

GLOMERULOPATÍAS

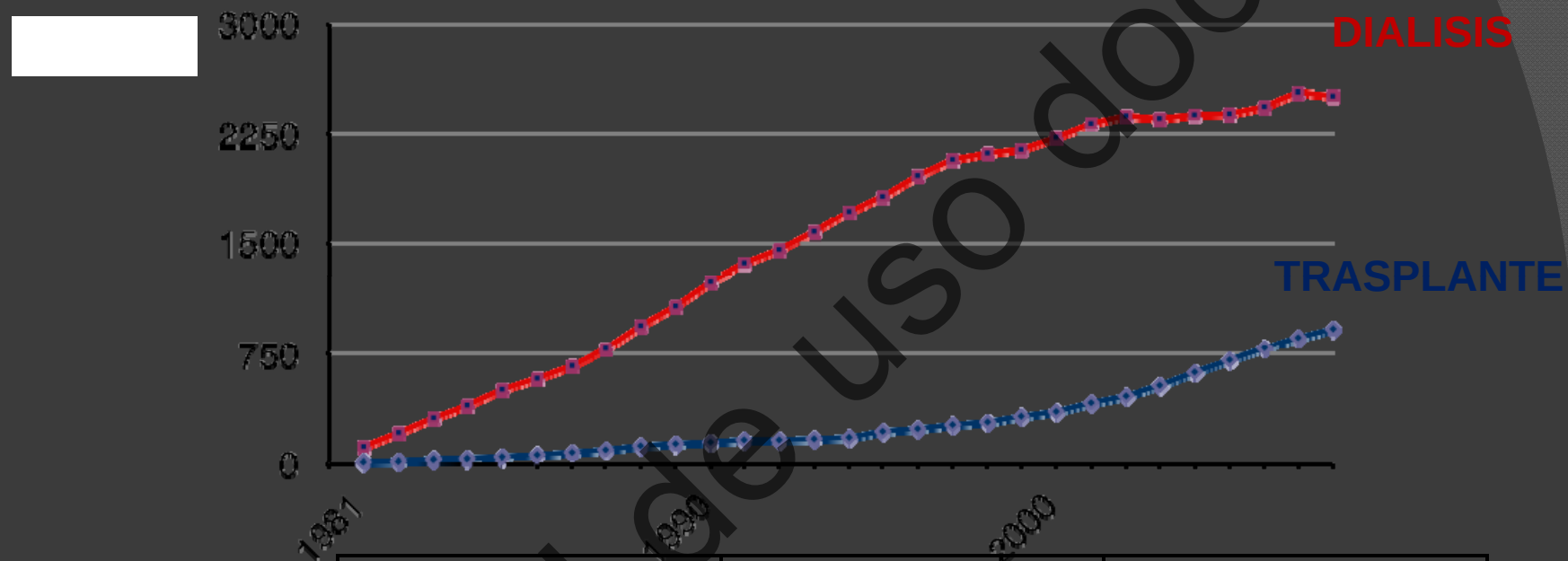
Dr. Oscar Noboa
Junio 2015



URUGUAY

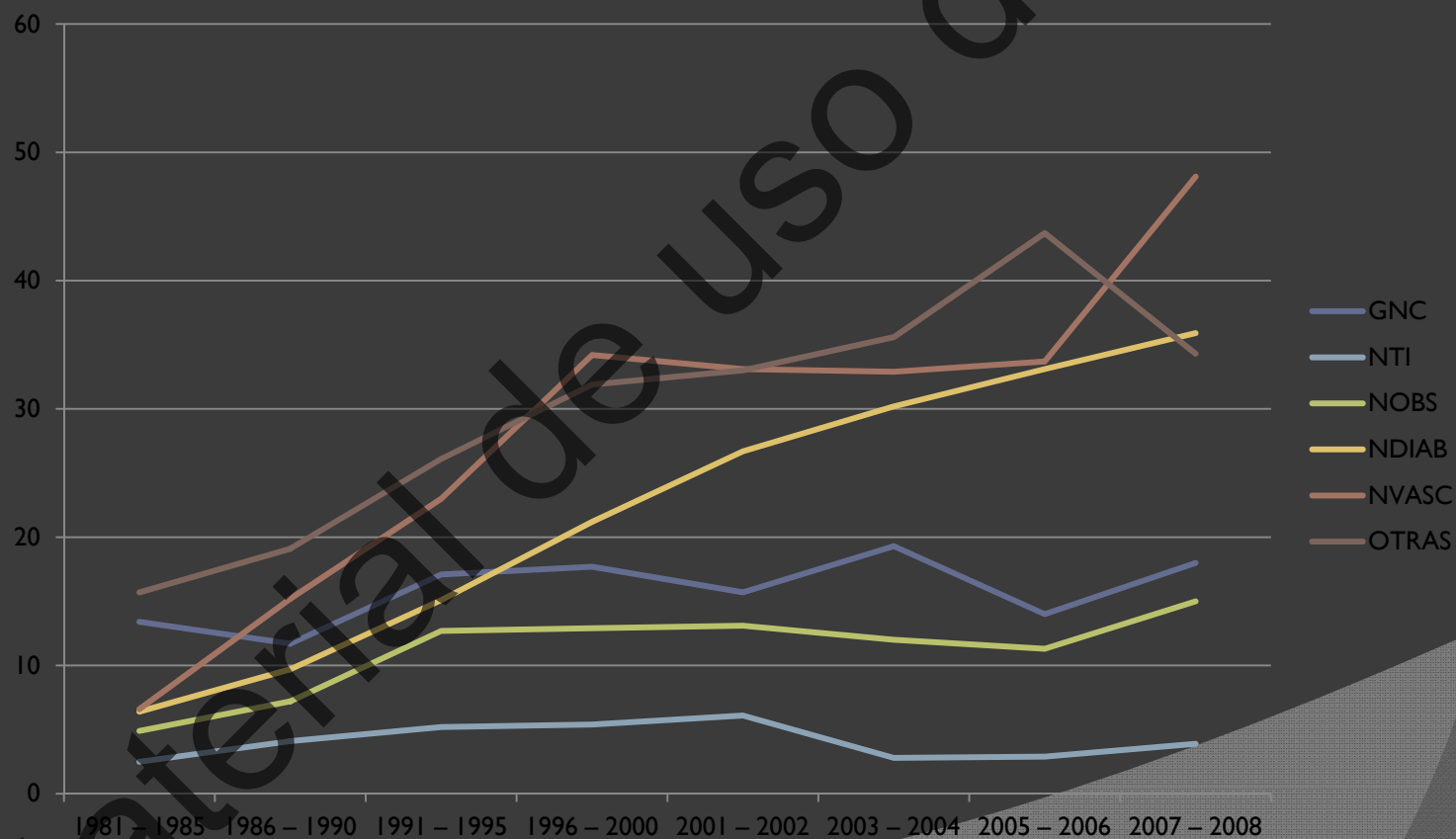
TRATAMIENTO SUSTITUTIVO DE LA FUNCIÓN RENAL

PACIENTES PREVALENTES SEGÚN MODALIDAD: DIÁLISIS Y TRASPLANTE RENAL



PREVALENTES 2010	PACIENTES	pmp
DIALISIS	2.514 (72%)	749
TRASPLANTE	963 (28%)	287
TOTAL	3.477	1036

Incidencia de ERC según nefropatía



RUD 2009

The incidence of primary glomerulonephritis worldwide: a systematic review of the literature

Anita McGrogan¹, Casper F.M. Franssen² and Corinne S. de Vries¹

Nephrol Dial Transplant (2010) 1 of 17
doi:10.1093/ndt/gfq665

Nephrol Dial Transplant (2010): Editorial Review

7

Table 1. Continued

Study	Cases	RUE	ROE	Biopsy rate	Description
Kim <i>et al.</i> [38] Study type: retrospective Location: New Orleans	163	**	**	Not given	Case definition: nephrotic syndrome defined as heavy proteinuria, oedema and hypoalbuminaemia; some underwent renal biopsy. Case identification: record review and two main referral hospitals.
Sehic <i>et al.</i> [37] Study type: retrospective Location: Shelby County, Tennessee, USA	17	**	*	Not given	Case definition: patients <18 years and resident in study area. Diagnosis of IgA nephropathy made by renal biopsy.
Orta-Sibu <i>et al.</i> [45] Study type: retrospective Location: Venezuela	505	**	***	Not given	Case definition: <15 years; Acute GN with haematuria, oedema, arterial hypertension present. Nephrotic syndrome was diagnosed on the basis of proteinuria >40 mg/h per m ² body surface area with or without oedema, hypoproteinaemia and hypercholesterolaemia. Case identification: information obtained by contacting 17 centres with a questionnaire. Data collected by chart review of patients.
Mazzuchi <i>et al.</i> [17] Study type: prospective Location: Uruguay	5058	***	*	Not given	Case definition: diagnosed by biopsy defined by minimal glomerular lesions, levels of proteinuria, serum creatinine, arterial hypertension and glomerular filtration rate. Case identification: national registry.

RUE, risk of underestimation; ROE, risk of overestimation; *, low; **, medium; ***, high; ESR, erythrocyte sedimentation rate; ANA, anti-nuclear antibodies; GBM, glomerular basement membrane; ELISA, enzyme-linked immunosorbent assay; biopsy rate: /100 000/year.

5058

↓
Abst

106

↓
Revisión

40

Incidencia de Gp primarias entre 0.2 a 2.5 /100000/año

- Síndromes clínicos
- Clasificación de enfermedades glomerulares
- Epidemiología
- Lesión glomerular mínima
- Esclero hialinosis segmentaria y focal
- Nefropatía membranosa
- Nefropatía IgA
- Otras

Síndromes Clínicos

- **alteraciones urinarias asintomáticas**
 - presencia de microhematuria o proteinuria menor de 3.5 grs por día, sin hematuria macroscópica, sin hipertensión arterial, sin disminución de la función renal y sin hipoproteinemia.
- **síndrome nefrítico agudo**
 - comienzo brusco, con hematuria asociada a uno cualquiera de los síntomas siguientes: hipertensión arterial, edemas, aumento de la azoemia o de la creatininemia.

Síndromes clínicos

- **proteinuria nefrótica**
 - proteinuria mayor de 3.5 grs por día.
- **síndrome nefrótico**
 - proteinuria mayor de 3.5 grs por día y albuminemia menor de 3 gr/dl.
- **síndrome nefrítico crónico**
 - proteinuria, microhematuria e hipertensión asociado a lento deterioro de la función renal.
- **hipertensión arterial**
 - en el adulto cifras de presión arterial mayores o iguales a 140/90. Sin otras alteraciones clínicas, salvo las alteraciones urinarias.
- **insuficiencia renal**
 - **Deterioro del filtrado glomerular.** creatinina plasmática mayor de 2 mg/dl. (*sólo como criterio de clasificación*)
- **otros síndromes**, que frecuentemente son expresión clínica de otras nefropatías, se registrarán como "otros".

Síndromes Clínicos

- **síndrome de hematuria aislada**
 - comienzo brusco o insidioso, con hematuria macroscópica, con proteinuria y sin otros elementos clínicos de síndrome nefrítico.
- **síndrome de glomerulonefritis rápidamente progresiva**
 - comienzo brusco o insidioso con proteinuria, hematuria y rápido deterioro de la función renal. Se entiende por rápido deterioro de la función renal los casos en que en menos de 3 meses la creatinina plasmática supera los 3 mg/dl y/o duplica su valor anterior.

Registro Uruguayo de Glomerulopatias

Informe referente a los años 2010-2012

Grupo coordinador Oscar Noboa, Liliana Gadola, Dres. Hena Caorsi, Mariela Garau, Francisco Gonzalez Martinez.

Patólogos que reportan al registro en el período. Dr. Nelson Acosta. Dra Ana Panuncio. Dra Maria Auchaina. Dra Silvia Melesi, Dra Carmen Gutiérrez.

Nefrólogos que reportan al registro en el período.
Dr Luis Vilardo , Dr Pablo Ríos, Dra Beatriz Gelabert

PPTG 2014

Distribución de las biopsias según grandes grupos. 2010-2012

Diagnóstico	Frecuencia	%
Sin diagnóstico con biopsia inclasificable	44	9.7
Glomerulopatías primarias	281	62.2
Glomerulopatías secundarias	127	28.1
Total	452	100.0



CLASIFICACIÓN DE LAS ENFERMEDADES GLOMERULARES

NATURAL HISTORY OF BRIGHT'S DISEASE *
CLINICAL, HISTOLOGICAL AND EXPERIMENTAL
OBSERVATIONS

ARTHUR ELLIS, O.B.E., M.D. TORONTO, F.R.C.P.
DIRECTOR OF THE MEDICAL UNIT AT THE LONDON HOSPITAL;
PROFESSOR OF MEDICINE IN THE UNIVERSITY OF LONDON

- Nefritis tipo 1 173 casos ,
 - con infección previa , oliguria , hematuria macroscópica, y microscópica en 99%, con leucocitos , con elevación de urea
 - ✦ Complicaciones infecciones, encefalopatía hipertensiva, edema pulmonar.
 - ✦ Evolución
 - Recuperación
 - Fallece en agudo
 - Rápidamente progresiva
 - Curso lento
 - Histología aumento de la celularidad, semilunas ,
- Nefritis tipo 2 145 casos
 - Edema (nefrosis), derrame pleural , proteinuria , sin globulos rojos
 - ✦ Complicaciones, infecciones y peritonitis
 - ✦ Evolución
 - Lenta progresión
 - Histologia , depósito focal de hialina

The Lancet 1942

Criterios de clasificación

- Interpretación clínica
 - Primitivas (idiopáticas) / secundarias
 - Primarias/sistémicas
- Mecanismo de daño renal
- Lesiones histológicas
 - Focales, segmentarias, difusas
- Inmunofluorescencia
- Temporal
 - Agudas / crónicas
- De acuerdo a celularidad
 - Inflamatorias / no inflamatorias
 - ✦ Sedimento urinario
 - ✦ Marcadores inflamatorios

Interpretación causal

- Primarias

- Sólo el riñón

- Sistémicas

- Enfermedad sistémica que también afecta el riñón

- Primarias

- Idiopáticas (Primitivas)
 - Se desconoce la causa
 - Secundarias
 - Se conoce la causa

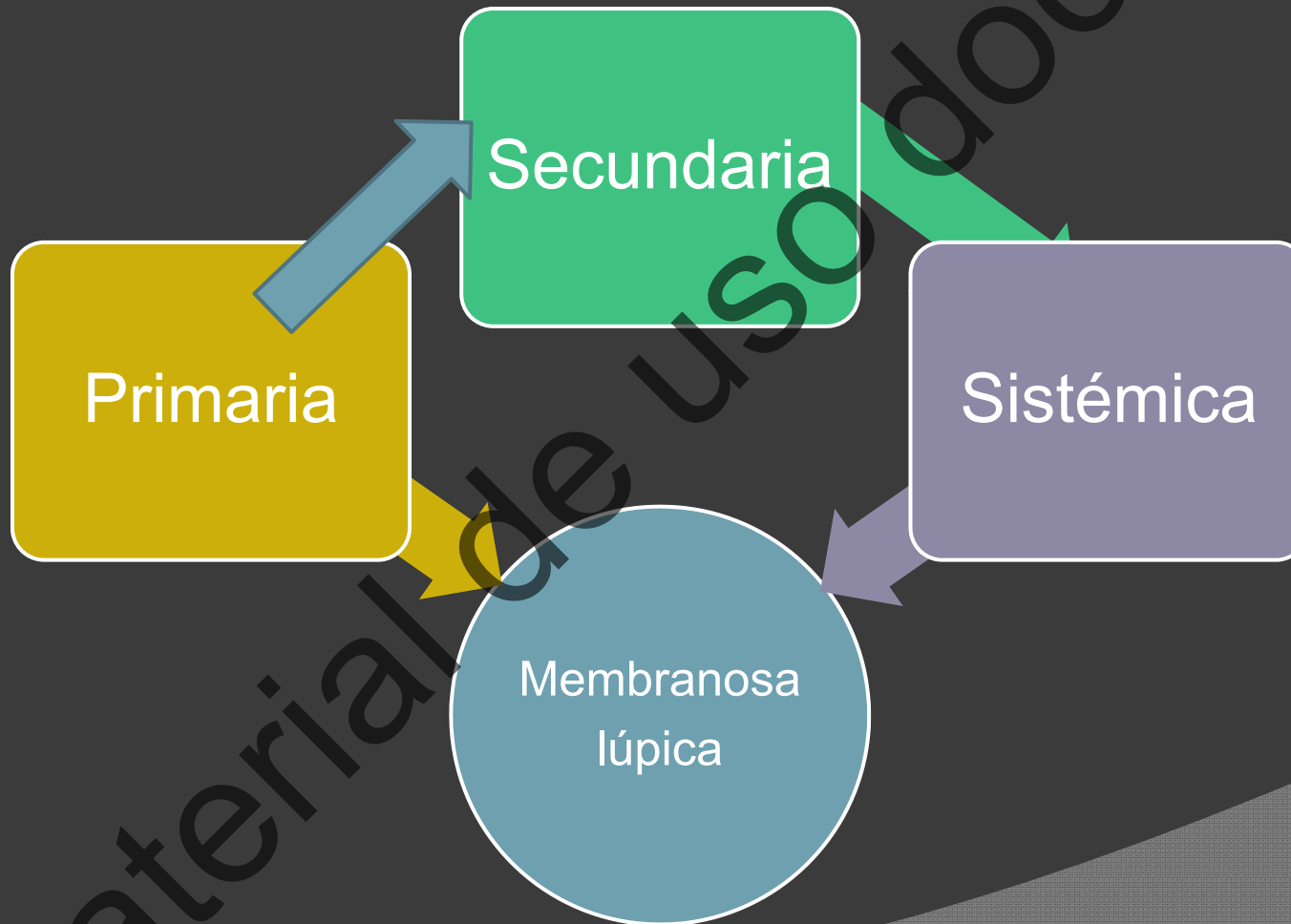
Mecanismo de daño glomerular

- Genética
- Depósito de proteínas o fragmentos
- Mecánico
- Metabólico
- Depósito de inmunocomplejos (Tipo III)
- Anticuerpos anti MBG (tipo II)
- Por citoquinas
- Pauciinmune (tipo IV)

Anatomía Patológica

- Patrones histopatológicos
 - Pueden no corresponder con la presentación clínica
 - Pueden estar presentes en diferentes glomerulopatías
 - No identifican por si solos la causa determinante
- Inmunofluorescencia
- Microscopía electrónica

Problemas semánticos



Forma clínica de presentación

Período 2010-2012

	Frecuencia	Porcentaje	Porcentaje válido
Sin síntomas	1	,2	,4
S.No.	85	18,8	38,1
S.Ni.Ag	3	,7	1,3
S.Ni.Cr.	4	,9	1,8
Macrohematuria	7	1,5	3,1
GNRP	32	7,1	14,3
AUA	69	15,3	30,9
HTA	2	,4	,9
IRA	4	,9	1,8
IRC	16	3,5	7,2
Total	223	49,3	100,0
Sin dato	229	50,7	

Forma de presentación: Síndrome nefrótico

	Frecuencia	Porcentaje
SIN DIAGNÓSTICO con BIOPSIA INCLASIFICABLE	2	2.4
LESION GOMERULAR MÍNIMA	18	21.2
HIALINOSIS FOCAL Y SEGMENTARIA	10	11.8
GN MEMBRANOSA	30	35.3
GN MEMBRANOPROLIFERATIVA	2	2.4
N. IgA	5	5.9
GN POST INFECCIOSA	1	1.2
NEFROPATÍA LÚPICA	13	15.3
NEFROPATÍA DIABÉTICA	2	2.4
AMILOIDOSIS	2	2.4
Total	85	100.0

Forma de presentación: AUA

	Frecuencia	Porcentaje
SIN DIAGNÓSTICO con BIOPSIA INCLASIFICABLE	16	23,2
HIALINOSIS FOCAL Y SEGMENTARIA	6	8,7
GN MEMBRANOSA	3	4,3
N. IgA	25	36,2
GN MESANGIAL (NO IgA)	1	1,4
GN EXTRACAPILAR (limitada al riñón)	1	1,4
GN ESCLEROSANTE CRÓNICA	1	1,4
NEFROPATÍA LÚPICA	11	15,9
NEFROPATÍA DIABÉTICA	2	2,9
VASCULITIS.	2	2,9
AMILOIDOSIS	1	1,4
Total	69	100,0

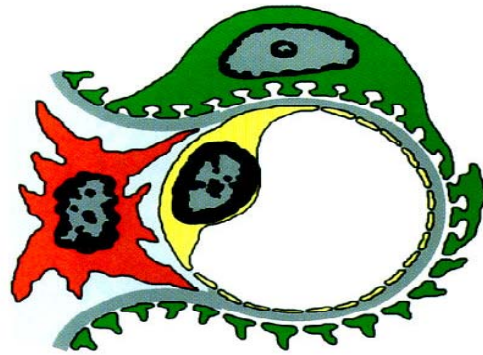
Incidencia de glomerulopatías primarias. Período 2010-2012

Diagnóstico	Frecuencia	Porcentaje	Tasa de incidencia pmp
Lesion gomerular mínima	40	14,2	5.19
Hialinosis focal y segmentaria	47	16,7	6.09
Gn membranosa	61	21,7	7.91
Gn membranoproliferativa	17	6,0	2.20
N. IgA	100	35,6	12.97
Gn intracapilar difusa	4	1,4	0.52
Gn focal (No IgA)	1	0,4	0.13
Gn mesangial (No IgA)	3	1,1	0.39
Gn post infecciosa	2	0,7	0.26
Gn esclerosante crónica	3	1,1	0.39
Otras glomerulopatías	3	1,1	0.39
TOTAL G. PRIMARIAS	281	100,0	44.3

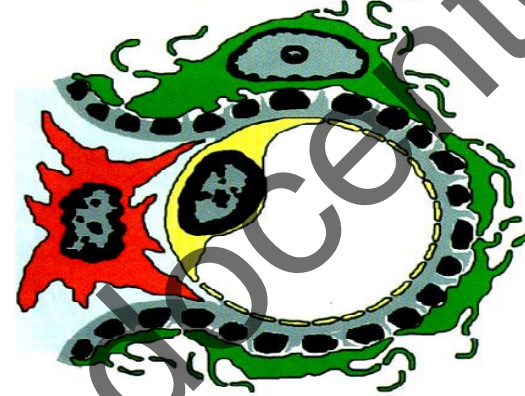
Incidencia de glomerulopatías primarias. Período 2010-2012

	1998-1999		2003-2004		2008-2009		2010-2012	
Diagnóstico	n	TI	n	TI	n	TI	n	TI
Sin diagnóstico c/biopsia	39	7.76	17	3.33	30	5.71	44	5.70
LGM	18	3.58	22	4.31	18	3.43	40	5.19
HFS	51	10.15	41	8.02	22	4.19	47	6.09
G. Membranosa	22	4.38	19	3.72	33	6.28	61	7.91
G. Membranoproliferativa	7	1.39	3	0.59	2	0.38	17	2.20
N. IgA	28	5.57	37	7.24	66	12.57	100	12.97
G. intracapilar difusa	2	0.4	3	0.59	3	0.57	4	0.52
G. Focal (No IgA)	3	0.6	3	0.59	1	0.19	1	0.13
G. Esclerosante crónica	7	1.39	3	0.59	6	1.14	3	0.39

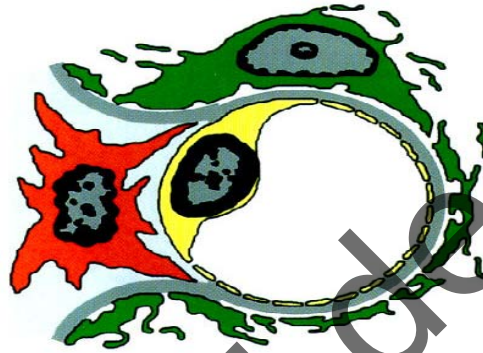
Normal Glomerular Capillary



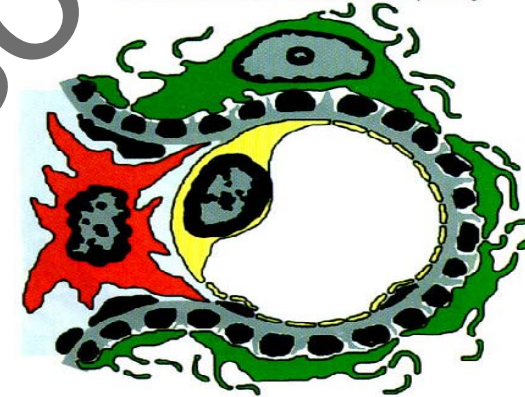
Idiopathic
Membranous Glomerulopathy



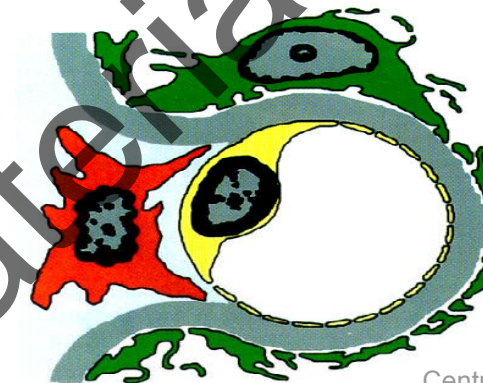
Minimal Change Glomerulopathy



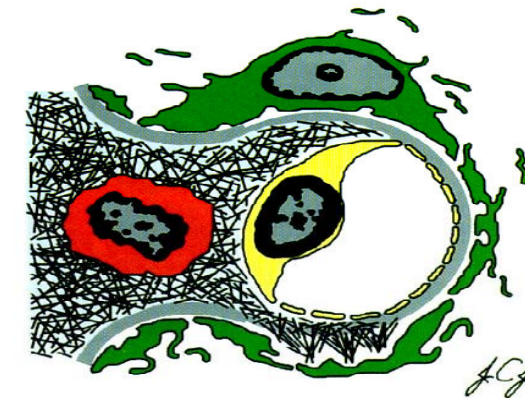
Secondary
Membranous Glomerulopathy



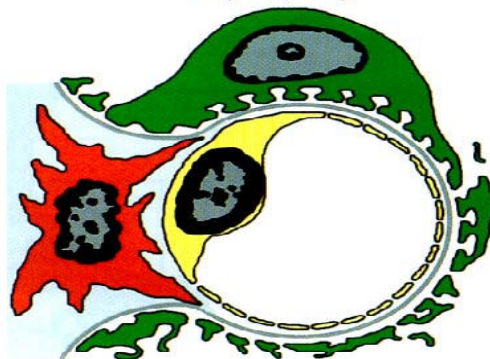
Diabetic Glomerulosclerosis



Amyloidosis



Thin Basement Membrane
Nephropathy



Proliferative Lupus
Glomerulonephritis



Mesangioproliferative
Glomerulonephritis



Type I Membranoproliferative
Glomerulonephritis



Acute Postinfectious
Glomerulonephritis



Type II Membranoproliferative
Glomerulonephritis



GLOMERULOPATÍAS

FORMAS ANATOMO-CLÍNICAS

- **NO PROLIFERATIVAS**

- LESIÓN GLOMERULAR MÍNIMA
- ESCLEROHIALINOSIS SEGMENTARIA Y FOCAL
- MEMBRANOSA

- **PROLIFERATIVAS**

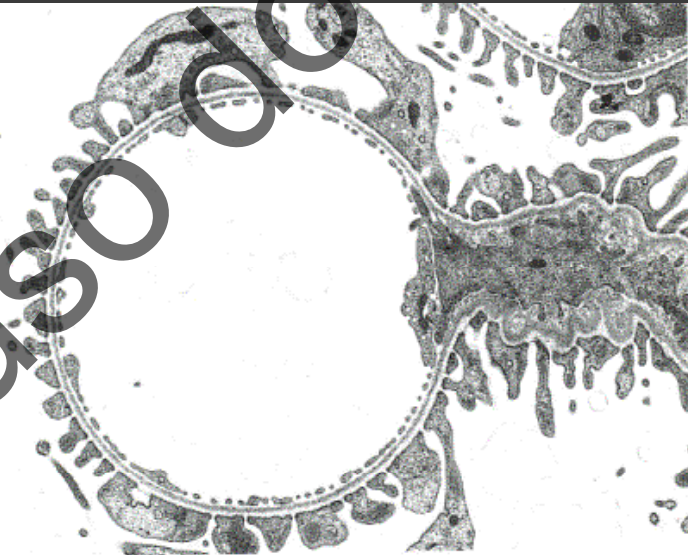
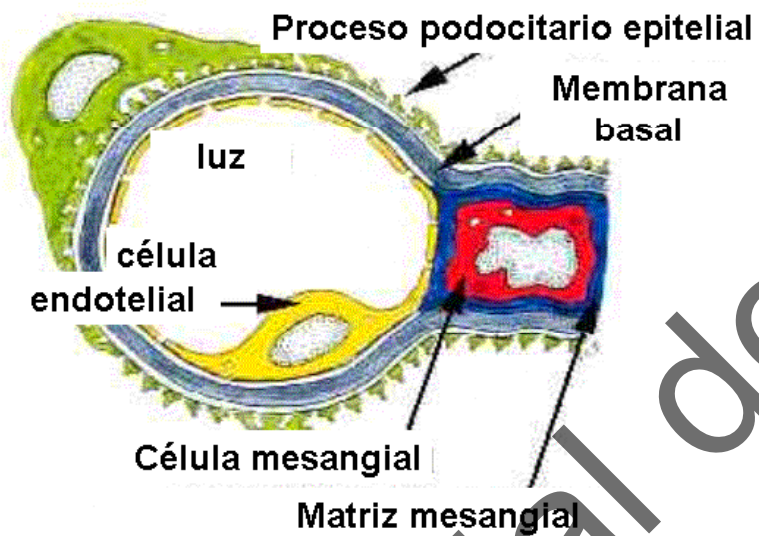
- INTRACAPILAR O DIFUSA O AGUDA POST-INFECCIOSA
- INTRA Y EXTRACAPILAR O RÁPIDAMENTE PROGRESIVA
- MEMBRANOPROLIFERATIVA

- **A DEPÓSITOS DE Ig A**

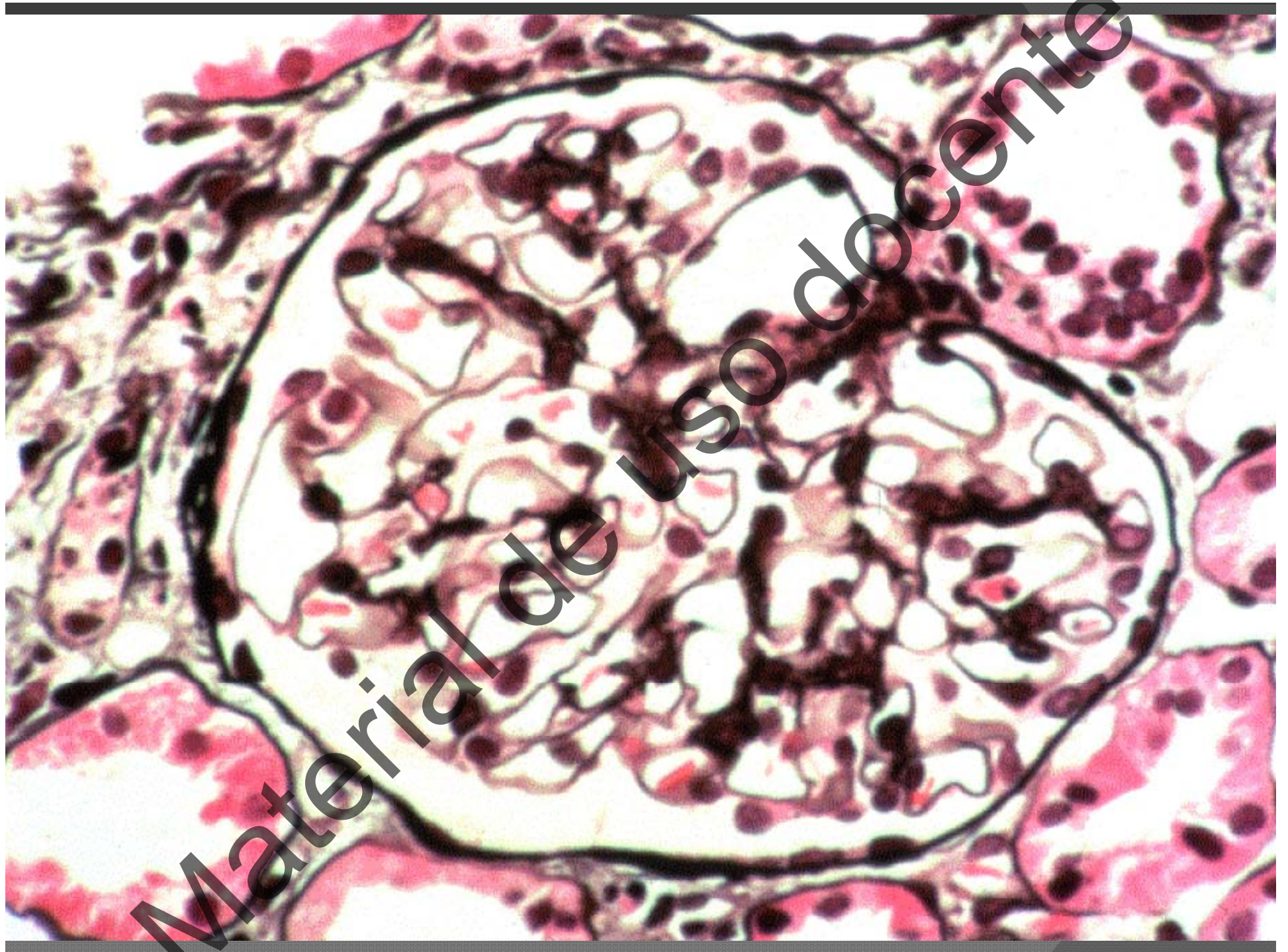
GLOMERULOPATÍAS NO PROLIFERATIVAS

- SE EXPRESAN POR S NEFRÓTICO
 - O AUA (PROTEINURIA NO NEFRÓTICA O PROTEINURIA Y MICROHEMATURIA)
- CONSECUENCIA DE PODOCITOPATÍA
- DOS MECANISMOS:
 - FACTOR SOLUBLE QUE AFECTA PODOCITO
 - DEPÓSITO DE AC SUBEPITELIALES, ACTIVACIÓN DE COMPLEMENTO Y LESIÓN DEL PODOCITO

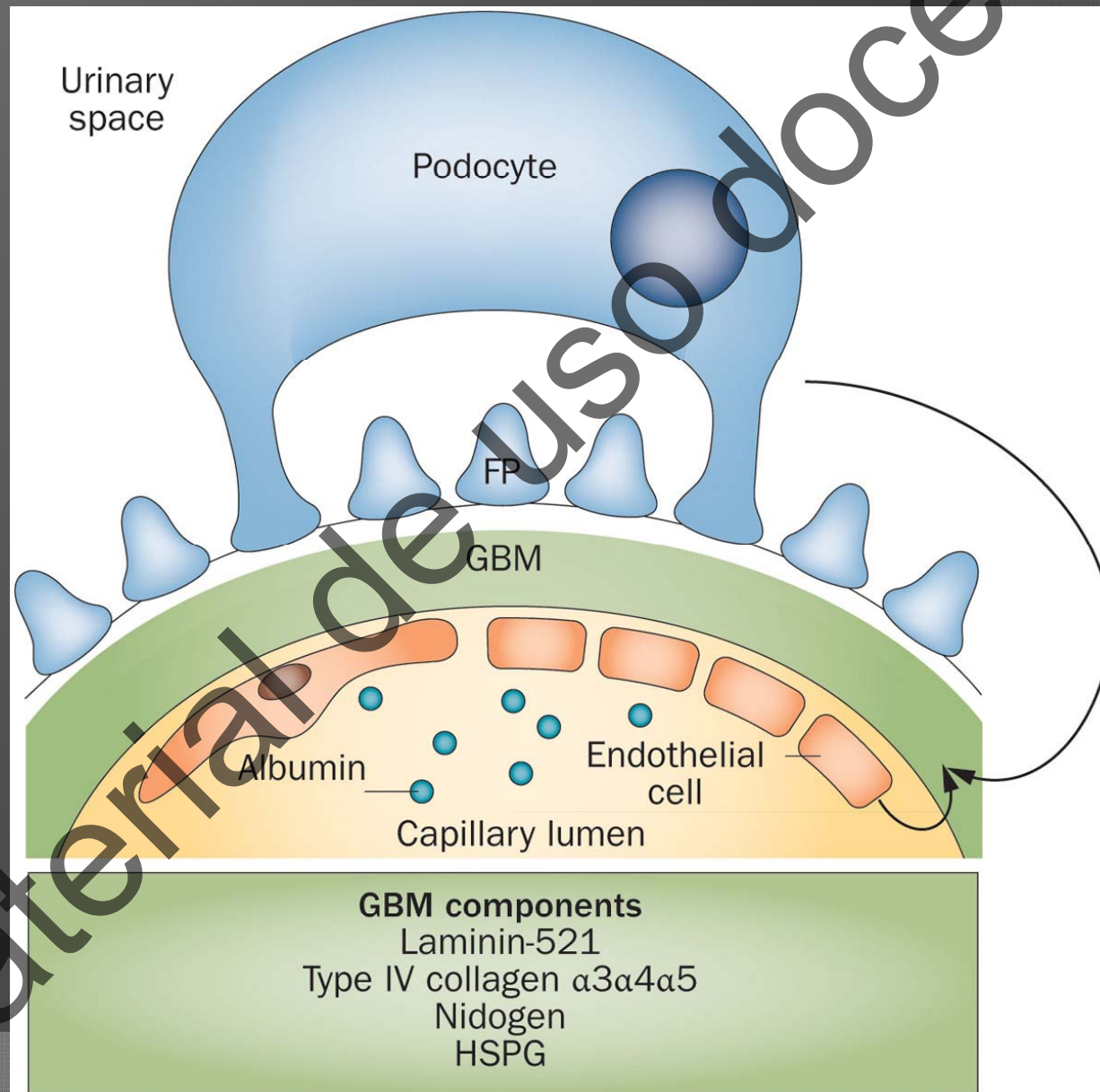
Capilar glomerular normal







Mecanismo de generación de la proteinuria



Suh, J. H. &
Miner, J. H. (2013)
The glomerular
basement
membrane as a
barrier to albumin
Nat. Rev. Nephrol.
doi:10.1038/nrnep

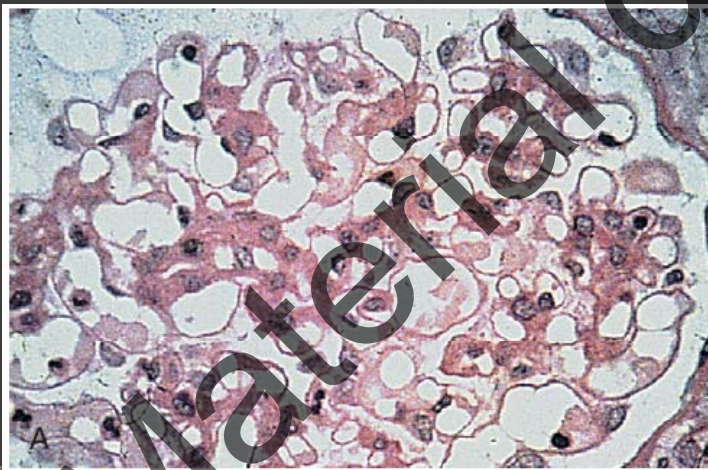
CAPÍTULO 1.

Tratamiento de Lesión Glomerular Mínima.

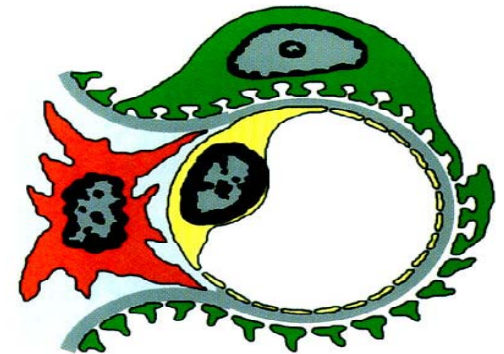
Este capítulo describe las recomendaciones para el tratamiento de la Lesión Glomerular Mínima en adultos.

1.1: Introducción

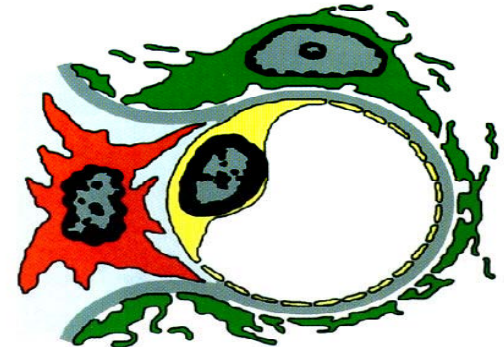
La Lesión glomerular mínima (LGM) determina entre un 10 a 15% de los síndromes del adulto y el 90% de los niños.¹⁻⁴ El estudio anatomopatológico al microscopio óptico característicamente no muestra lesiones glomerulares ó muestra cambios de acentuación mesangial. La inmunofluorescencia es negativa (ó presenta C3 débil) siendo característica la pérdida de procesos podocitarios sin depósitos electrónicos al microscopio electrónico¹⁻².



Normal Glomerular Capillary



Minimal Change Glomerulopathy



LESION GLOMERULAR MINIMA

- SINDROME NEFROTICO PURO UNICO O RECURRENTE
- PROTEINURIA SELECTIVA
- CAUSA MAS COMUN EN EL NIÑO (95%)
- PATOGENIA:
 - DESCONOCIDA
 - BASE INMUNOLOGICA
 - ASOCIACION CON INFECCIONES, VACUNACIONES, ATOPIA, RESPUESTA A ESTEROIDES E INMUNODEPRESORES, MEJORIA POR SARAMPION
- AP
 - MO: NORMAL
 - IF: NO DEPOSITOS
 - ME: FUSION DE PEDICELIOS

CHAPTER 16 Introduction to Glomerular Disease: Histologic Classification and Pathogenesis



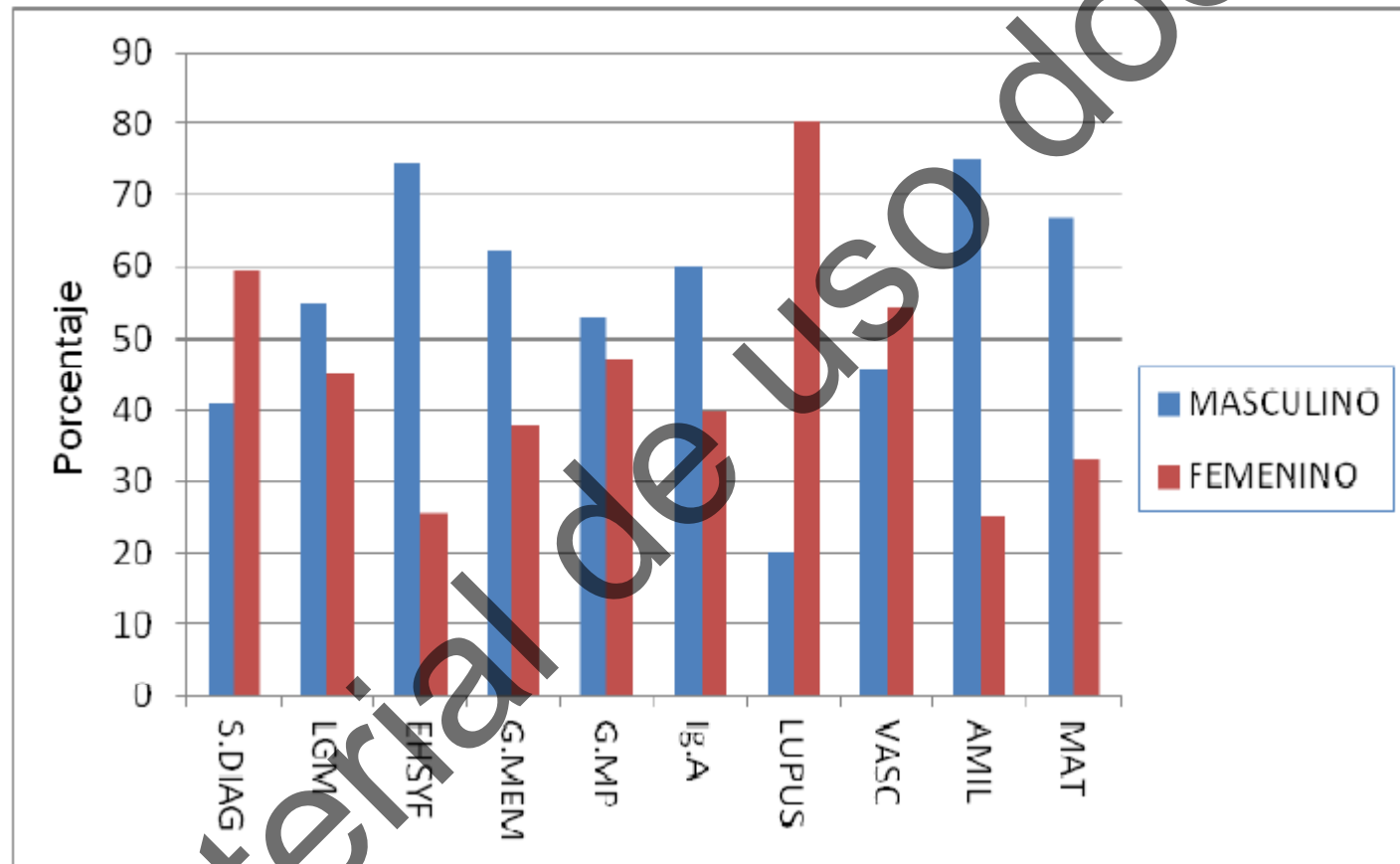
Factors Associated with the Onset of Nephrotic Syndrome in Minimal Change Disease	
Drugs	
Nonsteroidal anti-inflammatory drugs (NSAIDs)	
Interferon alfa	
Lithium: rare (usually causes chronic interstitial nephritis)	
Gold: rare (usually causes membranous nephropathy)	
Allergy	
Pollens	
House dust	
Insect stings	
Immunizations	
Malignancy	
Hodgkin's disease	
Mycosis fungoides	
Chronic lymphocytic leukemia: uncommon (usually associated with membranoproliferative glomerulonephritis)	

Figure 17.1 Factors associated with the onset of nephrotic syndrome in minimal change disease.

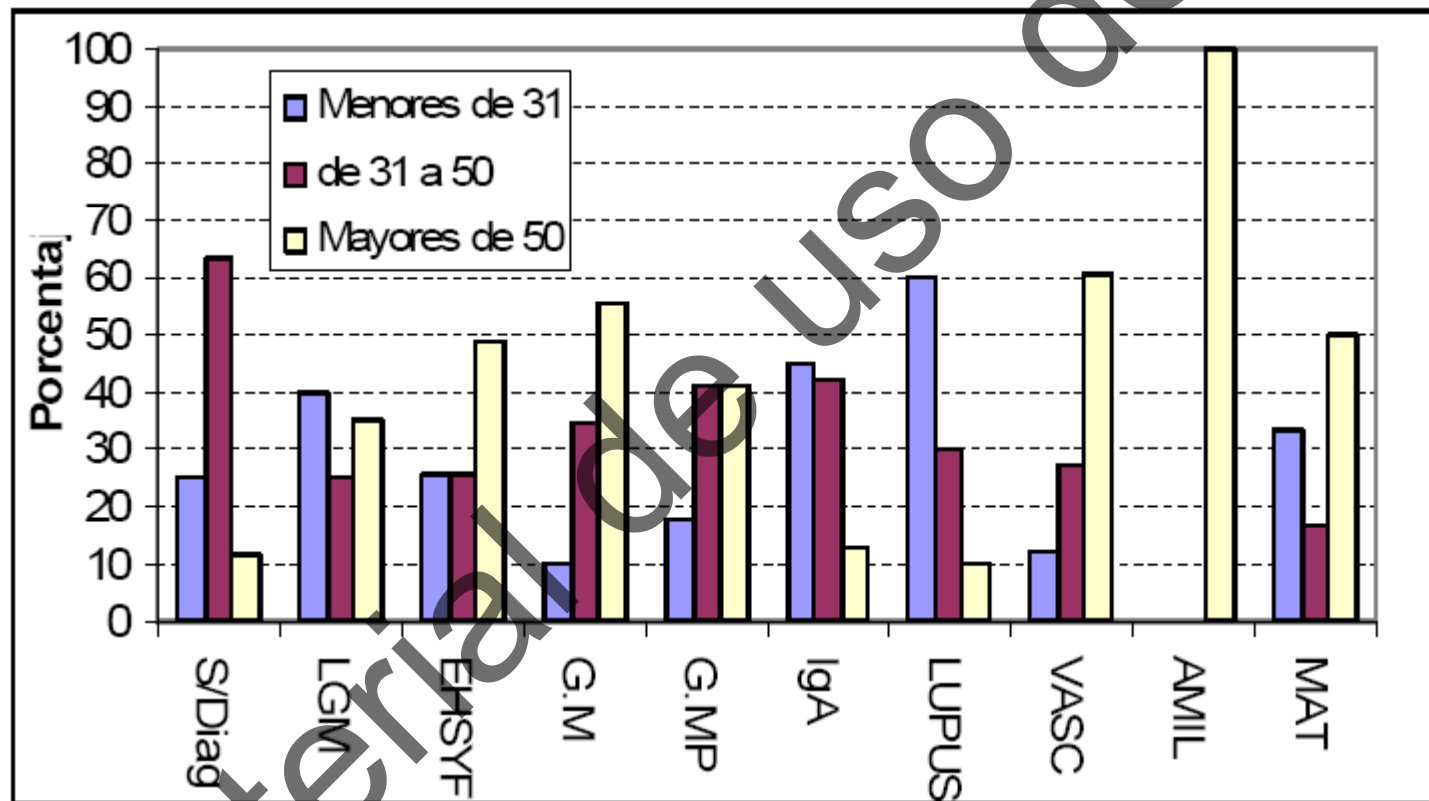
Minimal Change Nephrotic Syndrome

Philip D. Mason, Peter F. Hoyer

Distribución por sexo en las diferentes glomerulopatías. Período 2010-2012.



Edad al momento de la biopsia según glomerulopatía. Período 2010-2012



CAPITULO 2.

Esclerohialinosis Focal y Segmentaria (EHFS)

2.1: Introducción

La EHFS constituye uno de los patrones más comunes de lesión glomerular. En nuestro medio se ha comprobado en pacientes mayores de 15 años una reducción de su incidencia en tres periodos estudiados, de 10 ppm a 4 ppm (RUG)¹. Constituye la tercera glomerulopatía primaria biopsiada en el país. El término EHFS define un patrón anatomopatológico característico en la microscopia óptica pero con múltiples etiologías posibles. Los hallazgos típicos incluyen aumento segmentario de la matriz mesangial con obliteración de los capilares, esclerosis, hialinosis, células espumosas, cicatrización segmentaria, y la adhesión entre el ovillo glomerular y la cápsula de Bowman.

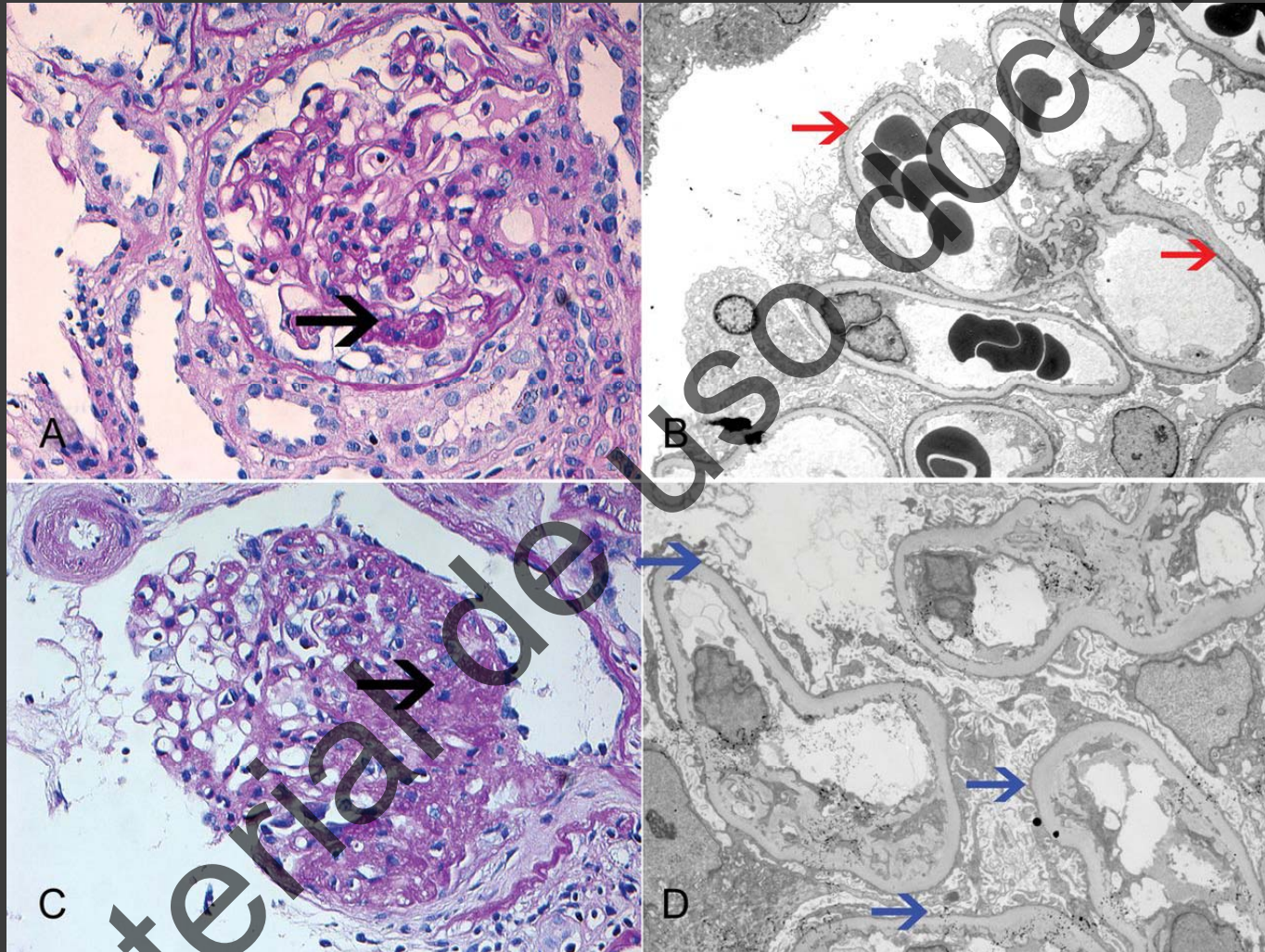
La EHFS se clasifica en primaria o secundaria en función de que se identifique o no una causa responsable, lo que tiene implicancias terapéuticas. A nivel histológico, al microscopio electrónico, en la lesión primaria se observa una extensa lesión podocitaria, con esfacelo de los pies de los podocitos, en tanto que en las EHFS la lesión podocitaria es segmentaria.²

La lesión primaria se define por exclusión de cualquier otra causa identificable de la EHFS secundaria (Tabla I). Las causas secundarias de la EHFS deben ser evaluados por un análisis detallado en cada caso de la historia clínica, el examen físico, los antecedentes familiares, las imágenes renales y la histología renal, incluyendo estudios de microscopía electrónica.

ESCLEROHIALINOSIS SEGMENTARIA Y FOCAL

- **SINDROME NEFROTICO IMPURO CORTICORRESISTENTE**
 - **CAUSA MAS COMUN EN JOVEN**
 - **PATOGENIA:**
 - **DESCONOCIDA**
 - **BASE INMUNOLOGICA**
 - **ALTERACION DE LA CARGA ELECTRICA DE MEMBRANA GLOMERULAR**
 - **FACTOR SOLUBLE: RECIDIVA EN HORAS EN TRASPLANTE**
 - **FORMA SECUNDARIA A ADAPTACION ESTRUCTURAL Y FUNCIONAL: HIPERFILTRACION, OBESIDAD, NEFRECTOMIA 5/6, ETC.**
 - **HIPERTROFIA, <DENSIDAD EPITELIAL - RETRACCION DE PODOCITOS, MODIFICACION DE PERMEABILIDAD - ACUMULACION HIALINA - COLAPSO CAPILAR SEGMENTARIO**
 - **AP**
 - **MO: ESCLEROSIS SEGMENTARIA Y FOCAL**
 - **IF: C3 E IgM**
 - **ME: FUSION DE PEDICELIOS**
-

FSGS.



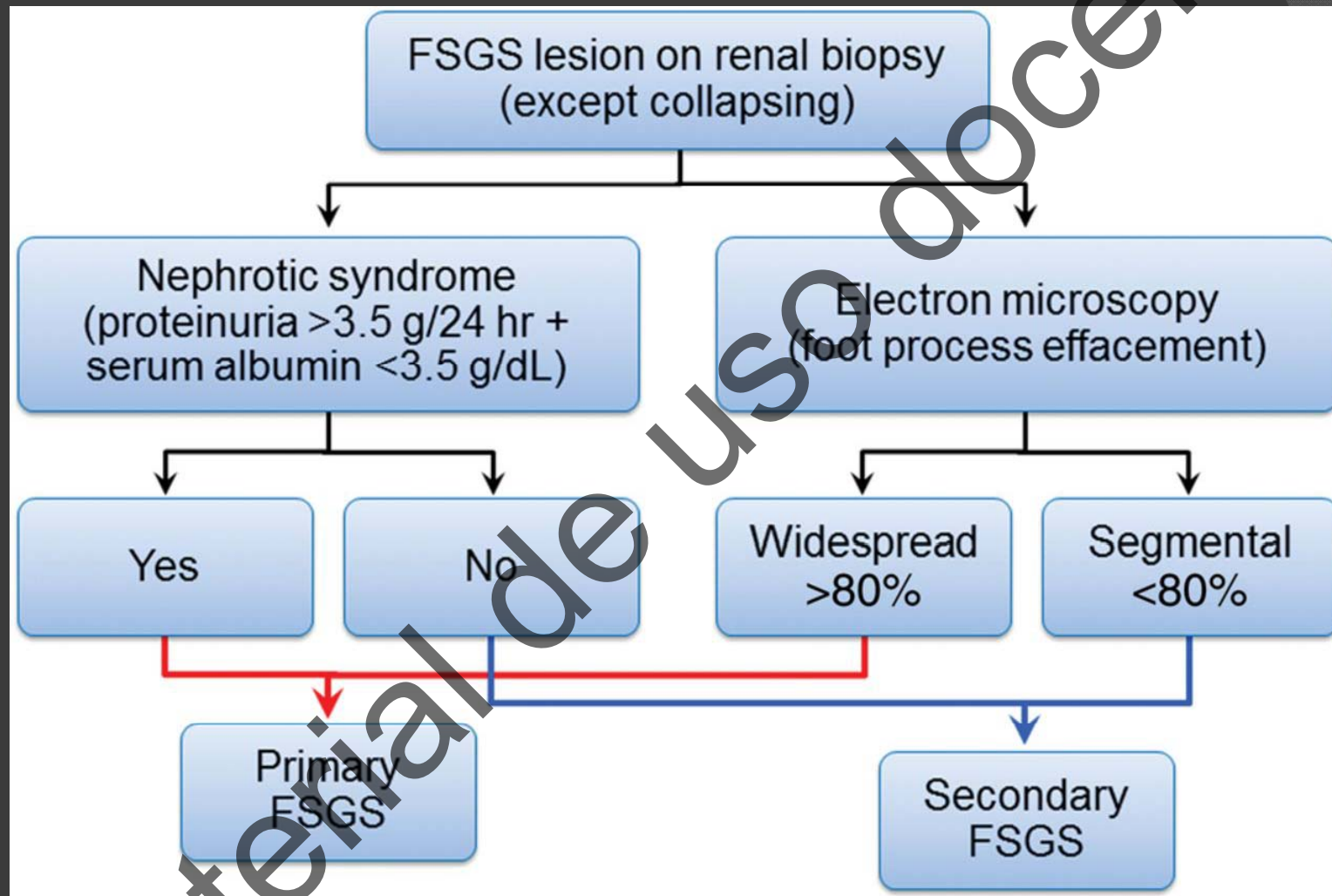
Sanjeev Sethi et al. Nephrol. Dial. Transplant. 2015;30:375-384

Table 1. Worldwide distribution of biopsy-proven glomerular diseases

Country	Reference	Primary GN (%)	Secondary GN (%)
America			
USA	3	IgAN (22) ^a	LN (13) ^a
Brazil	1	FSGS (25) ^b	LN(42) ^b
Europe			
Italy	5	IgAN (37) ^b	LN (26) ^b
Spain	7	IgAN (17) ^a	LN (11) ^a
Czech Republic	8	IgAN (34) ^b	LN (23) ^b
Hungary	10	IgAN (15) ^a	LN (7) ^a
Macedonia	11	MN (13) ^b	
Romania	12	MPGN (29) ^b	LN (29) ^b
Serbia	13	Non-IgA mesangioproliferative (25) ^b	LN (76) ^b
UK	21	IgAN (39) ^b	
Asia			
China	14	IgAN (45) ^b	LN (54) ^b
Korea	16	IgAN (28) ^b	LN (9) ^b
Middle East			
Saudi Arabia	17	FSGS (21) ^b	LN (57) ^b
Australia	18	IgAN (34) ^a	LN (14) ^a

^aPercentage of total glomerular diseases. ^bPercentage of primary or secondary glomerulonephritis.

Proposed diagram to differentiate between primary and secondary FSGS based on clinical presentation and EM examination (collapsing FSGS is excluded).



Sanjeev Sethi et al. Nephrol. Dial. Transplant. 2015;30:375-384

Focal Segmental Glomerulosclerosis

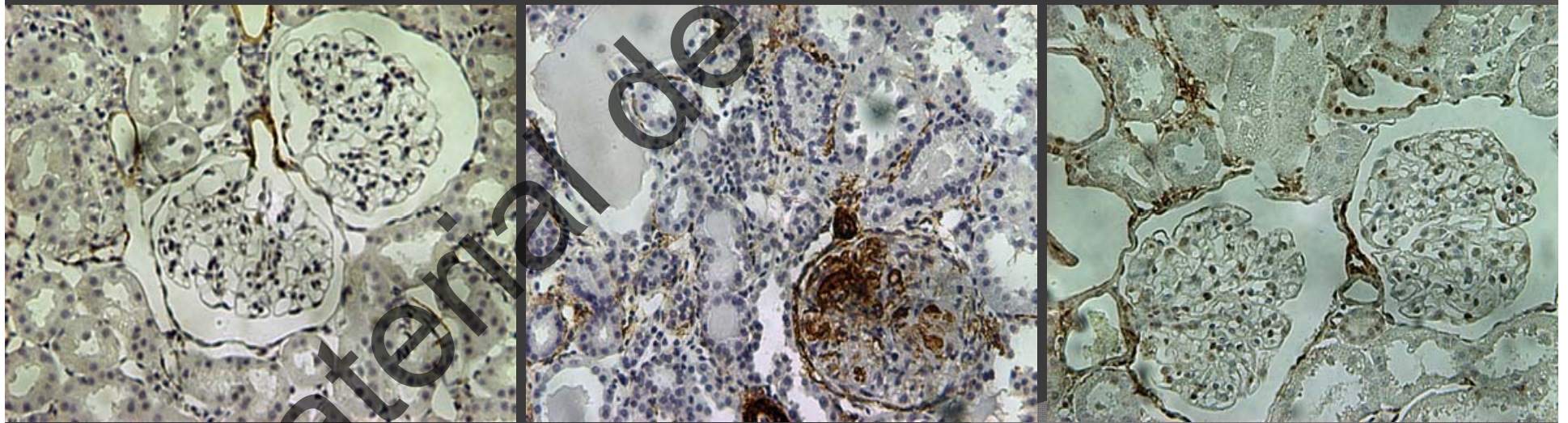
Vivette D. D'Agati, M.D., Frederick J. Kaskel, M.D., Ph.D., and Ronald J. Falk, M.D.

Table 1. Causes of Focal Segmental Glomerulosclerosis.

Type of Disease	Cause
Primary (idiopathic) form	Specific cause unknown; mediated by circulating permeability factors
Secondary forms	
Familial or genetic	Mutations in specific podocyte genes*
Virus-associated	Human immunodeficiency virus type 1, parvovirus B19, simian virus 40, cytomegalovirus, Epstein–Barr virus
Drug-induced	Heroin; interferons alfa, beta, and gamma; lithium; pamidronate; sirolimus; calcineurin-inhibitor nephrotoxicity; anabolic steroids
Adaptive†	Conditions with reduced renal mass: oligomeganephronia, very low birth weight, unilateral renal agenesis, renal dysplasia, reflux nephropathy, sequela to cortical necrosis, surgical renal ablation, renal allograft, aging kidney, any advanced renal disease with reduced functioning nephrons Conditions with initially normal renal mass: systemic hypertension, acute or chronic vaso-occlusive processes (atheroembolization, thrombotic microangiopathy, renal-artery stenosis), elevated body-mass index (obesity, increased lean body mass [e.g., bodybuilding]), cyanotic congenital heart disease, sickle cell anemia

* For details regarding genetic mutations associated with focal segmental glomerulosclerosis, see the table in the Supplementary Appendix.

† The adaptive form is mediated by adaptive structural–functional responses to glomerular hypertension caused by elevated glomerular capillary pressures and flows.



Kurdián M, Herrero-Fresneda I, Lloberas N, Gimenez-Bonafe P, et al. (2012) Delayed mTOR Inhibition with Low Dose of Everolimus Reduces TGF β Expression, Attenuates Proteinuria and Renal Damage in the Renal Mass Reduction Model. PLoS ONE 7(3): e32516. doi:10.1371/journal.pone.0032516 march 2012
<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0032516>

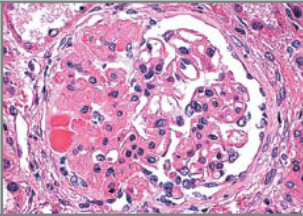
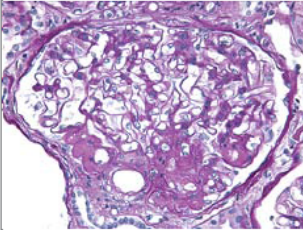
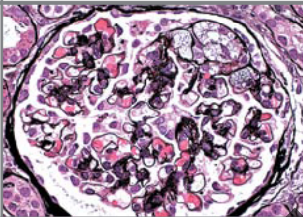
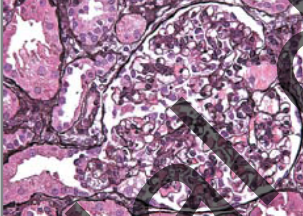
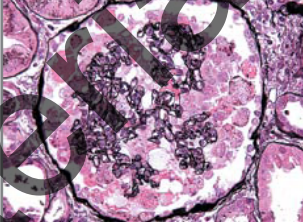
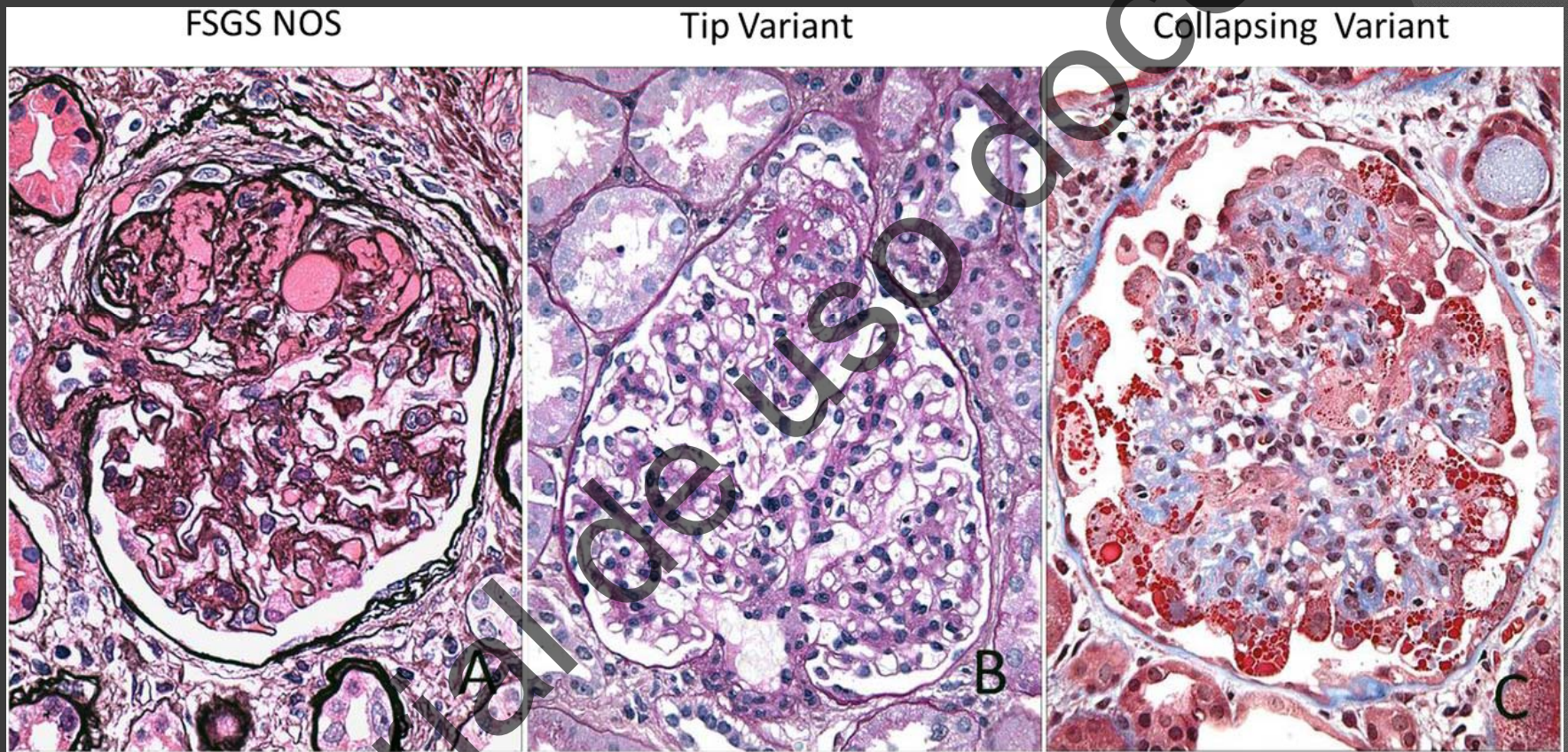
Histologic Subtype	Glomerular Lesion	Defining Features	Associations	Clinical Features
NOS		The usual generic form of FSGS. FSGS(NOS) does not meet defining criteria for any other variant. Foot-process effacement is variable.	Primary or secondary (including genetic forms and other diverse secondary causes). Cross-sectional studies suggest this is the most common subtype. Other variants can evolve into FSGS (NOS) over time.	May present with the nephrotic syndrome or subnephrotic proteinuria.
Perihilar		Perihilar hyalinosis and sclerosis involving the majority of glomeruli with segmental lesions. Perihilar lesions are located at the glomerular vascular pole. In adaptive FSGS, there is usually glomerular hypertrophy (glomerulomegaly). Foot-process effacement is relatively mild and focal, which probably reflects the heterogeneous adaptive responses of glomeruli.	Common in adaptive FSGS associated with obesity, elevated lean body mass, reflux nephropathy, hypertensive nephrosclerosis, sickle cell anemia, and renal agenesis. Predisposition for vascular pole is probably due to normally increased filtration pressures at the proximal afferent end of glomerular capillary bed, which are heightened under conditions of compensatory demand and vasodilatation of the afferent arteriole.	In adaptive FSGS, patients are more likely to present with subnephrotic proteinuria and normal serum albumin levels.
Cellular		Expansile segmental lesion with endocapillary hypercellularity, often including foam cells and infiltrating leukocytes, with variable glomerular epithelial-cell hyperplasia. There is usually severe foot-process effacement.	Usually primary, but also seen in a variety of secondary forms. This is the least common variant. It is thought to represent an early stage in the evolution of sclerotic lesions.	Usually presents with the nephrotic syndrome.
Tip		Segmental lesion involving the tubular pole, with either adhesion to tubular outlet or confluence of podocytes and tubular epithelial cells. Compared with other variants, it has the least tubular atrophy and interstitial fibrosis. There is usually severe foot-process effacement.	Usually primary. Probably mediated by physical stresses on the paratubular segment owing to the convergence of protein-rich filtrate on the tubular pole, causing shear stress and possible prolapse.	Usually presents with abrupt onset of the nephrotic syndrome. More common in white race. Best prognosis, with highest rate of responsiveness to glucocorticoids and lowest risk of progression.
Collapse		Implosive glomerular-tuft collapse with hypertrophy and hyperplasia of the overlying visceral epithelial cells. Hyperplastic glomerular epithelial cells may fill the urinary space, resembling crescents. Severe tubular injury and tubular microcysts are common. There is usually severe foot-process effacement.	Primary or secondary to Viruses: HIV-1, parvovirus B19, SV40, EBV, CMV, hemophagocytic syndrome Drugs: pamidronate and interferon Vaso-occlusive disease: athero-emboli, calcineurin inhibitor nephrotoxicity, and chronic allograft nephropathy	Most aggressive variant of primary FSGS with black racial predominance and severe nephrotic syndrome. Worst prognosis, with poor responsiveness to glucocorticoids and rapid course to renal failure.

Figure 3. Histologic Variants of Focal Segmental Glomerulosclerosis (FSGS).

CMV denotes cytomegalovirus, EBV Epstein-Barr virus, HIV-1 human immunodeficiency virus type 1, NOS not otherwise specified, and SV40 simian virus 40.

Major histologic variants are illustrated.



D'Agati V D et al. CJASN 2013;8:399-406

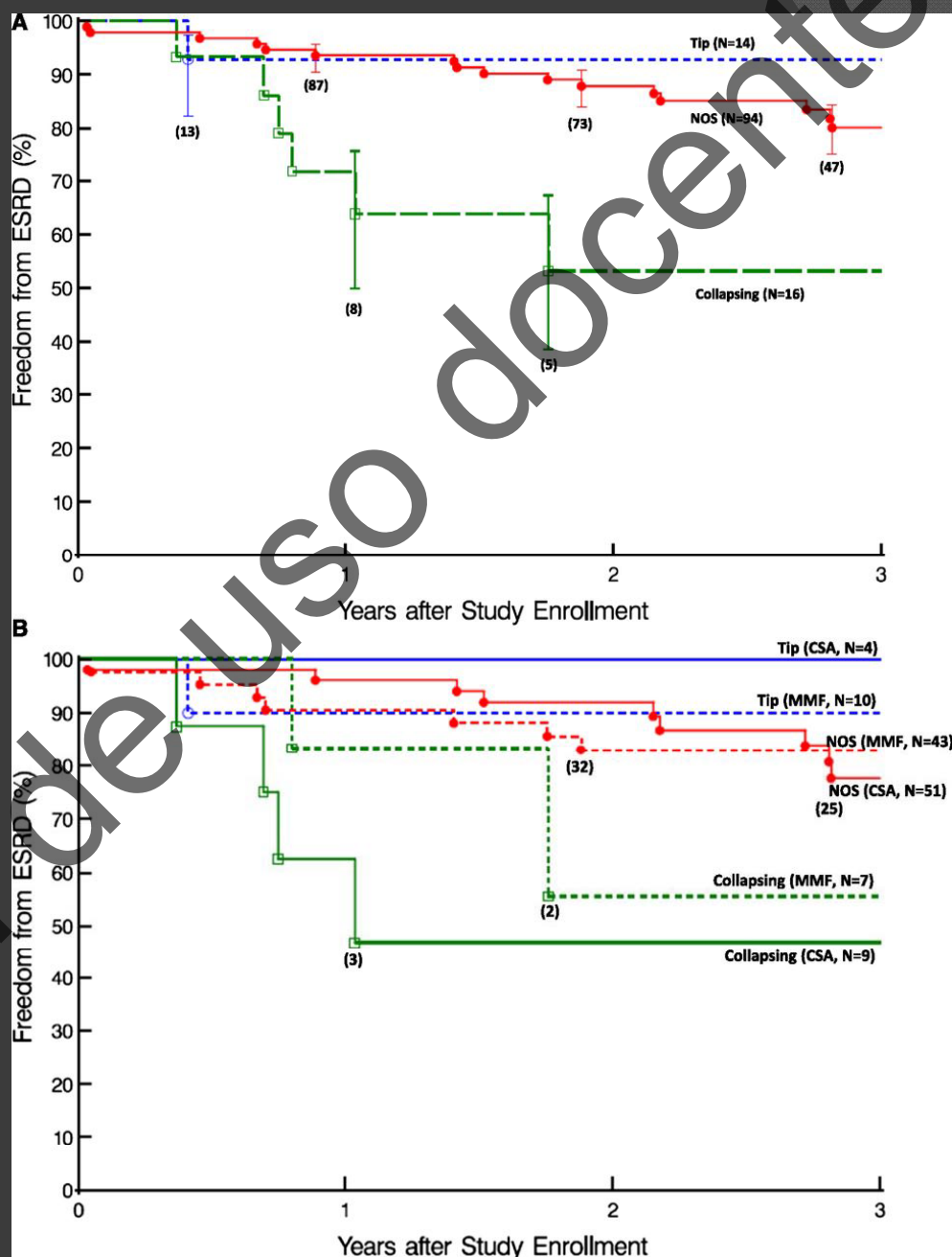
CJASN

Table 1. Demographic and presenting clinical data by FSGS histologic subtype

Demographic and Presenting Clinical Data	Not Otherwise Specified	Tip	Collapsing	P Value
Total number of cases	94	14	16	—
Age at onset (yr)	13 (8, 17)	15 (10, 29)	16.5 (14, 30.5)	0.02
Age group at onset (yr)				0.03
2–12 (children)	44 (47%)	4 (29%)	1 (6.3%)	
13–17 (teenagers)	27 (29%)	4 (29%)	9 (56%)	
≥18 (adults)	23 (24%)	6 (43%)	6 (38%)	
Age at biopsy (yr)	14 (9, 18)	15 (10, 30)	16.5 (14.5, 31.5)	0.05
Male sex	50 (53%)	8 (57%)	8 (50%)	0.93
Black race	37 (39%)	2 (14%)	10 (63%)	0.03
Birth weight (kg; <i>n</i> *)	3.4±0.7 (70)	3.2±0.5 (13)	2.7±0.8 (10)	0.08
Obesity at onset (<i>n</i> *)	12 (20%) (59)	2 (17%) (12)	2 (18%) (11)	0.91
Hypertension	55 (59%)	8 (57%)	7 (44%)	0.54
Edema	34 (36%)	8 (57%)	11 (69%)	0.03
Nephrosis level				0.03
Mild	29 (31%)	1 (7%)	1 (6%)	
Intermediate	37 (39%)	8 (57%)	6 (38%)	
Severe	28 (30%)	5 (36%)	9 (56%)	
Severe or intermediate nephrosis	65 (69%)	13 (93%)	15 (94%)	0.03
Urine protein/creatinine ratio	3.61 (1.77, 6.70)	4.75 (3.49, 8.94)	7.55 (4.35, 10.70)	0.02
Urine protein/creatinine ratio by level				0.01
1–1.99	29 (31%)	1 (7%)	1 (6%)	
2–3.99	23 (24%)	4 (29%)	3 (19%)	
4–7.99	20 (21%)	4 (29%)	4 (25%)	
≥8	22 (23%)	5 (36%)	8 (50%)	
Serum albumin (g/dl)	2.98±0.93	2.54±0.95	2.49±0.74	0.04
Cholesterol (mg/dl; <i>n</i> *)	347±175 (86)	429±109 (13)	420±114 (15)	0.002
LDL (mg/dl; <i>n</i> *)	197±132 (73)	309±119 (11)	253±102 (11)	<0.001
Serum creatinine (mg/dl)	0.86±0.61	0.84±0.43	1.33±0.50	0.003
Baseline estimated GFR (ml/min per 1.73m ²)	121 (83, 206)	120 (87, 180)	82 (58, 108)	0.006

Values are mean ± SD, median (25th, 75th percentile), or count (percent); *n** is the available *n* for a given value. Where not specified, the available *n* is the same as the total number of cases in the top row. *P* values were calculated using Kruskal–Wallis tests for continuous variables, Pearson chi-squared tests for nominal categorical variables, and Cochran–Mantel–Haenszel tests for ordinal categorical variables.

The rate of progression to ESRD for the three major subgroups is illustrated using Kaplan–Meier curves and the log-rank test.



Three distinct pathways of injury and repair characterize the podocytopathies.

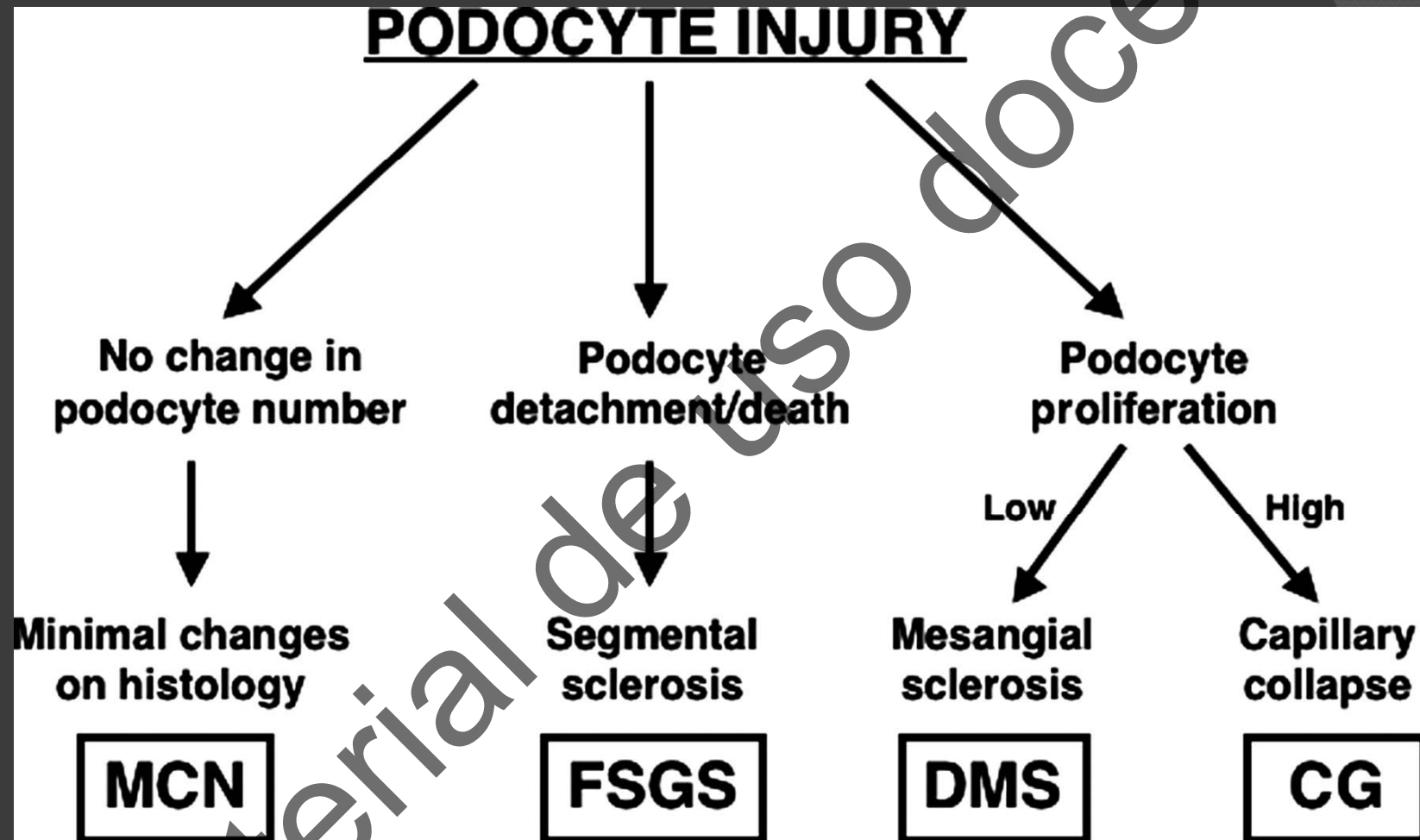
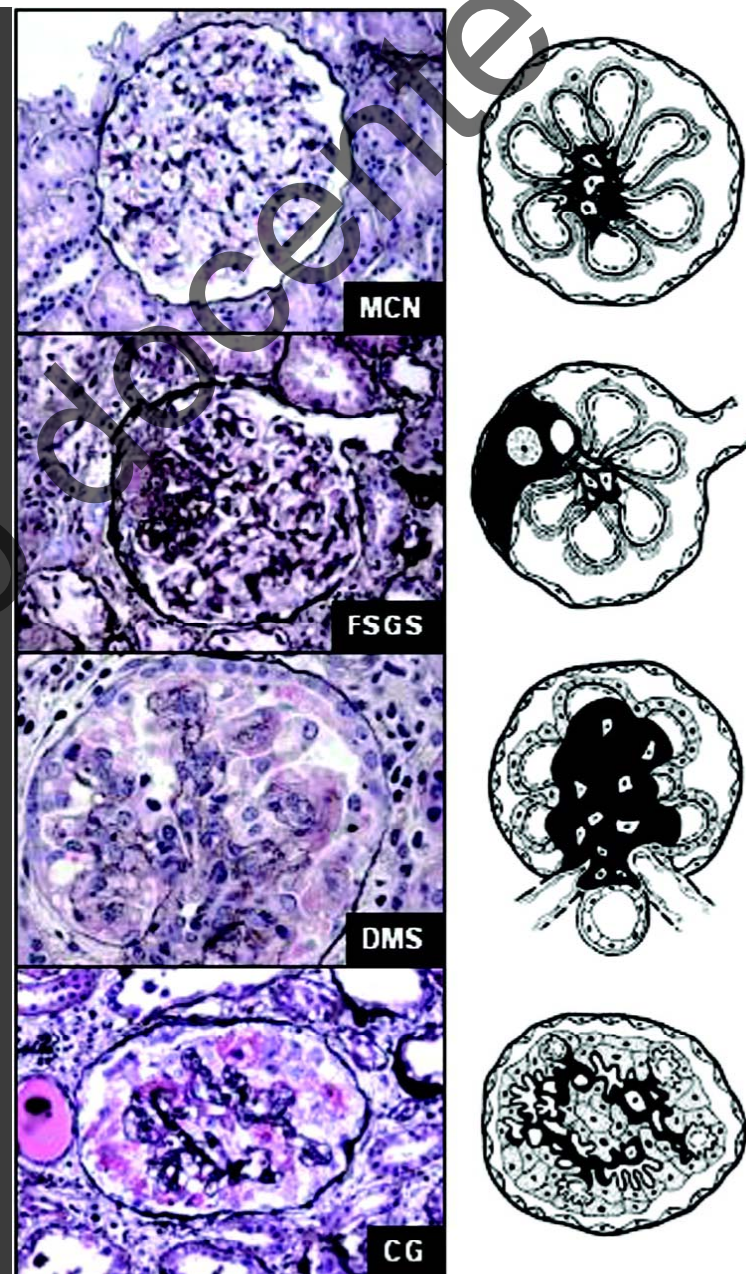


Table 2. Taxonomy of the podocytopathies

Podocytopathy	Idiopathic Forms	Genetic Forms	Reactive Forms
Minimal-change nephropathy	Idiopathic MCN steroid-sensitive steroid-resistant	Nonsyndromic <i>NPHS2</i> Syndromic <i>DYSF</i> (limb-girdle muscular dystrophy 2B)	Reactive MCN Hodgkin disease Immunogenic stimuli Medication-associated: nonsteroidal anti-inflammatory agents, gold, penicillamine, lithium, IFN- α and - β , pamidronate
Focal segmental glomerulosclerosis	Idiopathic FSGS	Nonsyndromic <i>NPHS1</i> + <i>NPHS2</i> <i>NPHS2</i> <i>ACTN4</i> <i>CD2AP</i> <i>TRPC6</i> <i>WT1</i> mtDNA tRNA ^{Leu} <i>PLCE1</i> Syndromic <i>WT1</i> (Frasier) mt DNA tRNA ^{Leu} (MELAS) <i>PAX2</i> (renal-coloboma syndrome with oligomeganephronia) <i>LMX1B</i> (nail-patella) <i>COQ2</i> <i>ITGB4</i> <i>COL4A3, A4, A5</i> (Alport) <i>GLA</i> (Fabry)	Postadaptive FSGS Reduced nephron mass: renal dysplasia, surgical renal mass reduction, reflux nephropathy, chronic interstitial nephritis Initially normal nephron mass: obesity, increased muscle mass, sickle cell anemia, cyanotic congenital heart disease, hypertension ^b Medication-associated FSGS: cyclosporine, tacrolimus, IFN- α , lithium, pamidronate
Diffuse mesangial sclerosis	Idiopathic DMS	Nonsyndromic <i>NPHS1</i> (congenital nephrotic syndrome, Finnish type) <i>WT1</i> <i>NPHS2</i> <i>PLCE1</i> Syndromic <i>LAMB2</i> (Pierson) <i>WT1</i> (Denys-Drash)	
Collapsing glomerulopathy	Idiopathic CG	Nonsyndromic <i>COQ2</i> Syndromic action myoclonus-renal failure	Infection-associated CG viruses (HIV-1, parvovirus B19 ^b , CMV ^b) other (Loa loa filariasis ^b , visceral leishmaniasis ^b , <i>Mycobacterium tuberculosis</i> ^b) Disease associations: Adult Still disease ^b , thrombotic microangiopathy, multiple myeloma ^b Medication-associated CG: IFN- α , pamidronate

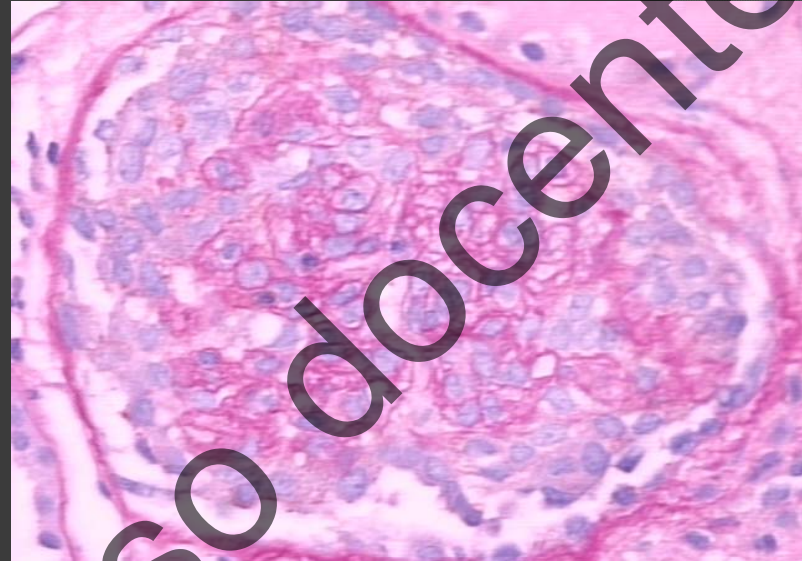
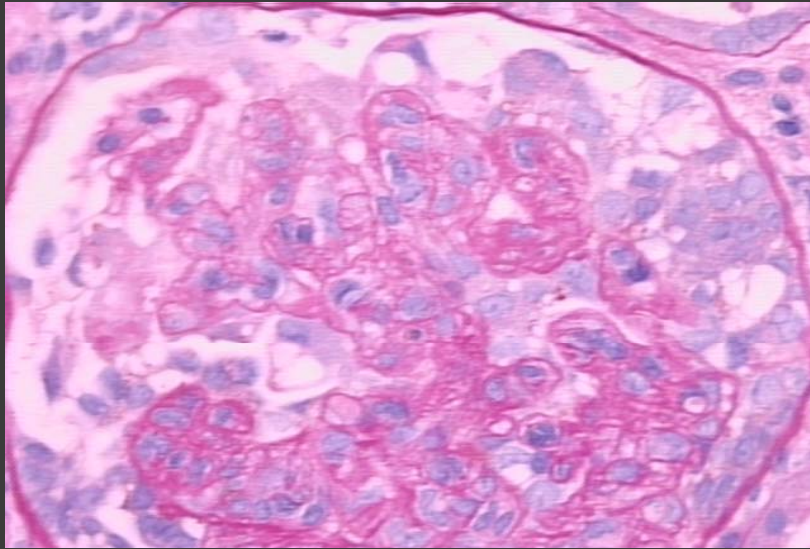
^aThe primary podocytopathies are organized into four morphologic patterns and three etiologic categories. Named syndromes are shown. *ACTN4*, α -actinin 4; FSGS, focal segmental glomerulosclerosis; *CD2AP*, CD2-associated protein; CMV, cytomegalovirus; *COL4*, type IV collagen; *COQ2*, co-enzyme Q synthetase 2; *DYSF*, dysferlin; FSGS, focal segmental glomerulosclerosis; *GLA*, α -galactosidase A; *ITGB4*, $\beta 4$ -integrin; *LAMB2*, laminin $\beta 2$ chain; *LMX1B*, Lim homeobox transcription factor 1B; MELAS, mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes; *NPHS1*, nephrin; *NPHS2*, podocin; *PAX2*, paired homeobox protein 2; *PLCE1*, phospholipase C $\epsilon 1$; *TRPC6*, transient receptor potential cation channel, member 6; *WT1*, Wilms' tumor-1.

^bDisease associations for which causation has not been clearly established.

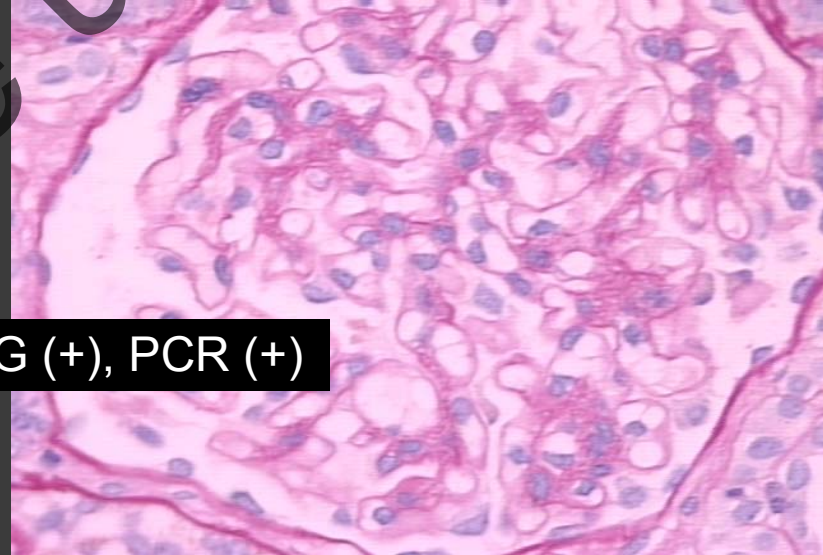


Caso clínico

- 32 años SF
- Diabética tipo 1
- DP hace 8 años
- TX reno pancreas hace 6 años, ambos injertos funcionantes
- Tacrolimus , MMF prednisona
- Deseo concepcional , azatioprina
- A los dos meses Pu 3 g/d creatininemia 2,3 mg/dl, Glicemia 0.8
- PBR



Colapso del ovillo. Podocitos desprendidos.

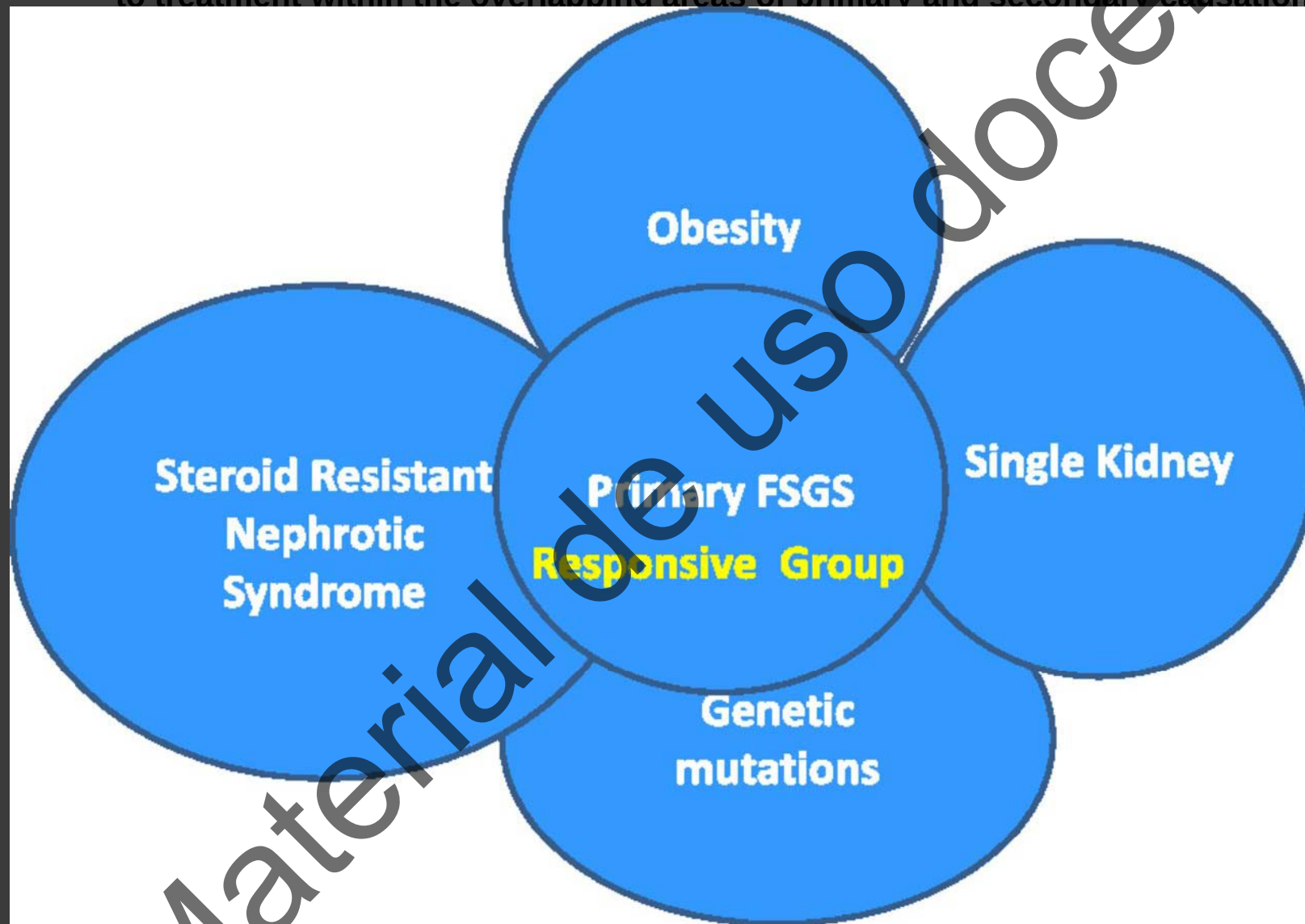


Parvovirus B19 IgM/IgG (+), PCR (+)

Hialinización de asas capilares

Discreta acentuación mesangial

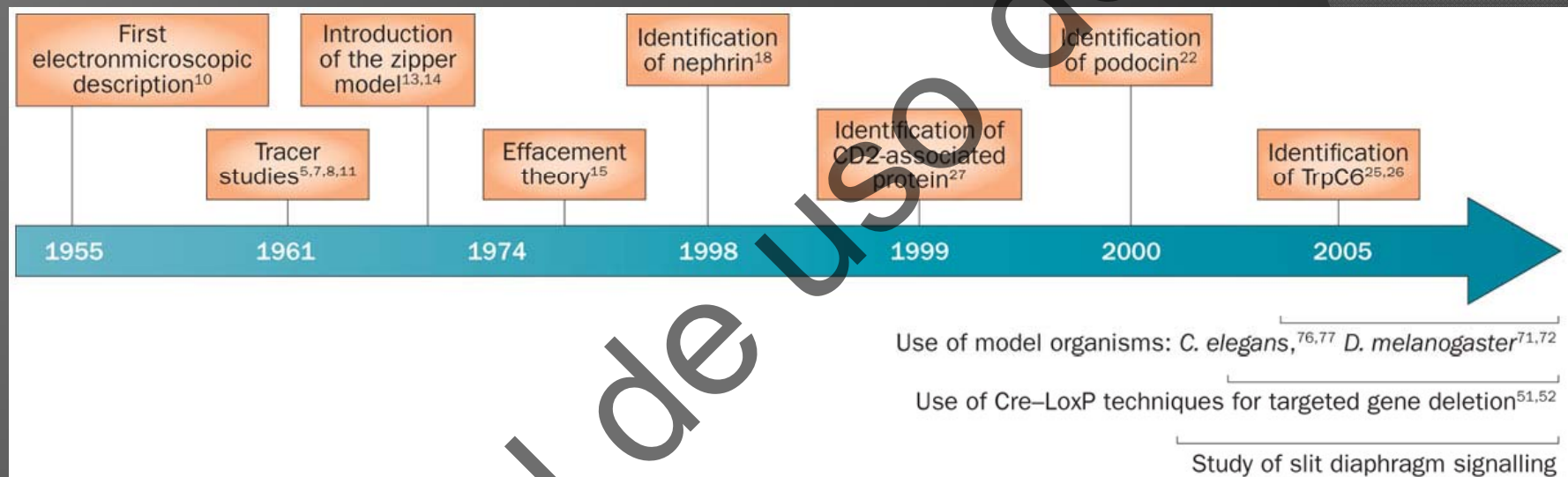
Overlap of different causal categories of FSGS. There is a complex interaction between different causes of FSGS. The overlap area conceptually indicates patients who may respond to treatment within the overlapping areas of primary and secondary causations.



Mecanismos de HFS

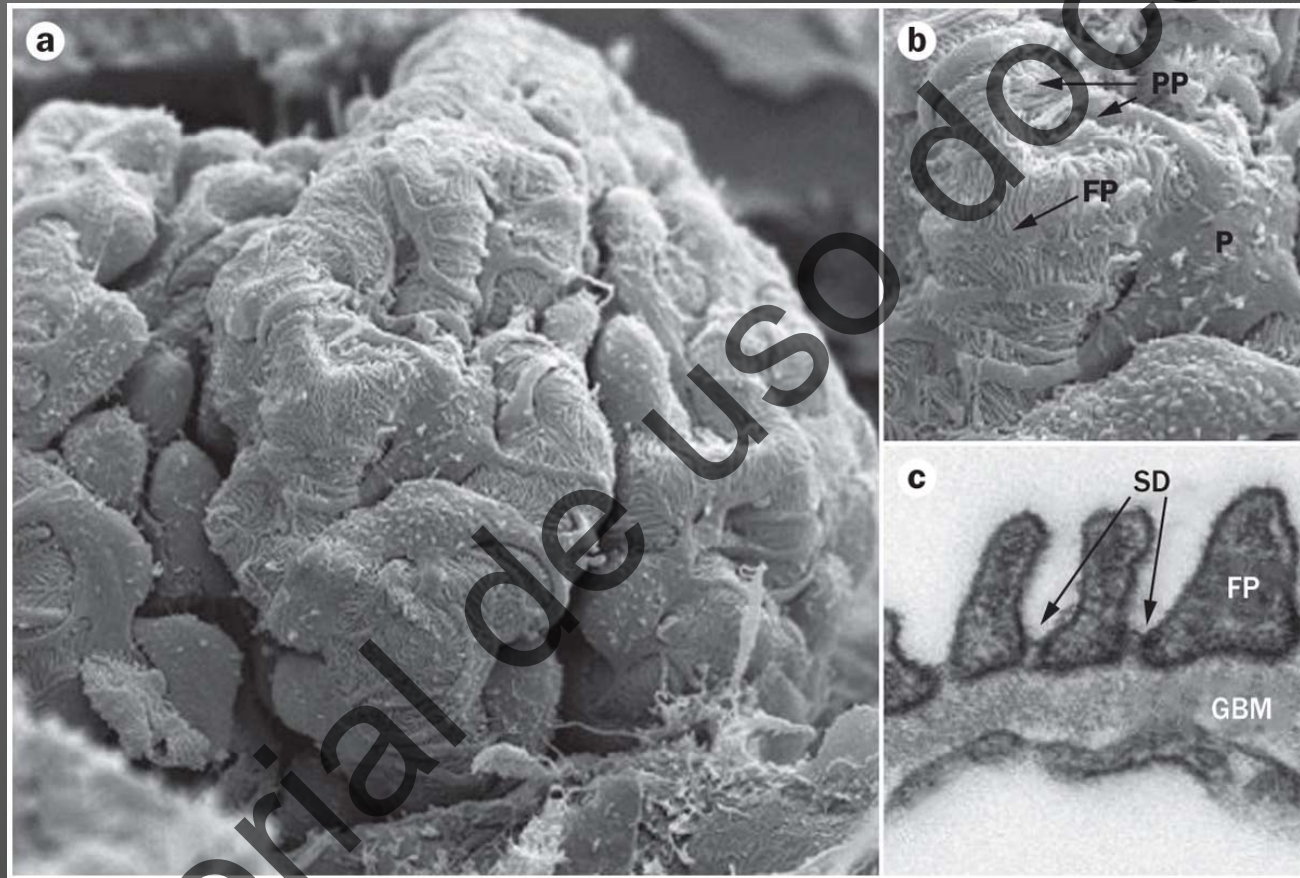
- suPAR (Receptor soluble de la urokinasa)
- Causas Genéticas
- APOL1
- Adaptativas

Figure 1 Timeline of major discoveries relating to the slit diaphragm



Grahammer, F. *et al.* (2013) The podocyte slit diaphragm—from a thin grey line to a complex signalling hub
Nat. Rev. Nephrol. doi:10.1038/nrneph.2013.169

Figure 2 Electron micrographs of the slit diaphragm and surrounding structures



Grahammer, F. *et al.* (2013) The podocyte slit diaphragm—from a thin grey line to a complex signalling hub

nature
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Figure 2 The role of podocyte dysfunction in proteinuria

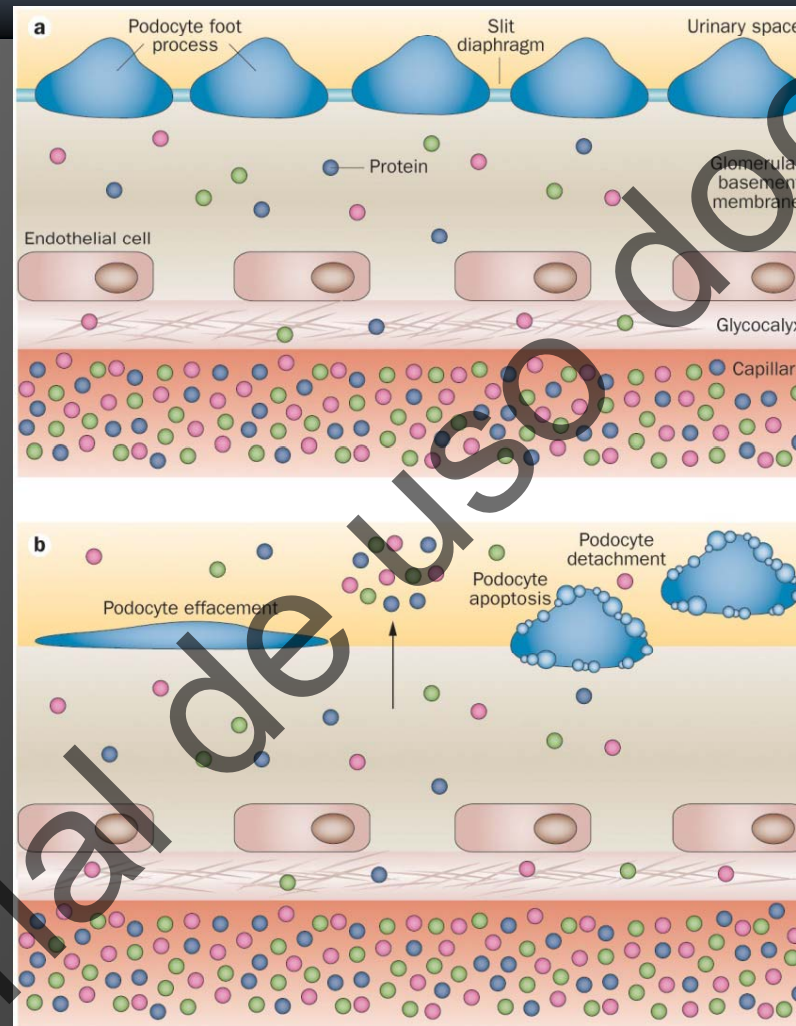
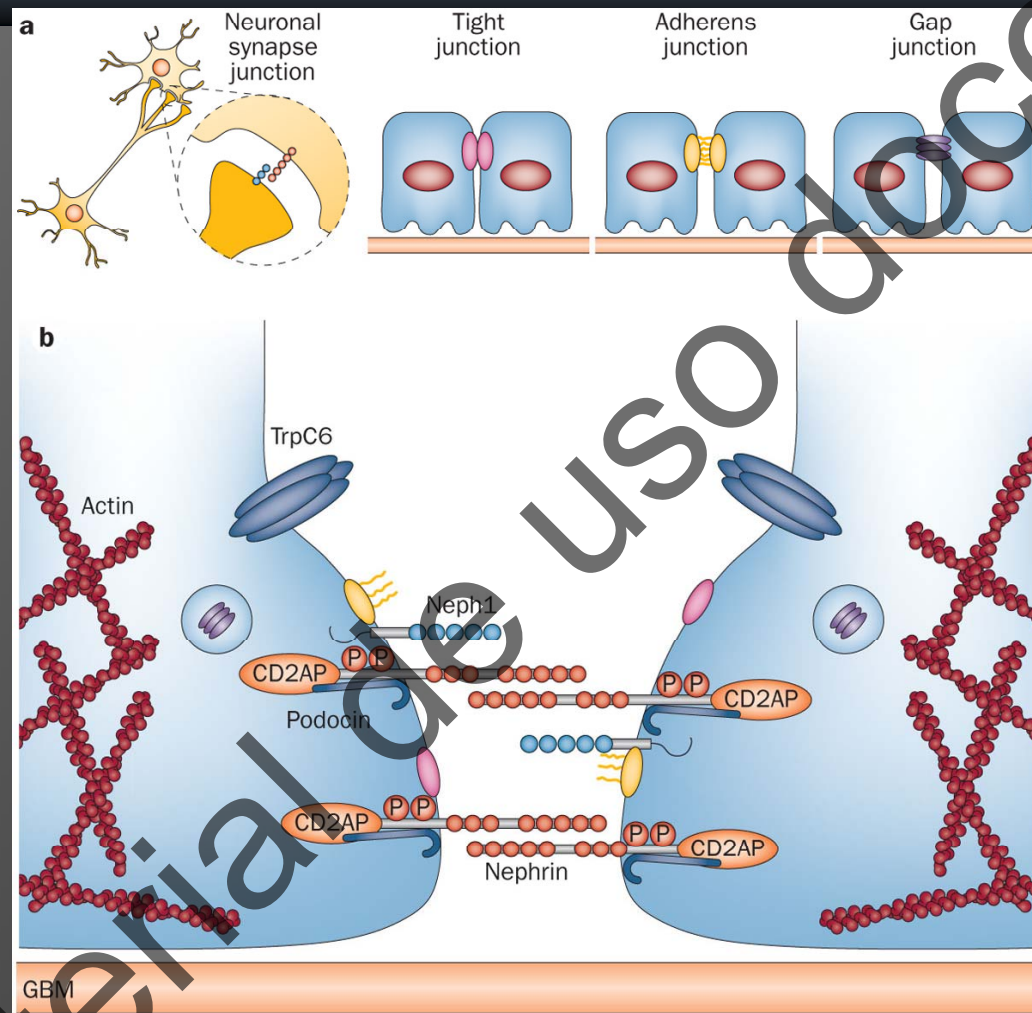
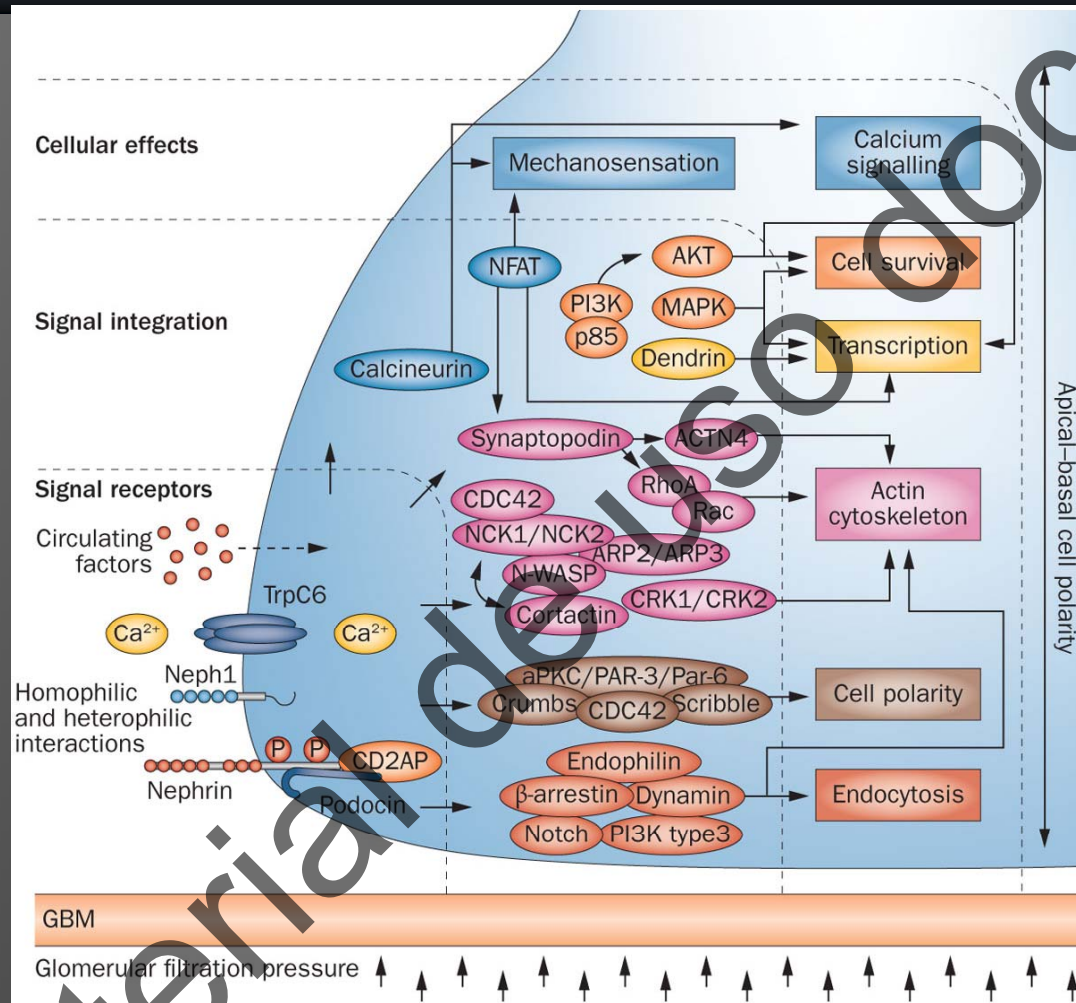


Figure 3 Molecular components of the podocyte slit diaphragm



Grahammer, F. *et al.* (2013) The podocyte slit diaphragm—from a thin grey line to a complex signalling hub
Nat. Rev. Nephrol. doi:10.1038/nrneph.2013.169

Figure 4 A comprehensive overview of signalling pathways converging at the slit diaphragm



Grahammer, F. et al. (2013) The podocyte slit diaphragm—from a thin gate to a complex signalling hub
Nat. Rev. Nephrol. doi:10.1038/nrneph.2013.169

nature
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Table 1
Comprehensive
list of genes
mutated in
diseases
associated with
nephrotic
syndrome

Table 1 Comprehensive list of genes mutated in diseases associated with nephrotic syndrome				
Gene	Protein	Mode of inheritance	Clinical phenotype	Reference
<i>Encode SD proteins</i>				
<i>NPHS1</i>	Nephrin	Autosomal recessive	CNS and infantile SRNS	18
<i>NPHS2</i>	Podocin	Autosomal recessive	Infantile and childhood SRNS	22
<i>CD2AP</i>	CD2-associated protein	Autosomal recessive	Infantile SRNS	27,159
<i>TRPC6</i>	Short transient receptor potential channel 6	Autosomal dominant	Juvenile and adult-onset FSGS	25,26
<i>Encode actin-regulating proteins</i>				
<i>ACTN4</i>	α -Actinin-4	Autosomal dominant	Juvenile and adult-onset FSGS	30
<i>INF2</i>	Inverted formin-2	Autosomal dominant	Juvenile and adult-onset FSGS	34
<i>ARHGAP24</i>	Rho-GTPase-activating protein 24	Autosomal dominant	Infantile and juvenile FSGS	36
<i>ARHGDIA</i>	Rho GDP-dissociation inhibitor 1	Autosomal recessive	CNS	37
<i>Encode transcription factors</i>				
<i>WT1</i>	Wilms tumour protein	Autosomal dominant	Denys-Drash syndrome, Frasier syndrome or isolated SRNS	38
<i>LMX1B</i>	LIM homeobox transcription factor 1 β	Autosomal dominant	Nail patella syndrome	45,46
<i>SMARCA1</i>	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A-like protein 1	Autosomal dominant	Schimke immuno-osseous dysplasia	47
<i>Encode GBM proteins</i>				
<i>LAMB2</i>	Laminin subunit β 2	Autosomal recessive	CNS (either isolated or as an aspect of Pierson syndrome)	39
<i>ITGB4</i>	Integrin β 4	Autosomal recessive	Epidermolysis bullosa	40
<i>Encode mitochondrial proteins</i>				
<i>COQ2</i>	4-hydroxybenzoate-polyprenyltransferase, mitochondrial	Autosomal recessive	Early onset SRNS, coenzyme Q ₁₀ deficiency	32
<i>COQ6</i>	Ubiquinone biosynthesis monooxygenase COQ6	Autosomal recessive	SRNS with sensorineural deafness	33
<i>PDSS2</i>	Decaprenyl-diphosphatesynthase subunit 2	Autosomal recessive	SRNS, coenzyme Q ₁₀ deficiency	42
<i>MTTL1</i>	Mitochondrial Leu (UUR) tRNA	Autosomal recessive	MELAS, diabetes, deafness and glomerular lesions	43,44
<i>Encode lysosomal proteins</i>				
<i>SCARB2</i>	Lysosome membrane protein 2	Autosomal recessive	Action myoclonus and renal failure	41
<i>Encode other podocyte proteins</i>				
<i>PLCE1</i>	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase ϵ 1	Autosomal recessive	Infantile and early childhood SRNS	28
<i>PTPRO</i>	Receptor-type tyrosine-protein phosphatase O	Autosomal recessive	SRNS	31
<i>MYO1E</i>	Unconventional myosin 1e	Autosomal recessive	FSGS	35
<i>APOL1</i>	Apolipoprotein L1	Autosomal recessive	FSGS	29
Abbreviations: CNS, congenital nephrotic syndrome; FSGS, focal segmental glomerulosclerosis; GBM, glomerular basement membrane; MELAS, mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes; SD, slit diaphragm; SRNS, steroid-resistant nephrotic syndrome.				

Grahammer, F. *et al.* (2013) The podocyte slit diaphragm—from a thin grey line to a complex signalling hub
Nat. Rev. Nephrol.
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Inverted formin 2 mutations with variable expression in patients with sporadic and hereditary focal and segmental glomerulosclerosis

Rasheed A. Gbadegesin^{1,2}, Peter J. Lavin^{2,3}, Gentzon Hall^{2,3}, Bartłomiej Bartkowiak^{1,2}, Alison Homstad^{1,2}, Ruiji Jiang^{1,2}, Guanghong Wu^{2,3}, Alison Byrd^{2,3}, Kelvin Lynn⁴, Norman Wolfish⁵, Carolina Ottati⁶, Paul Stevens⁷, David Howell⁸, Peter Conlon⁹ and Michelle P. Winn^{2,3}

¹Department of Pediatrics, Duke University Medical Center, Durham, North Carolina, USA; ²Center for Human Genetics, Duke University Medical Center, Durham, North Carolina, USA; ³Department of Medicine, Duke University Medical Center, Durham, North Carolina, USA; ⁴Department of Medicine, Division of Nephrology, Christchurch Hospital, Christchurch, New Zealand; ⁵Department of Pediatrics, Division of Nephrology, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada; ⁶Centro de Nefrología Hospital de Clínicos Dr Manuel Quintela, Montevideo, Uruguay; ⁷Department of Nephrology, East Kent Hospital University NHS, Canterbury, UK; ⁸Department of Pathology, Duke University Medical Center, Durham, North Carolina, USA and ⁹Department of Nephrology, Beaumont Hospital, Dublin, Ireland

Table 2 | Clinical phenotype of eight families with FSGS and mutations in INF2

Individual number	Race/country	Mutation	Age onset (years)	Symptomatic individuals ^a	Histology	Median age at ESKD (years)
6502	C/USA	Exon 4 608C>A A203D ^b	14–24	2/2	FSGS	42
6505	C/USA	Exon 4 550G>C E184Q ^b	20–37	8/8	FSGS	33
6507	C/USA	Exon 4 530G>A R177H	28–34	2/4	FSGS	36
6515	C/Canada	Exon 4 653G>A R218Q	16–46	2/3	FSGS	U
6518	C/New Zealand	Exon 4 605A>G N202D ^b	19–24	2/2	FSGS	U
6529	C/Belgium	Exon 4 641G>A R214H	22–45	6/6	FSGS	45.5
6556	C/United Kingdom	Exon 4 641G>A R214H	27–30	3/5	FSGS	40
6635	H/Uruguay	Exon 4 641C>T R214C	20	1/3	FSGS	U

Abbreviations: C, Caucasian; ESKD, end-stage kidney disease; FSGS, focal and segmental glomerulosclerosis; H, Hispanic; INF2, inverted formin 2; U, unknown.

^aNumerator: number of individuals with FSGS, nephrotic syndrome, or chronic kidney disease in the family. Denominator: number of individuals with the mutation.

^bNew mutations in this study.

Table 1. Classification of FSGS by Underlying Cause

Classification	Etiology	Causes
Primary	Circulating permeability factor	• Idiopathic
Secondary	Glomerular hyperfiltration	• Reduced nephron mass ○ Congenital (low birthweight, kidney dysplasia) ○ Acquired nephron loss (eg, reflux nephropathy, diabetic kidney disease) • Adaptive response (obesity, sickle cell disease, cyanotic congenital heart disease)
	Viral infection	• HIV, parvovirus B19, cytomegalovirus
	Drugs and toxins	• Heroin, pamidronate, lithium, anabolic steroids
Familial	Podocyte gene disorders	• Nephrin, podocin, IFN2, α-actinin-4, CD2AP, WT1; TRPC6; phospholipase Cϵ1

Figure 1

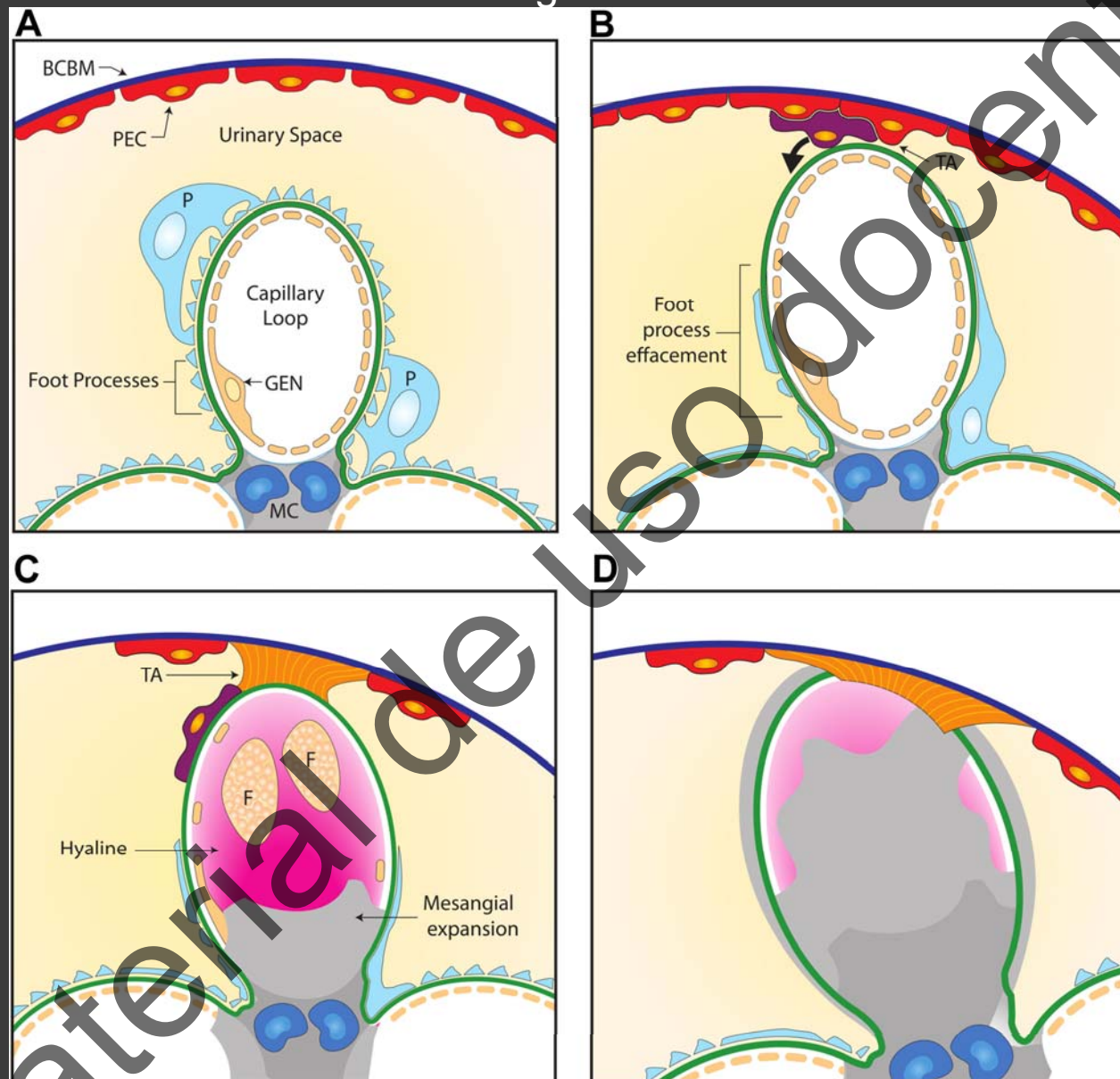


Figure 2

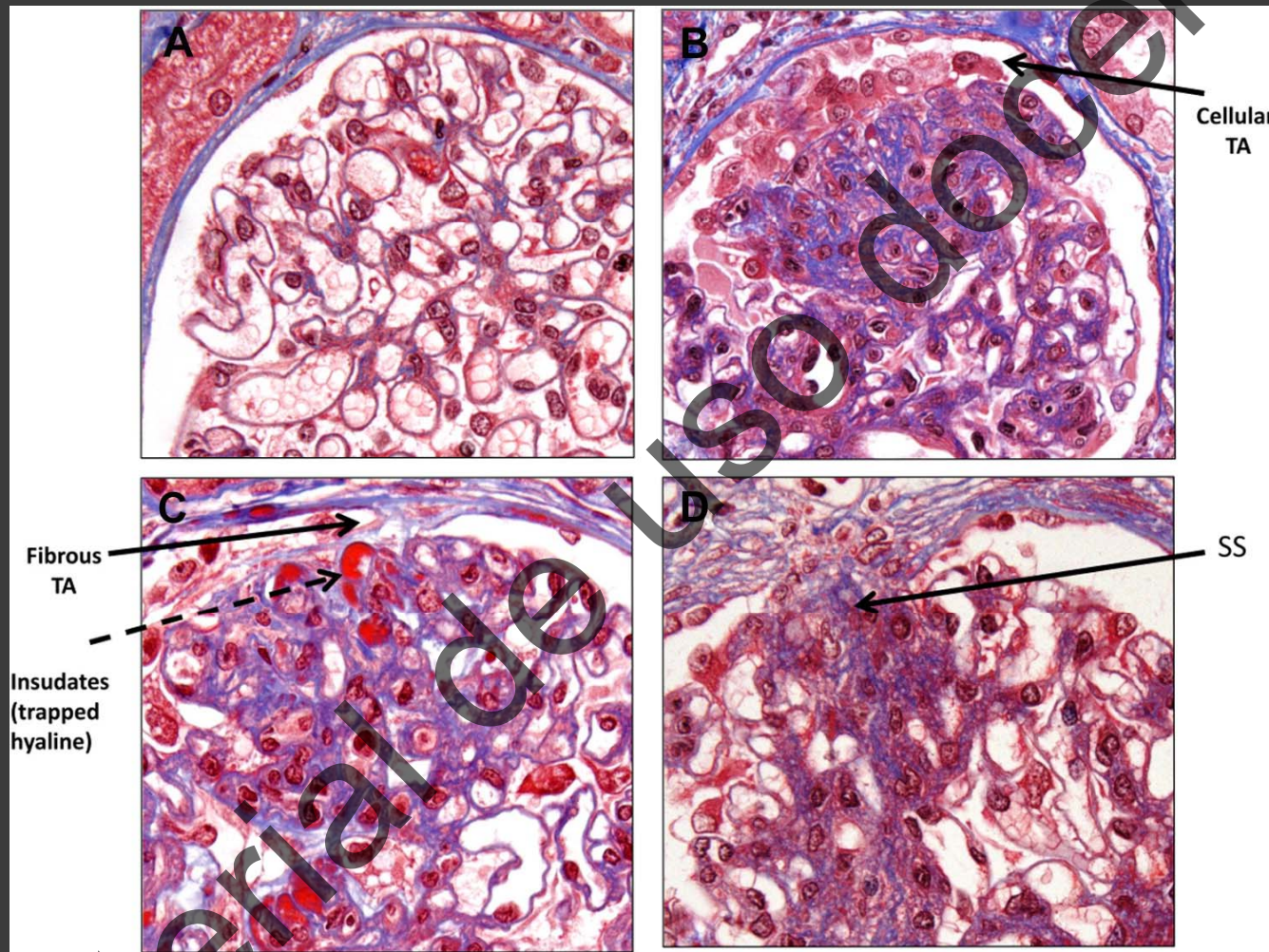


Figure 3

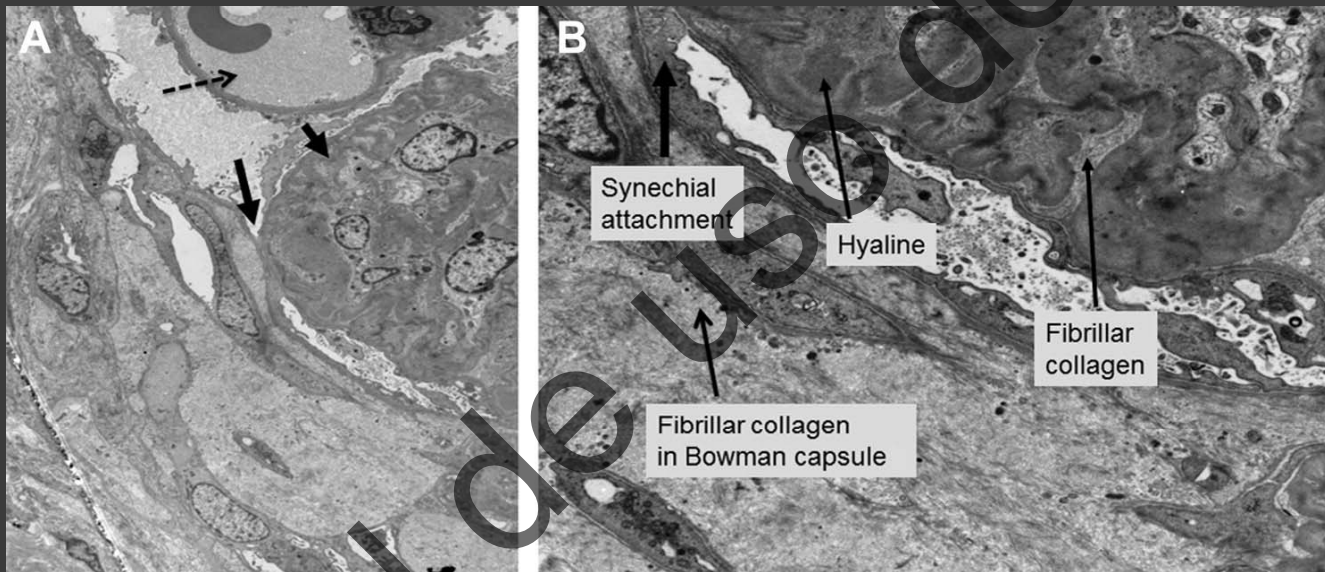
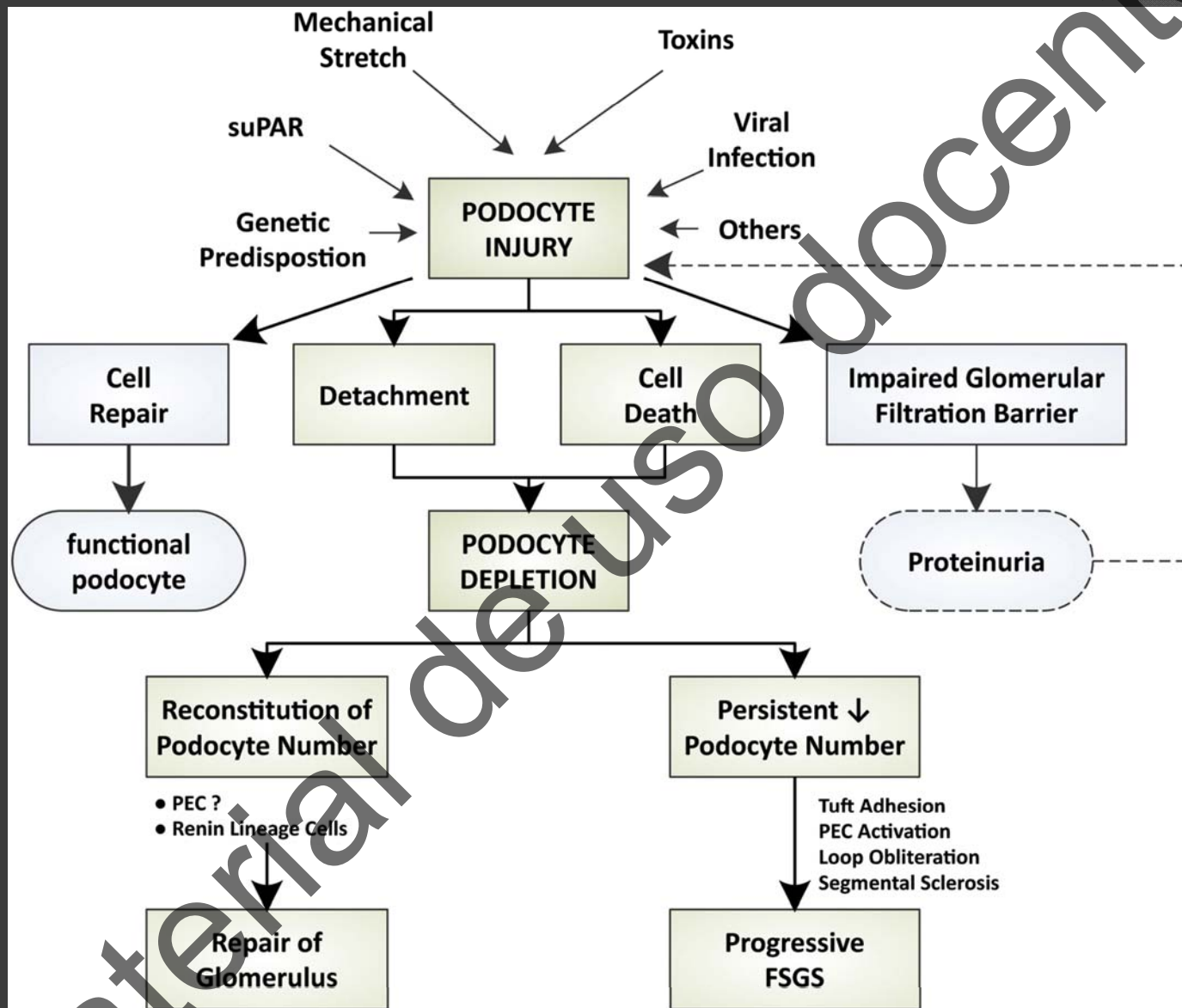
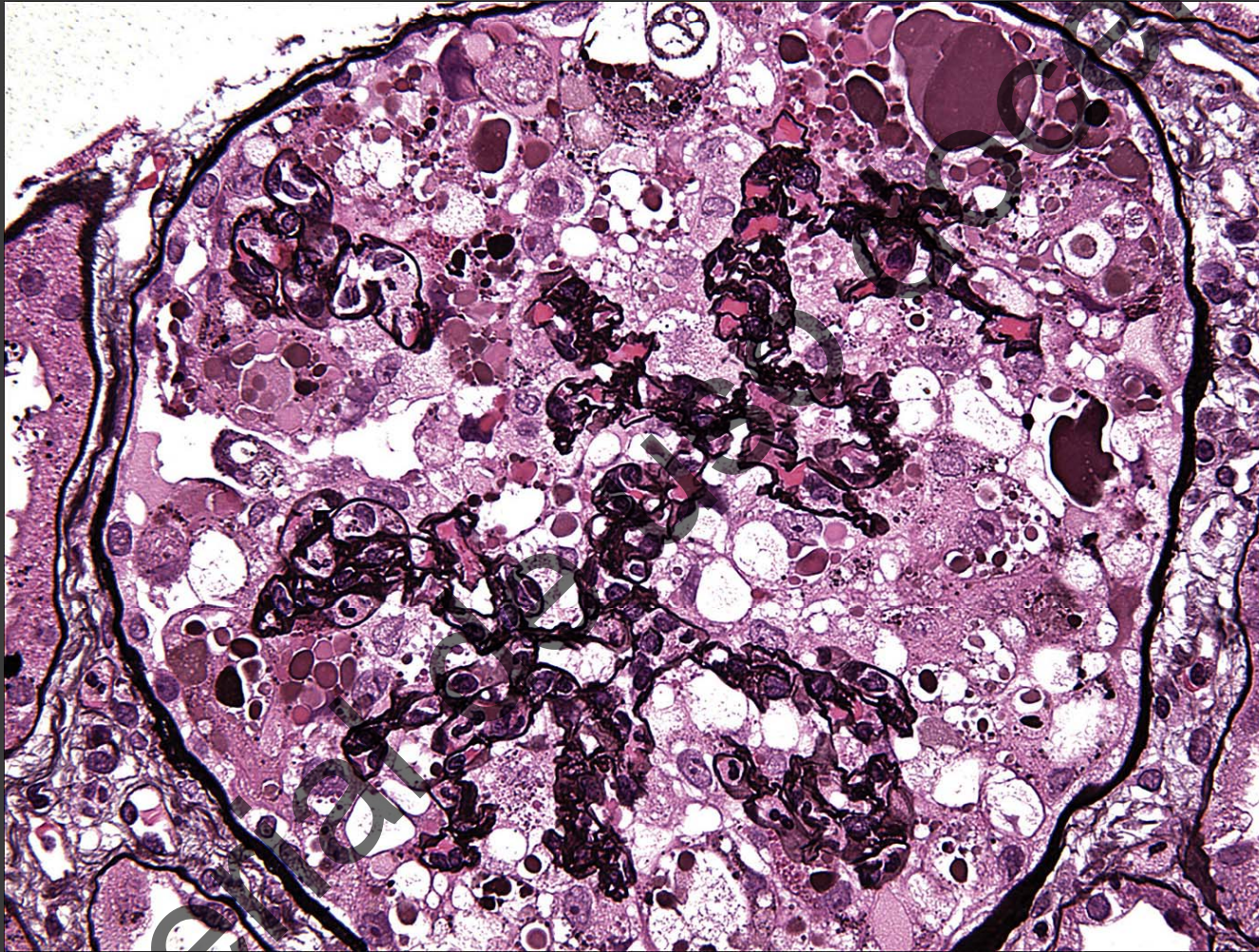


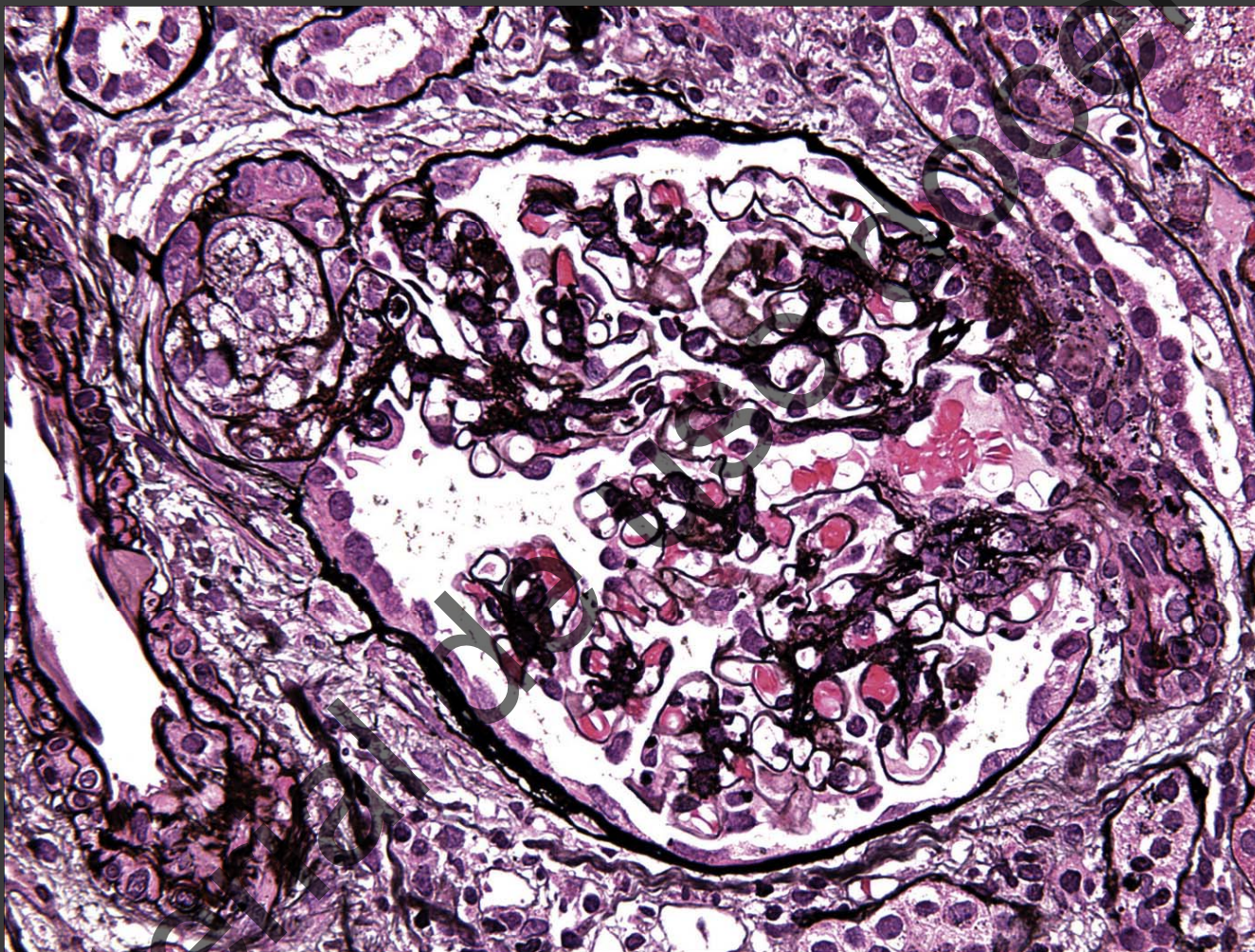
Figure 4



Colapsante



Tip variant



Variante Celular

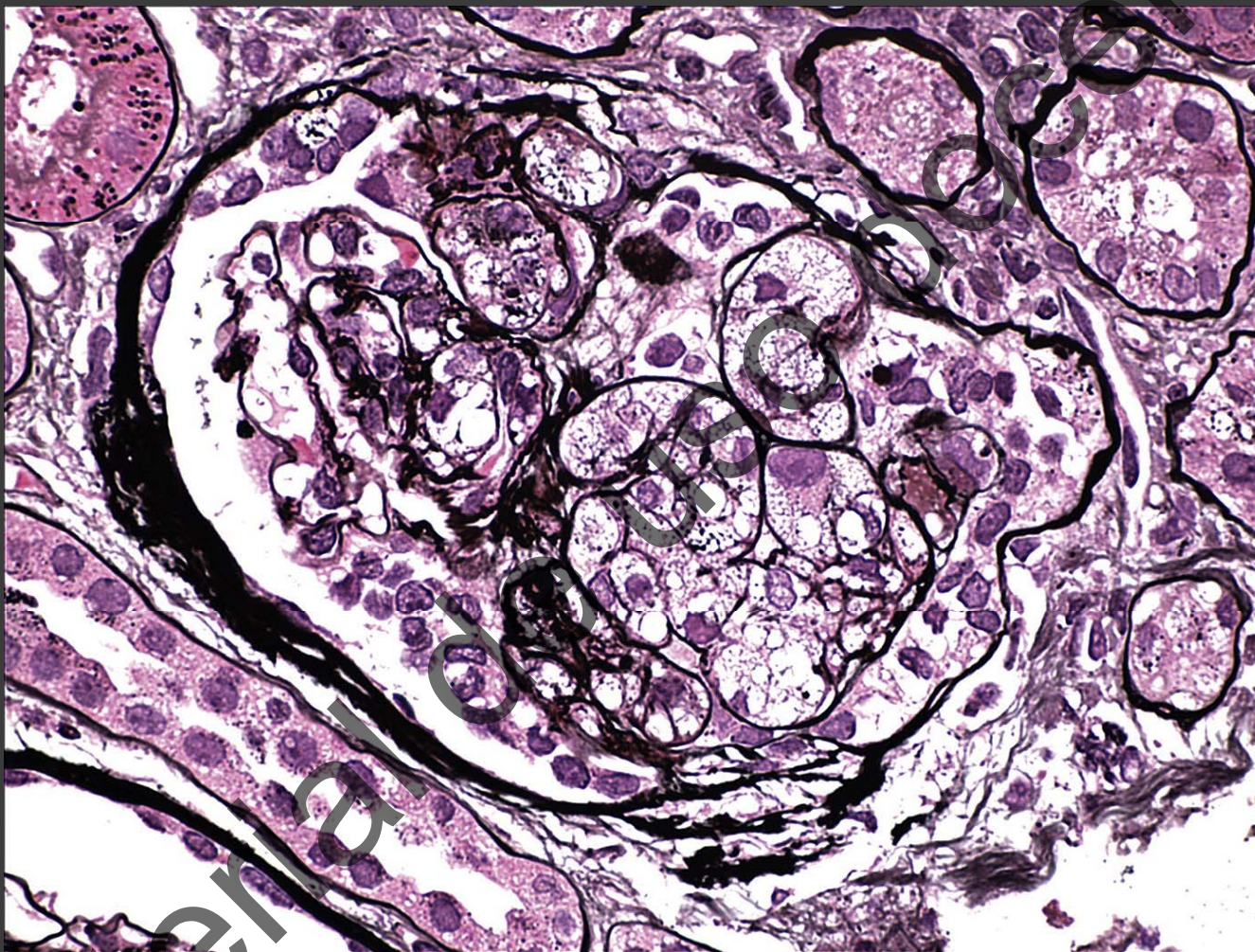


Figure 4

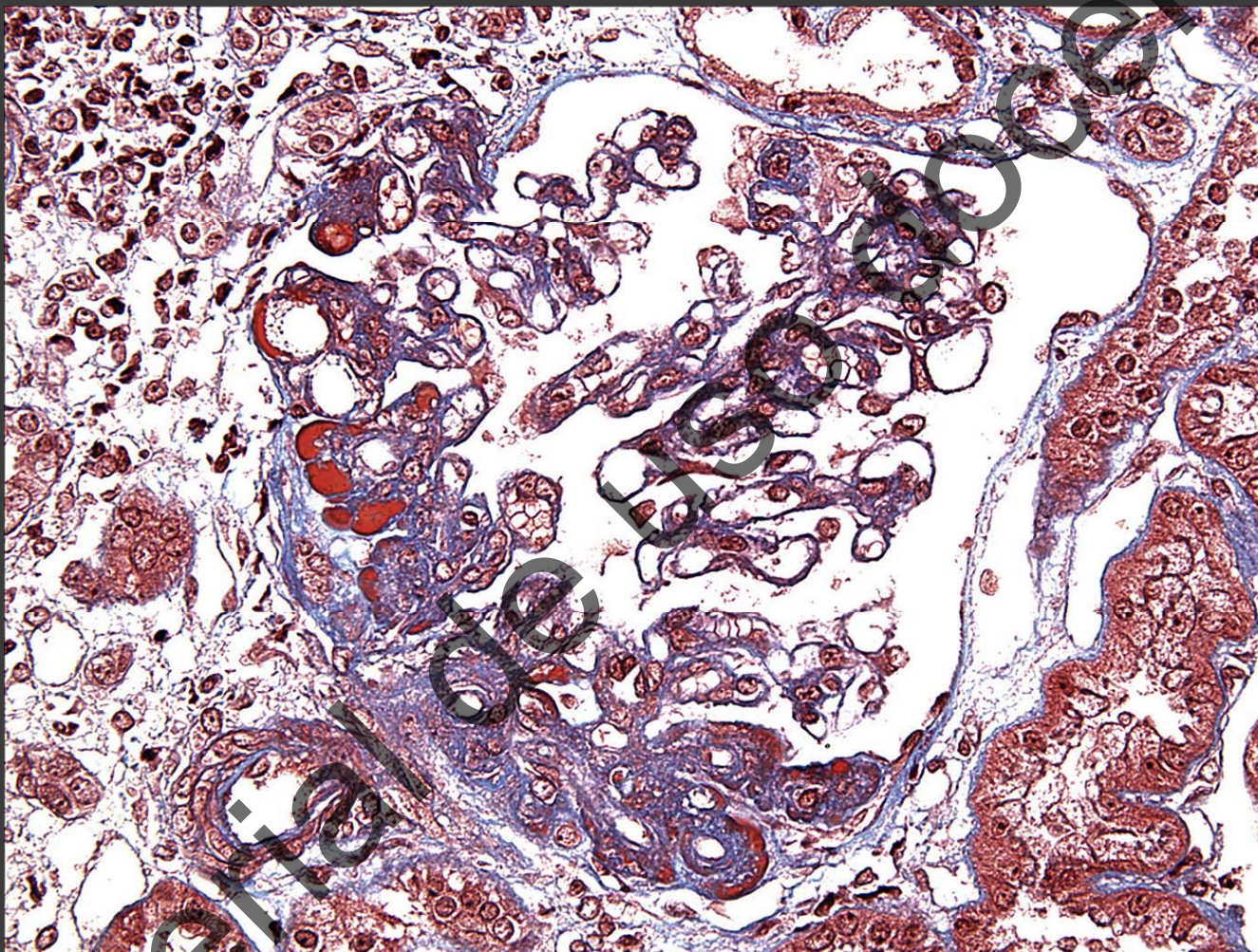
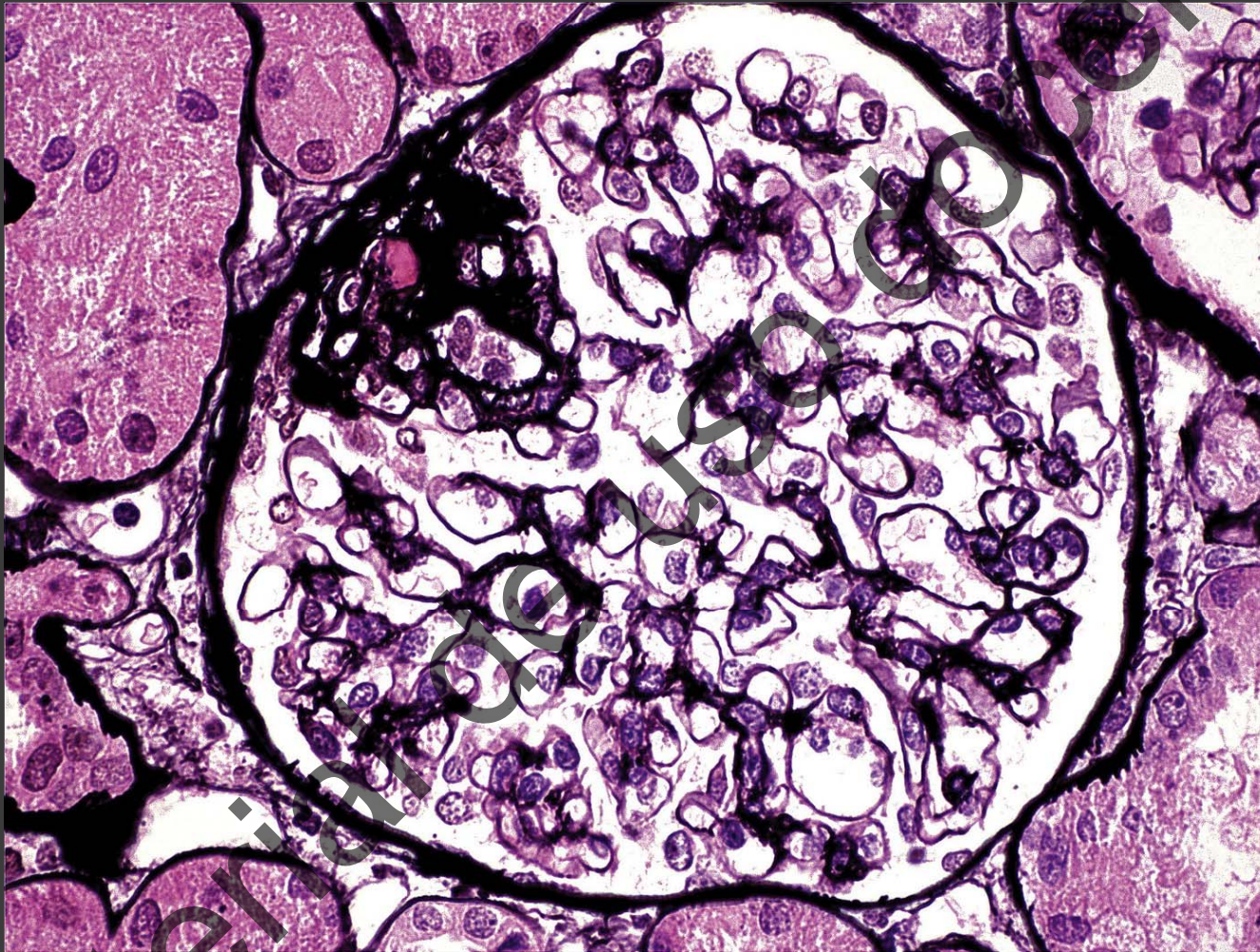
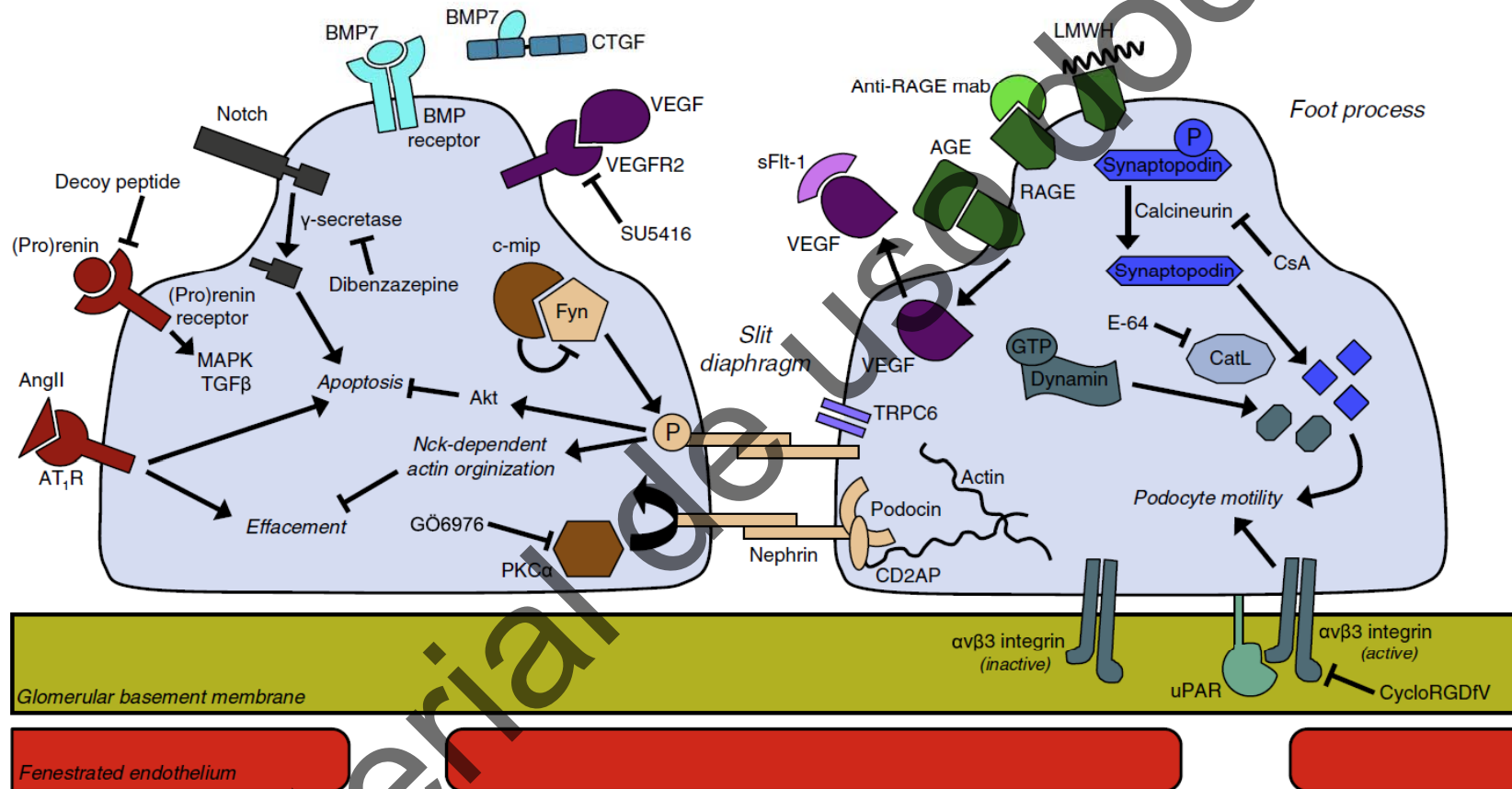
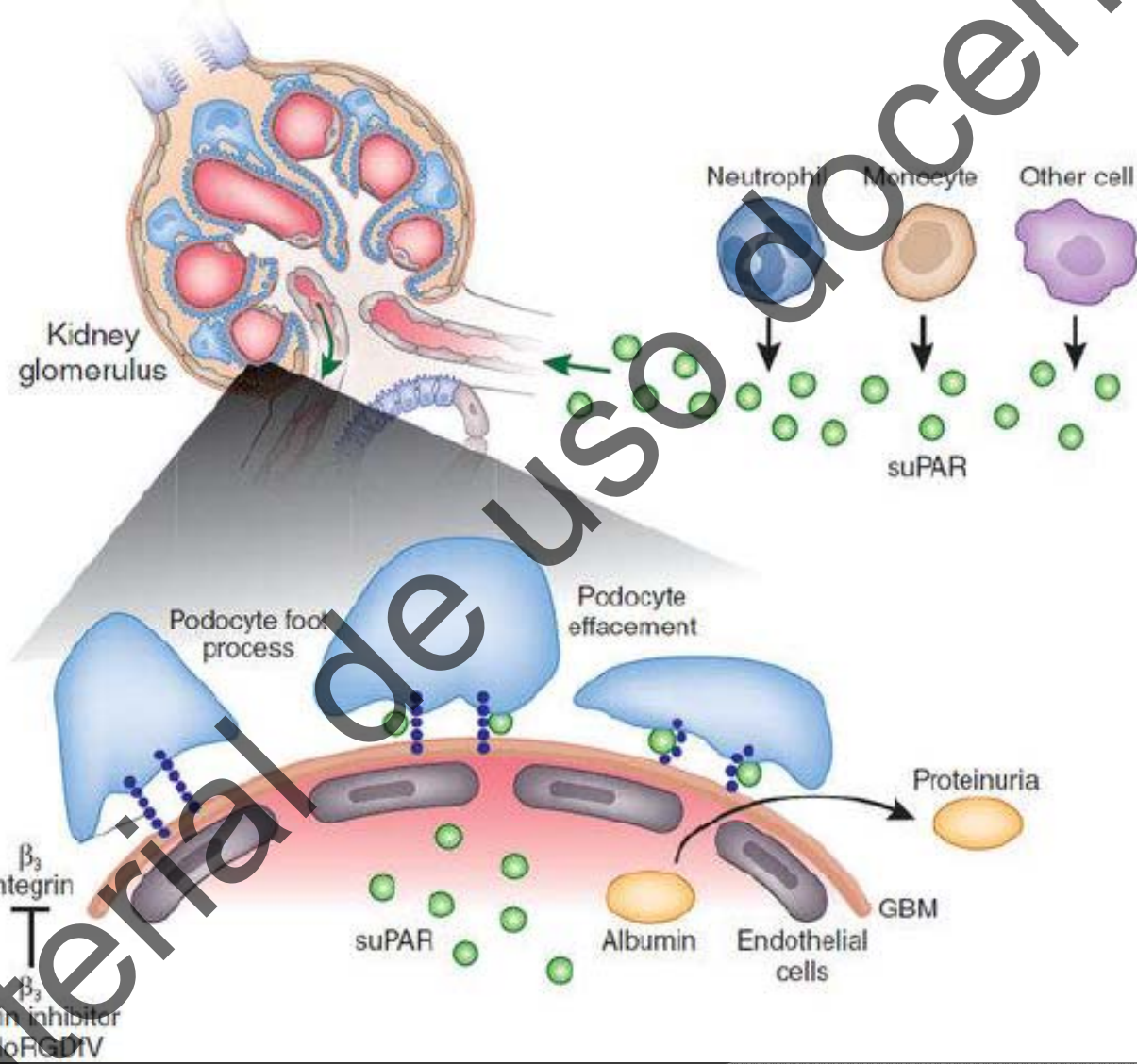


Figure 5

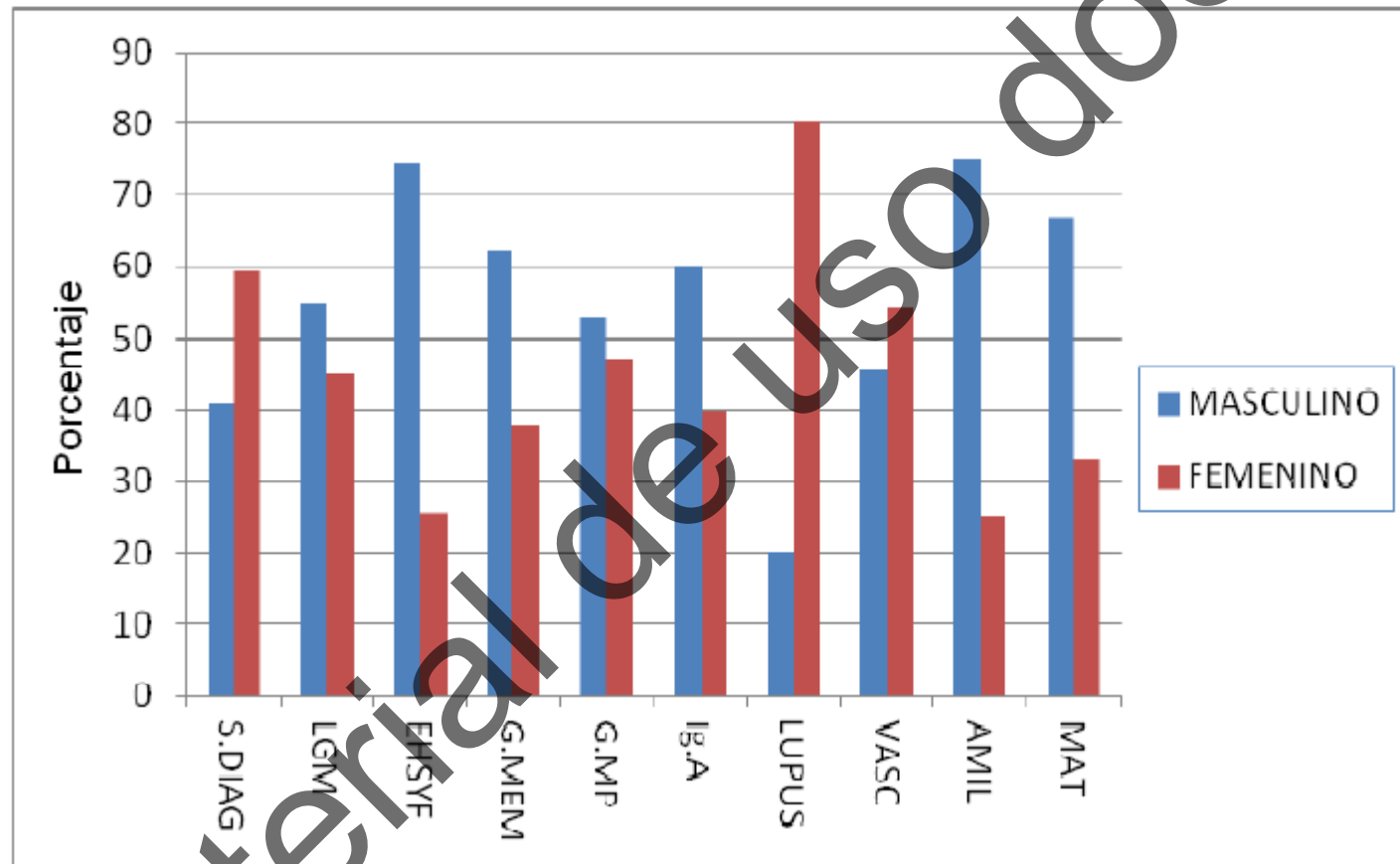


suPAR y activación de integrinas en Podocitos

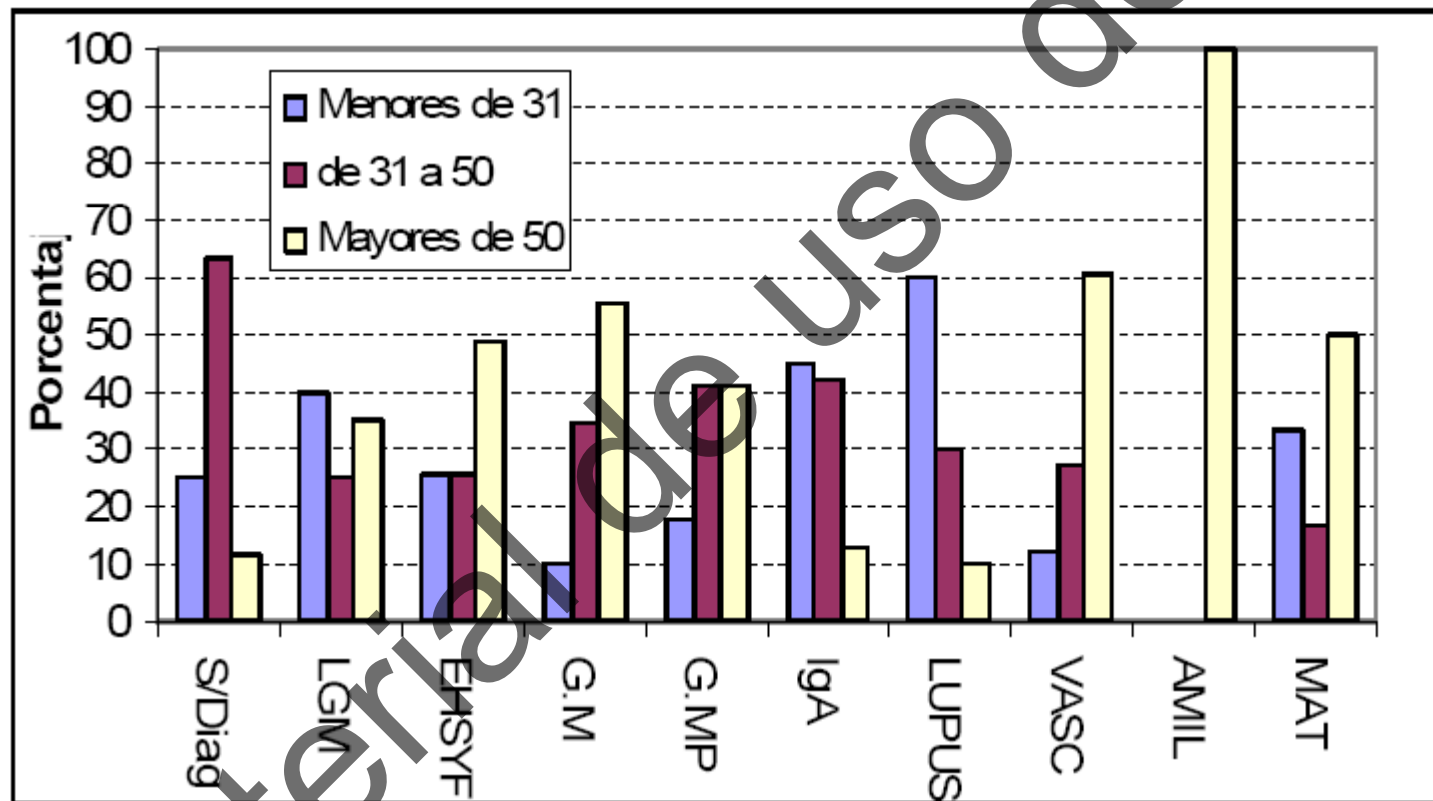




Distribución por sexo en las diferentes glomerulopatías. Período 2010-2012.



Edad al momento de la biopsia según glomerulopatía. Período 2010-2012



CAPÍTULO 3

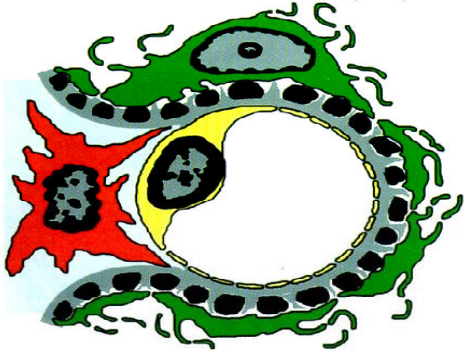
Nefropatía Membranosa.

3.1: Introducción.

En este capítulo se tratarán las recomendaciones de la Nefropatía Membranosa Idiopática (NMI).

El diagnóstico de Nefropatía Membranosa (NM) es realizado por biopsia renal y sus rasgos más importantes son el espesamiento de la pared capilar glomerular, celularidad glomerular, deposición de IgG y C3 a lo largo de la pared capilar en la inmunofluorescencia y cambios en la microscopía electrónica. La NM es una enfermedad típicamente

Idiopathic
Membranous Glomerulopathy



Secondary
Membranous Glomerulopathy



Membranosa

Idiopática (Ac PLA2R)

Secundaria

Neoplasmas

Infecciones

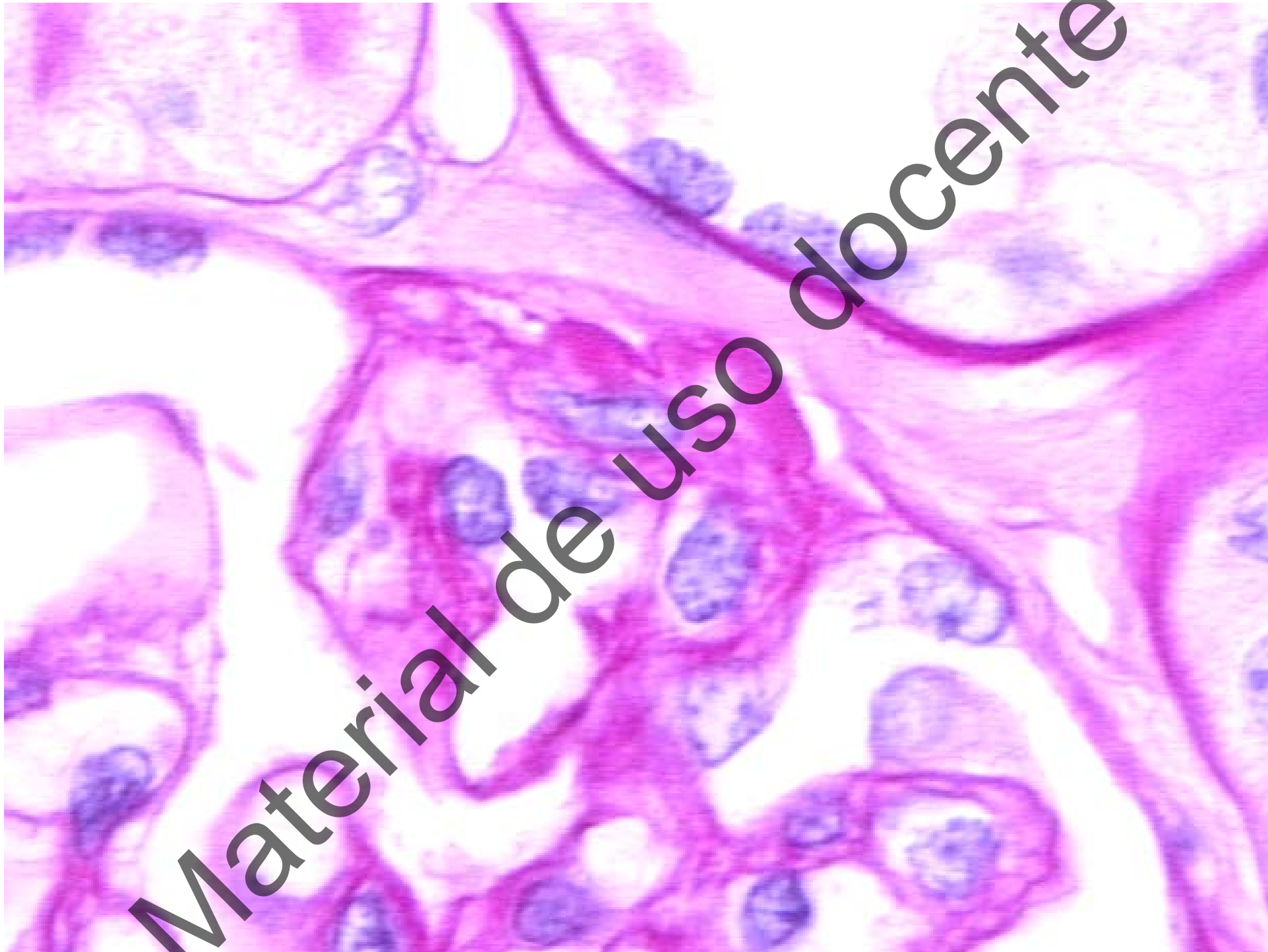
Drogas

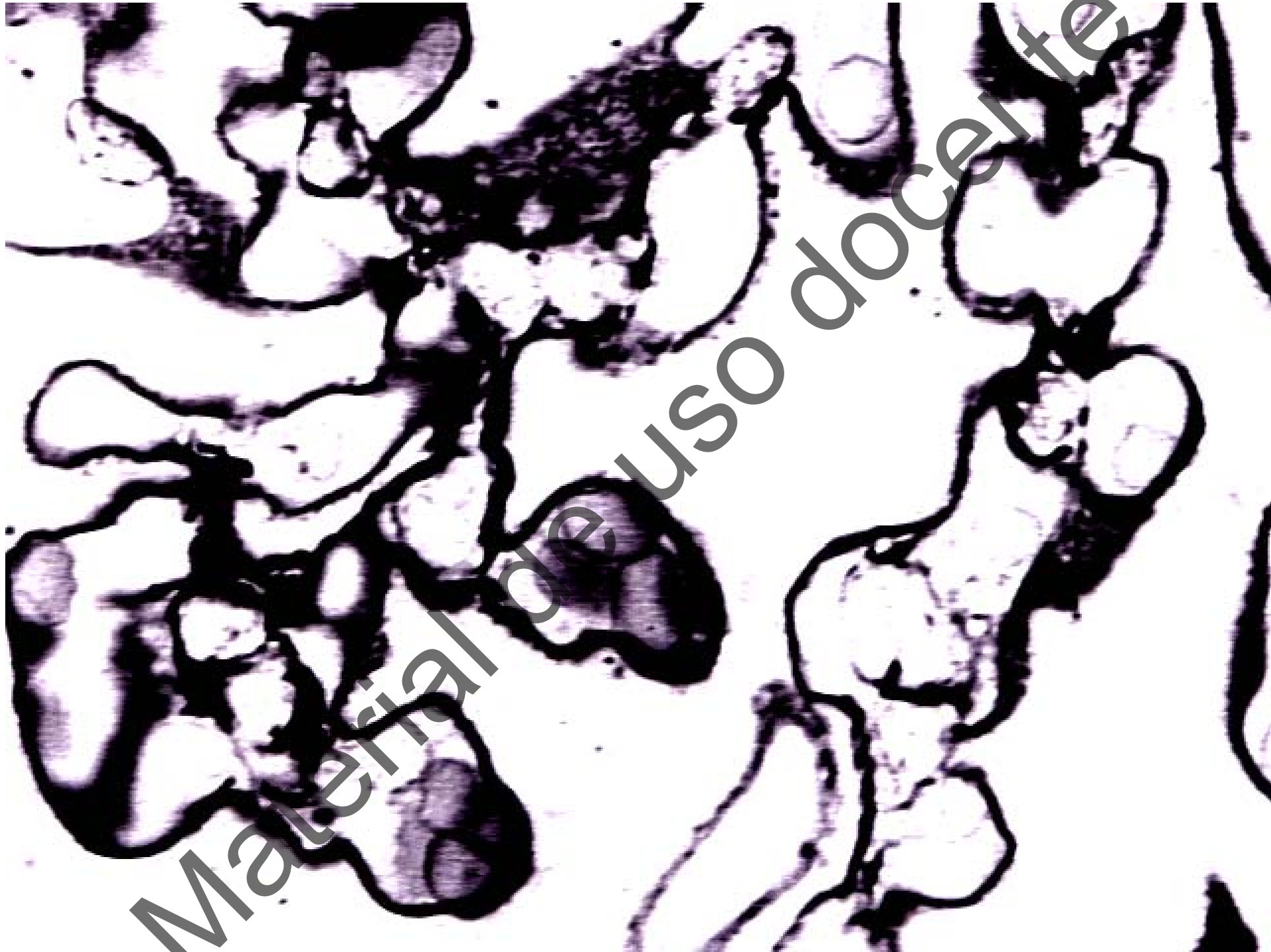
Tabla I. Causas de Glomerulopatía Membranosa secundaria

Infecciones	Neoplasias	Enf. Autoinmunes	Medicamentos
Hepatitis virus B Hepatitis virus C Sífilis Lepra Sarna Malaria Esquistosomiasis	Carcinoma de pulmón Mama Colon Estomago Riñón Esófago Melanoma Leucemia Linfoma (s/t no Hodgkin)	LES Conectivopatía mixta Poliartritis reumatoidea S de Sjogren Dermatomiositis Sarcoidosis Tiroiditis de Hashimoto Miastenia gravis S. de Guillan-Barre Snd. Antifosfolípidos Penfigoide bulloso Dermatitis herpetiforme	Penicilamina Sales de oro Captopril AINES.

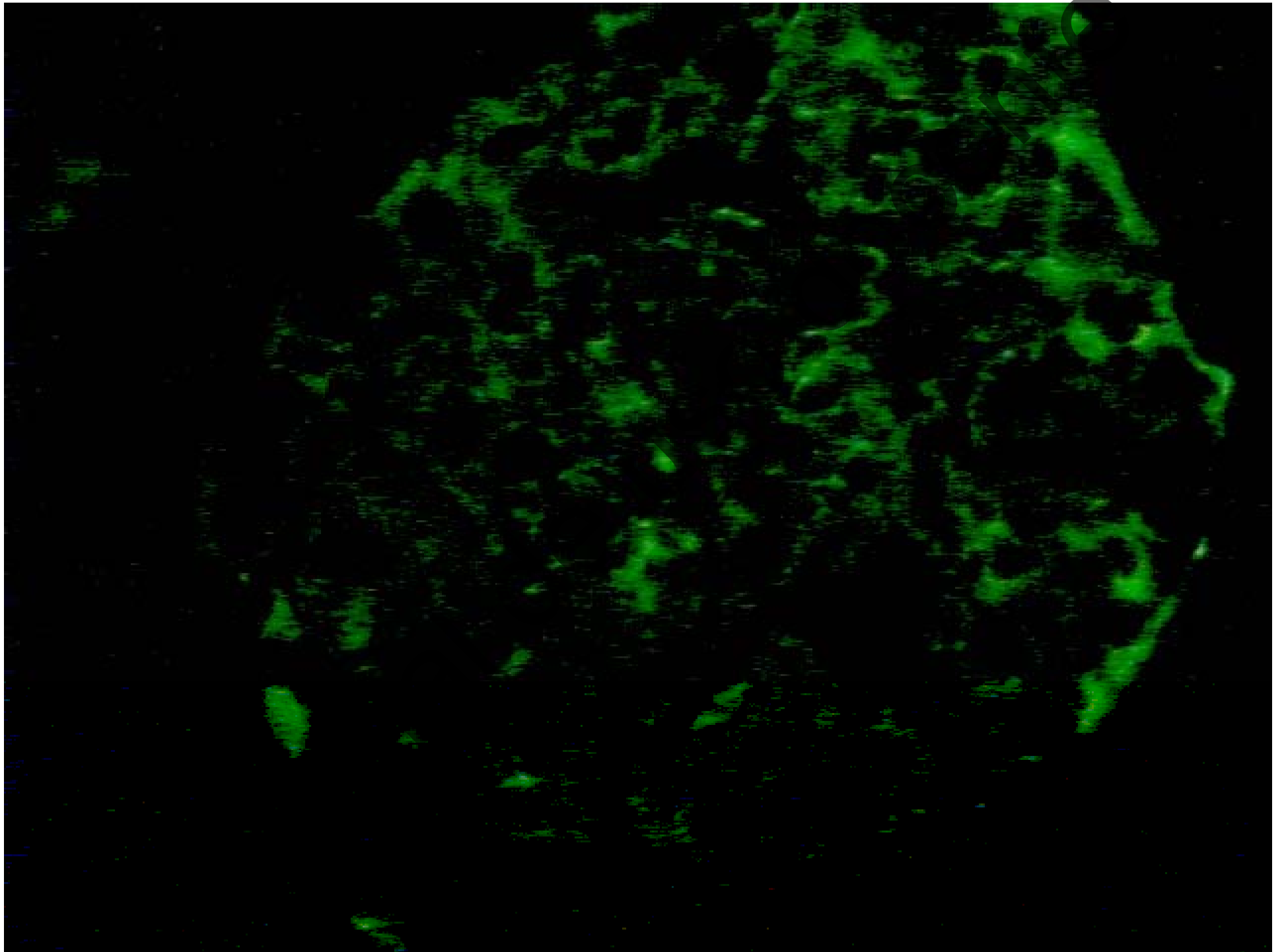
Para descartar estas etiologías, además de una anamnesis y examen físico completos, deberán solicitarse: serología y PCR virales y, según corresponda: mamografía, Fibrogastro y autoanticuerpos. Fibrocolonoscopia, TAC corporal total y/o PET y

Material de uso docente









● Neutral endopeptidase

● Phospholipase A₂ receptor

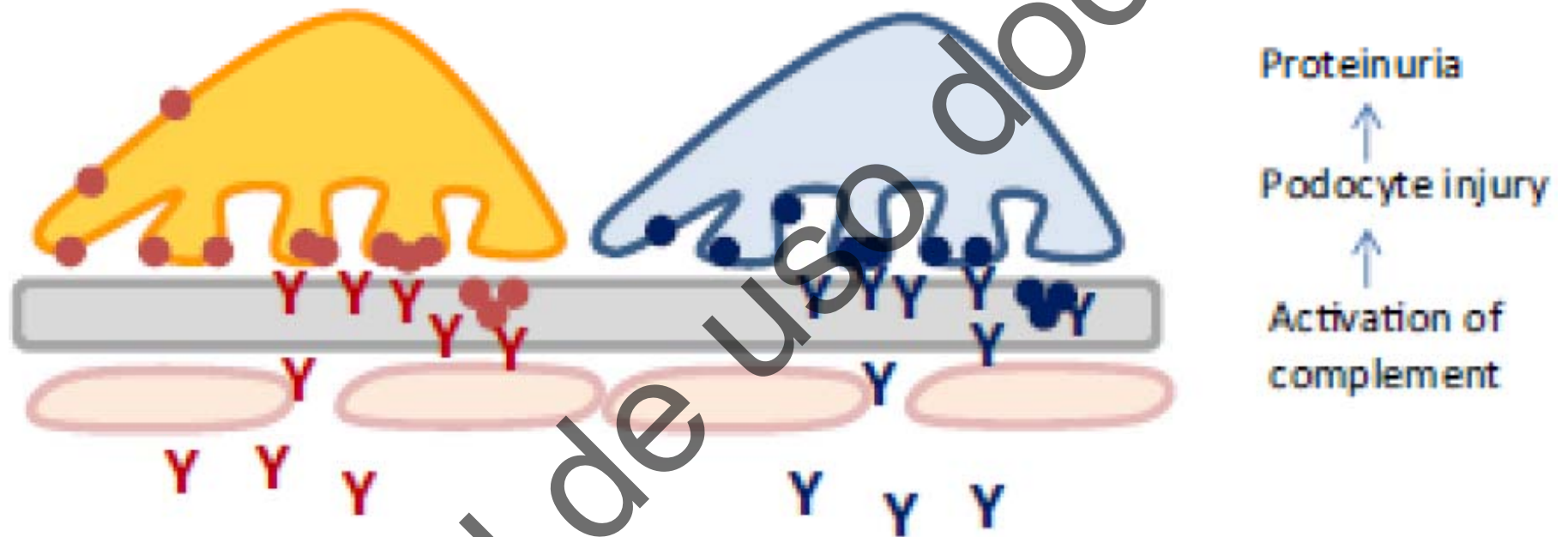


Figure 1. Proposed scheme of in situ formation of immune deposits in membranous nephropathy (MN). The in situ formation of immune complexes involves circulating antibodies binding to a native podocyte protein. Two antigenic targets have been identified: neutral endopeptidase (in alloimmune MN) and phospholipase A₂ receptor (in idiopathic MN). In both cases, the pathogenic antigens are integral glycoproteins of podocytes. The formation of subepithelial immune deposits and complement activation are responsible for functional impairment of the podocytes and proteinuria.

RONCO, DABIEC, 2010

Am J Nephrol 2014;40:29-35

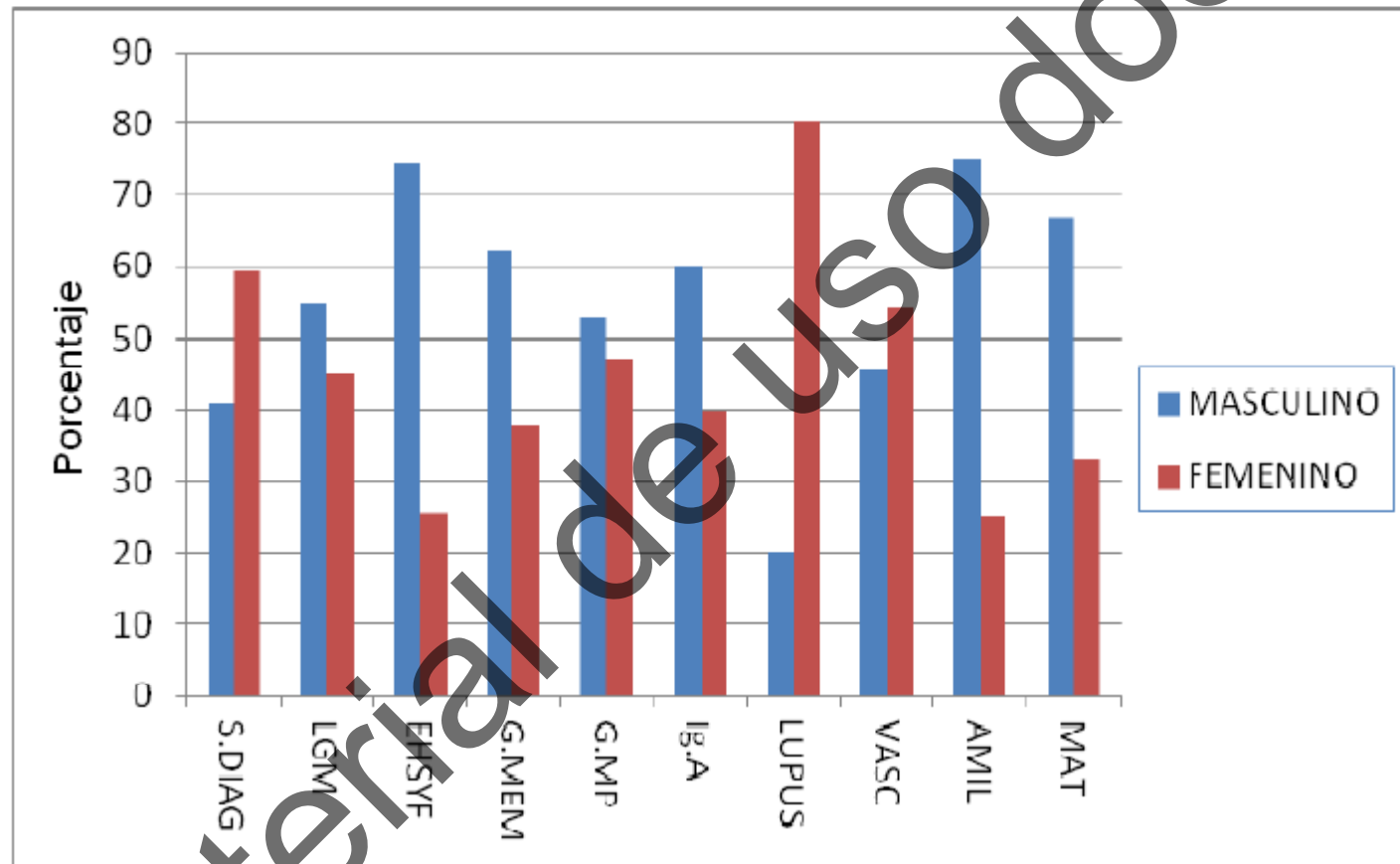
Prevalence of Cancer in Membranous Nephropathy: A Systematic Review and Meta-Analysis of Observational Studies

Leeaphorn N.a · Kue-A-Pai P.a · Thamcharoen N.a · Ungprasert P.c · Stokes M.B.b · Knight E.L.a

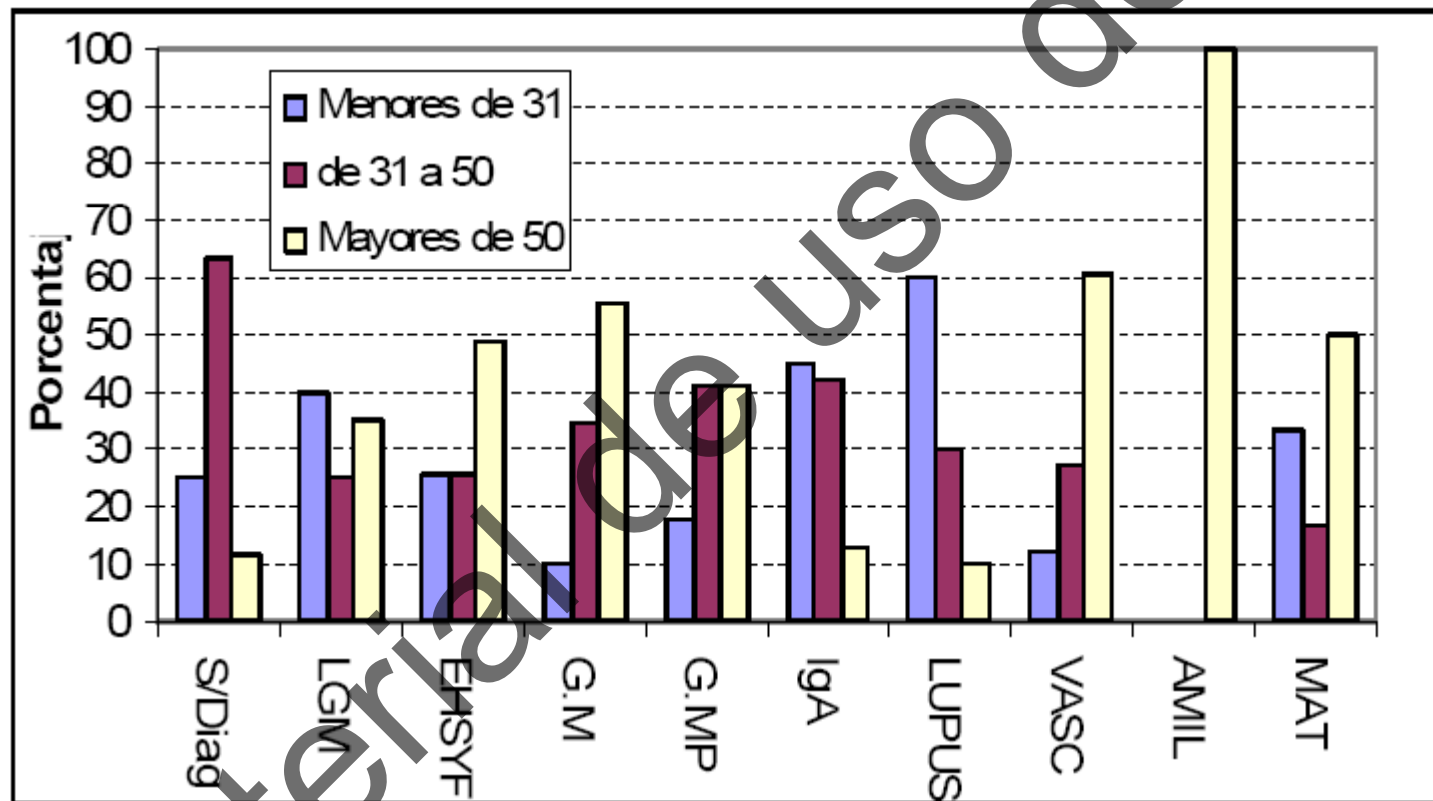
Type of malignancy	Bjørneklett et al. [9]	Lefaucheur et al. [8]	Rihova et al. [22]	Burstein et al. [6]	Cahen et al. [5]	Row et al. [4]	Total
Lung	6 (18.18)	8 (33.33)	3 (37.5)	2 (22.22)	1 (25)	2 (28.57)	22 (25.88)
Prostate	7 (21.21)	5 (20.83)	1 (12.5)	0 (0)	0 (0)	0 (0)	13 (15.29)
Hematologic	5 (15.15)	2 (8.33)	0 (0)	2 (22.22)	1 (25)	2 (28.57)	12 (14.11)
Colon/rectal	4 (12.12)	1 (4.16)	1 (12.5)	1 (11.11)	0 (0)	2 (28.57)	9 (10.58)
Breast	4 (12.12)	1 (4.16)	0 (0)	1 (11.11)	0 (0)	0 (0)	6 (7)
Stomach/esophagus	1 (3)	2 (8.33)	0 (0)	1 (11.11)	1 (25)	0 (0)	5 (5.8)
Bladder	2 (6)	1 (4.16)	0 (0)	1 (11.11)	0 (0)	0 (0)	4 (4.7)
Renal cell carcinoma	0 (0)	0 (0)	0 (0)	1 (11.11)	1 (25)	0 (0)	2 (2.35)
Larynx	0 (0)	1 (4.16)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Thymus	0 (0)	1 (4.16)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Mediastinum	0 (0)	1 (4.16)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Cervix/uterus	1 (3)	1 (4.16)	1 (12.5)	0 (0)	0 (0)	0 (0)	3 (3.5)
Hepatocellular	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)	1 (1.17)
Cholangiocarcinoma	0 (0)	0 (0)	1 (12.5)	0 (0)	0 (0)	0 (0)	1 (1.17)
Melanoma	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Skin, nonmelanoma	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Disseminated, unknown	1 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.17)
Wilms' tumor	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (14.28)	1 (1.17)

Values are number of cases (percentage). Number and percent of cases (in parentheses).

Distribución por sexo en las diferentes glomerulopatías. Período 2010-2012.



Edad al momento de la biopsia según glomerulopatía. Período 2010-2012



Glomerulopatía IgA

- Enfermedad glomerular crónica
 - Depósitos mesangiales predominantes de IgA
 - Diversas formas clínicas:
 - Hematuria recurrente
 - Alteraciones urinarias aisladas
 - Insuficiencia renal
-

Glomerulopatía IgA

↑ IgA1 circulante con
pobre galactosilación

Formación de Ac
anti IgA1 ↓ galactosil.

Depósitos o formación
Mesangial de IC IgG-IgA1

Receptores IgA	Activación de C'
-------------------	---------------------

- Daño mesangial
- Activación vías secundarias

Post-transplant Henoch-Schonlein
purpura de novo: Clinical/histological
discordance

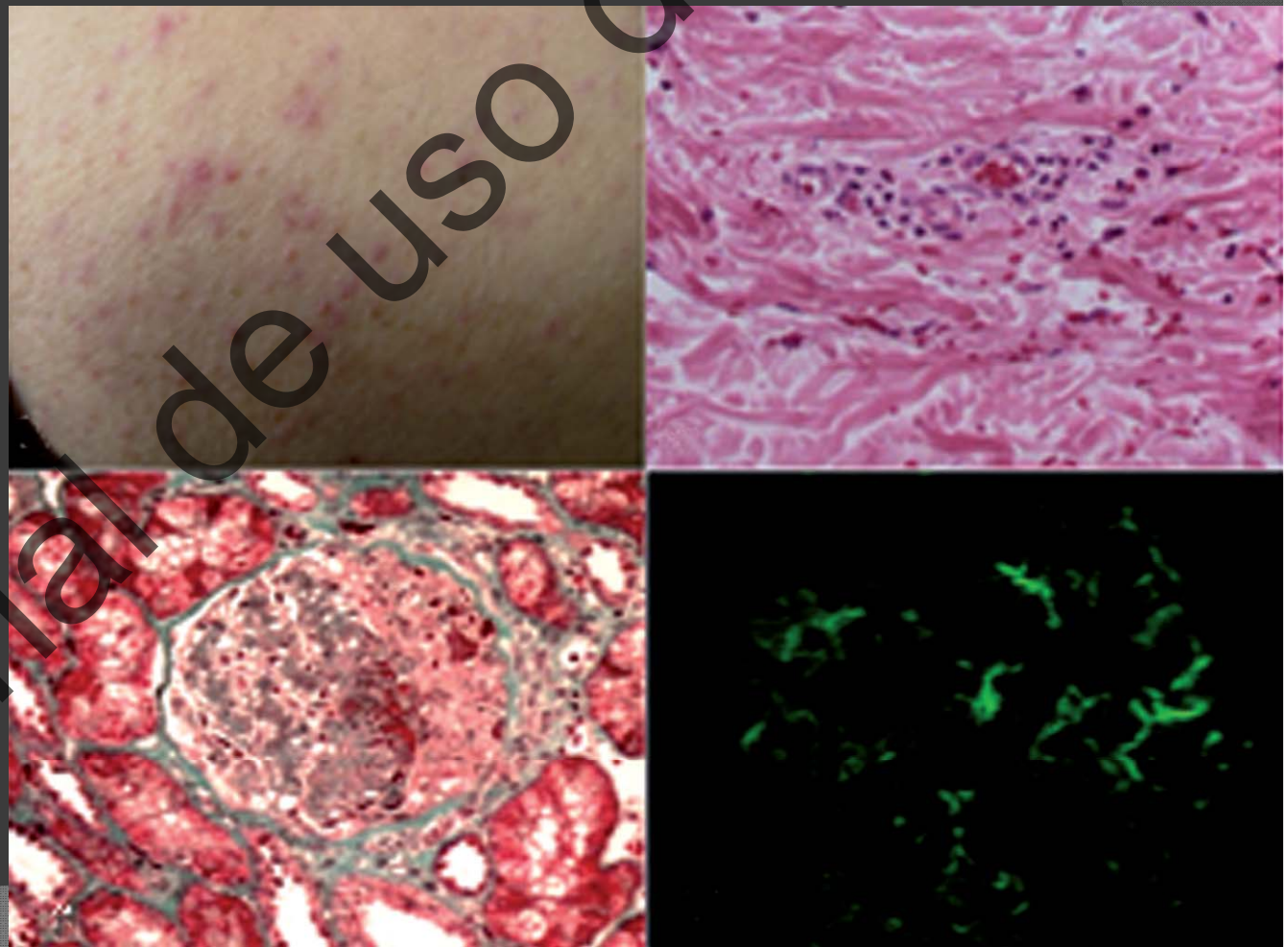
Nefrologia 2012;32(6):850-2

doi:10.3265/Nefrologia.pre2012.Jun.11468

Marcelo Nin¹, Rossana
Cordero¹, Lidice
Doufrechou², Alejandra
Larre-Borges²,
Virginia Coria¹, Nelson
Acosta¹,
Liliana Gadola¹, Sergio
Orihuela¹,
Francisco González¹,
Oscar Noboa¹

¹ Centro de Nefrología.
Facultad de Medicina.
Universidad de la
República. Montevideo
(Uruguay).

² Servicio de
Dermatología.
Facultad de Medicina.
Universidad
de la República.
Montevideo (Uruguay).



Nefropatía IgA en Uruguay: presentación clínica y evolución

Dres. Liliana Gadola*, Jimena Cabrera†, Nelson Acosta Marichal‡, Ana Panuncio§, María Haydé Aunchaina¶, Virginia Coria***, Alicia Petraglia††, Gabriela Ottati‡‡, Silvia Melessi§§, Pablo Ríos Sarro¶¶, Beatriz Gelabert***, Cristina Verdaguer†††, Nelson Dibello‡‡‡ Cecilia Burgos§§§, Raquel Arregui¶¶¶, José Santiago****, Federico García Rey††††, Fernanda Varela††††, Sebastián Marton††††, Gabriela Campeas‡‡‡, María García Taibo§§§§, Mercedes Chá¶¶¶¶, Luis Vilardo*****, Eduardo Rugnitz†††††, Raúl Mizraji‡‡‡‡, Alfredo Maino§§§§§, Sylvia Ballardini¶¶¶¶¶, Alejandro Operti*****, Pierina Borggini†††††, Patricia Cuña‡‡‡‡, Ben Szpinak§§§§§, Soledad Brovia¶¶¶¶¶, Mary Antúnez*****, Graciela Desiderio†††††, Óscar Noboa‡‡‡‡‡, Emma Schwedt‡‡‡‡‡, Hena Caorsi‡‡‡‡‡, Francisco González-Martínez‡‡‡‡‡, Carlota González§§§§§§, Mariela Garau¶¶¶¶¶¶



Tabla 1. Características y forma de presentación clínica (según declaración de nefrólogo tratante al RUG) de la cohorte global y de las poblaciones de los períodos 1985-1999 y 2000-2009.

	<i>Cohorte global</i>	<i>1985-1999</i>	<i>2000-2009</i>
Número total de pacientes incluidos	341	113	228
Sexo masculino	220 / 341	79 / 113	141 / 228
Edad (años) media $\pm$ DS	31 $\pm$ 13	30 $\pm$ 13	31 $\pm$ 13
Creatininemia inicial (mg/dl) media $\pm$ DS	1,6 $\pm$ 1,8	1,5 $\pm$ 1,4	1,6 $\pm$ 2
PAS inicial (mmHg) media $\pm$ DS	134 $\pm$ 26	133 $\pm$ 22	135 $\pm$ 28
PAD inicial (mmHg) media $\pm$ DS	82 $\pm$ 18	82 $\pm$ 16	81 $\pm$ 18
Alteraciones urinarias asintomáticas (%)**	41,8	34,4	47 *
Macrohematuria (%)	24,7	33,7	20,5 *
Síndrome nefrótico (%)	9,7	9,1	10
Síndrome nefrítico (%)	8,7	7,1	9,5
IRC (%)	6,4	7,1	6
GNRP (%)	3,7	0	5,5 *
HTA (%)	3,3	5,1	2,5
IRA (%)	1,3	0	2

* χ^2 p < 0,05 1° vs 2° período

** Forma clínica: % de los pacientes con datos en cada grupo.

Cohorte global 298 ptes / 1° per 119 ptes / 2° per 179 ptes

Tabla 3. Factores de riesgo de progresión a filtrado glomerular estimado (FGe) menor de 60 ml/min, ingreso a TSR o fallecimiento.

	<i>Análisis univariado</i>	<i>Análisis multivariado</i>
Proteinuria inicial mayor a 1 g/d	0,023 *	
HTA	0,004 *	
FG inicial menor de 60 ml/min	< 0,001 *	
Creatininemia inicial mayor a 2,5 mg/dl	< 0,001 *	** < 0,05
Semilunas	0,025 *	
Proliferación endocapilar	0,007 *	
Daño túbulo-intersticial	< 0,001 *	

Análisis univariado, chi2 * $p < 0,05$ y análisis multivariado ** $p < 0,05$.

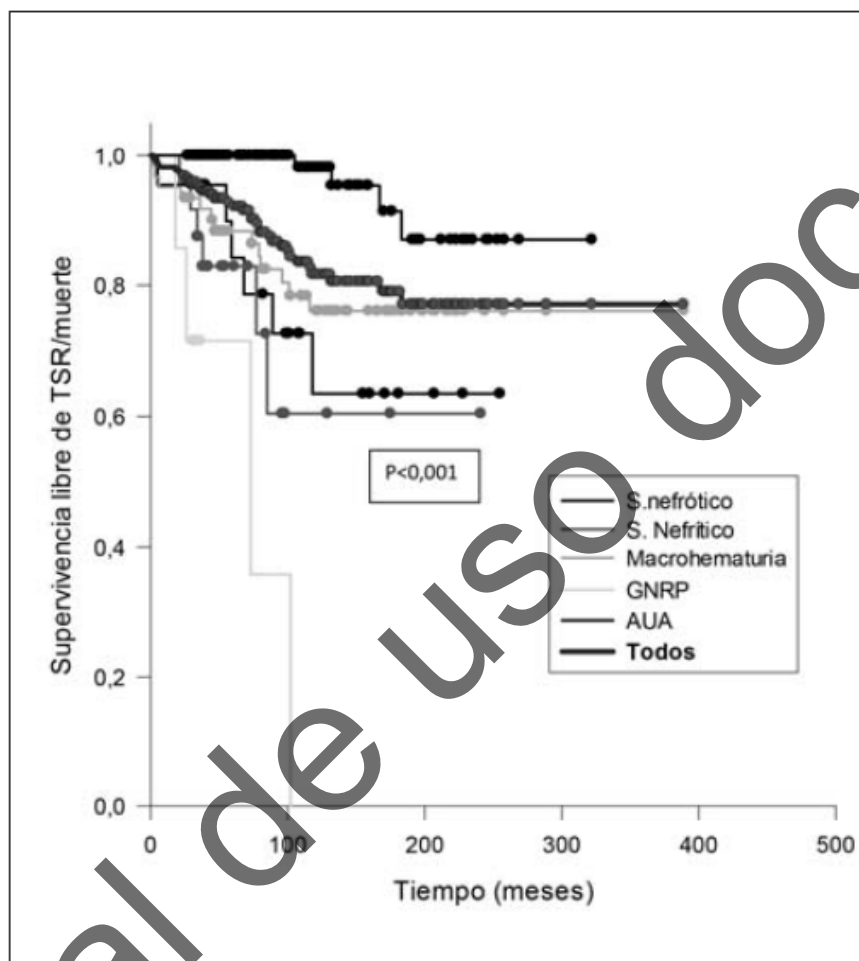


Figura 3. Curvas de supervivencia de pacientes con nefropatía IgA, global y según presentación clínica definida por nefrólogo tratante al ingreso al RUG. Síndrome Nefrótico. Síndrome Nefrítico. Macrohematuria. GNRP: Glomerulonefritis rápidamente progresiva, AUA: Alteraciones urinarias asintomáticas, (test de Breslow, * $p < 0,001$)

Review

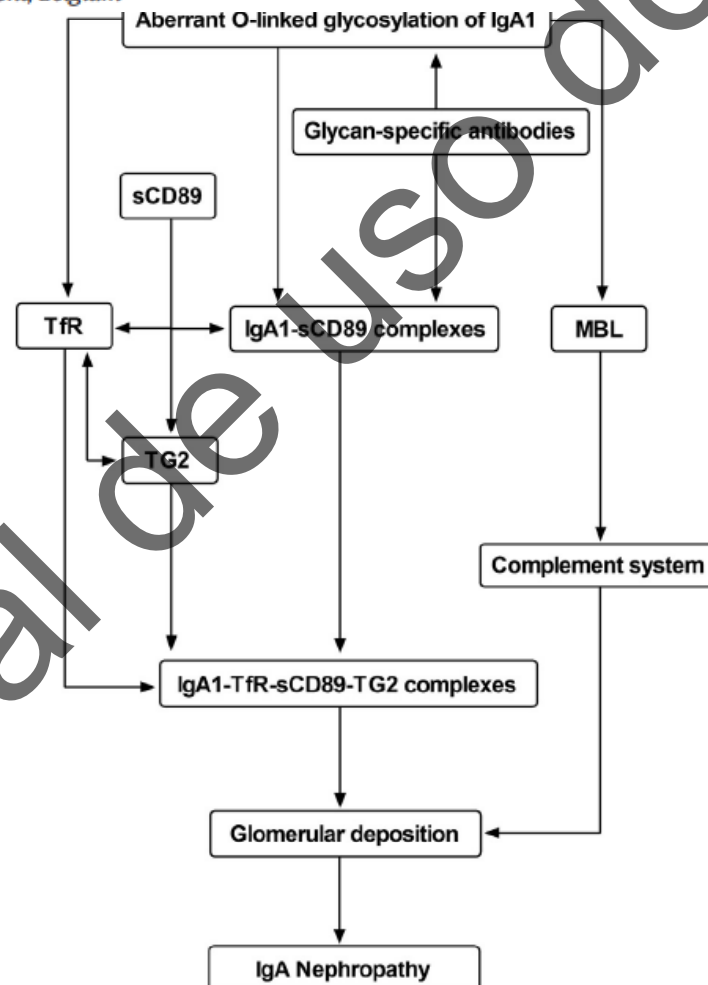
Diagnosis and monitoring of IgA nephropathy: the role of biomarkers as an alternative to renal biopsy

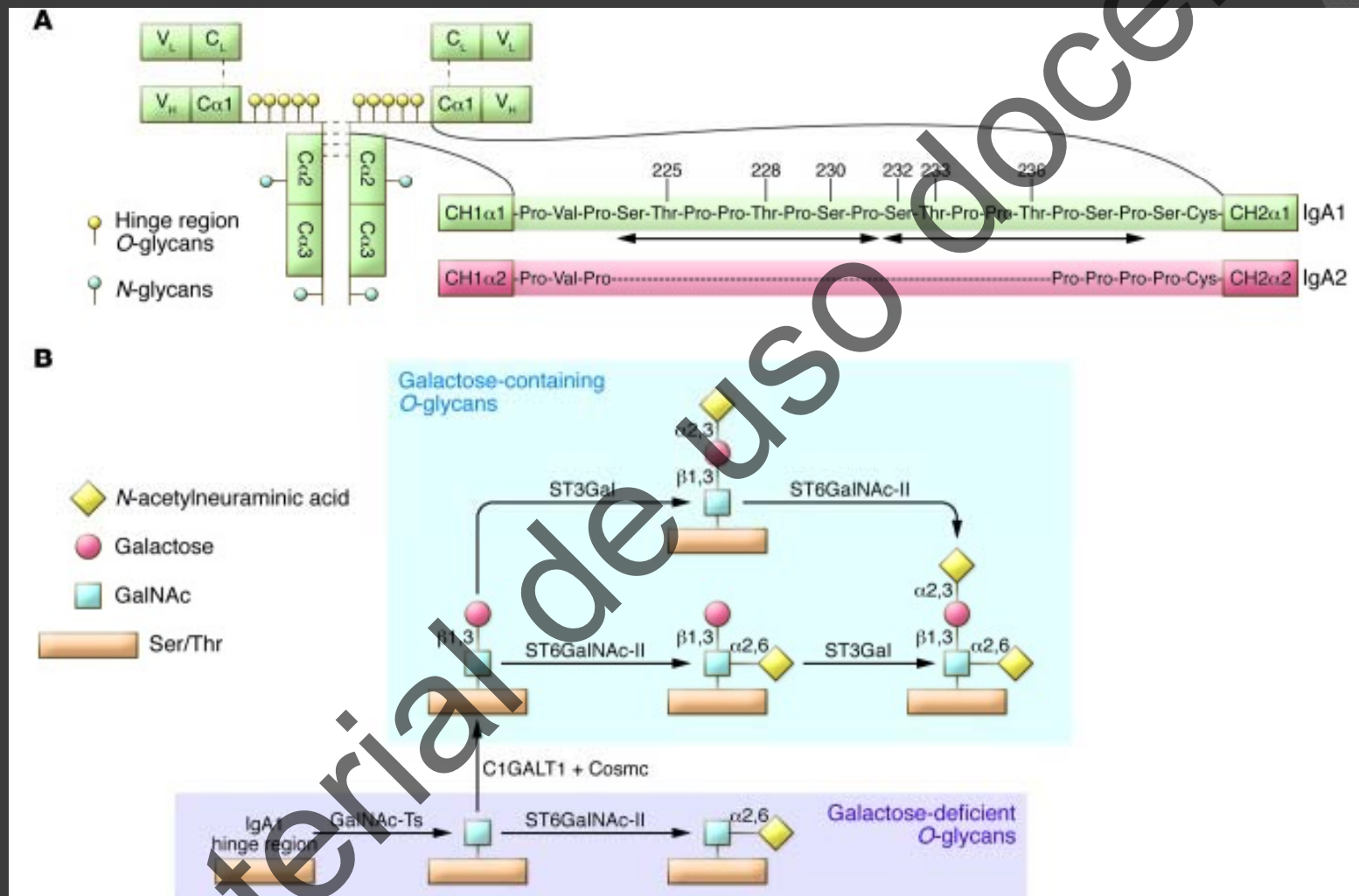
Rafael N. Moresco^{a,b}, Marijn M. Speeckaert^c, Joris R. Delanghe^{a,*}

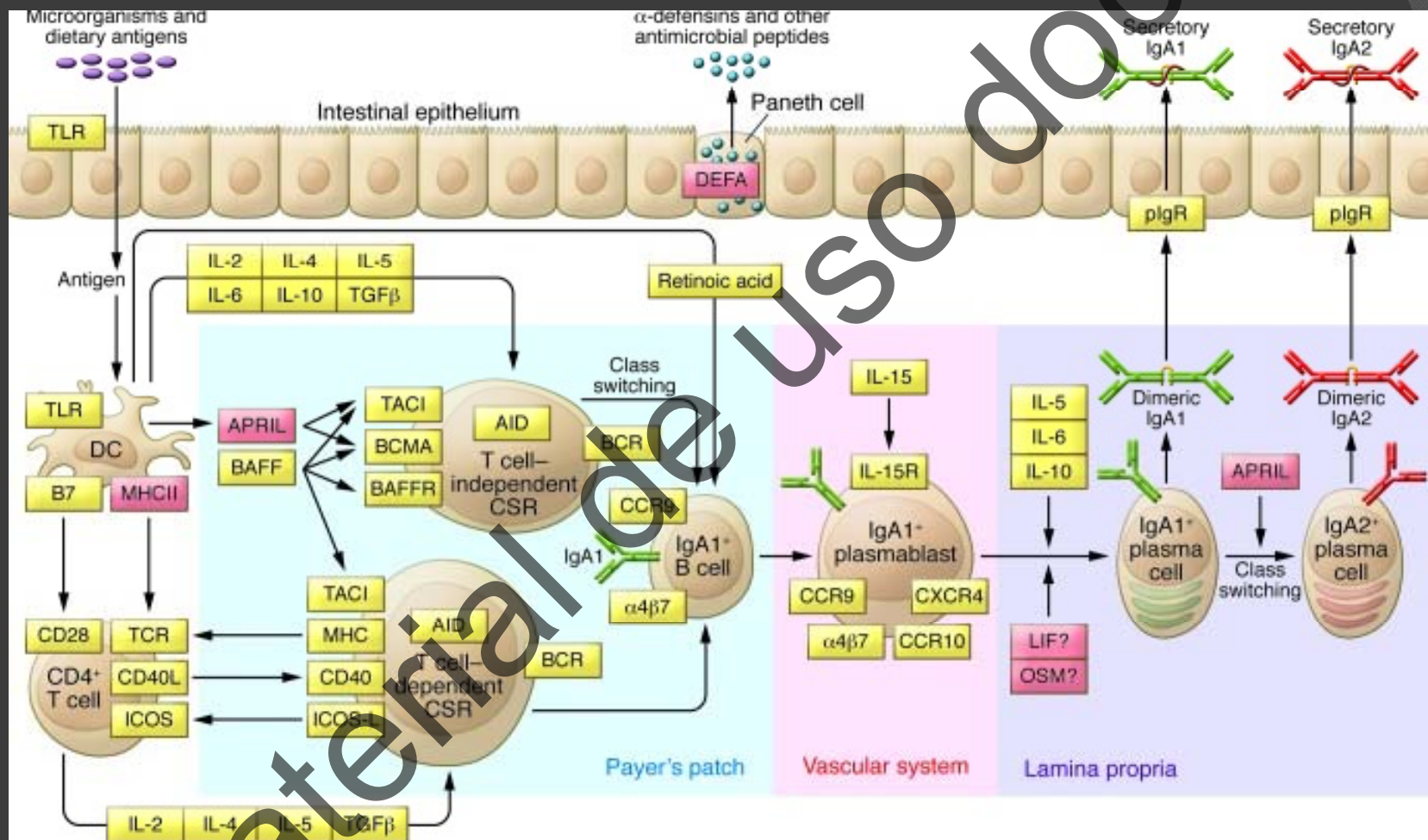
^a Department of Clinical Chemistry, Ghent University Hospital, Gent, Belgium

^b Department of Clinical and Toxicological Analysis, Federal University of Santa Maria, Santa Maria, Brazil

^c Department of Nephrology, Ghent University Hospital, Gent, Belgium







Incidencia de glomerulopatías primarias. Período 2010-2012

	1998-1999		2003-2004		2008-2009		2010-2012	
Diagnóstico	n	TI	n	TI	n	TI	n	TI
Sin diagnóstico c/biopsia	39	7.76	17	3.38	30	5.71	44	5.70
LGM	18	3.58	22	4.31	18	3.43	40	5.19
HFS	51	10.15	41	8.02	22	4.19	47	6.09
G. Membranosa	22	4.38	19	3.72	33	6.28	61	7.91
G. Membranoproliferativa	7	1.39	3	0.59	2	0.38	17	2.20
N. IgA	28	5.57	37	7.24	66	12.57	100	12.97
G. intracapilar difusa	2	0.4	3	0.59	3	0.57	4	0.52
G. Focal (No IgA)	3	0.6	3	0.59	1	0.19	1	0.13
G. Esclerosante crónica	7	1.39	3	0.59	6	1.14	3	0.39

Síndrome Nefrítico con complemento bajo

● Primaria

- Post-infecciosa
 - Strep β hemolítico
 - otros
- GN Membranoproliferativa
 - HVC
 - parásitos

● Sistémica

- LES
- Endocarditis
- crioglobulinemia

Síndrome Nefrítico con complemento normal

● Primaria

- IgA
- Alport's
- ANCA+ GNRP

● Sistémica

- Goodpasture's
- Vasculitis
- Schonlein Henoch
- TTP/HUS

Síndrome Nefrótico

● Renal

- LGM
- Membranosa
- HFS

● Sistémico

- DM
- MM/Amiloidosis
- LES

Síndrome Nefrítico con proteinuria nefrótica

● Renal

- NIgA
- Membranoproliferativas
- Post infecciosas

● Sistémico

- Schonlein Henoch
- LES

Clasificación

- ⦿ Clínica
- ⦿ Complemento
- ⦿ Patrón histopatológico
 - Óptica
 - IF
 - ME
- ⦿ Marcadores humorales
- ⦿ **Razonamiento clínico**