Quoi de Neuf en Nephrologie

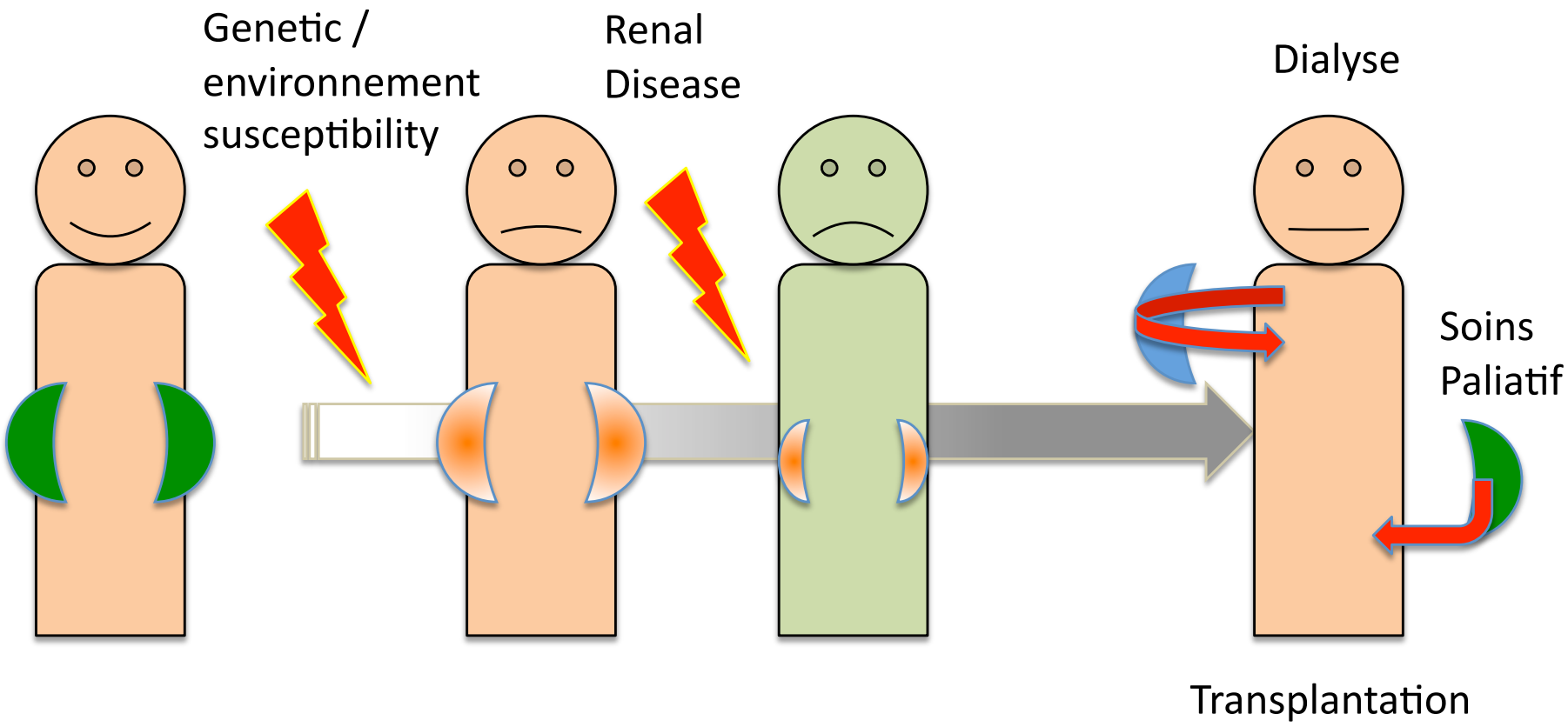
Dr Guillen Anaya Miguel Ange

R.U.M.B

8 / 11 / 2018

Le Chemin

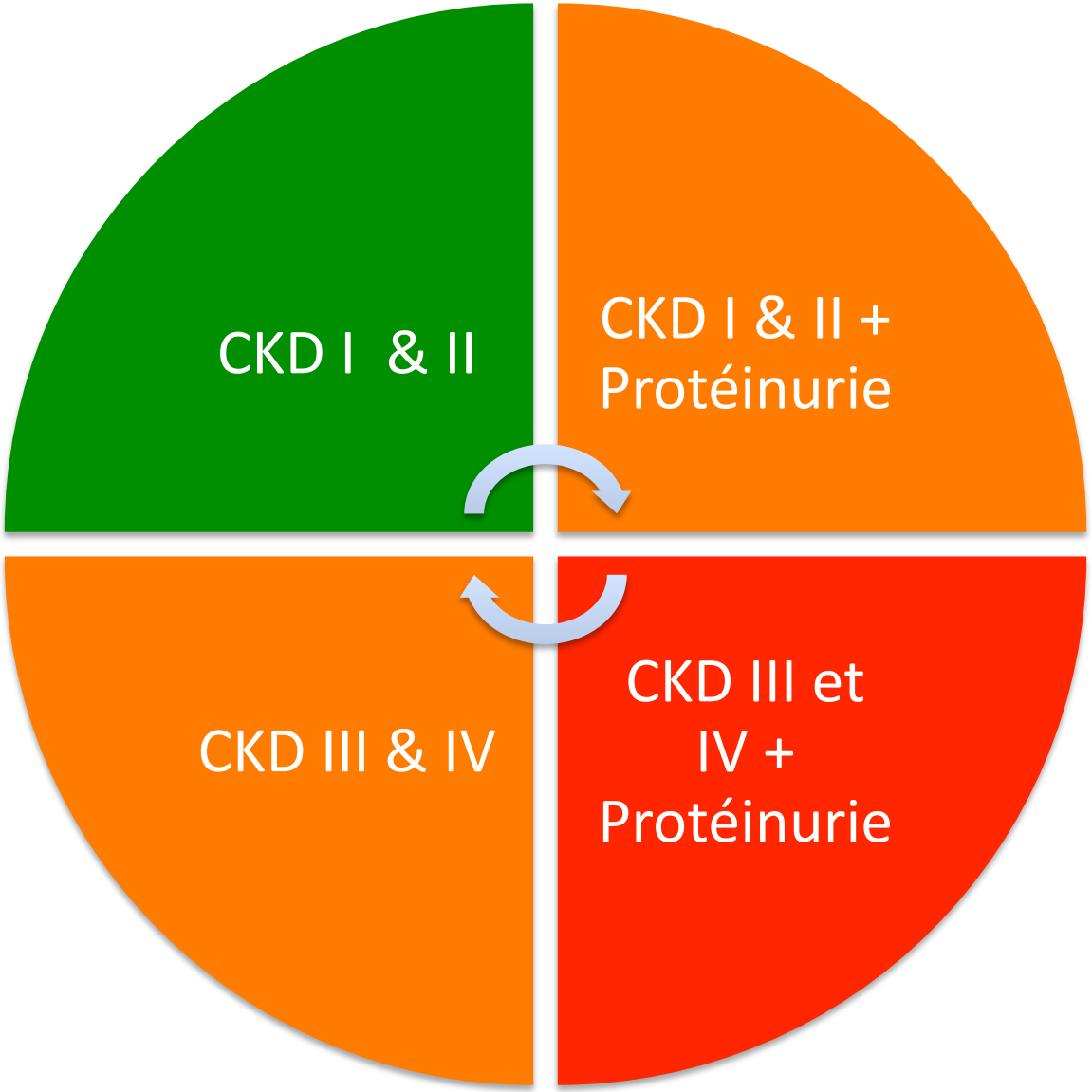
Le Chemin


Genetic / environnement susceptibility
Renal Disease
Dialyse
Soins Paliatif
Transplantation

GFR categories (ml/min/ 1.73 m²) Description and range				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
	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			

Classification MRC

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk;



Vue pratique personnelle.

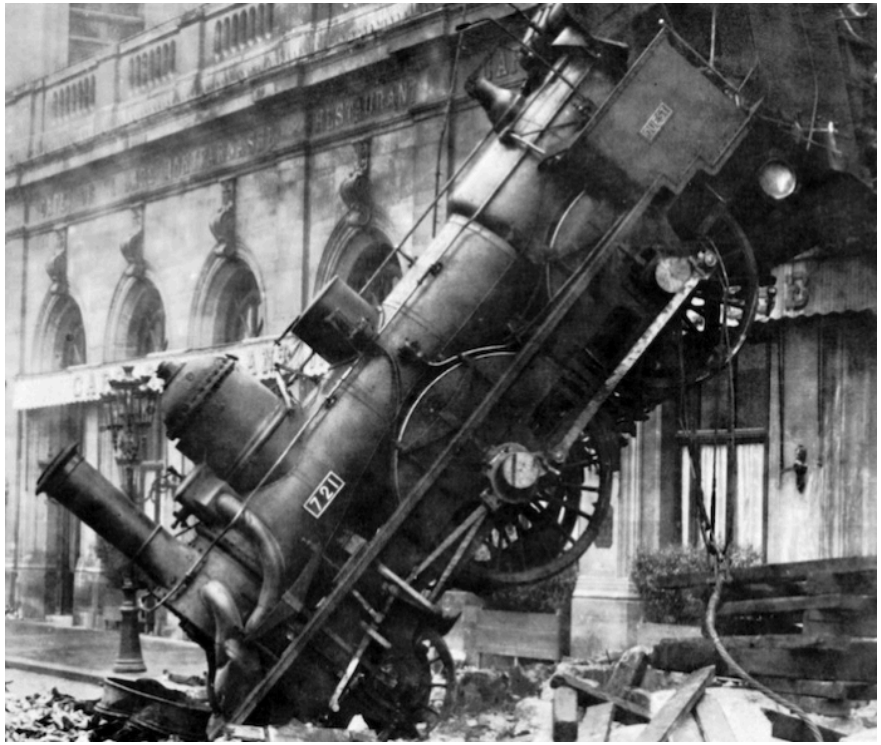
Classification Maladie Aigue (AKI)

STADE	Créatinine	Débit Urinaire
1	1,5 à 1,9 x valeur de base Ou > + 0,3 mg/dL	< 0,5 ml/Kg/h en 6-12 h
2	2,0 à 2,9 x valeur de base	< 0,5 ml/Kg/h en > 12h
3	>= 3,0 x valeur de base Ou Créatinine > 4 mg/dL Ou Initiation de dialyse	< 0,3 ml/Kg/h en 24h ou anurie de 12 h

MARCH 2012

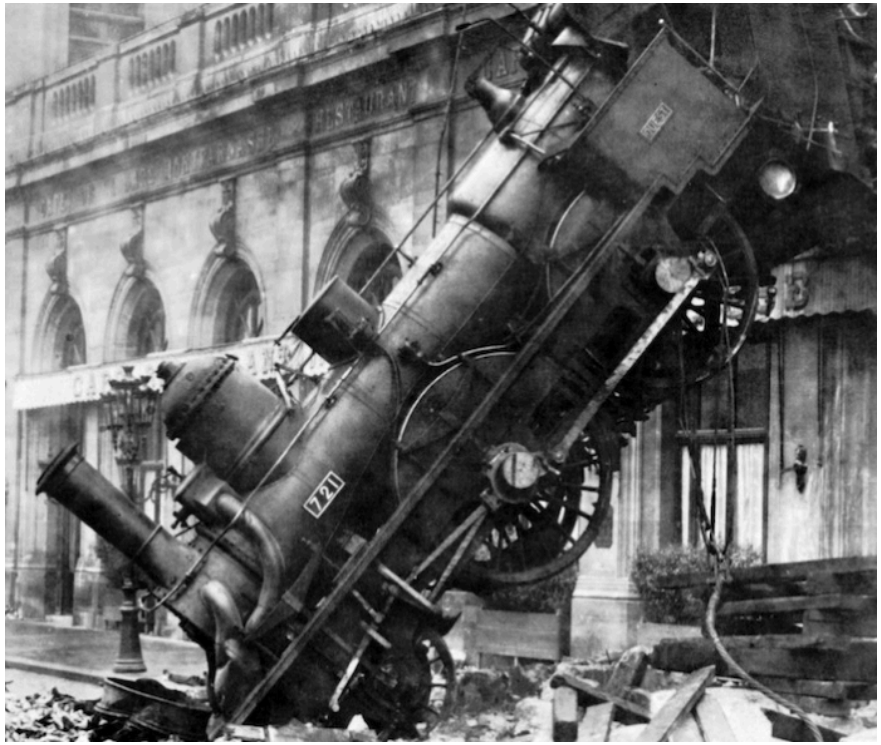
Que peut t on faire face à une maladie rénale ?

Diagnostic



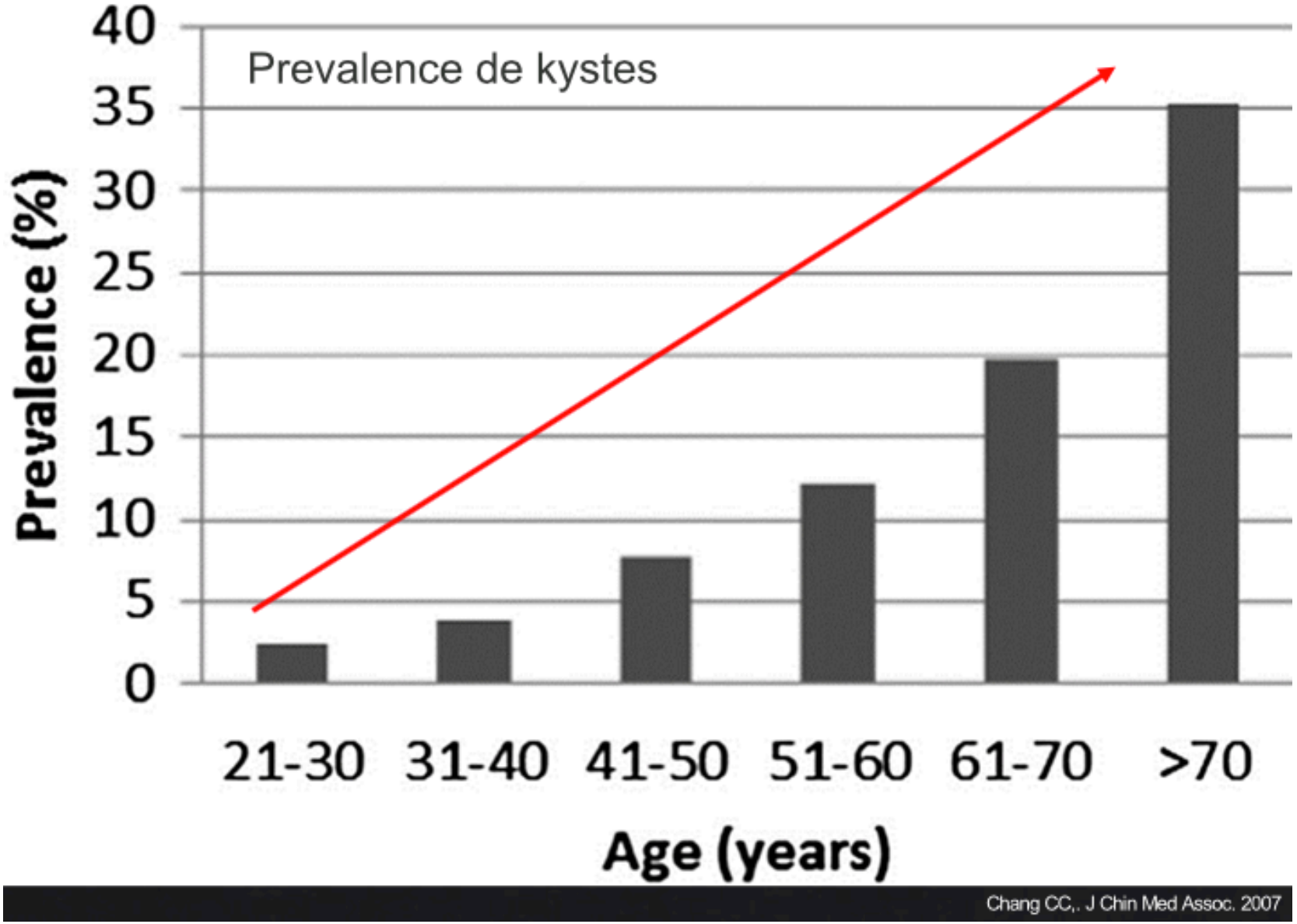
- URINE
- IMAGERIE
- SANG

Diagnostic

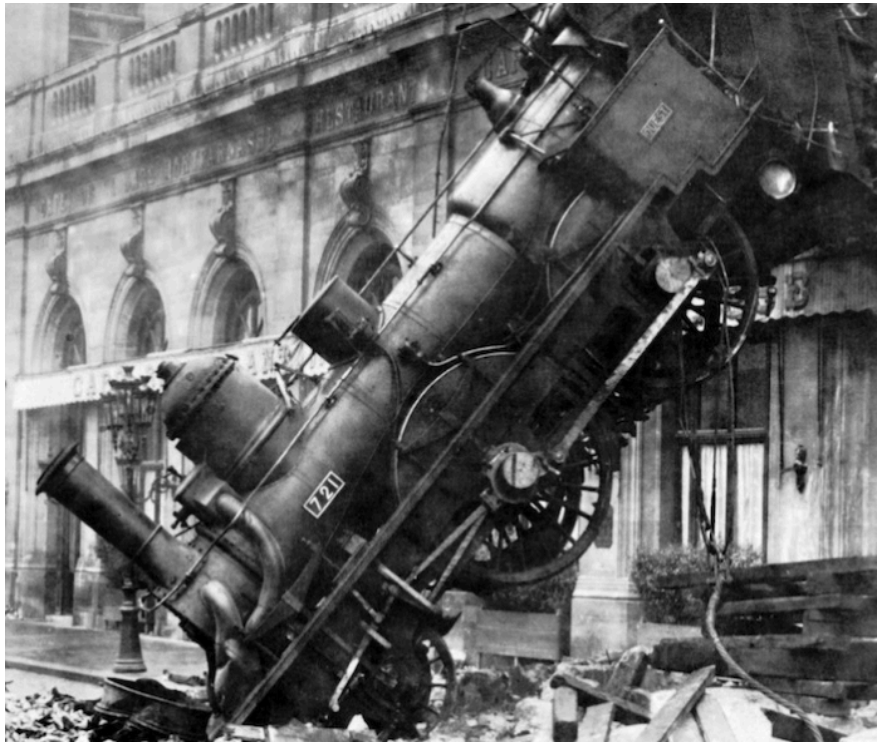


URINE

- Anomalie Mb basale
- Rupture Mb Basale
- Inflammation
- Cristaux
- Glycosurie
- …

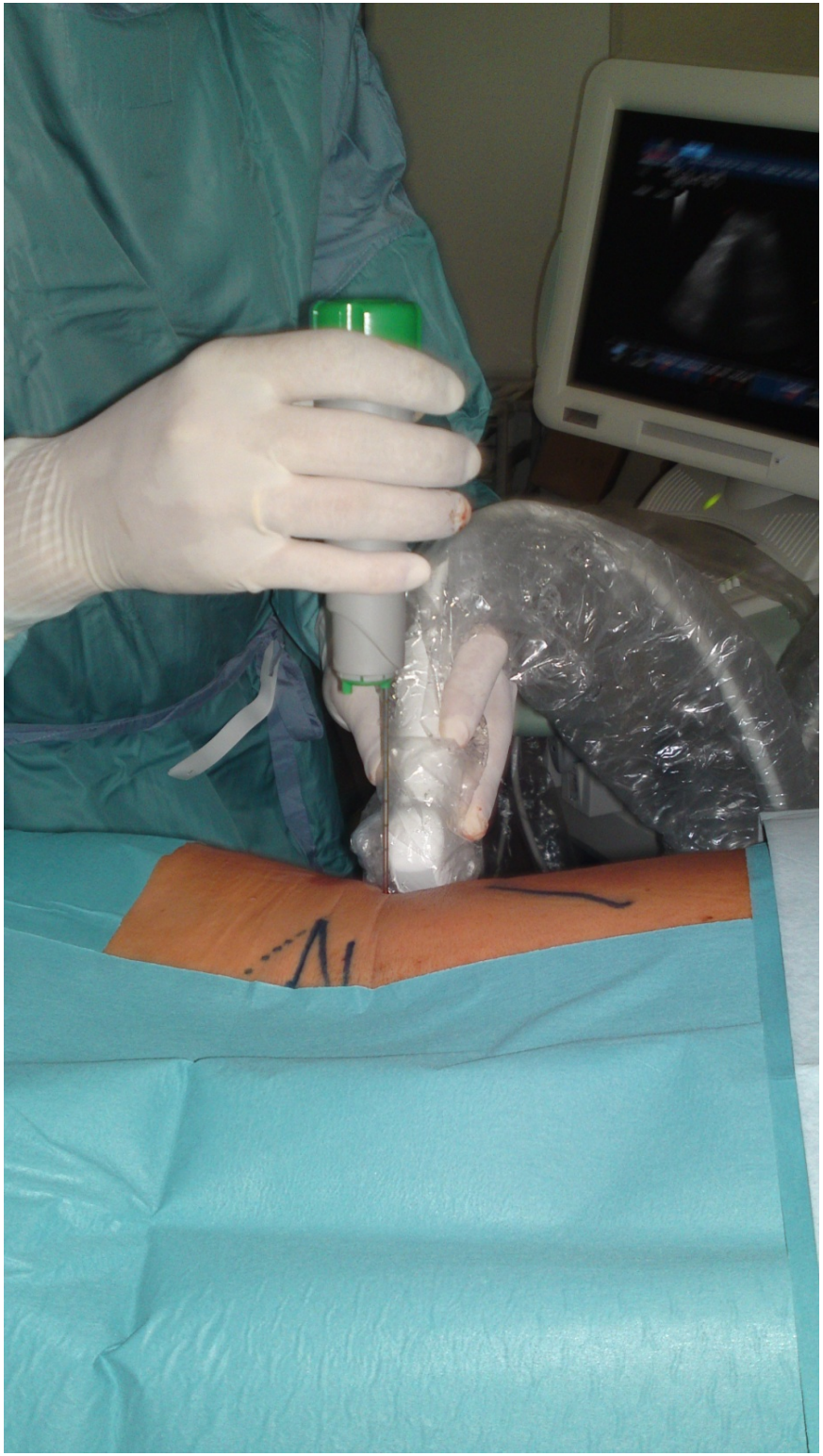

Prevalence de kystes
Prevalence (%)
40
35
30
25
20
15
10
5
0
21-30
31-40
41-50
51-60
61-70
>70
Age (years)
Chang CC,. J Chin Med Assoc. 2007

Diagnostic



SANG

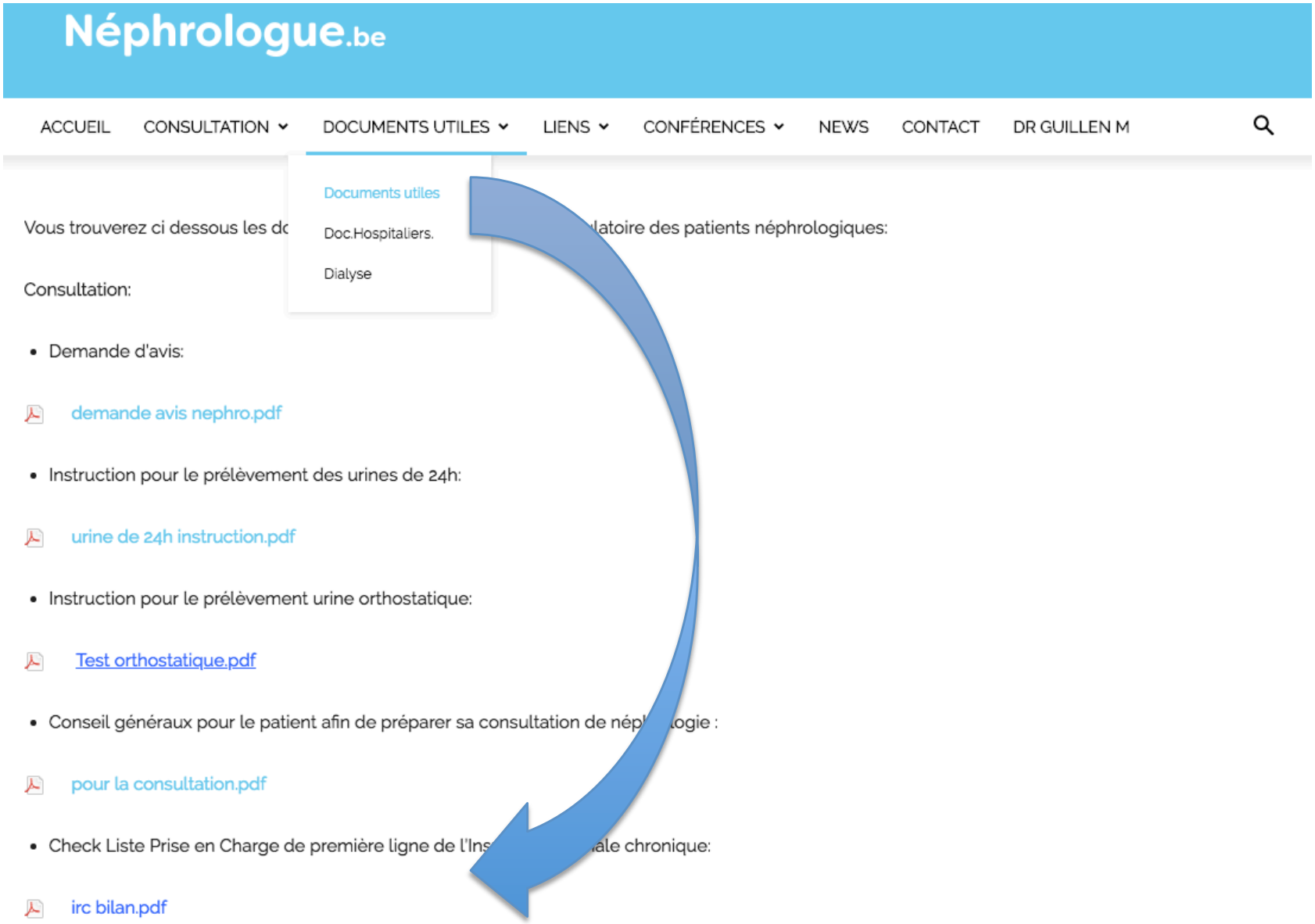
- classique
- Sérologie
- Complément
- Génétique
- Pharmaco
- Toxine Urémique



Biopsie Rénale

- Discussion locale
-
- Discussion Université
-
- Discussion Inter U.

Check Liste


Néphrologue.be
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DOCUMENTS UTILES
LIENS
CONFÉRENCES
NEWS
CONTACT
DR GUILLEN M
Documents utiles
Doc.Hospitaliers.
Dialyse
Vous trouverez ci dessous les do
latoire des patients néphrologiques:
Consultation:
Demande d'avis:
demande avis nephro.pdf
Instruction pour le prélèvement des urines de 24h:
urine de 24h instruction.pdf
Instruction pour le prélèvement urine orthostatique:
Test orthostatique.pdf
Conseil généraux pour le patient afin de préparer sa consultation de néph logie :
pour la consultation.pdf
Check Liste Prise en Charge de première ligne de l'Ins ale chronique:
irc bilan.pdf

Le DIAGNOSTIC

La protéinurie

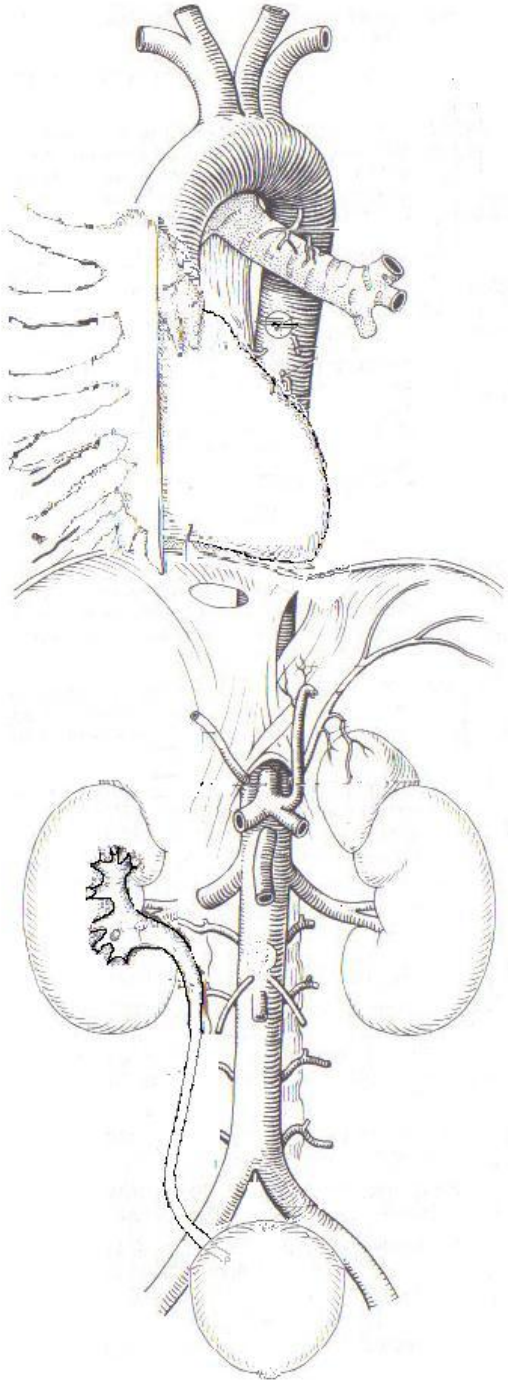
La Volémie, L'hypertension

L'Anémie

L'ostéodystrophie rénale

La kaliémie / L'acidose

Les Néphrotoxiques



Les FR généraux:

-l'Hypercholestérolémie

-La Sarcopénie

-INFLAMATION CHRONIQUE

- HYPERURICEMIE

- DIABETE

- TABAC

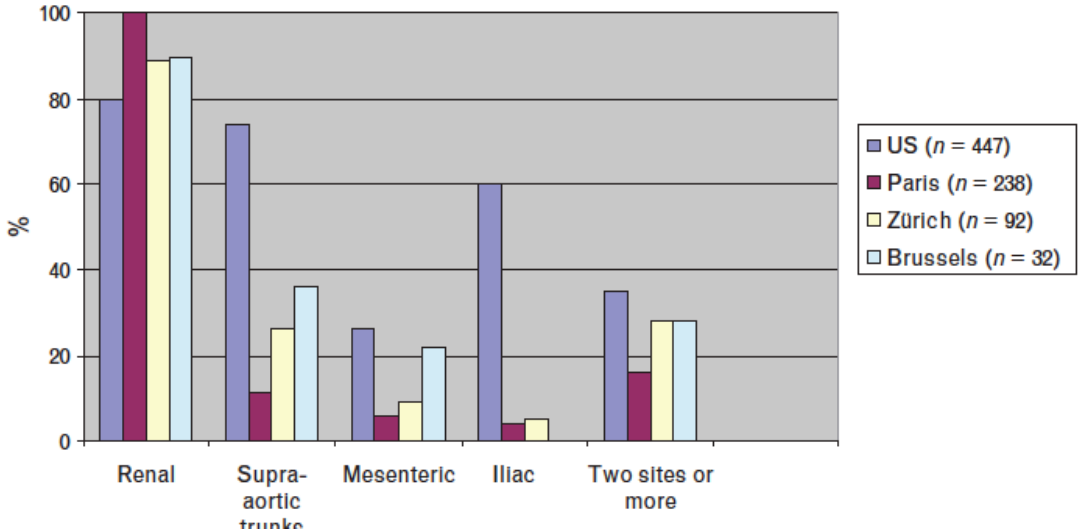
- ? microbiote ?

Pourquoi Creuser ?

FMD

European consensus on the diagnosis and management of fibromuscular dysplasia

Alexandre Persua,b, Alessandra Giavarinic,d, Emmanuel Touze´ e, Andrzej Januszewiczf,
Marc Sapovalg,h, Michel Azizic,h, Xavier Barrali, Xavier Jeunemaitreh,j, Alberto Morgantid,
Pierre-Franc¸ois Plouinc,h, Peter de Leeuwk, on behalf of the ESH Working Group 'Hypertension and the Kidney'



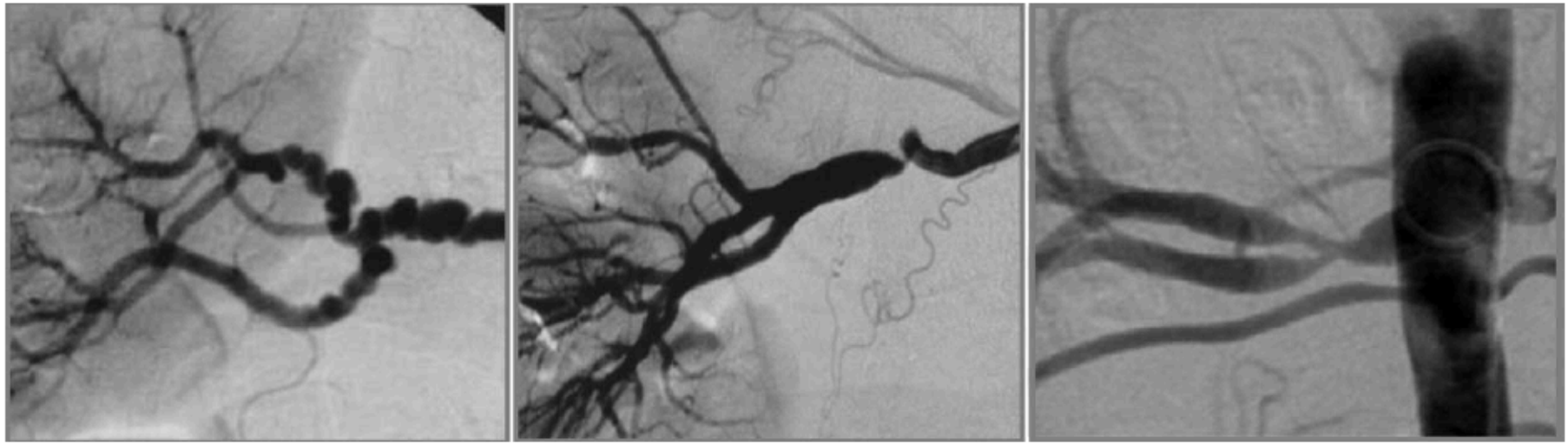


FIGURE 1 Angiographic classification of fibromuscular dysplasia (FMD) of the renal arteries. From left to right, 'string-of-beads' appearance of multifocal FMD, unifocal FMD, and tubular FMD (adapted from ref [1]).

Journal of Hypertension 2014, 32:

FMD REIN	Si Hypertension
1	Age < 30 ans, femme
2	Grade 3 HTA ou Hypertension artérielle ou HTA résistante
3	Petit rein sans histoire d'urologie
4	Souffle abdominale sans athéromatose
5	FMD dans un autre territoire

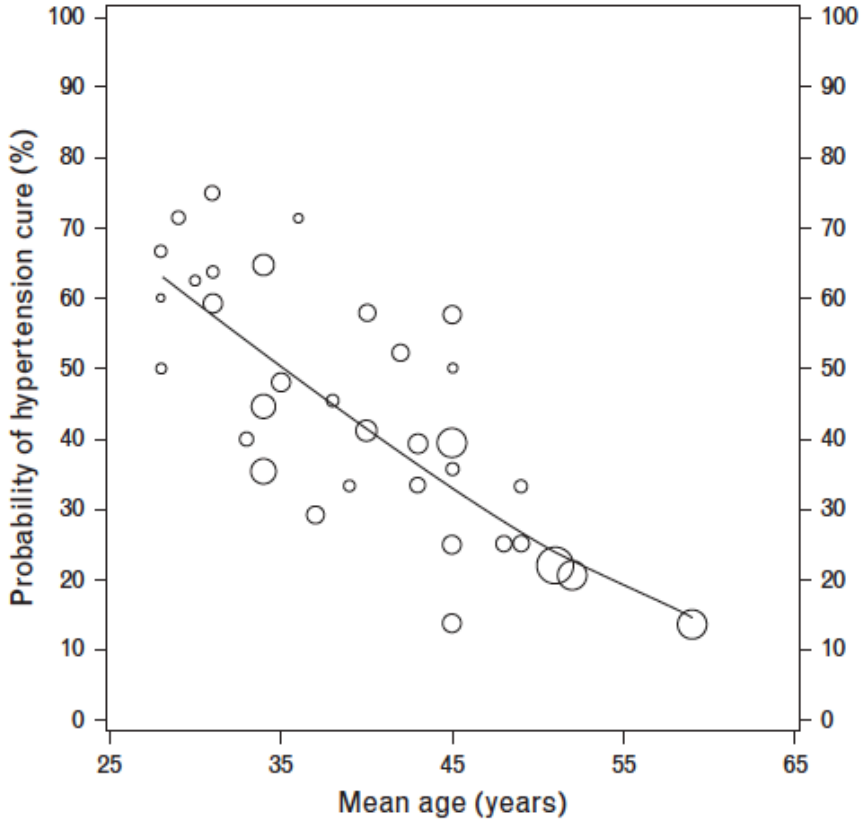


FIGURE 5 Meta-regression analysis assessing the relationship between the hypertension cure rate following percutaneous angioplasty and mean age (adapted from ref. [3]).

Si démontré dans un organe

Rein

- AnioCT
- Angio IRM

Cerveau

- Angio CT
- AngioIRM

Screening for FMD of the renal, iliac and cervicocephalic arteries is also recommended in case of spontaneous coronary artery dissection, particularly in presence of HTN or other suggestive symptoms.

In patients with renal artery and/or cervicocephalic FMD, screening of other, less often involved vascular beds should be considered in presence of suggestive symptoms or medical history.

A retenir

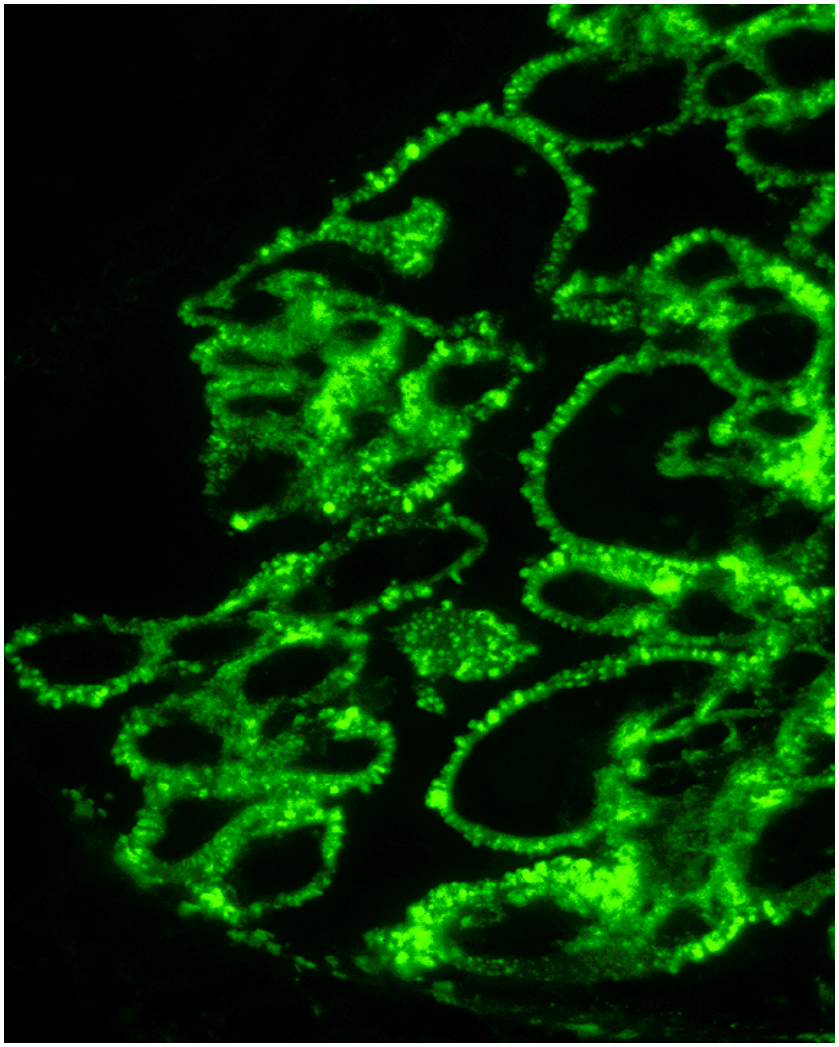
Donnée des donneurs de rein démontre une prévalence sous estimée
Dans les cohortes de FMD diagnostic à un âge moyen supérieur à 50 ans
FMDplus fréquent chez le femme de 30-50 ans mais aussi chez l'homme, et à tout âge de vie
FMD est une maladie systémique incluant les vaiseaux rénaux et cervicaux céphaliques
La FMD est associé à des dissection spontannée des coronaires
Le FMD est d'origine génétique

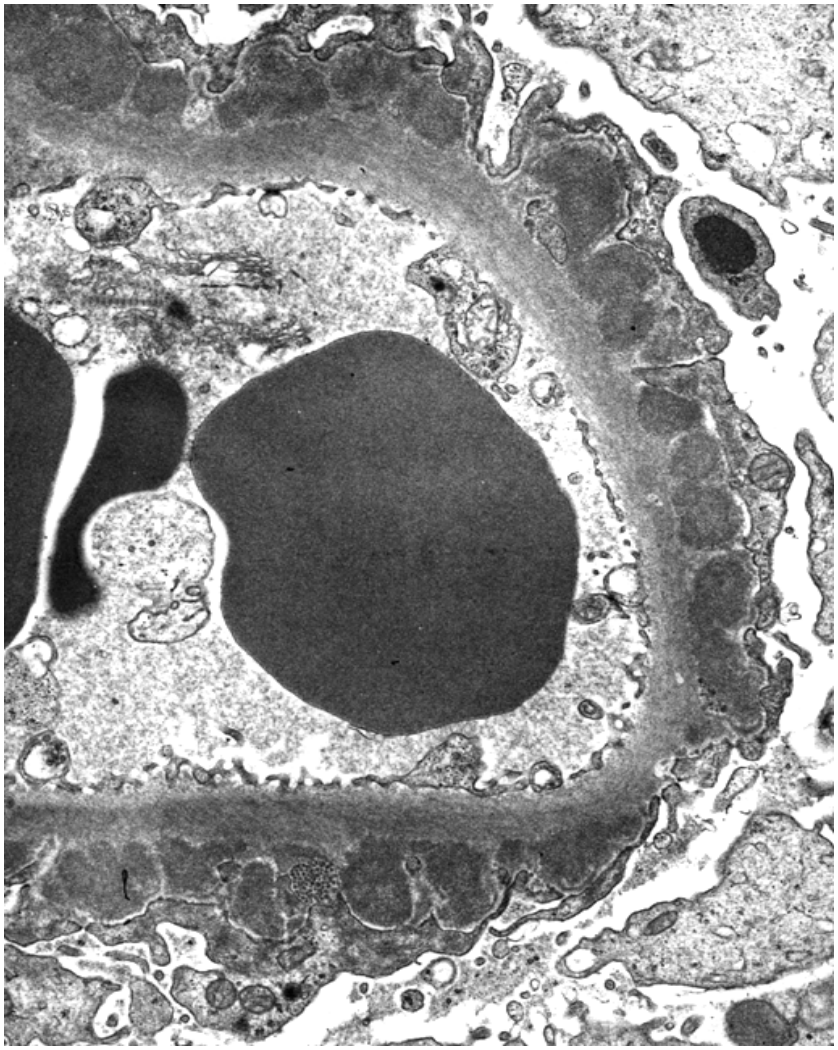
Néphropathie glomérulaire quoi de neuf

GEM

ANCA

Membranous Nephropathy





Major cause of nephrotic syndrome and chronic renal failure

G. Extramembraneuse
Membranous nephropathy

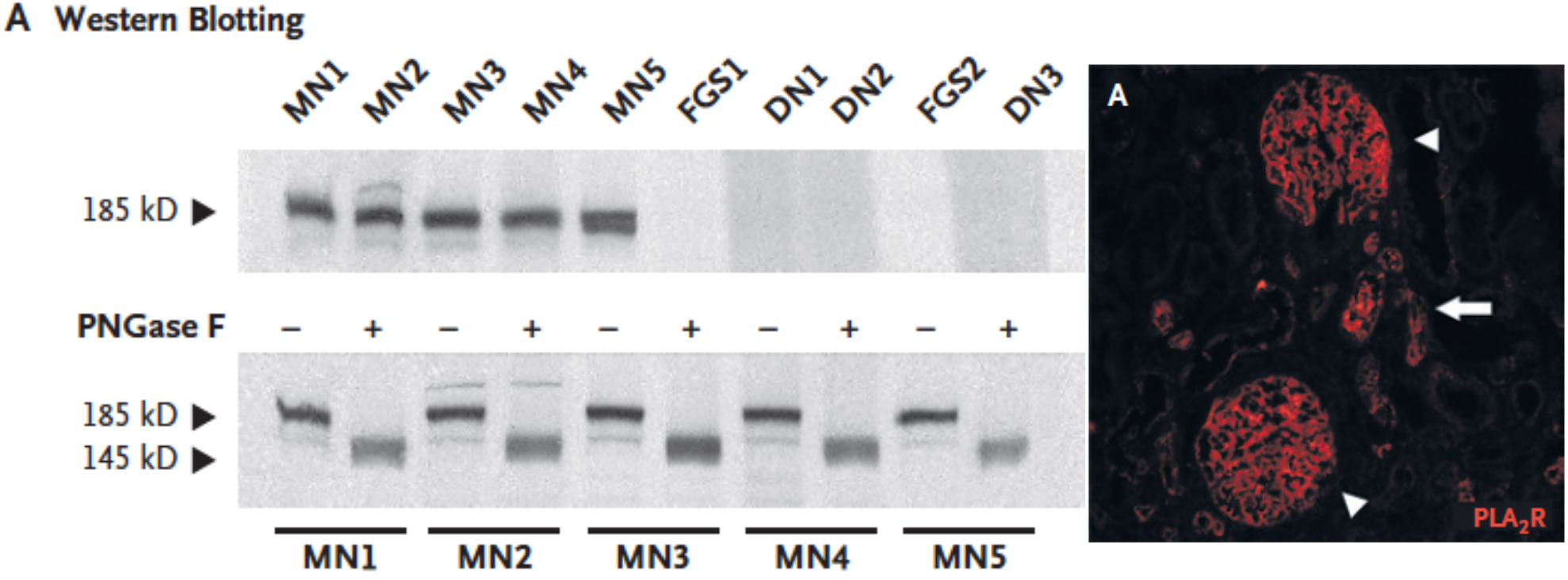
GEM	IgG sous classe	
Secondaire (30%)	Sous classe IgG 1/2/3	
Primaire (70 %)	Sous classe IgG 4	Traitement immunosupresseur mais lequel ? Protéinurie juste un marqueur indirect de la maladie
GEM Greffe de novo	Sous classe IgG 1	
GEM Greffe récurrente	Sous classe IgG 4	

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 2, 2009 VOL. 361 NO. 1

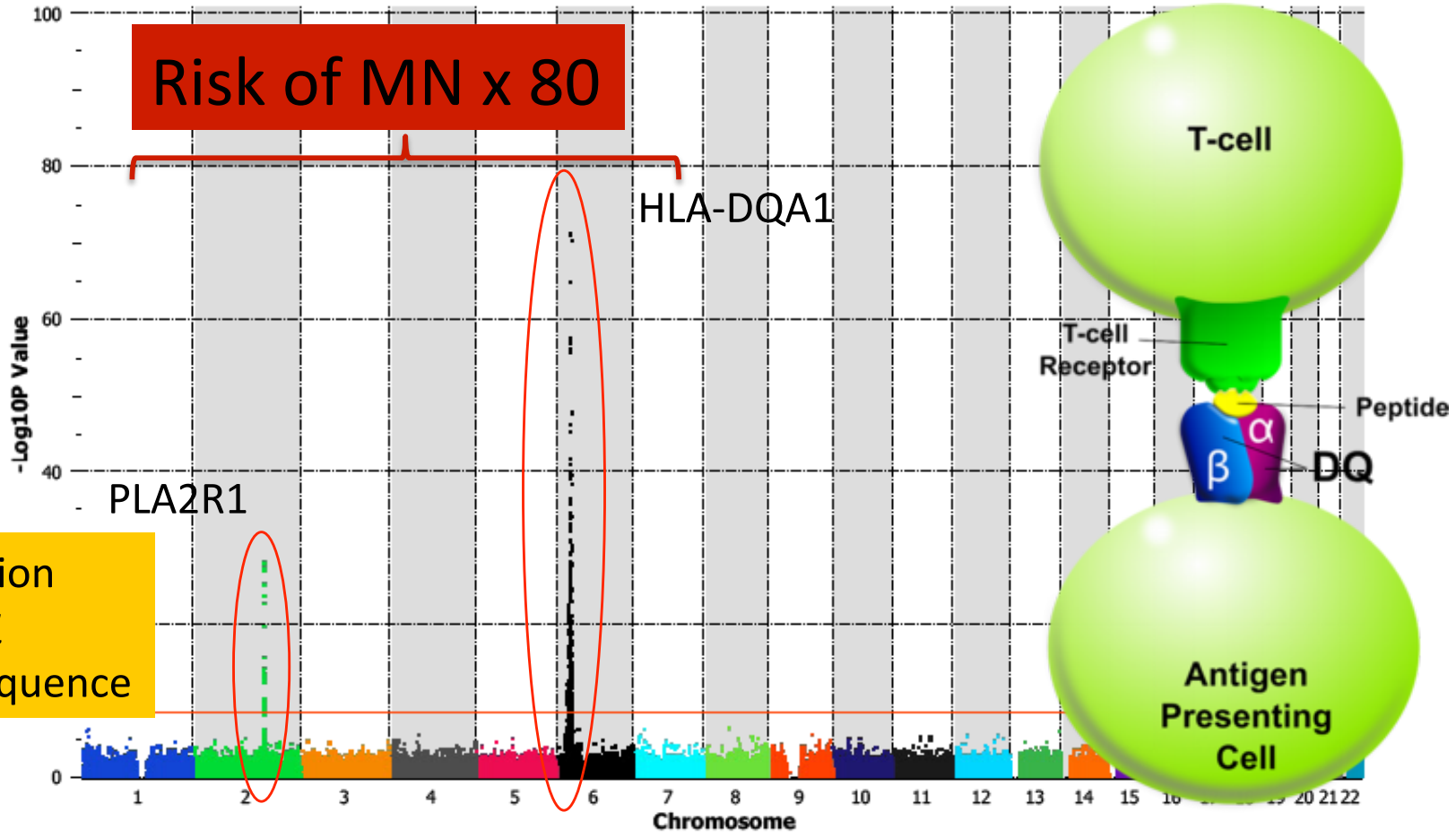
M-Type Phospholipase A_2 Receptor as Target Antigen in Idiopathic Membranous Nephropathy

Laurence H. Beck, Jr., M.D., Ph.D., Ramon G.B. Bonegio, M.D., Gérard Lambeau, Ph.D., David M. Beck, B.A., David W. Powell, Ph.D., Timothy D. Cummins, M.S., Jon B. Klein, M.D., Ph.D., and David J. Salant, M.D.



From polygenic disease to rare association of common variants

556 Patients ; 2338 controls (Euro MN Consortium = F+UK+NL)

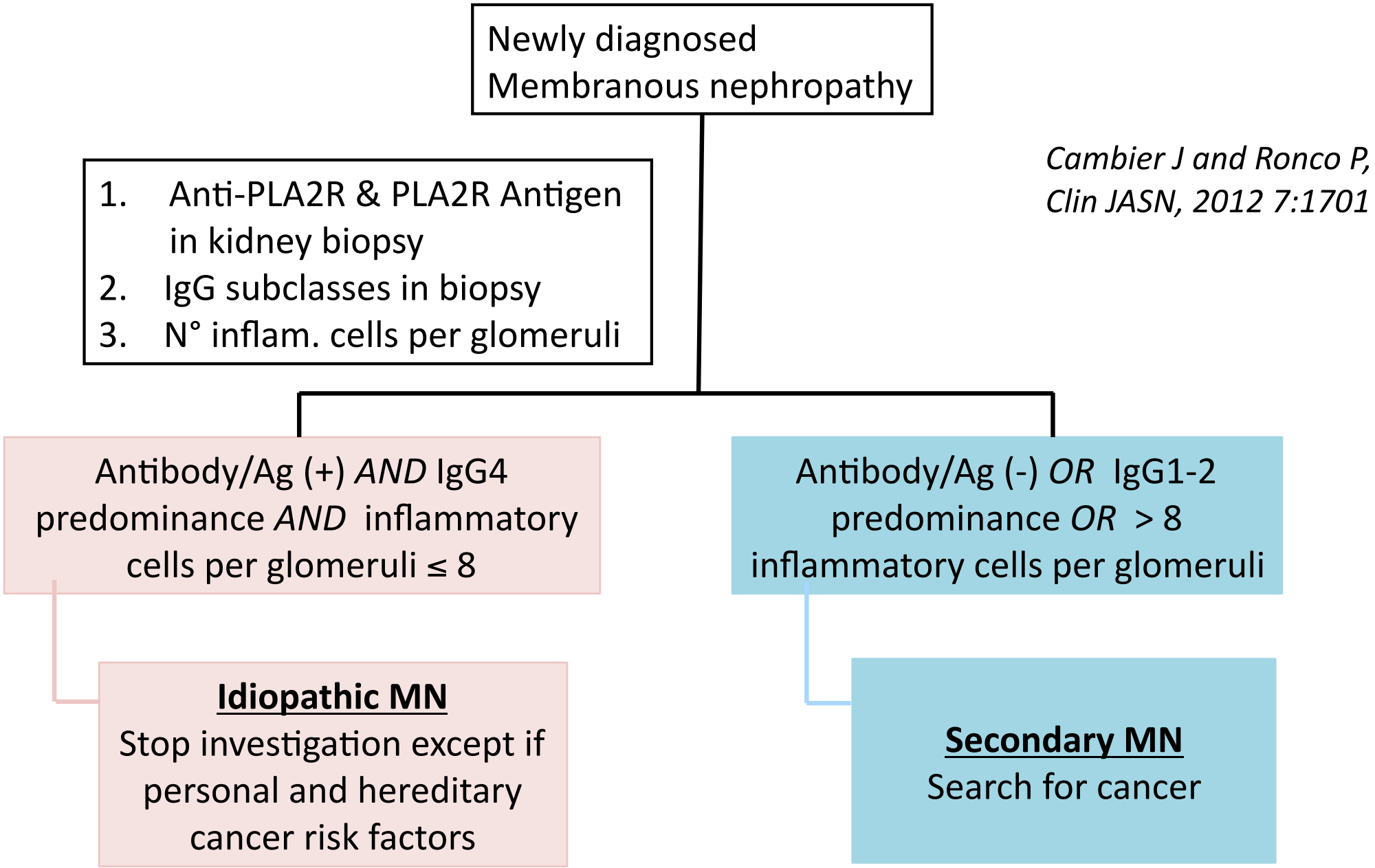


No mutation in *PLA2R1* coding sequence

Stanescu et al, New Engl J Med, 2011, 364: 616 ; Coenen et al, J Am Soc Nephrol, 2013,24:677

ANTI PLA2R	Syndrome nephrotique de l'adulte
cout	< 20 euros (-13 -)
spécificité	très bonne: 99 % (JASN 2011 &2012)
sensibilité	Dépende de la GEM: idiopathique 80 % (JASN 2011 &2012) (Nouvel Ag cible ***Thrombospondin type-1 domain containing 7A (THSD7A)***)
Evite la biopsie	Non Existe antipla2R paraneoplasique mais histologie différente + association avec sarcoidose et HBV Etat des lieux si GFR altérée Si taux taux négatif on peut retrouvé encore de l'antipla2R dans les biopsies
Taux ?	Cut off de ? 100 ? rU/ml prédictif mais idéalement
Spreading AG-Ag	Ce n'est pas un Ac monoclonal, polyclonalité marque d'activité ?
Monitoring	OUI - OUI et OUI
Traitement	Ponticelli modifié (€)→ Anti lympho B (RTXMB) (€€€) E.secondaire: €€€ Us €

Management of newly diagnosed MN

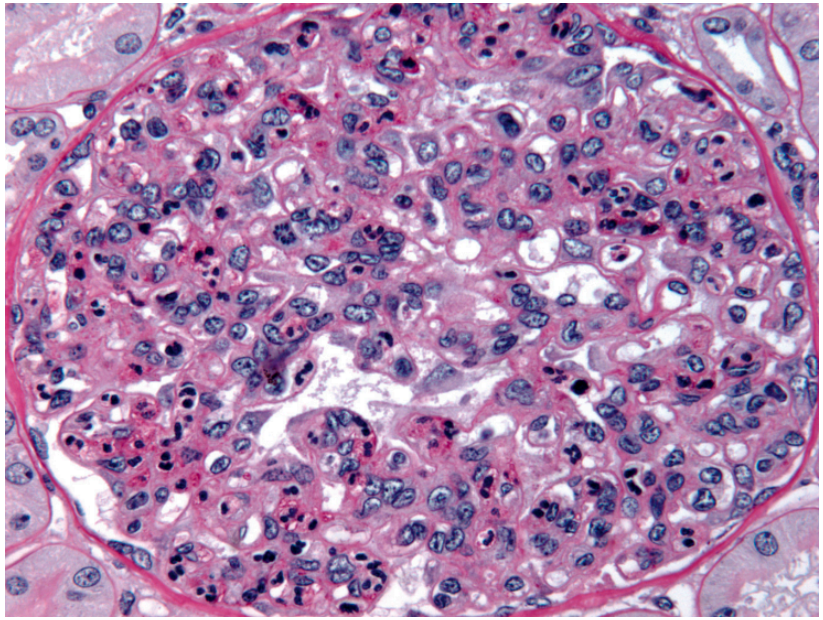


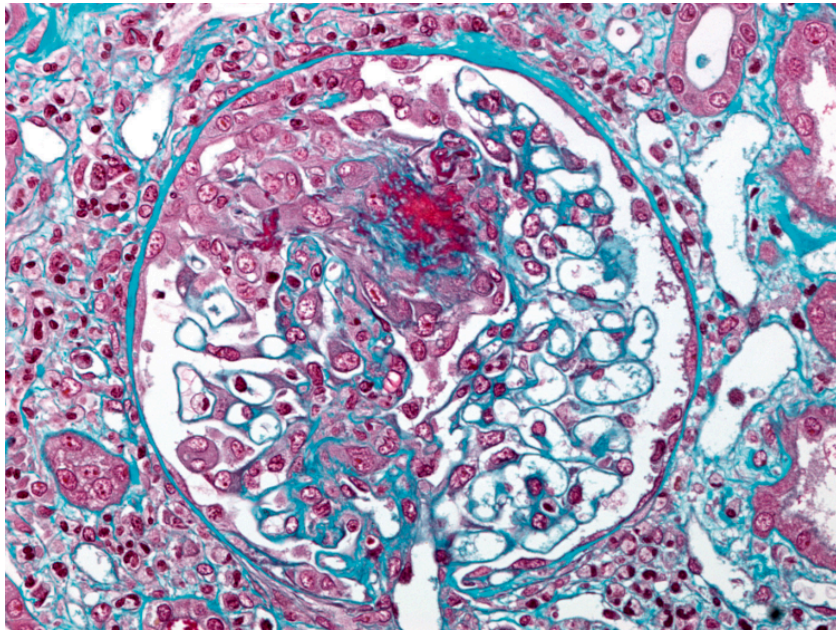
Cambier J and Ronco P, Clin JASN, 2012 7:1701

ANCA

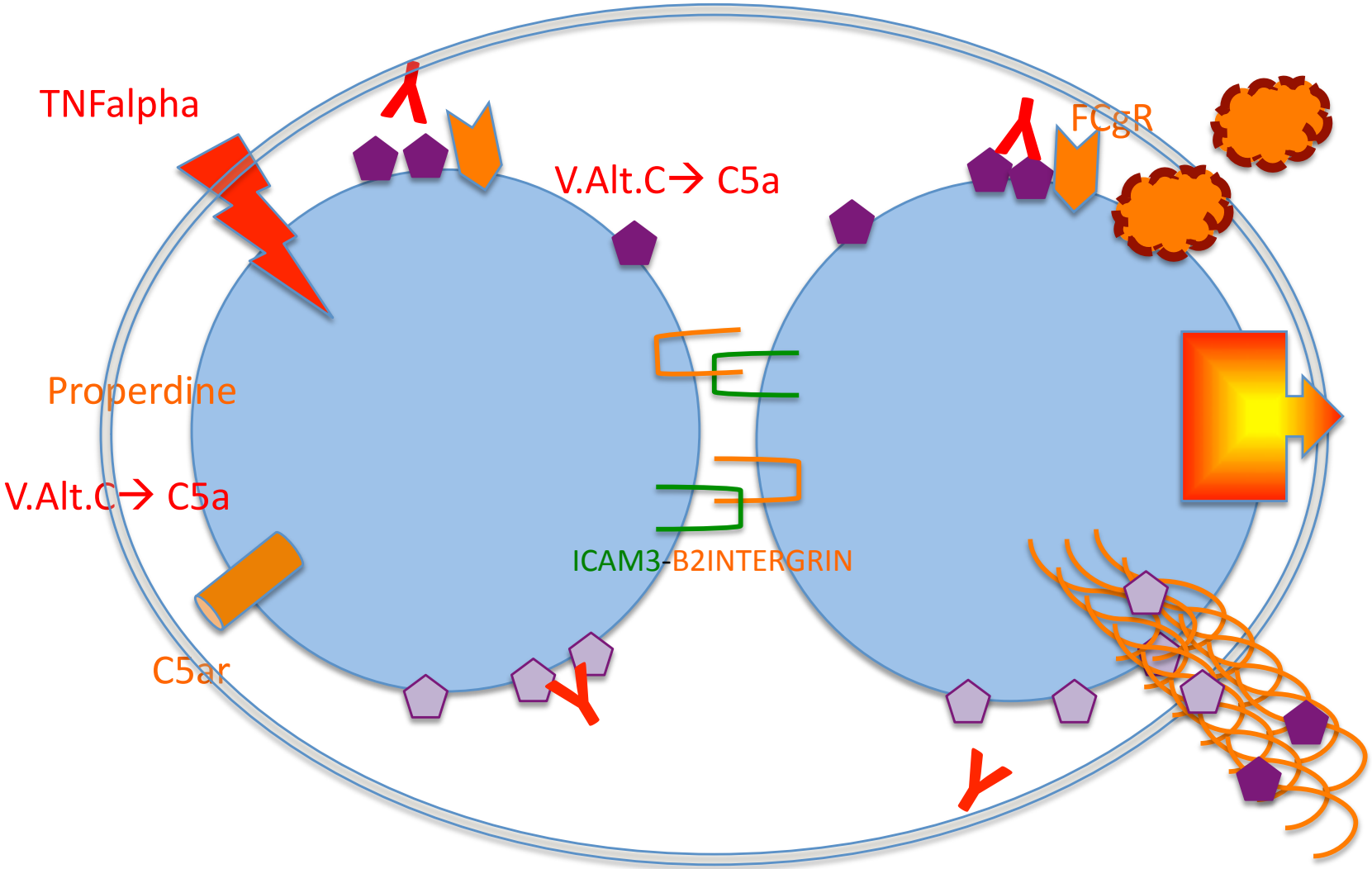
ANTI-NEUTROPHIL CYTOPLASMIC AUTOANTIBODIES WITH SPECIFICITY FOR MYELOPEROXIDASE IN PATIENTS WITH SYSTEMIC VASCULITIS AND IDIOPATHIC NECROTIZING AND CRESCENTIC GLOMERULONEPHRITIS

RONALD J. FALK, M.D., AND J. CHARLES JENNETTE, M.D.





Mécanisme - Netose



COMPLEMENT

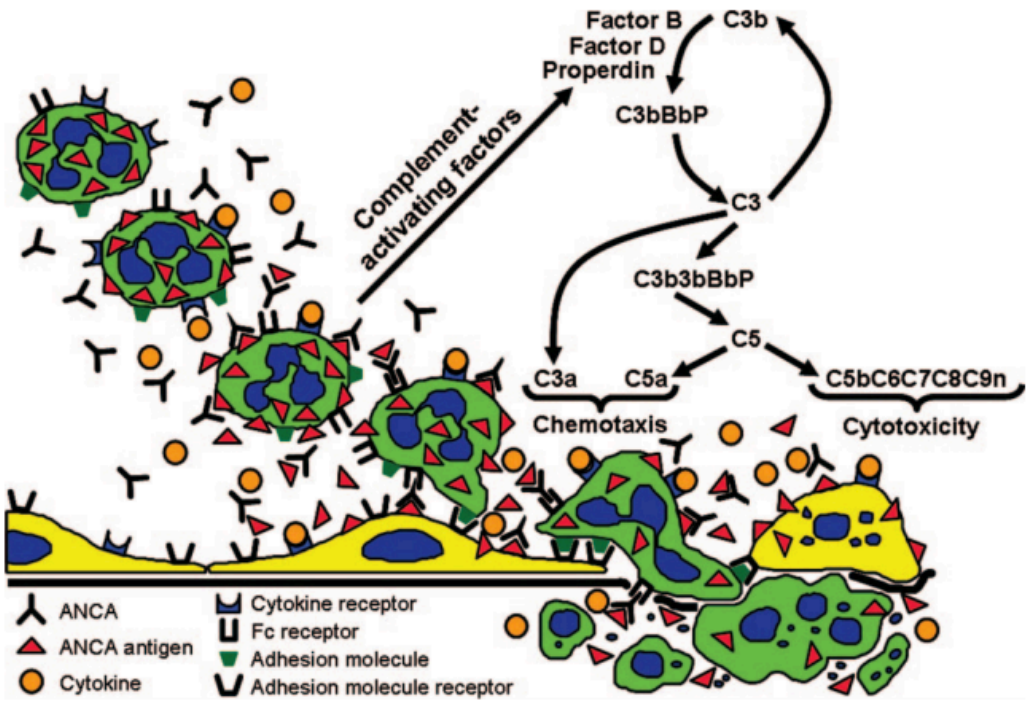
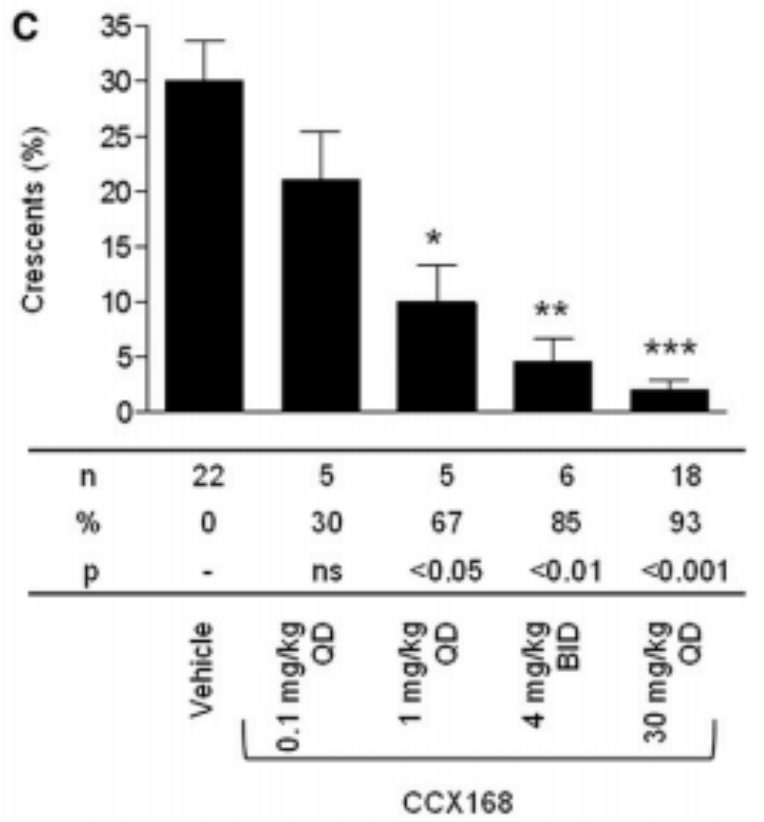
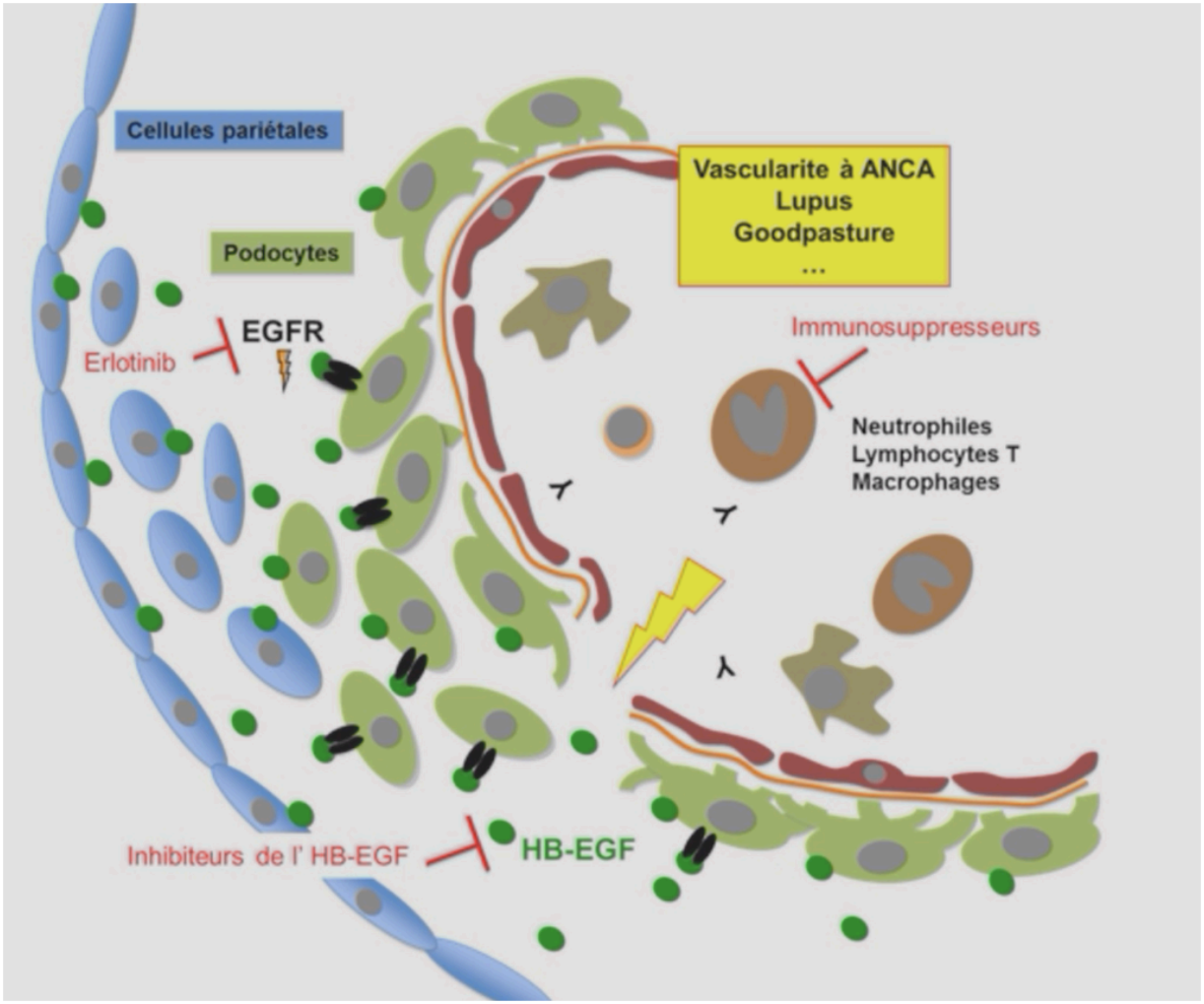


Figure 12. Diagram depicting a putative pathogenic mechanism for ANCA glomerulonephritis and vasculitis. Beginning in the top left, neutrophils are primed by cytokines to express more ANCA antigens (MPO and PR3) at the surface where they can interact with ANCA antibodies. This results in neutrophil activation both by Fc receptor engagement and Fab'2 binding. ANCA-activated neutrophils release factors (eg, properdin, proteases, oxygen radicals, and MPO) that activate the alternative complement pathway with the generation of the powerful neutrophil chemoattractant C5a and the membrane attack complex C5b-9. This complement activation amplifies neutrophil influx, neutrophil activation, and vessel damage, resulting in the aggressive necrotizing inflammation of ANCA disease.



Des Croissants



Nephrol Dial Transplant (2013) 0: 1–12
doi: 10.1093/ndt/gft318

ndt
Nephrology Dialysis Transplantation

Full Review

Impact of rituximab trials on the treatment of ANCA-associated vasculitis

The NEW ENGLAND JOURNAL of MEDICINE

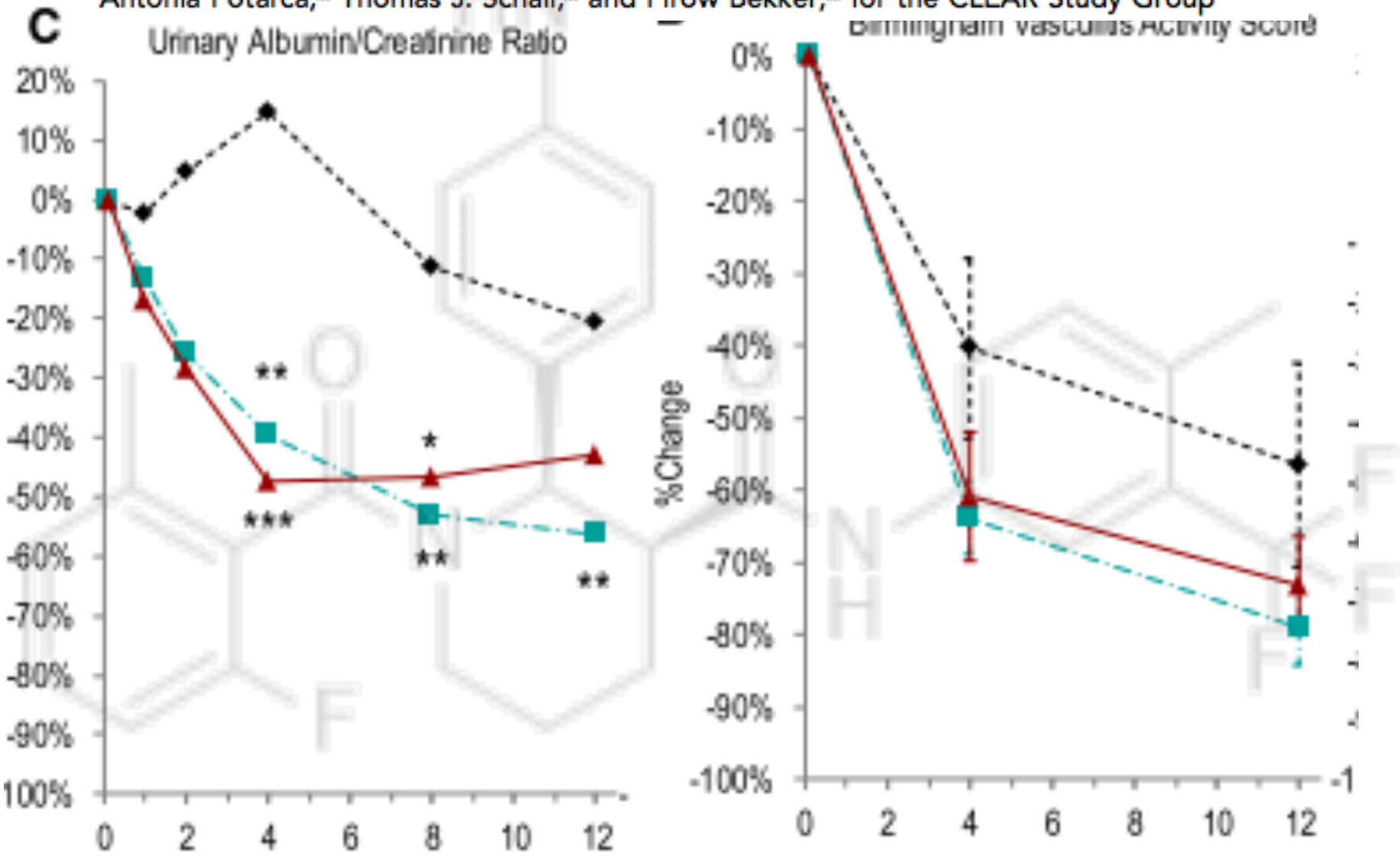
ESTABLISHED IN 1812 NOVEMBER 6, 2014 VOL. 371 NO. 19

Rituximab versus Azathioprine for Maintenance in ANCA-Associated Vasculitis

L. Guillevin, C. Pagnoux, A. Karras, C. Khouatra, O. Aumaître, P. Cohen, F. Maurier, O. Decaux, J. Ninet, P. Gobert, T. Quémeneur, C. Blanchard-Delaunay, P. Godmer, X. Puéchal, P.-L. Carron, P.-Y. Hatron, N. Limal, M. Hamidou, M. Ducret, E. Daugas, T. Papo, B. Bonnotte, A. Mahr, P. Ravaud, and L. Mouthon, for the French Vasculitis Study Group*

Randomized Trial of C5a Receptor Inhibitor Avacopan in ANCA-Associated Vasculitis

David R.W. Jayne,* Annette N. Bruchfeld,† Lorraine Harper,‡ Matthias Schaier,§ Michael C. Venning,‖ Patrick Hamilton,‖ Volker Burst,¶ Franziska Grundmann,¶ Michel Jadoul,** István Szombati,†† Vladimír Tesař,‡‡ Mårten Segelmark,§§ Antonia Potarca,‖‖ Thomas J. Schall,‖‖ and Pirow Bekker,‖‖ for the CLEAR Study Group



Traitement

2000

- Plasmapherese

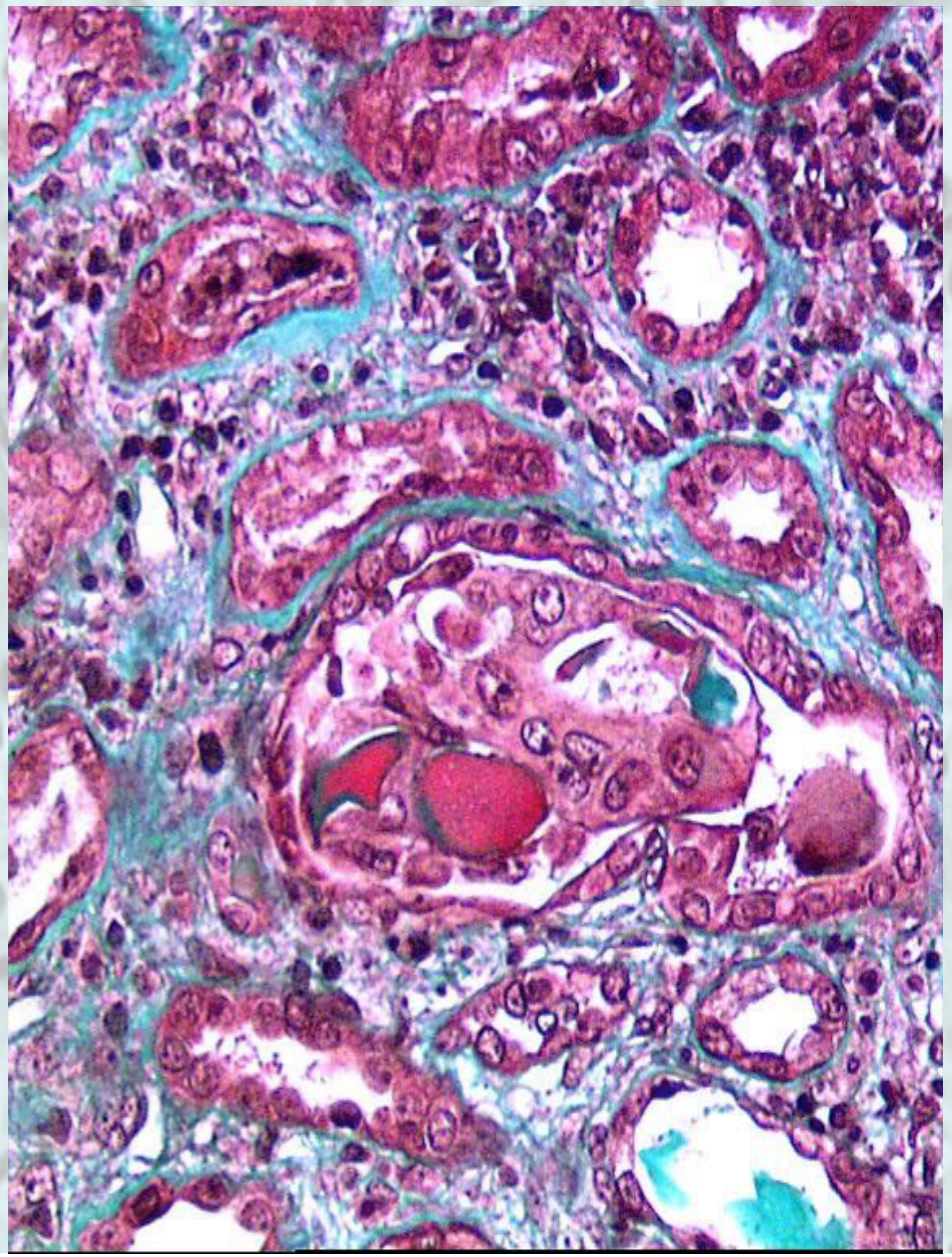
- Corticoide
- Endoxan

- → 25 % avec serious adverse event < 6mois

2020 - 2030

- IDES

- AVACOPAN
- Rituximab



Néphrite tubulo-interstitielle aigue

Intro médication cause 1

Mayo Clinic

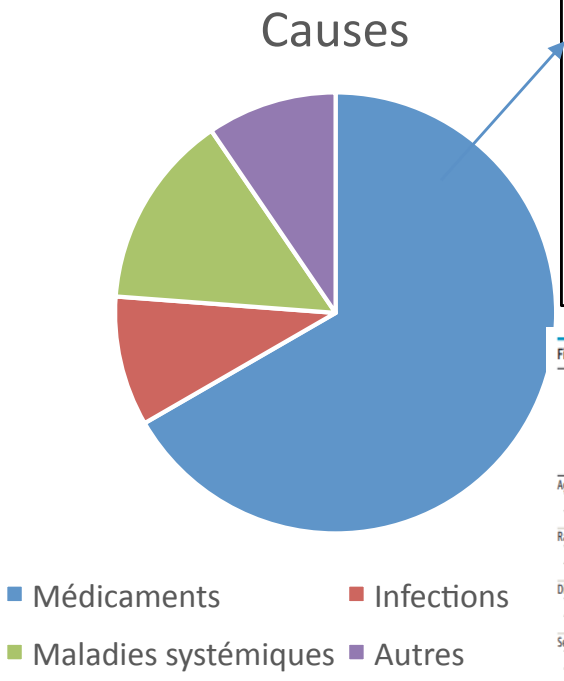
Table 2 | Causes of AIN by age group (*N* = 133)

Cause	Number of patients (%) ⩾65 years (*N* = 45)	<65 years (*N* = 88)
Drug induced	39 (87)	56 (64)
Antibiotics	21 (47)	26 (30)
NSAIDs	1 (2)	9 (10)
PPIs	8 (18)	5 (6)
Other drugs	3 (7)	8 (9)
Multiple drugs	6 (13)	8 (9)
Autoimmune/systemic disorders	3 (7)	24 (27)
Sarcoidosis	1 (2.3)	12 (13.6)
Sjogren's	1 (2.3)	5 (5.7)
TINU	0 (0)	3 (3.4)
IgG4 related	0 (0)	2 (2.3)
Other—sweets, MCTD/CREST	1 (2.3)	2 (2.3)
Infectious	1 (2)	4 (4.5)
Bacterial	1 (2)	2 (2.3)
Viral	0 (0)	1 (1.1)
Fungal	0 (0)	1 (1.1)
Other	1 (2)	4 (4.5)
Reactive interstitial nephritis (Councilman's disease)	0 (0)	2 (2.3)
Malignancy	1 (2)	1 (1.1)
CVID	0 (0)	1 (1.1)
Unknown	1 (2)	0 (0)

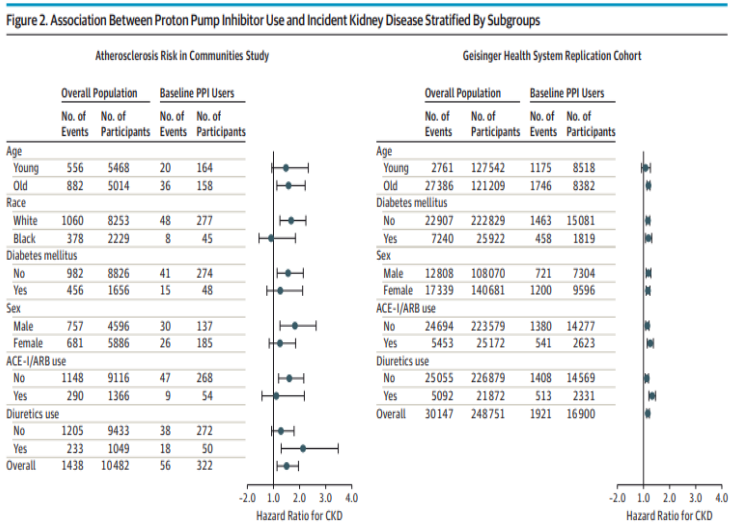
Clinical characteristics, causes and outcomes of acute interstitial nephritis in the elderly

Angela K. Muriithi[1], Nelson Leung[1], Anthony M. Valeri[2], Lynn D. Cornell[3], Sanjeev Sethi[3], Mary E. Fidler[3] and Samih H. Nasr[3]

[1]Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota, USA; [2]Division of Nephrology, Columbia University, College of Physicians and Surgeons, New York, New York, USA and [3]Division of Anatomic Pathology, Mayo Clinic, Rochester, Minnesota, USA



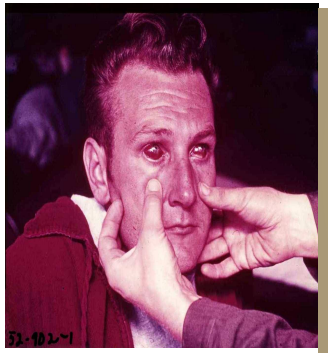
- **Antibiotiques** (pénicillines, céphalosporines, rifampicine, trimethoprim-sulfamethoxazole, ciprofloxacine)
- **IPP**
- **AINS**
- Diurétiques
- Allopurinol
- **Aminosalicylés**

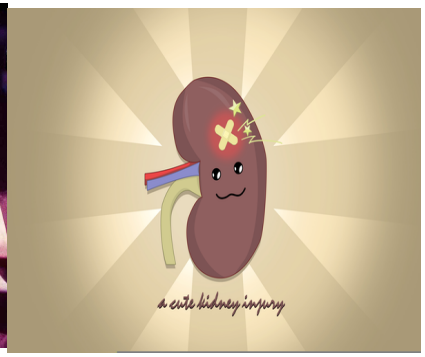


B Lazarus et al. JAMA Internal Medicine, 2016

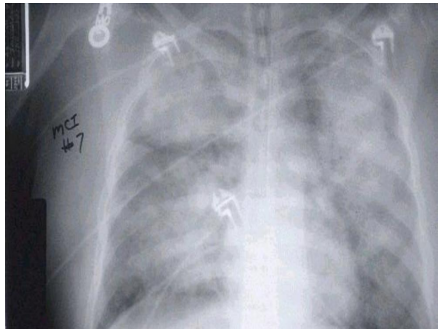
Hantavirus

Virus	Géographie	Réservoir	Maladie
Puumala	Europe ouest	Campagnol roussâtre	FHSR (forme bénigne : néphropathie épidémique)
Dobrava	Europe ouest	Mulot à collier	FHSR (forme grave)
Hantaan	Extrême Orient	Mulot	Fièvre hémorragique coréenne (FHSR)
Seoul	Ubiquiste	Rat	FHSR
Prospect Hill	Etats-Unis	Campagnol	?
Sin Nombre et autres	Amériques	Diverses espèces de rongeurs	Syndrome pulmonaire à Hantavirus





Otis Archives, National Museum of Health & Medicine, 1950.



IgG4 – Y penser

- Âge moyen: 60 ans
- Sex ratio: de 3:1 à 8:1 selon organe
- Critères biologiques ET histologiques
- **Diagnostics différentiels** :

hémopathie, infections systémiques, **Sd Sjögren**, LED, Vasculite, PR

« Critères diagnostiques » de la maladie associée aux IgG4 adaptés d'après Okazaki et al. [13].

Diagnostic d'IgG4-RD retenu si : (1)+(2) ou (1)+ ($3^{a/b}$) ou (2)+($3^{a/b}$) ou ($3^{a/b/c/d}$)

(1) Atteinte d'organe définie par
une dysfonction d'organe
et/ou une anomalie radiologique : hypertrophie focale ou diffuse, lésion(s) nodulaire(s) d'un ou de plusieurs organe(s)

(2) Élévation des IgG4 sériques (> 1,35 mg/mL)

(3) Lésions histologiques
a – Infiltration lymphocytaire et plasmocytaire avec fibrose tissulaire sans infiltration par des polynucléaires neutrophiles
b – Infiltration abondante par des plasmocytes IgG4+ (>10/CFG) et/ou ratio plasmocytes IgG4+/IgG+ >40 %
c – Fibrose engainante et mutilante (*swirling and storiform fibrosis*)
d – Lésions de phlébite oblitérante

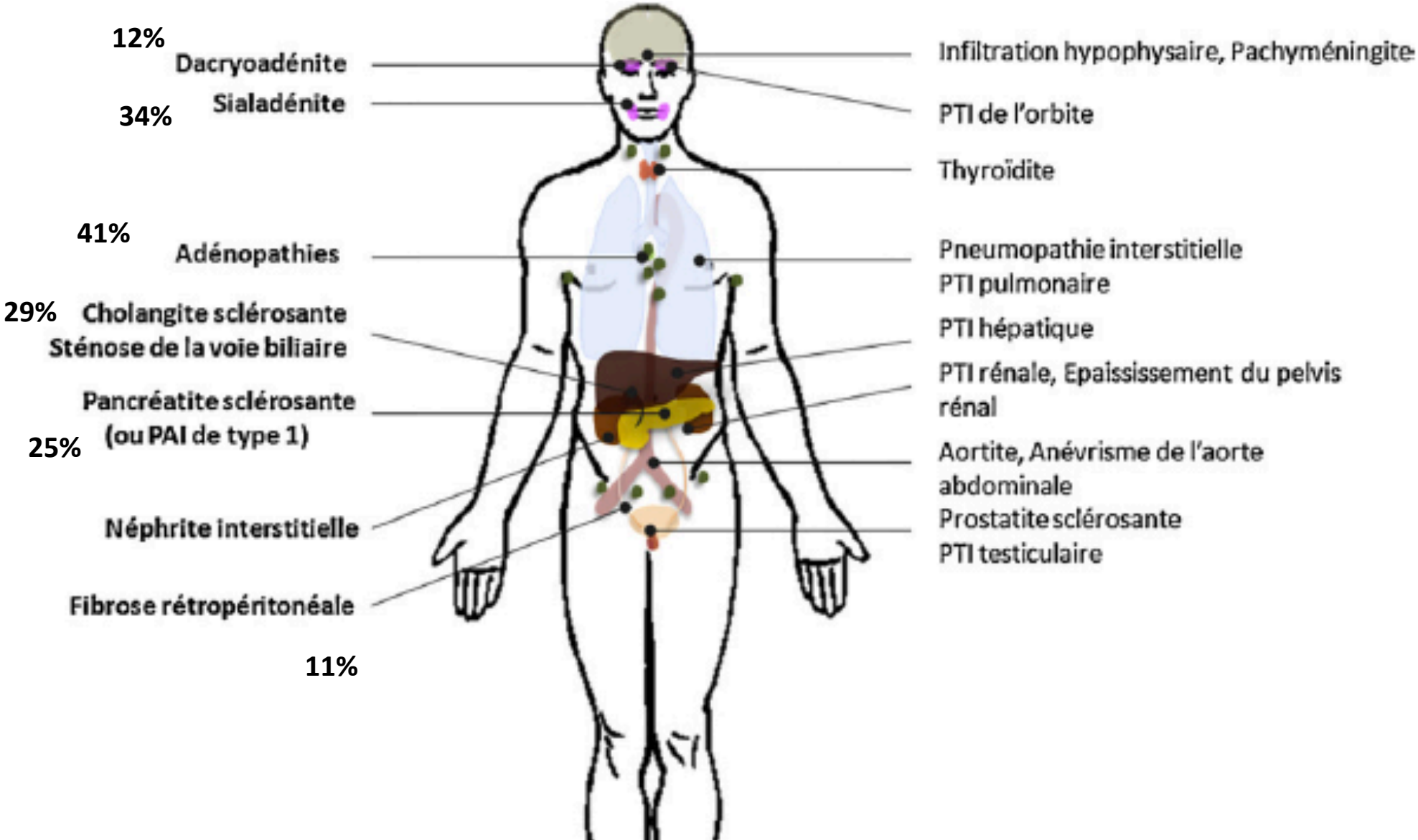
Diagnostics différentiels exclus (cf. Tableau 2 pour les formes systémiques)

Diagnostic exclu si les anticorps anti-SSA et/ou anti-SSB sont positifs[a]

CFG : champ à fort grossissement.
[a] Critère d'exclusion additionnel à ceux proposés par Okazaki et al.

M. Zaidan et al. / Néphrologie & Thérapeutique 8 (2012) 499–507

IgG4 – Présentation extra-rénale classique



IgG4 – Présentation rénale classique

- 10 - 30%
- Inaugurale, asymptomatique, découverte fortuite
- **Néphropathie tubulo-interstitielle non granulomateuse (NTI)**
  Protéinurie, IR modérée à sévère
- ± Atteinte glomérulaire (non isolée, GEM)

- Diagnostic :
  - **Histopathologique** : infiltrats lymphocytaires et plasmocytaires + fibrose
    - *Motif biopsie?* Dégradation fx rénale ou bilan masse
  - **Biologique** : IgG4 > **1,35 mg/mL,** hypocomplémentémie**,** leucocyturie, hématurie, protéinurie (non gomérulaire),

IgG4 – Imagerie rénale

- CT scanner

- Intérêt du PET-CT dans le **bilan d'extension** lésionnel initial et **l'évaluation** de la **réponse** thérapeutique

- Atteinte rénale
  - Hypertrophie rénale et/ ou multiples lésions nodulaires bilatérales, masse rénale unique, voire épaississement
  - DD: carcinome rénal!

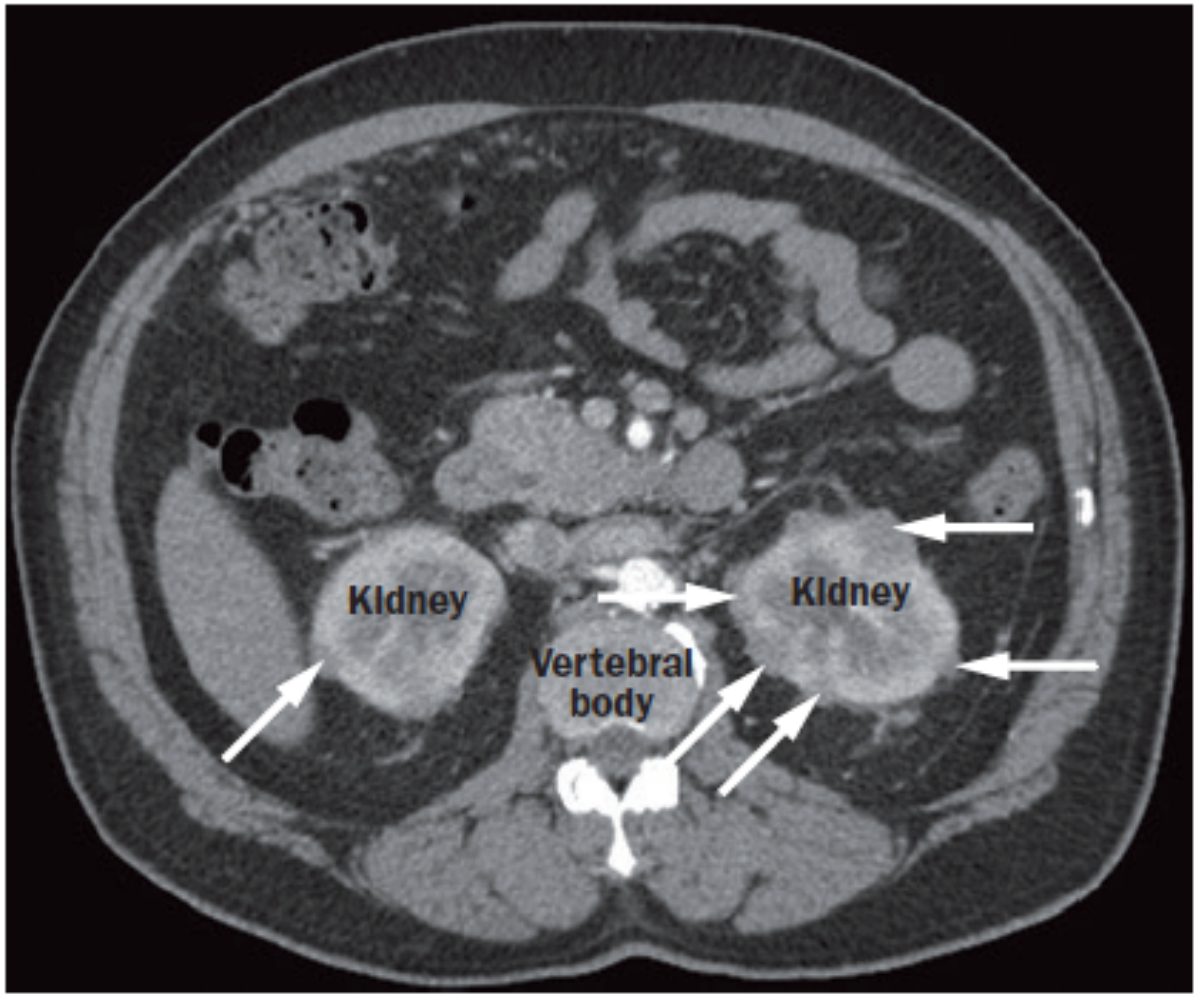
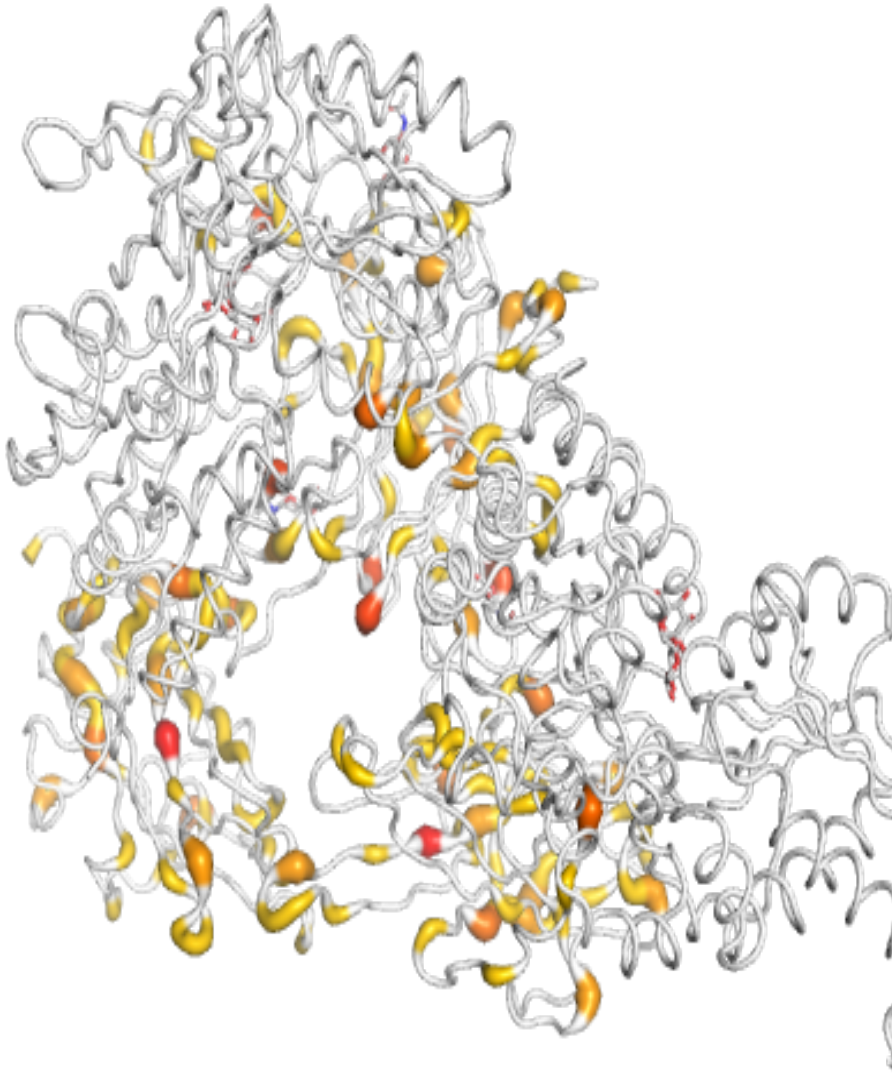


Figure 4 | CT scan of the kidneys in a patient with IgG4-related tubulointerstitial nephritis. Multiple cortical, hypodense lesions are visible (arrows).

IgG4 - Traitement

- **Corticoïdes :** en 1ère intention, très bonne réponse
  - 0,6mg/kg/j 2-4 semaines puis schéma dégressif sur 2-3 mois
  - En cas de rechutes : trt d'entretien par prednisolone 2,5 – 5 mg/j

- **Alternatives :** Azathioprine, MMF, Rituximab
  - en cas de dépendance, résistance ou C-I aux corticoïdes



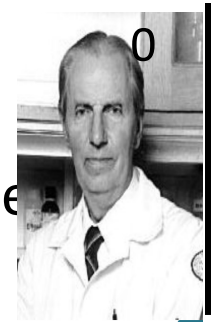
Néphrite tubulo-interstitielle chronique

UMOD

Uromoduline - C'est quoi? À quoi ça sert?

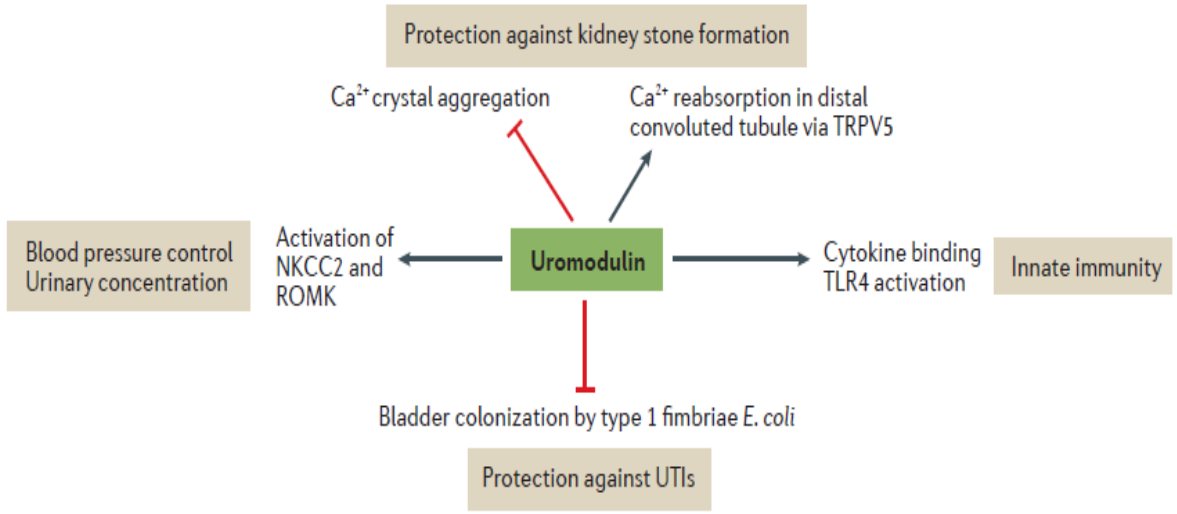
- Découverte en 1950: protéine de Tamm-Horsfall (THP)
- 1980's: uromoduline = THP
- Abondante dans l'urine **normale**
- Origine rénale: branche ascendante large de l'anse de Henlé
- Codée par le gène ***UMOD***
- RÔLES:
  -
  -

195
0



Igor Tamm

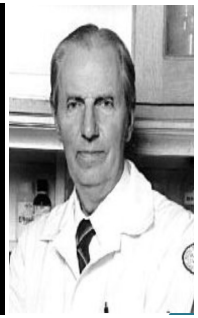
Frank Horsfall



Mutation Umod - Story

195

Frank Horsfall



Igor Tamm

J Am Soc Nephrol. 2001 Nov;12(11):2348-57.

Familial juvenile hyperuricemic nephropathy and autosomal dominant medullary cystic kidney disease type 2: two facets of the same disease?

Dahan K[1], Fuchshuber A, Adamis S, Smaers M, Kroiss S, Loute G, Cosyns JP, Hildebrandt F, Verellen-Dumoulin C, Pirson Y.

2001

Mutations of the *UMOD* gene are responsible for medullary cystic kidney disease 2 and familial juvenile hyperuricaemic nephropathy

T C Hart, M C Gorry, P S Hart, A S Woodard, Z Shihabi, J Sandhu, B Shirts, L Xu, H Zhu, M M Barmada, A J Bleyer

J Med Genet 2002;39:882–892

2002

J Am Soc Nephrol 14: 2883–2893, 2003

A Cluster of Mutations in the UMOD Gene Causes Familial Juvenile Hyperuricemic Nephropathy with Abnormal Expression of Uromodulin

KARIN DAHAN,* OLIVIER DEVUYST,† MICHÈLE SMAERS,* DIDIER VERTOMMEN,† GUY LOUTE,§ JEAN-MICHEL POUX,‖ BÉATRICE VIRON,¶ CHRISTIAN JACQUOT,# MARIE-FRANCE GAGNADOUX,** DOMINIQUE CHAUVEAU,†† MATHIAS BÜCHLER,‡‡ PIERRE COCHAT,§§ JEAN-PIERRE COSYNS,‖‖ BÉATRICE MOUGENOT,¶¶ MARK H. RIDER,‡ CORINNE ANTIGNAC,### CHRISTINE VERELLEN-DUMOULIN*, and YVES PIRSON†

Mutation UMOD: Présentation clinique

- Présentation commune aux AD

Table 2 | Usual clinical findings in patients with ADTKD

- Autosomal dominant inheritance
- Progressive loss of kidney function
- Bland urinary sediment
- Absent-to-mild albuminuria/proteinuria
- No severe hypertension during early stages
- No drug exposure potentially causing tubulointerstitial nephritis
- Normal or small-sized kidneys on ultrasound
- Nocturia or enuresis in children (owing to loss of renal concentration ability)

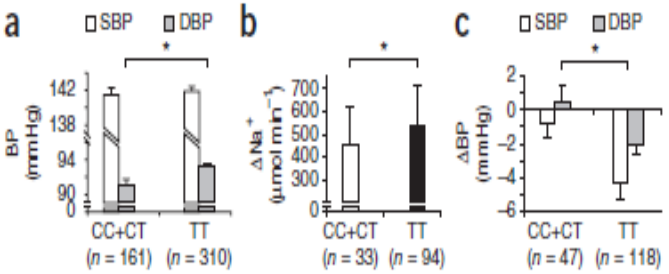
Abbreviation: ADTKD, Autosomal Dominant Tubulointerstitial Kidney Disease.

K-U Eckardt et al.: KDIGO Consensus Report on ADTKD

- Clinique**: Goutte**, ↓ progressive de la fx rénale
- Imagerie: ± kystes rénaux, rein de taille normale ou diminuée
- Biologique: **Hyperuricémie**, uromoduline urinaire basse, sédiment urinaire pauvre, ~~protéinurie~~, ~~albuminurie~~
- Histologique: **dépôts** tubulaires intracellulaires **d'uromoduline**, fibrose interstitielle, atrophie tubulaire, pas de dépôts d'Ig

➔ **Néphrite interstitielle chronique + hyperuricémie précoce**

Mutation UMOD: Allèle d'HTA?

- GWAS: variants du gène UMOD → susceptibilité pour HTA et IRC
  - Promoteur UMOD: allèle « *risk* » et allèle « *protective* »
- Modèle de souris:
  - Souris transgénique: HTA, HVG, + sensible au régime hyposodé, pattern histologique, + grande réponse au furosémide (rôle NKCC2)
- Ch
  - 

    Pad haute, + grande

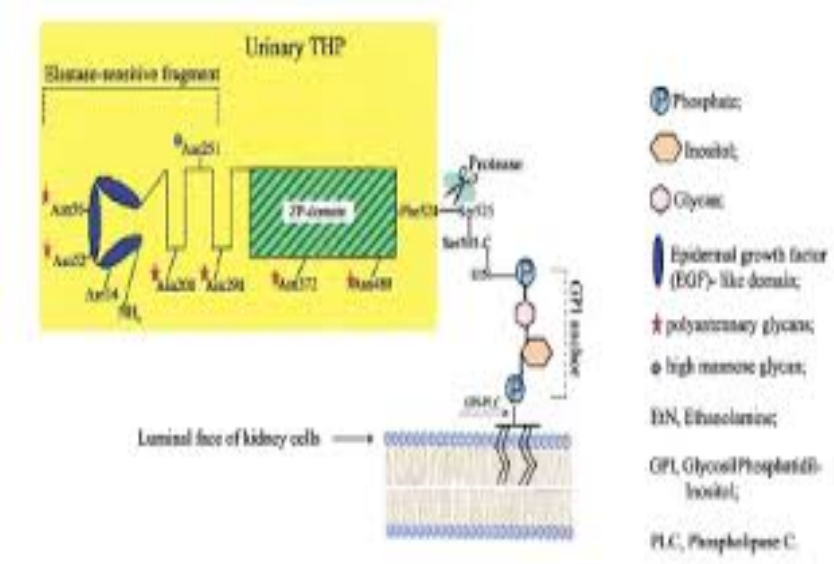
Figure 4 Increased blood pressure and response to furosemide in hypertensive patients homozygous for *UMOD* risk variants. (**a**) Average

Allèle UMOD et infection

The Uromodulin Gene Locus Shows Evidence of Pathogen Adaptation through Human Evolution

Silvia Ghirotto,* Francesca Tassi,* Guido Barbujani,* Linda Pattini,† Caroline Hayward,‡ Peter Vollenweider,§ Murielle Bochud,§ Luca Rampoldi,‖ and Olivier Devuyst¶

J Am Soc Nephrol 27: 2016



Tamm-Horsfall Protein Binds to Type 1 Fimbriated *Escherichia coli* and Prevents *E. coli* from Binding to Uroplakin Ia and Ib Receptors*

THE JOURNAL OF BIOLOGICAL CHEMISTRY Vol. 276, No. 13, Issue of March 30, pp. 9924–9930, 2001
Printed in U.S.A.

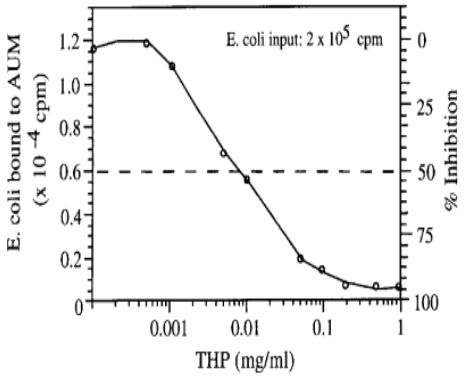
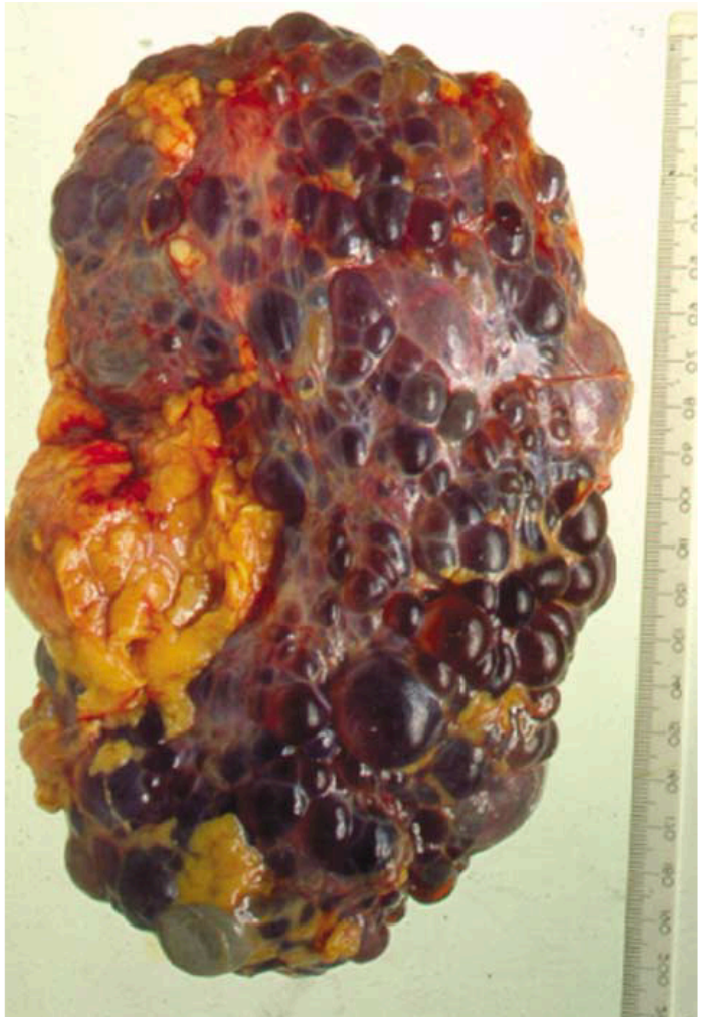


FIG. 7. **THP blocks the binding of type 1 fimbriated *E. coli* (SH48, MH type) to uroplakins.** A fixed amount of *E. coli* (2×10^5 cpm = 2×10^8 colony-forming units/ml) was incubated, in the presence of increasing amounts of THP, with immobilized AUMs (2 μg/well). Note that the binding of type 1 fimbriated *E. coli* to AUMs was greatly inhibited by THP.

ADPKD



- PKD 1
- PKD 2

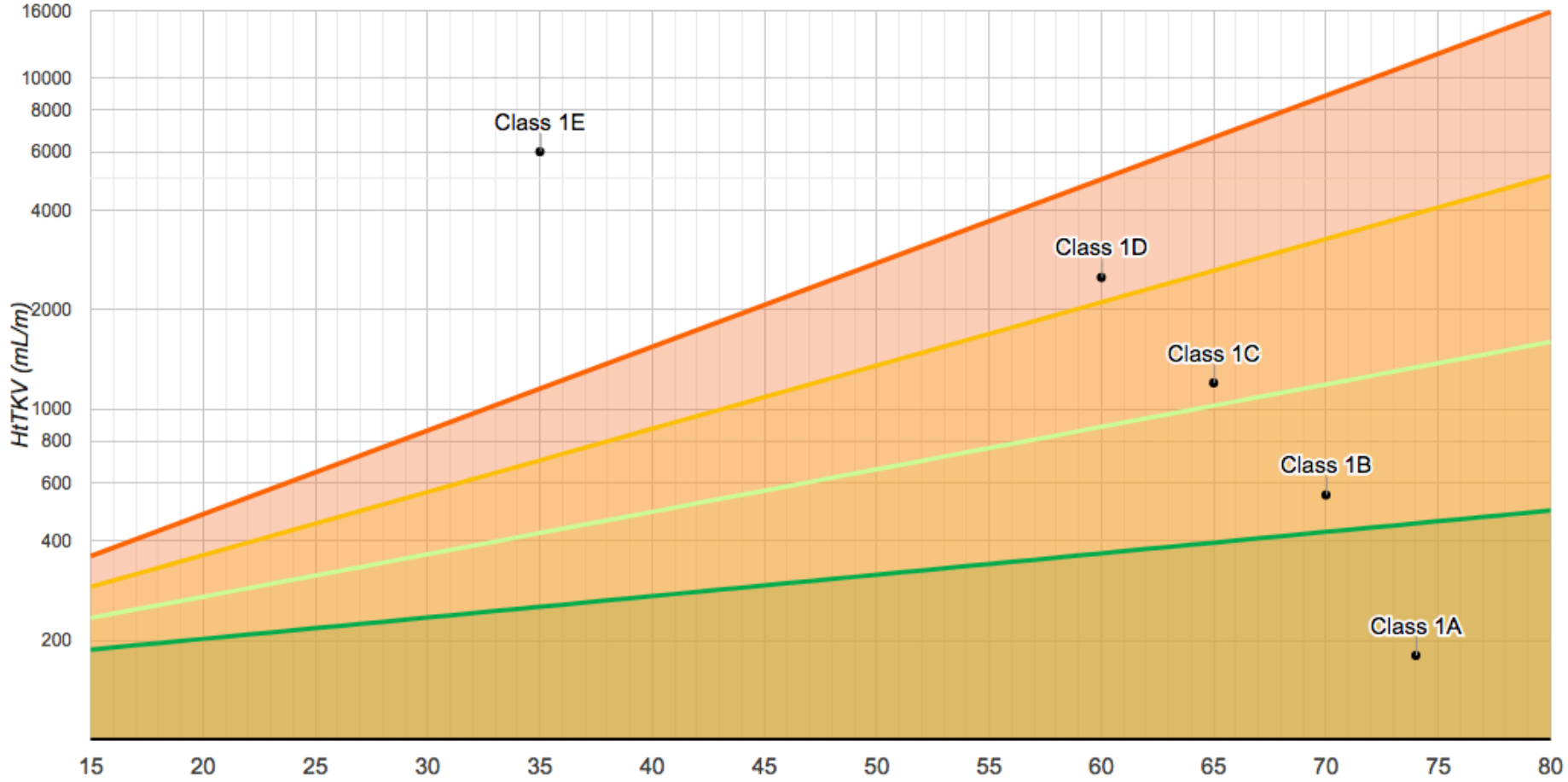
- → Variabilité ESRD 40-80 ans !

VOLUME RENAL et PROGRESSION

Table 1. Relationship between Total Kidney Volume and Glomerular Filtration Rate.

Variable	Total Kidney Volume			Glomerular Filtration Rate	
	Baseline Intercept	Slope	Slope	Baseline	Slope
	ml	*ml/yr*	*%/yr*	*ml/min*	*ml/min/yr*
Total kidney volume and age — mean ±SD (no. of patients)					
<750 ml and <30 yr	506±109 (45)	25.9±22.0 (45)	4.70±3.80 (45)	114±24.7 (47)	2.88±12.1 (46)
<750 ml and ≥30 yr	572±130 (48)	23.0±22.2 (48)	3.70±3.42 (48)	108±24.2 (49)	1.03±7.06 (48)
750–1500 ml and <30 yr	978±193 (28)	53.4±36.1 (28)	5.33±3.15 (28)	122±30.8 (28)	−0.38±7.66 (28)
750–1500 ml and ≥30 yr	1052±191 (61)	55.4±44.0 (61)	5.16±3.88 (61)	101±26.8 (61)	−1.62±10.9 (61)
>1500 ml and <30 yr	1859±333 (12)	173±81.3 (12)	9.48±4.61 (12)	99.6±23.8 (13)	−2.69±10.2 (12)
>1500 ml and ≥30 yr	2155±543 (38)	144±92.2 (38)	6.76±3.78 (38)	94.0±29.2 (38)	−5.04±5.86 (39)
P values for analysis-of-variance factors					
Total-kidney-volume group		<0.001	<0.001	0.009	0.005
Age group		0.20	0.02	0.005	0.20
Interaction		0.30	0.24	0.15	0.95

MAYO

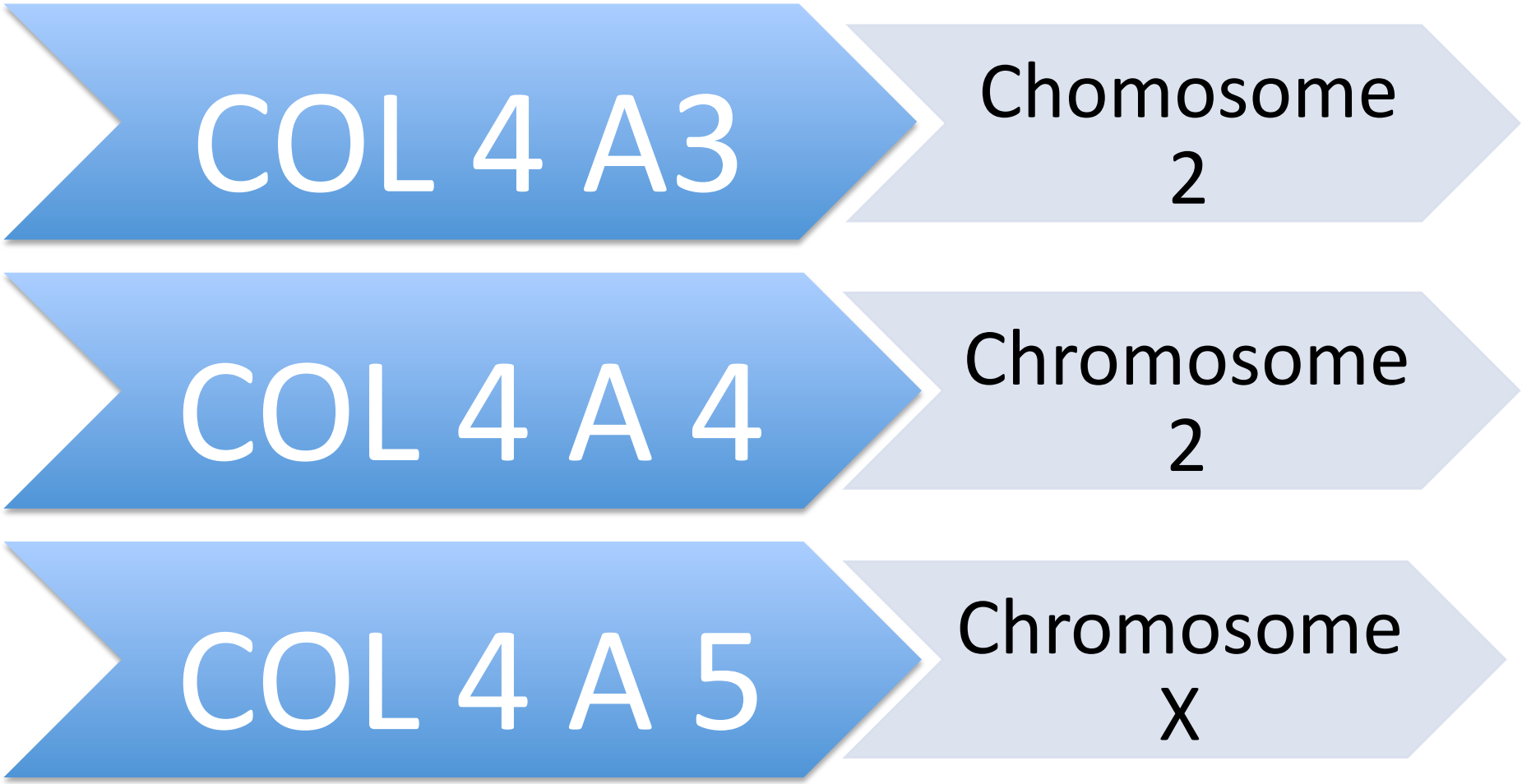

16000
10000
8000
6000
4000
2000
1000
800
600
400
200
HtTKV (mL/m)
Class 1E
Class 1D
Class 1C
Class 1B
Class 1A
15
20
25
30
35
40
45
50
55
60
65
70
75
80

VAPTAN

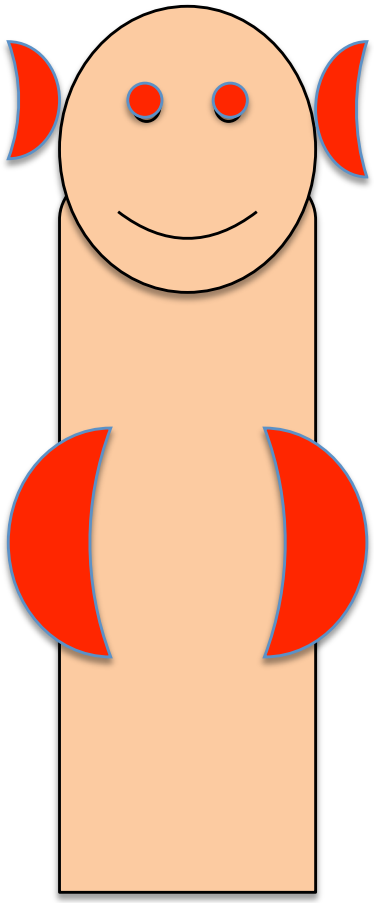
- TKV increased 2.8% per year in the tolvaptan group
- and 5.5% per year in the placebo group (P< 0.001). Tolvaptan
- significantly reduced the decline in eGFR from 10.1 to 6.8 mL/
- min/1.73 m2 over 3 years

UMOD et les Autres

Alport syndrome: a unified classification of genetic disorders of collagen IV a345



Syndrome d'Alport



- Maladie Glomérulaire
  - IgA Like !
- Surdité partielle (O.I)
- Anomalie Cornéene

- Thin Membrane nephropathy
- HSF

	Recommandation à la pratique
Juste Hématurie	Contrôle Annuel
+ Microalbuminurie	Contrôle semestriel Considère IEC surtout pour lespatients avec mutations sévères
+ Protéinurie	Start IEC
+ Protéinurie sous iRAAs	Contrôle sévère de la pression artérielle

Table 2 | Clinical practice recommendations for monitoring and treatment of Alport syndrome

Hematuria with normal UACR[a] and UPCR[b]	Annual blood pressure, serum creatinine, UACR, UPCR Report outcome to national or international registry
Hematuria + microalbuminuria	Increase monitoring to every 6 mo Consider ACEi,[c] especially for - patients with severe mutations (deletion, nonsense, frameshift, splicing) - SNHL[d] - family history of ESRD before age 30 yr Report outcome to national or international registry
Hematuria + overt proteinuria	Monitor every 6 mo Start ACEi, dose according to published recommendations[11,12]; Effective contraception recommended for female subjects of child-bearing age Report outcome to national or international registry
Progressive proteinuria (despite ACEi)	Consider add on therapy, such as - stringent blood pressure control including ARBs,[e] aldosterone-antagonists, calcium channel blockers, diuretics - statins in patients with high cholesterol levels or nephrotic patients with dyslipoproteinemia - paricalcitol in patients with secondary hyperparathyroidism Watch for future upcoming therapies Report outcome to national or international registry

HNF1B Janus Gene

Major criteria	Minor criteria
Fetal bilateral hyperechogenic kidneys	Ectopic kidney
Multicystic dysplastic kidney	Vesico-ureteral reflux
Renal agenesis	Hydronephrosis
Hypoplastic or dysplastic kidneys	
Cysts from unknown origin	
Extra-renal criteria	**Positive familial history**
Diabetes mellitus	Abnormalities in kidney
Hypomagnesaemia	Abnormalities in urogenital tract
Hypokalaemia	Gout
Hyperuricaemia	Liver function abnormalities
Liver function abnormalities	Diabetes or exocrine pancreas dysfunction

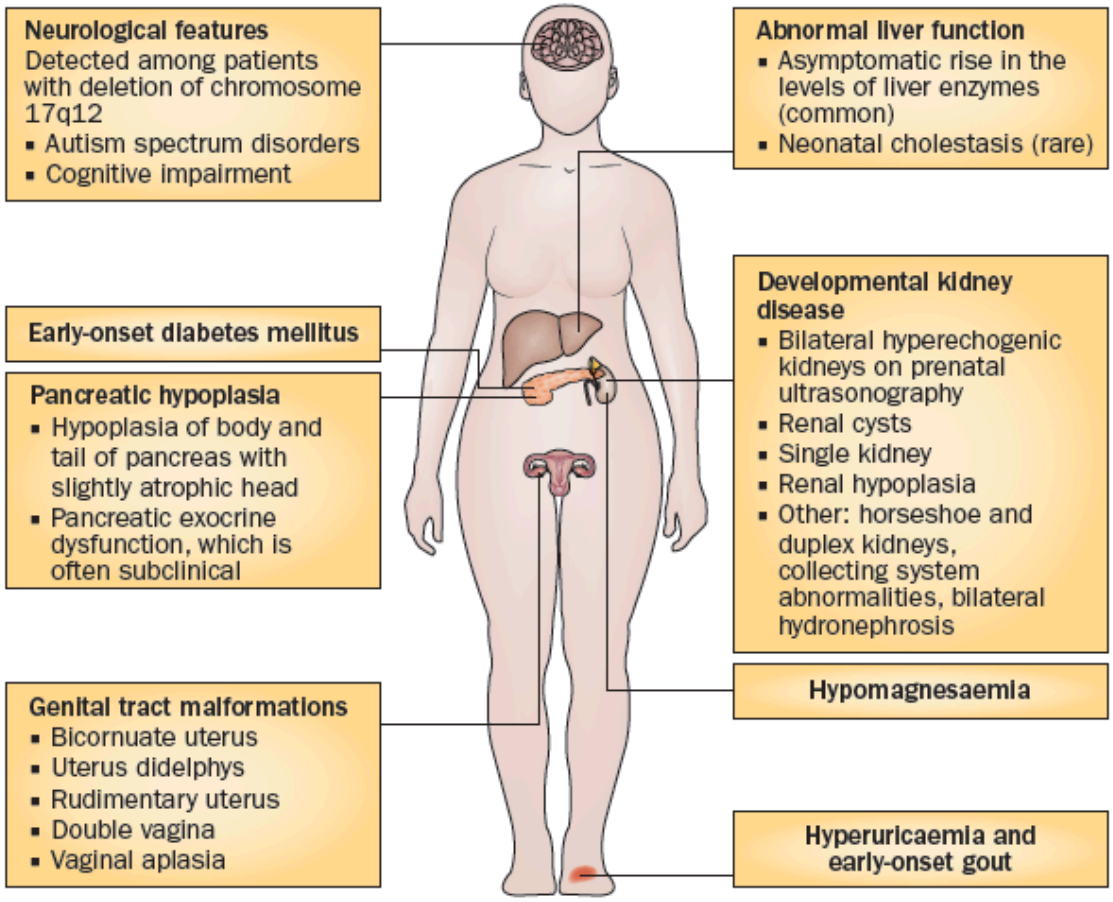
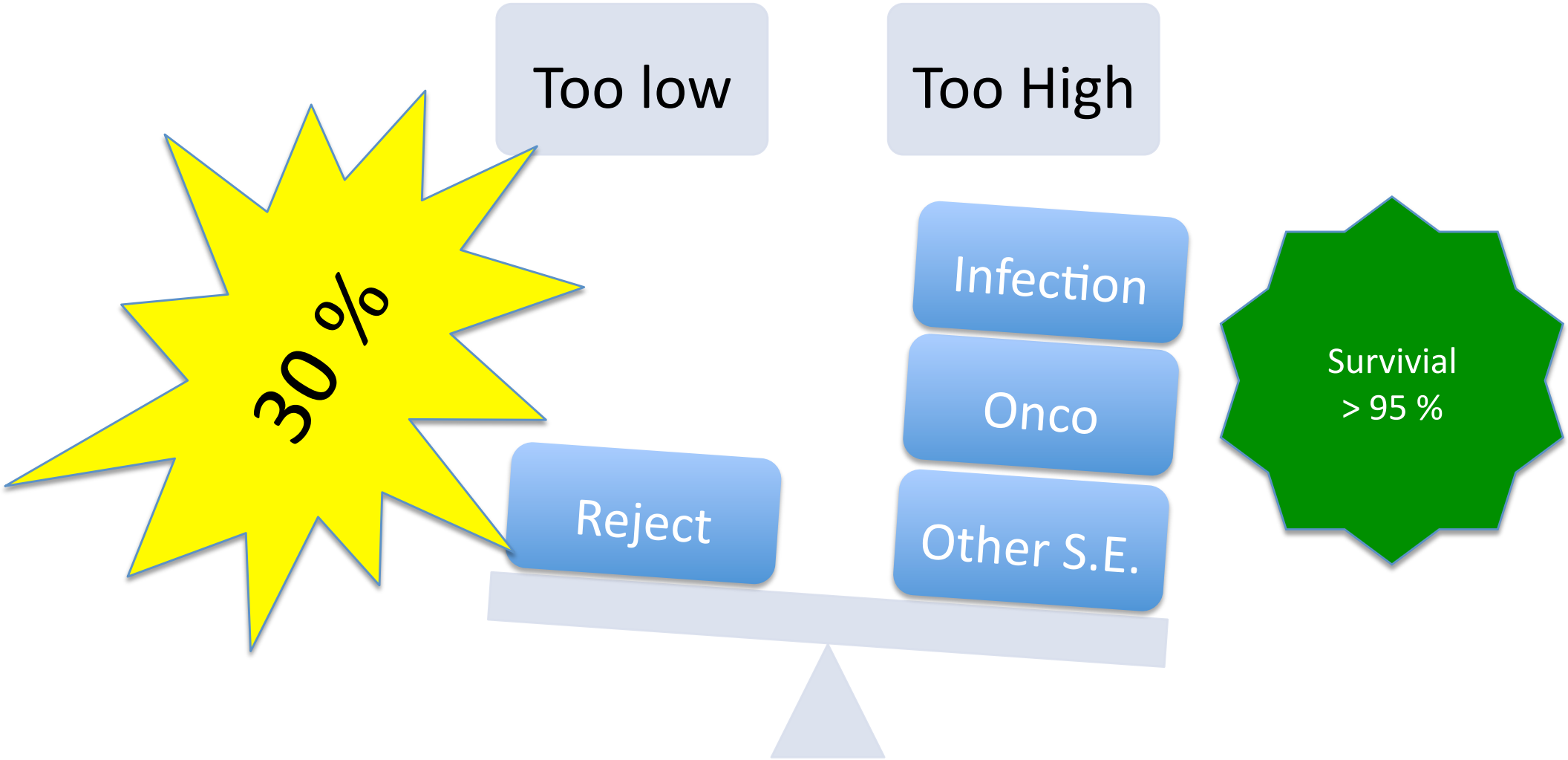


Figure 1 | Renal and extra-renal phenotypes frequently observed among patients with hepatocyte nuclear factor 1β-associated disease.

Transplantation Rénale

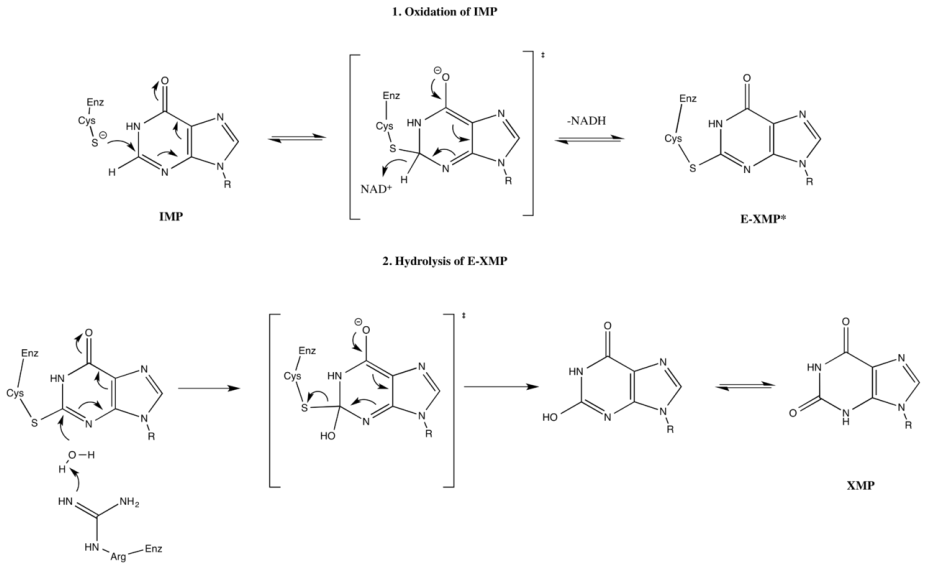
Ne regardez pas comment je tombe
mais comment je me relève de
chaque chutes

Treatment


Too low
Too High
30 %
Infection
Onco
Other S.E.
Reject
Survivial
> 95 %

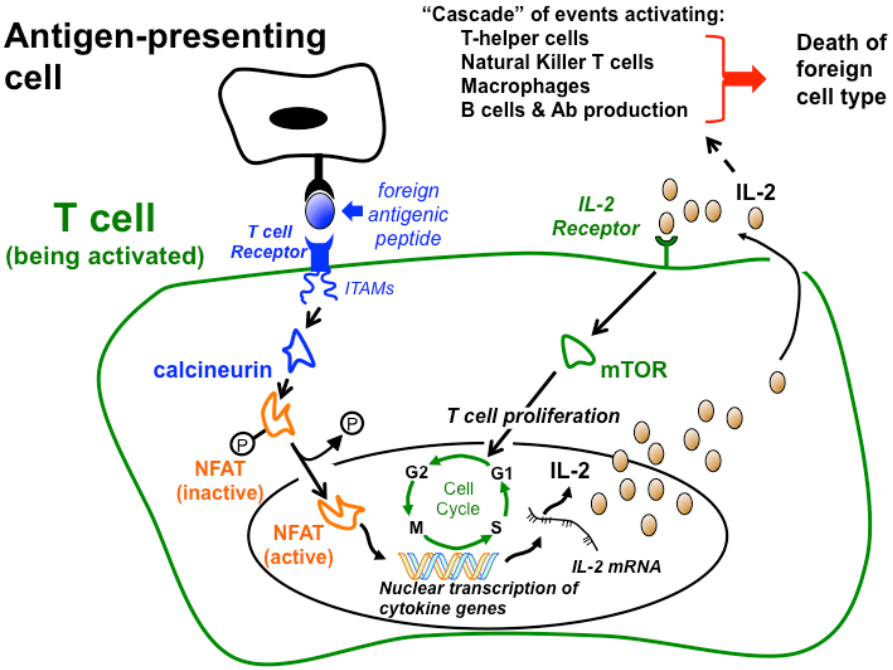
Comment cela marche

AZA MMF:



inosine 5'-phosphate → xanthosine 5'-phosphate → GUANINE (ADN)
Empeche la réplicatin cell immune

CSA FK506



Empêche la stimulation du système immune

Immunosupression

- AZA → MMF
- Cyclosporine/MMF→ Tacrolimus / MMF
- (Everolimus), mTOR inhibiteur (place onco TPR)
- Protocole Csfree: pas dans les recommandations (recherche)

Transplantation. 1996 Apr 15;61(7):1029-37.
A blinded, randomized clinical trial of mycophenolate mofetil for the prevention of acute rejection in cadaveric renal transplantation. The Tricontinental Mycophenolate Mofetil Renal Transplantation Study Group.(n 503)

CELL CEPT / MY FORTIC : Mycophenolate

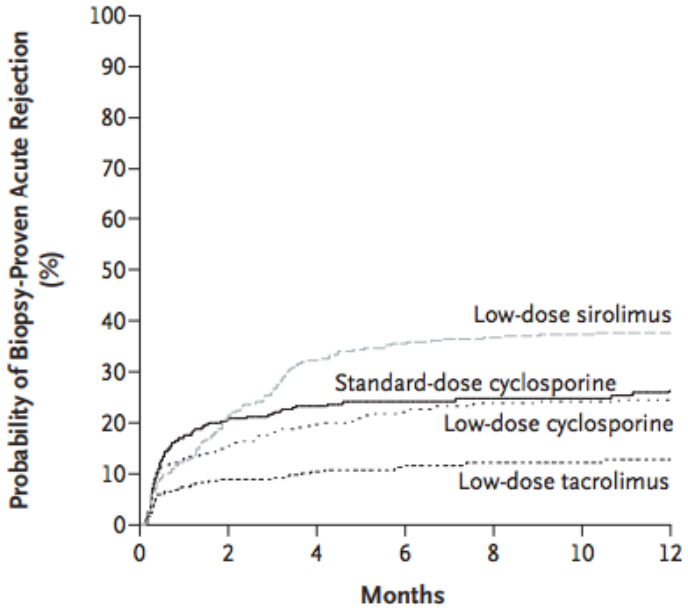
Biopsy-proven rejection occurred in 15.9% of patients in the MMF 3 g group and 19.7% in the MMF2 g group, compared with 35.5% in the AZA group

DIARHEE

Following these welldesigned double-blind controlled trials, several open-label studies did report an improvement in GI complaints following a switch from MMF to EC-MPS

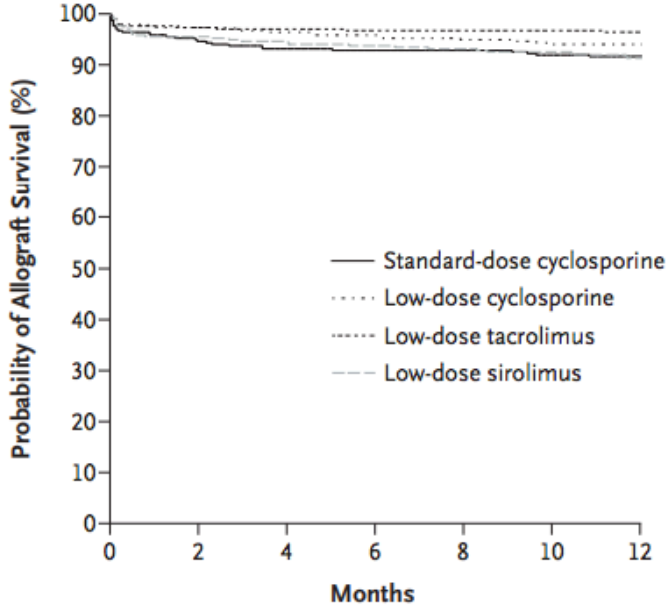
Etude Elite Symphony

A



No. at Risk							
Standard-dose cyclosporine	390	293	277	272	268	265	257
Low-dose cyclosporine	399	326	308	297	289	283	276
Low-dose tacrolimus	401	350	340	334	328	324	309
Low-dose sirolimus	399	297	252	236	228	225	214

B



No. at Risk							
Standard-dose cyclosporine	390	359	345	341	338	333	325
Low-dose cyclosporine	399	381	371	367	363	355	345
Low-dose tacrolimus	401	381	374	371	367	363	349
Low-dose sirolimus	399	373	364	358	349	344	329

TACROLIMUS (ADVAGRAFT): TAUX 5 - 7

Les Barrières

La Barrière ABO

Technique

- Doser les Anticorps
- Plasmaphérèse.
- Immunoabsorption
- IgG Endopeptidase

Resultat

- Bon avenir: 92 % us 94 % à trois ans
- Rejet : risque ++ 1ere année
- Mortalité à 1 ans +1 % (2%)
  - ABOi: infection 49%
  - ABOc: infection 13 %
- Rejet: Surtout ABMR (anticorps médiés). RR 3,86

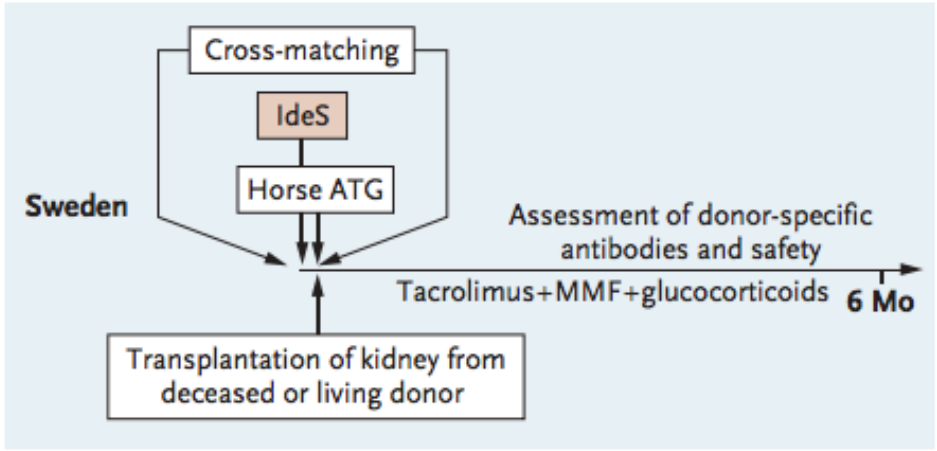
ABO-Incompatible Kidney Transplant Outcomes
A Meta-Analysis
Annelies E. de Weerd and Michiel G.H. Betjes

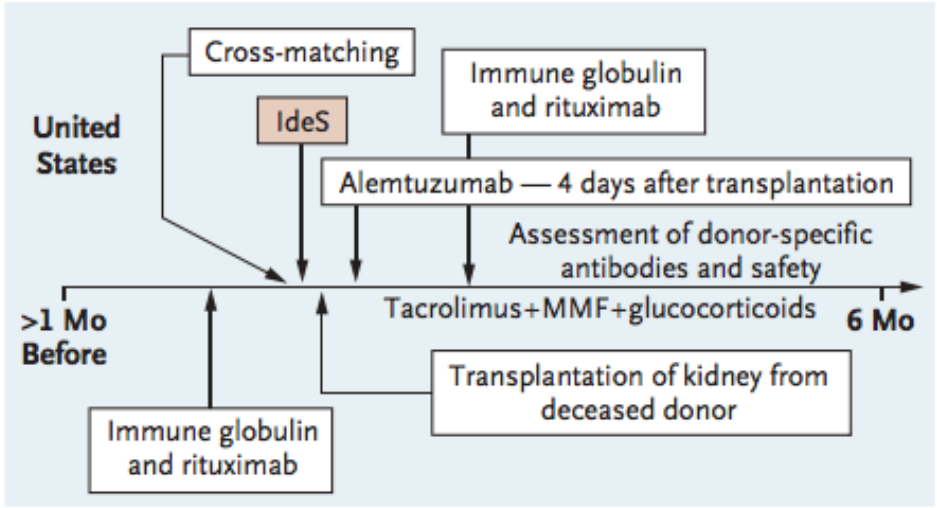
ORIGINAL ARTICLE

IgG Endopeptidase in Highly Sensitized Patients Undergoing Transplantation

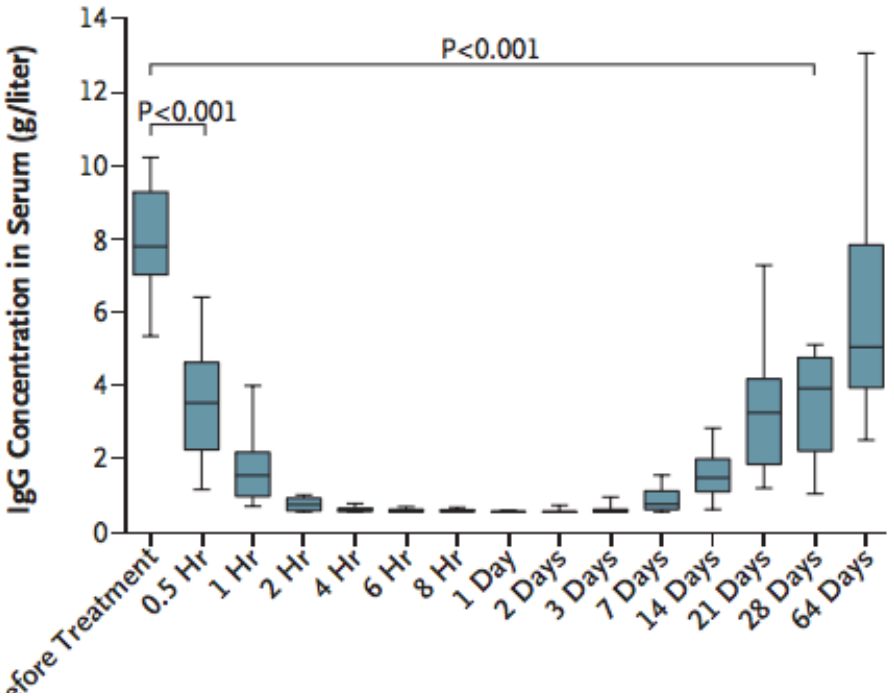
S.C. Jordan, T. Lorant, J. Choi, C. Kjellman, L. Winstedt, M. Bengtsson, X. Zhang, T. Eich, M. Toyoda, B.-M. Eriksson, S. Ge, A. Peng, S. Järnum, K.J. Wood, T. Lundgren, L. Wennberg, L. Bäckman, E. Larsson, R. Villicana, J. Kahwaji, S. Louie, A. Kang, M. Haas, C. Nast, A. Vo, and G. Tufveson

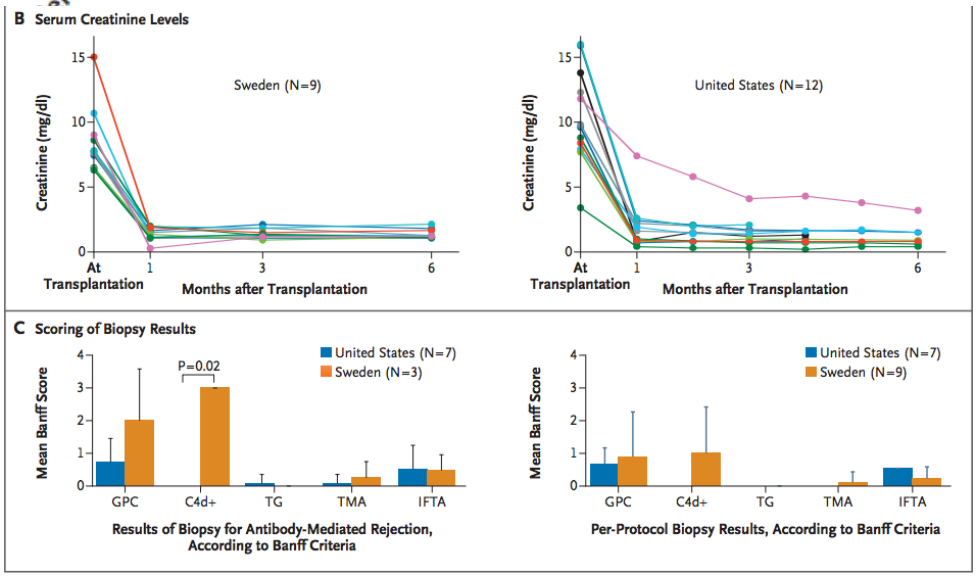
B Immunosuppressive Regimens



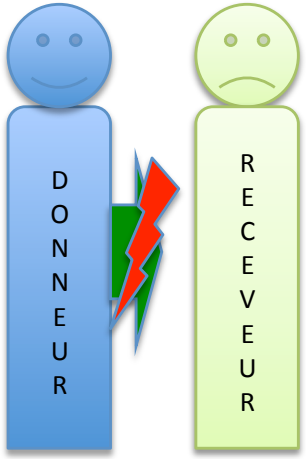


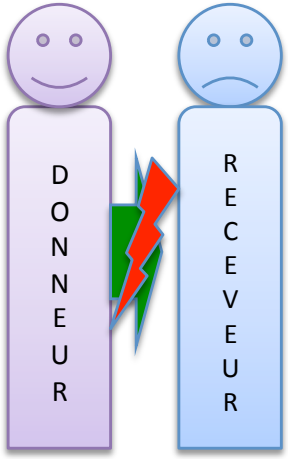
D Effect of IdeS on Circulating IgG Levels in Highly Sensitized Patients

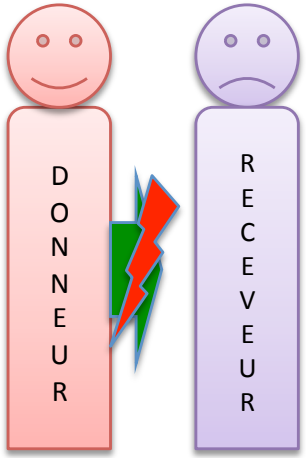


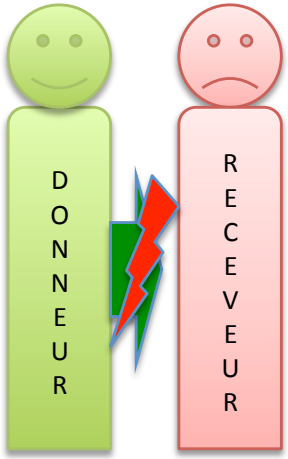


Donneurs vivants et incompatibilité









Avantage Donneur vivant:

- Survie du greffon meilleur
- Délais d'attente moins long (donc survie patient meilleur).

- Mais:
  - ABO incompatibilité
  - Positive Cross match
  - HLA incompatible

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The Dutch National Living Donor Kidney Exchange Program

Marry De Klerk, Karin M. Keizer, Frans H. J. Claas, Marian Witvliet, Bernadette J. J. M. Haase-Kromwijk, Willem Weimar

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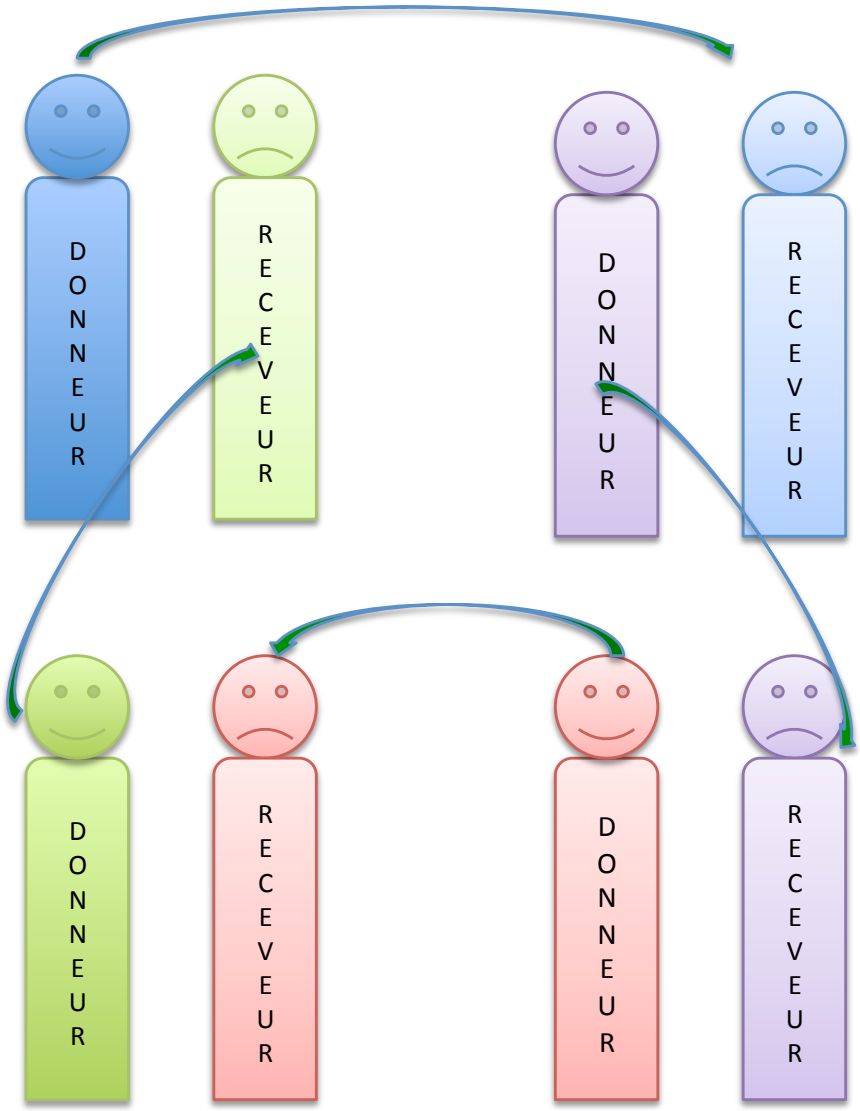
Donneurs vivants et incompatibilité



- Sept 2006 : first national workshop in Belgium
- Nov 2007 : Protocol for LDEP (7 transplant centers), in agreement with Belgian law on organ TP
- In cooperation with ET (license of Dutch program – NTS) – pts on ET waiting list
- The graft travels to recipient center ; not the donor
- Equitable, fair exchange …. No financial compensation
- Responsible national coordinators : Mrs Nelly Mauws (UZ Gent) and Vanessa De Meester (UCL)
- Run : 2-3x year
- Run 1 : 6 couples (april 2013) ; run 4 : 18 couples (march 2015)

Perte de Greffon et Infection: BK Virus

BK virus

NEW HUMAN PAPOVAVIRUS (B.K.) ISOLATED FROM URINE AFTER RENAL TRANSPLANTATION

SYLVIA D. GARDNER ANNE M. FIELD

Virus Reference Laboratory, Central Public Health Laboratory, Colindale Avenue, London N.W.9

DULCIE V. COLEMAN B. HULME

Department of Histopathology and Cytology and Medical Unit, St. Mary's Hospital, London W.2

THE LANCET, JUNE 19, 1971

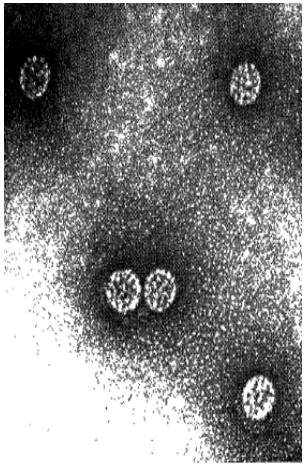


Fig. 1a—B.K. virus particles from urine. (×180,000.)

BK Virus Infection in a Kidney Allograft Diagnosed by Needle Biopsy

Raman Purighalla, MBBS, Ron Shapiro, MD, Jerry McCauley, MD, and Parmjeet Randhawa, MD

American Journal of Kidney Diseases, Vol 26, No 4 (October), 1995: pp 671-673

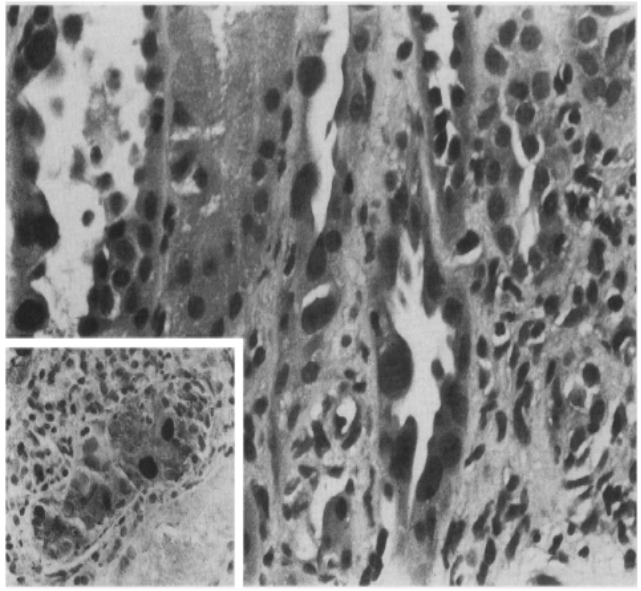


Fig 2. Electron micrograph showing a cluster of viral particles within a tubular epithelial cell. Measurements with a calibration grid indicated an average diameter of 51 nm, consistent with that described for the human polyoma virus. (original magnification ×30,800; inset, original magnification ×140,000).

BK virus

- Polyomavirus, famille papovavirus
- **1971** (S. Gardner): BK virus isolé dans urine d'un transplanté rénal avec sténose urétérale à 4 mois de la greffe
- **1995**: néphrite à BK virus chez transplanté rénal
- 4 génotypes: type I (séroprévalence pop gén: 80%)
- **Transmission**: voies respiratoires, transfusion, transplacentaire, transplantation
- **Latence**: Lymphocytes B, cellules épithéliales tubulaires rénales, cellules urothéliales
- **Réactivation**
  - Chez immunocompétents: virurie asymptomatique
  - Chez immunodéprimés: symptomatique
    - Cystite hémorragique chez greffés moelle osseuse

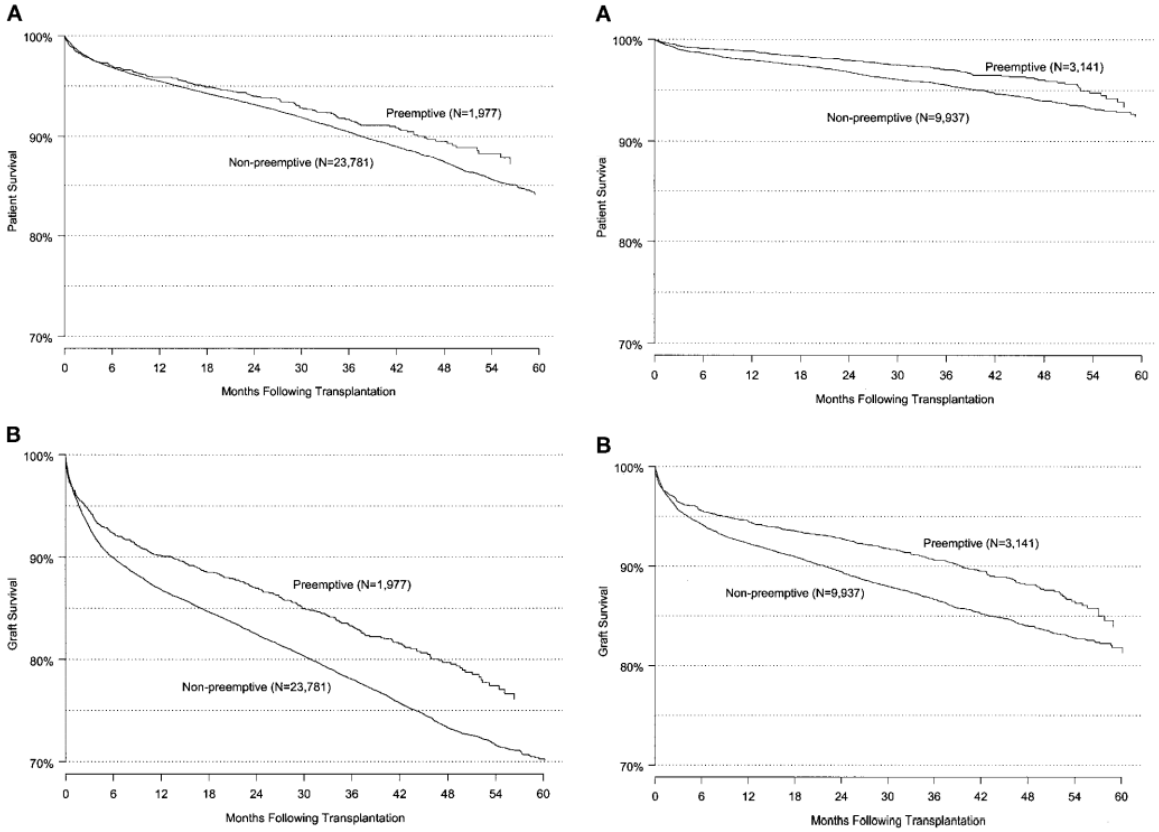
BK virus et transplantation rénale

- **Histoire naturelle:**
  - Virurie et virémie (10-15%)
    - **Néphropathie tubulo-interstitielle**!! (5%)
      - Perte du greffon
- **Dépistage**? 1x/mois pdt 6mois puis 1x/3mois pdt 2ans, si ↑ créat, biopsie évocatrice → **1° Urines: PCR -> virurie** >10^7copies/ml (Se 100%, Sp 91,8%)
- **Diagnostic**: PCR plasma: **Virémie** > 10^4 copies/ml → suspicion néphropathie!! (Se 100%, Sp 97,4%)
- **Prise en charge:**
  - Diminution IS: modalités au cas par cas, /!\rejet humoral/cellulaire
  - Switch IS
  - *Autres: léflunomide, inhibiteurs mtor, Ig IV, quinolones, cidofovir (néphrotoxique) ou le brincidofovir (non néphrotoxique) → peu efficaces*

GREFFE AVANT DIALYSE

Greffe Pré- emptive

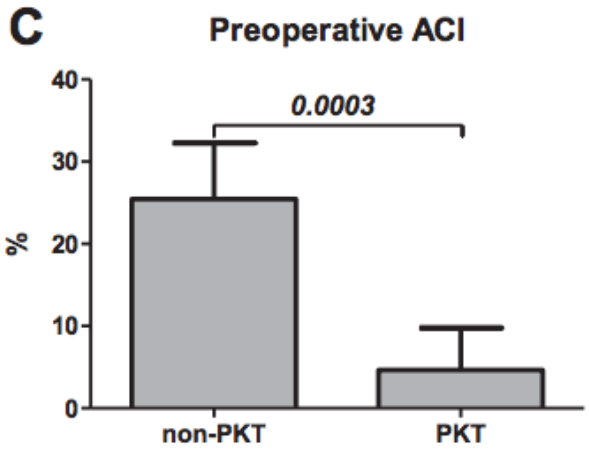
- Conditions.
- Avantages.
- Meilleurs survie
- Inconvénients

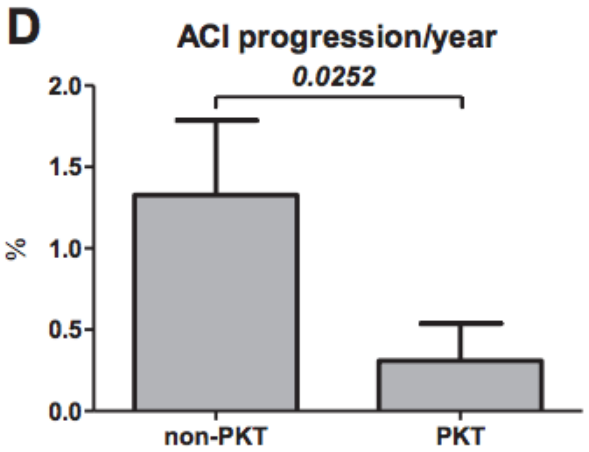


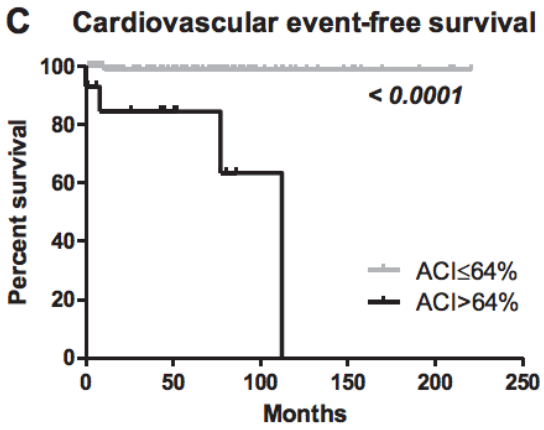
J Am Soc Nephrol 13: 1358–1364, 2002

Greffe Pré- emptive

- Conditions.
- Avantages.
- Meilleurs survie patient/greffon







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