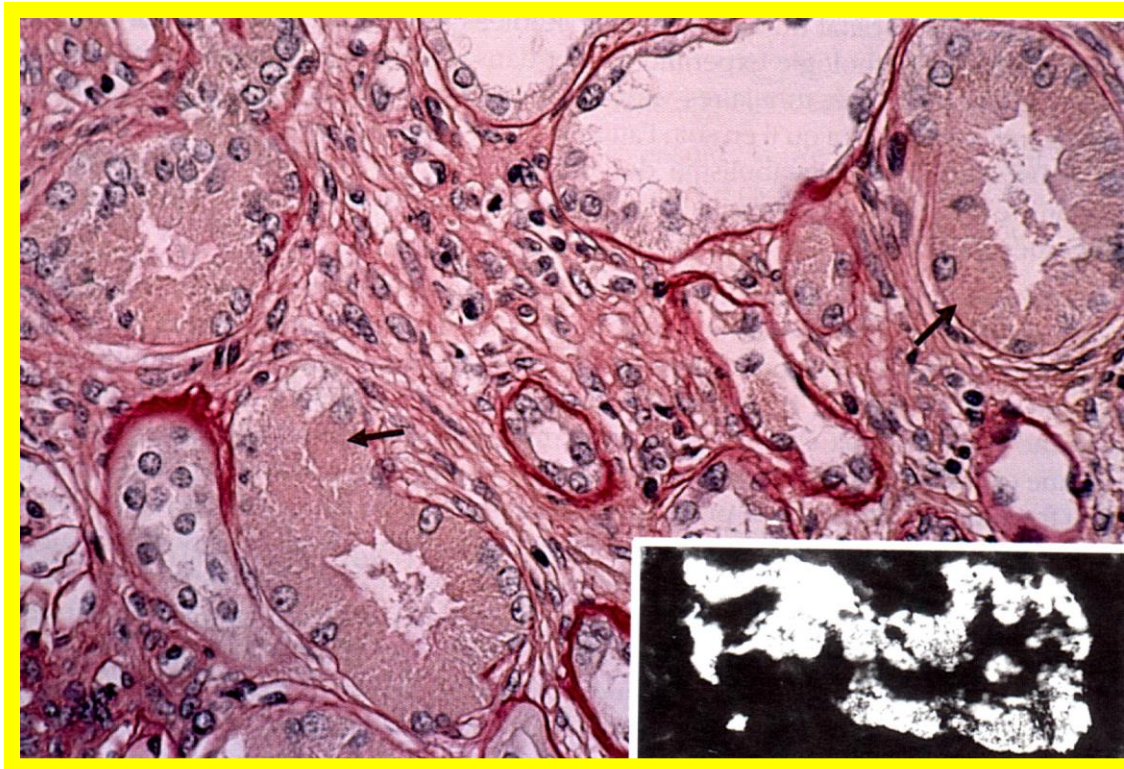


**Cilindri mielomatosi in IF colorati cu
ATC anti κ**



**Cilindri mielomatosi in IF colorati cu
ATC anti λ**

Sindrom Fanconi



Celule epiteliale cu citoplasma modificata de depozite cristaloide, epiteli tubulare alterate - TCP la IF epiteli de TCP (+) pentru lanturi λ

AMILOIDOZA

Boala generata de depunerea extracelulara a unui material fibrilar , avand caractere biochimice specifice - amiloid

Tipuri de amiloid - AA - apolipoproteina A - amiloidoze

secundare reactive

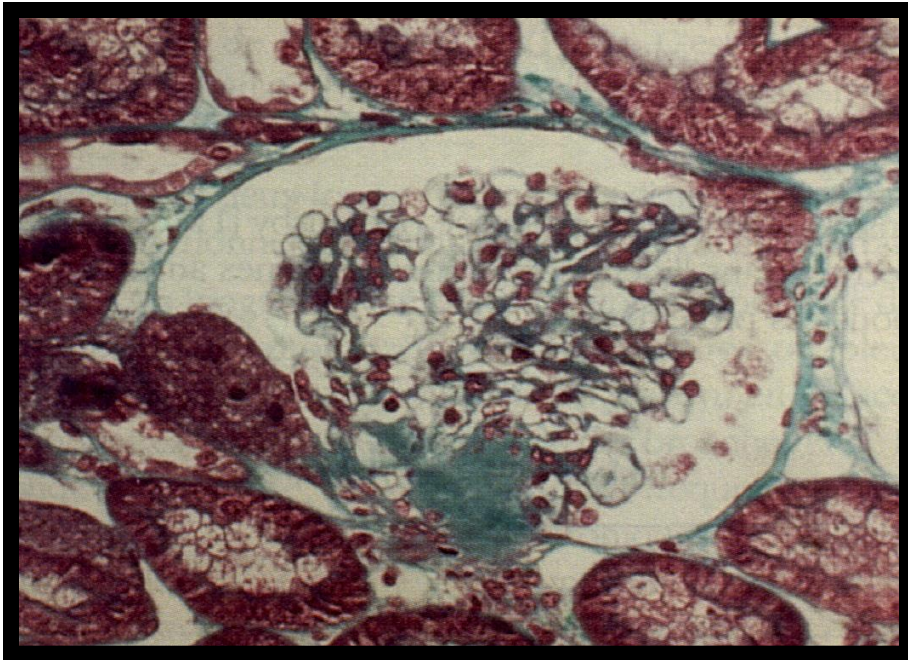
- AH - β 2 micro.g. - dializa

**- AL - lanturi κ si λ - amil.primara si
mielom**

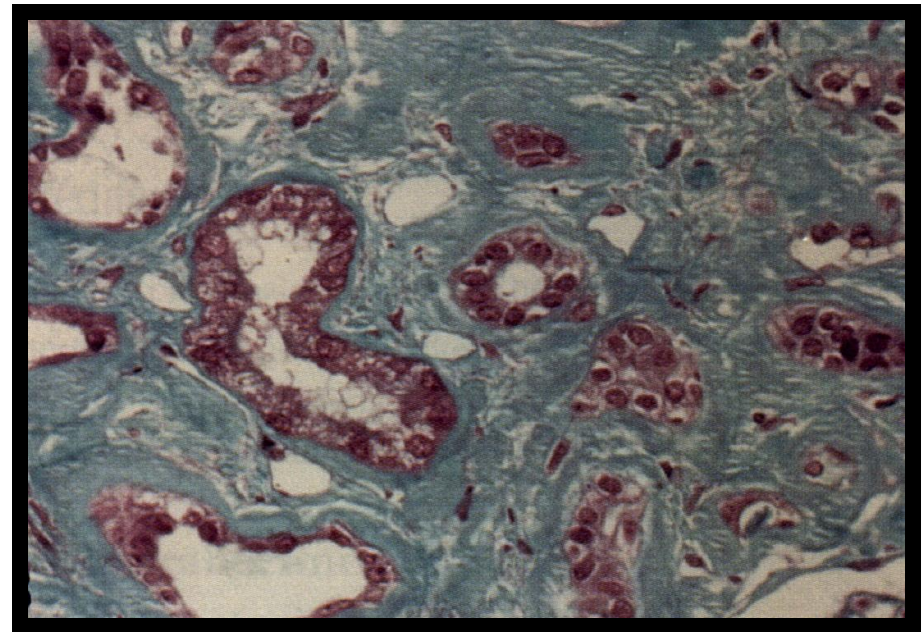
- AE - precursori de calcitonina

- tumori tiroidiene

- AS - senilitatea

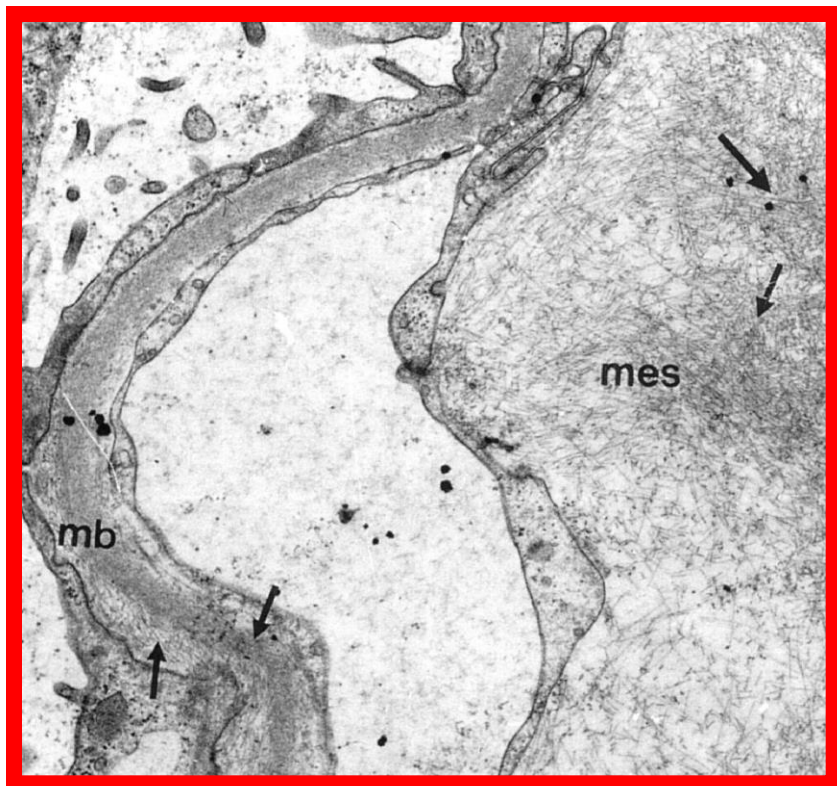


Depozit mezangial de amiloid

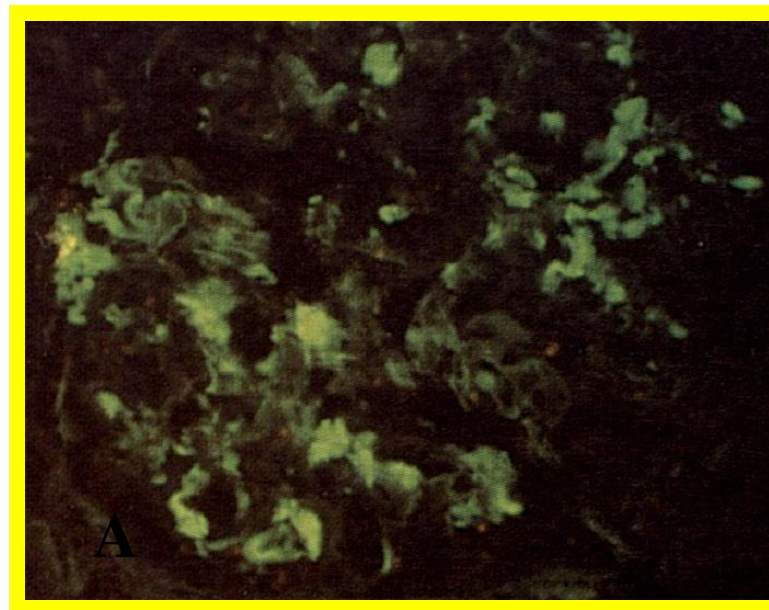


Depozit interstitial si peritubular masiv de amiloid

**Depozite glomerulare (A) si
peritubulare si perivascularare (B)**



**Fibrile amiloide in mezangiu si in
MBG la ME**



TABLOU CLINIC

- **Afectarea in amiloidoza este sistemica : depuneri in ficat, splina, inima, tub digestiv , rinichi**
- **Afectarea renala - depunere mezangiala, MBG, subendo si subepitelial - manifestare clinica - SN , proteinurie izolata**
- **Diagnostic (+) evidentierea depozitelor gingival, rectal, renal utilizand coloratii : Rosu de Congo, Tioflavina T (fluorescenta in UV)**