Anti-glomerular basement membrane disease

Professor Stephen McAdoo
Consultant Nephrologist, Hammersmith Hospital, Imperial College Healthcare NHS Trust
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FVSG Meeting, Paris France
2nd April 2026

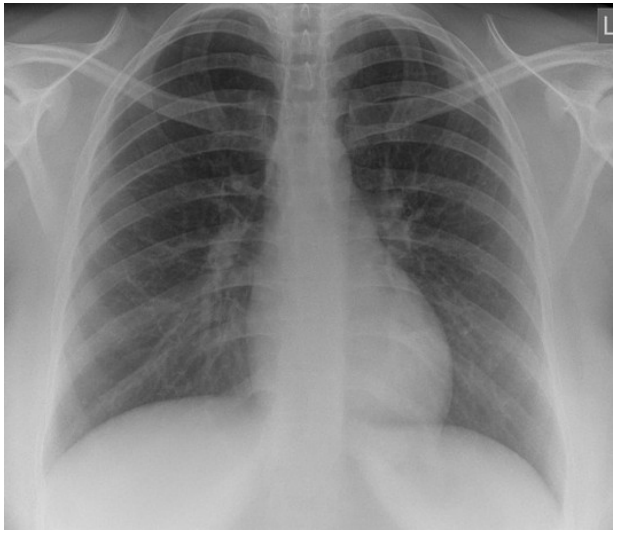
Case 1

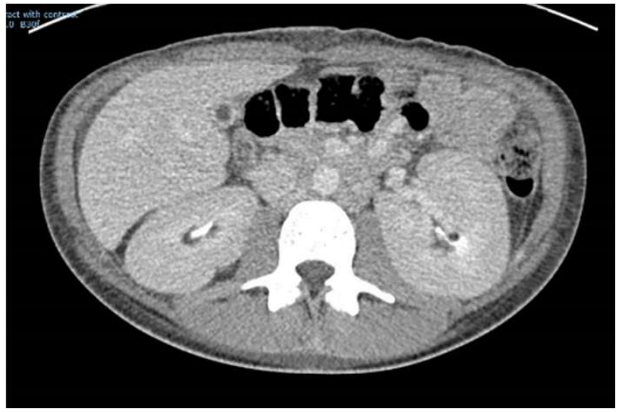
29F Waitress
No past medical history, non-smoker
1w fever, loin pain, visible haematuria
Treated for UTI by GP

Low grade fever
Systems examination normal
Urinalysis: blood 3+, protein trace, leucocytes 3+, nitrites negative
Creatinine 290 µmol/L, CRP 152 mg/L

Normal CXR
Unobstructed kidneys, ‘large relative to size’

Treated for pyelonephritis



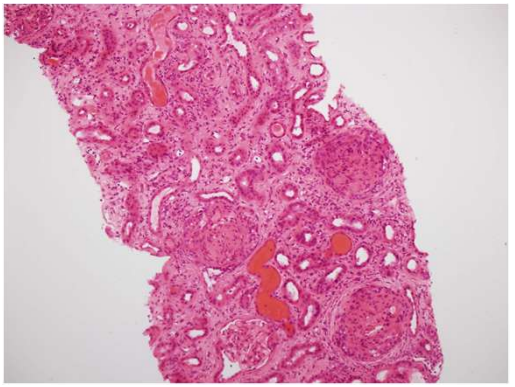


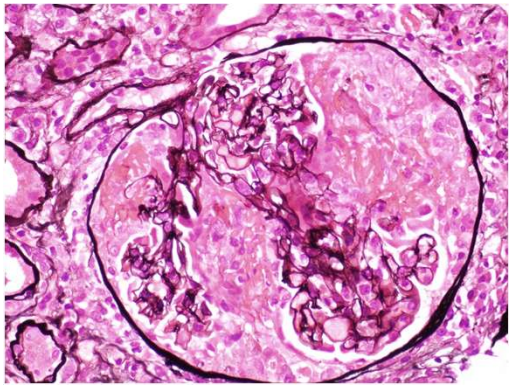
Case 1

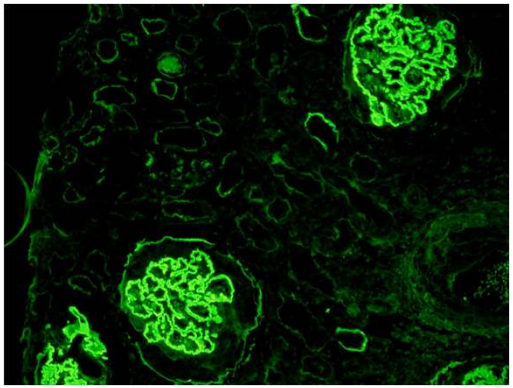
Day 5: Creatinine risen to 454 µmol/L

Urgent transfer to renal unit for biopsy

- 11/18 glomeruli with fibrinoid necrosis and cellular crescents
- None obsolete, no significant IFTA
- Strong linear IgG







Same days results:

- Anti-GBM antibody: 220 iu (NR <15)
- ANCA negative
- Creatinine 512 µmol/L

Case 1

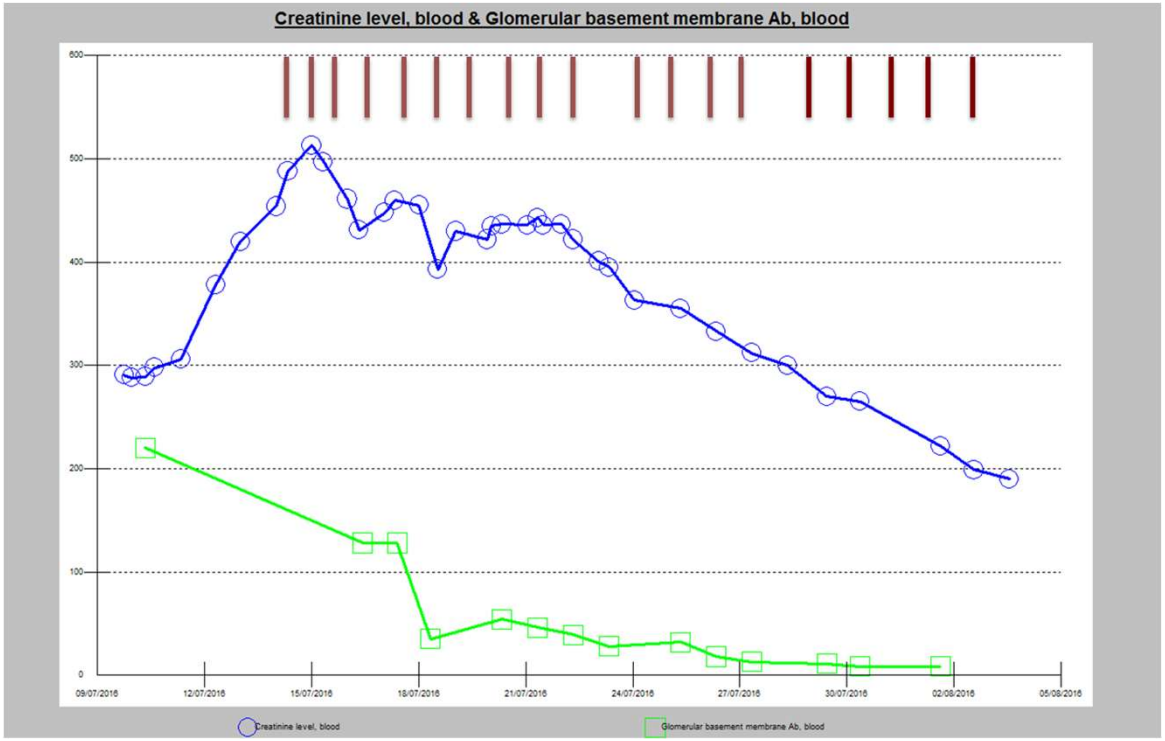
Commenced treatment

- Plasma exchange: 14 ->19 sessions
- Oral Prednisolone 60mg OD
- Oral Cyclophosphamide 2 mg/kg/day
- Adjunctive prophylaxis

Recovery to normal eGFR

Successful pregnancy after ~18 month

No relapses



Case 2

57M non-smoker

Presented October 2022: non-specifically unwell for 4 weeks

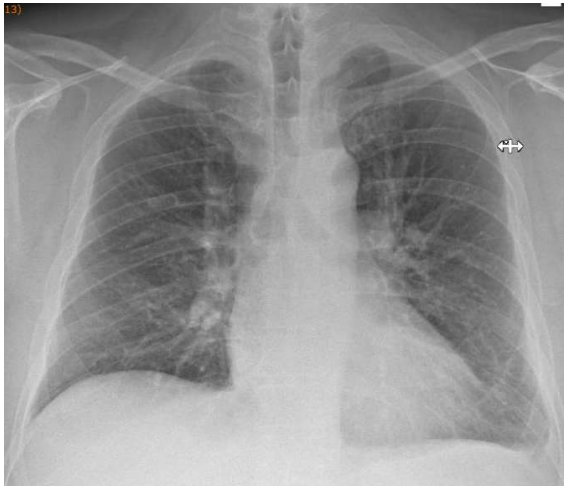
sCr 812 µmol/L, dialysis-dependent, UO 0.8 L/day

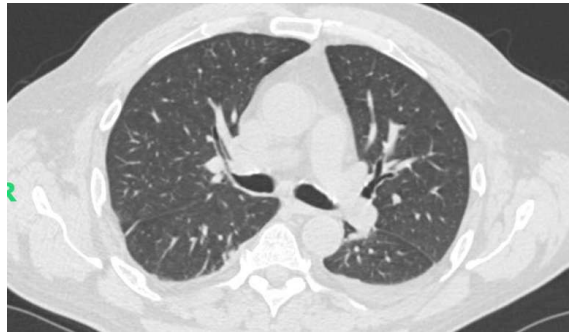
Anti-GBM >650 iu; ANCA negative

No evidence of lung haemorrhage

No biopsy before treatment

Treated with PEX, Oral CyP, RTX and Oral Pred





Case 2

Non-recovery of renal function

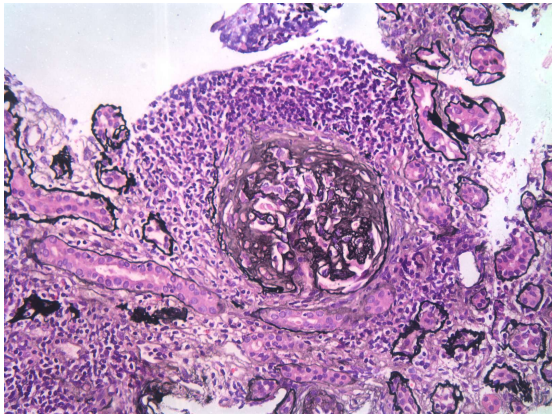
Progressive oligoanuria

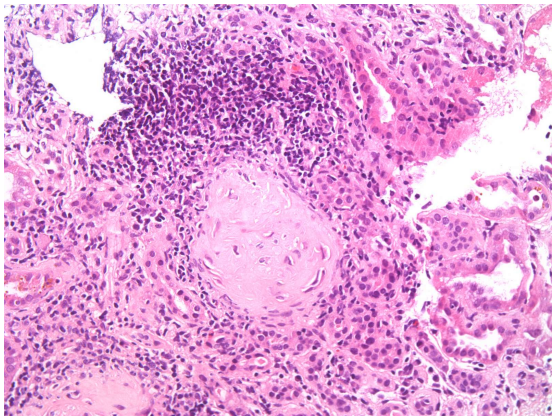
Biopsy after PEX #14

11/15 gloms obsolete, remainder with crescents

Anti-GBM 48 iu

Discharged after 3.5 weeks on maintenance HDx





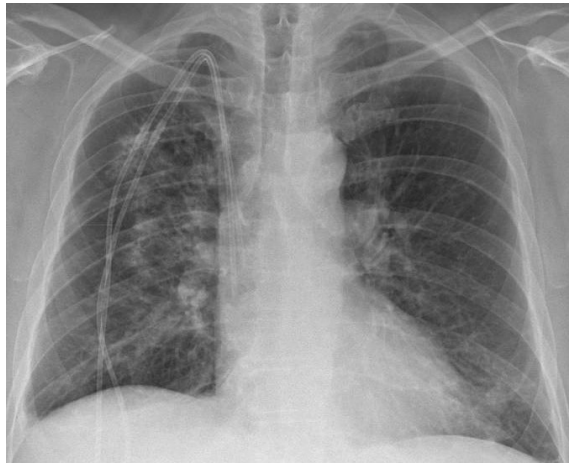
Case 2

Represented after 10 days

Dyspnoea, blood-stained sputum

2g fall in Hb

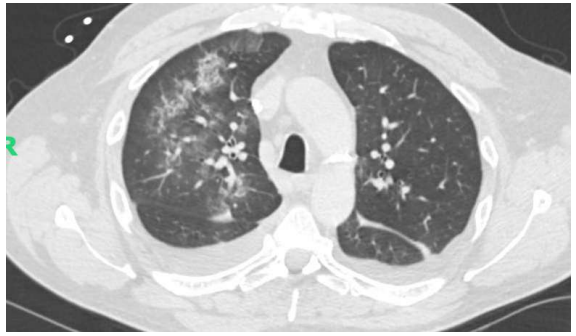
Anti-GBM rebound to 280 iu



Pulmonary ‘relapse’ in context of pulmonary oedema ± infection

Re-introduction of PEX

Total >20 exchanges



Resolution of lung haemorrhage, with non-recovery of kidney function

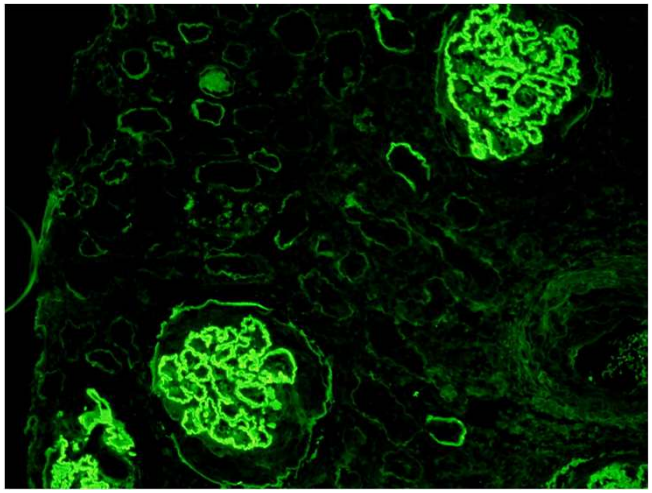
CMV viraemia, pneumonia, new-onset diabetes

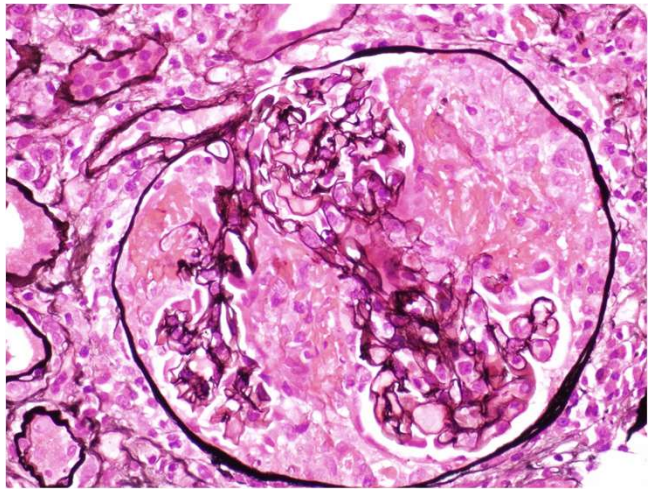
Anti-glomerular basement membrane disease

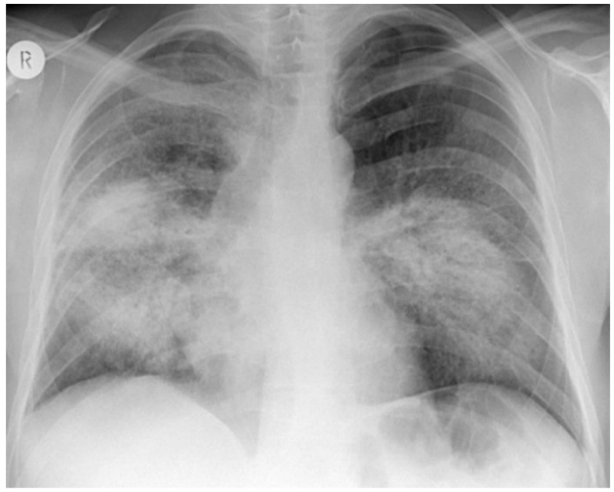
Vasculitis affecting glomerular capillaries, pulmonary capillaries, or both

Presents with rapidly progressive glomerulonephritis and/or diffuse alveolar haemorrhage

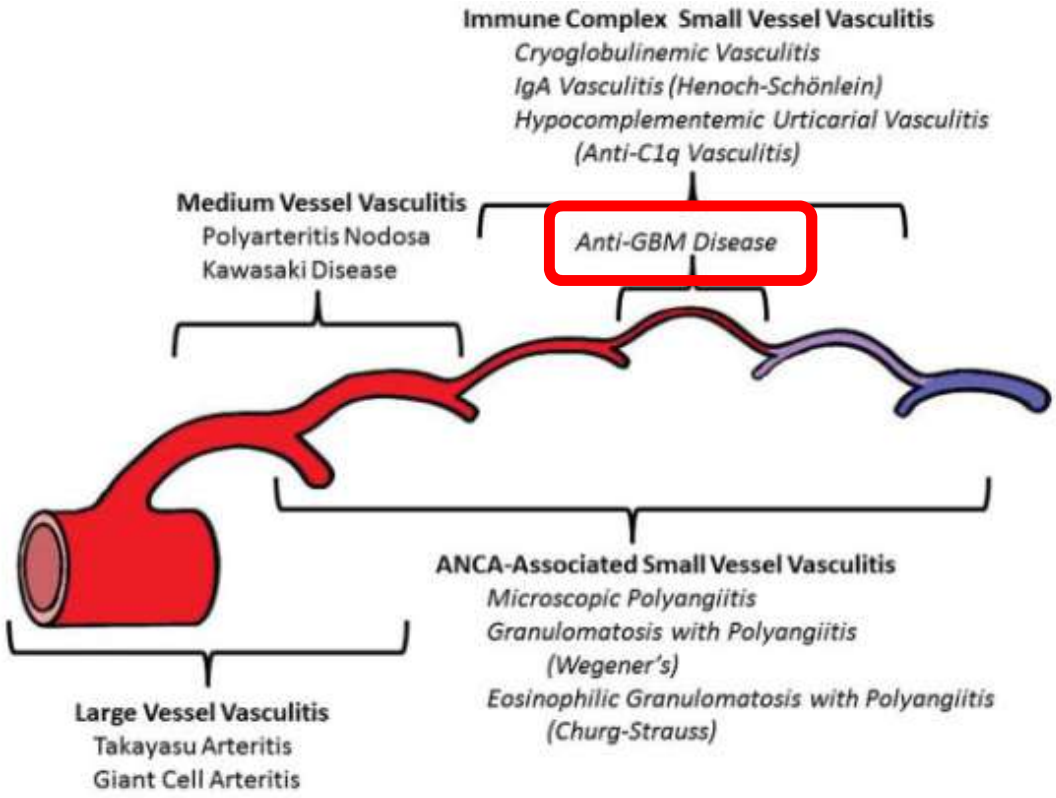
Characterised by autoreactivity to GBM, and deposition of anti-GBM autoantibodies in particular







Anti-glomerular basement membrane disease



Jennette, *Arthritis Rheumatol* 2013

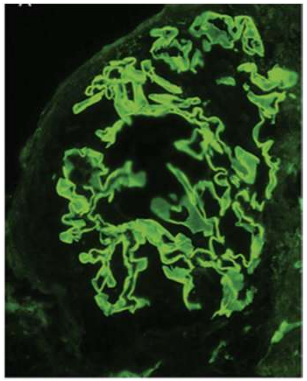
Goodpasture Disease

THE SIGNIFICANCE OF CERTAIN PULMONARY LESIONS IN RELATION TO THE ETIOLOGY OF INFLUENZA.

By Ernest W. Goodpasture, M.D.,
Boston, Massachusetts.

(From the Department of Pathology, Harvard Medical School.)

The great variations in the results of bacteriological analyses of the lungs and respiratory tract of those dead of influenza have left no common ground for agreement upon any one microörganism as the etiological agent of this disease. Although in certain sections of the country evidence seemed to be strongly in favor of Pfeiffer's bacillus,[1] the failure to find this microörganism and the predominance of other invading bacteria in different localities have served



Goodpasture Disease

GOODPASTURE'S SYNDROME
(PULMONARY HÆMORRHAGE ASSOCIATED WITH GLOMERULONEPHRITIS)[1]

M. C. STANTON[2] and J. D. TANGE[3]
From the Department of Pathology, University of Melbourne

SUMMARY

Nine cases, which show a combination of pulmonary hæmorrhage and glomerulonephritis, have been recorded : as the ætiology of the condition is obscure, brevity and precedence are urged to justify the name " Goodpasture's syndrome ".

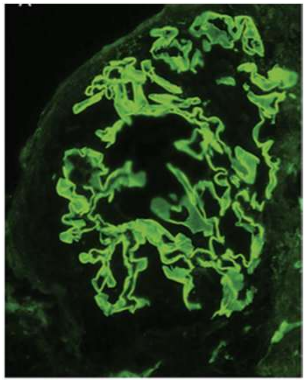
Only twelve other cases could be collected from the literature, but this probably does not reflect its real frequency.

The pulmonary lesions appear to be produced by some derangement of the humoral mechanisms of the body, similar to that operating in uncomplicated glomerulonephritis or related conditions, and are distinct and different from the pulmonary changes seen in the lungs in uræmia.

The renal lesion is predominantly glomerular and widespread ; in most cases, the change is proliferative with hyaline change in the late stages. Active organization with giant-cell formation is a feature of some cases.

The lung changes are characteristically congestion and thickening of alveolar walls with some disintegration and rupture. Alveoli contain a cellular exudate ; in later stages organization occurs.

Usually the first manifestation of the syndrome is hæmoptysis ; and as there may be only a trace, or even no albumin in the urine, early diagnosis may be exceedingly difficult. This may influence or mask the real prognosis of the syndrome. As it is a killing disease of young adults, it deserves further study.



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Goodpasture Disease

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June 1964

Annals of
Internal Medicine

Immune Aspects of the Glomerulonephritis Associated with Pulmonary Hemmorhage

ROBERT L. SCHEER, M.D., and MURRAY A. GROSSMAN, M.D.

Syracuse, New York

THE SIMULTANEOUS APPEARANCE of pulmonary hemorrhage and an acute glomerulonephritis has been observed often enough to warrant the conclusion that this represents a distinct clinical entity (1–12). This disease has been called Goodpasture's syndrome, although there is some doubt that the patient described by Goodpasture in 1919 actually met the criteria for the syndrome (1). Numerous reports have emphasized the fulminant course of the disease. The etiology of this syndrome is obscure, but the nature of the tissue reaction suggests that an immune mechanism is at least partially responsible for its pathogenesis. Immunologic studies of two women who died of pulmonary hemorrhage and acute glomerulonephritis demonstrate that an immune mechanism probably was operative in the kidneys.

Physical examination revealed a pale young woman who was not in acute distress. The only other significant abnormality was a grade II blowing systolic murmur over the base of the heart. Laboratory data on admission revealed a hemoglobin of 5 g/100 ml and a hematocrit reading of 15%. The leukocyte count was 10,650/mm³, of which polymorphonuclear cells were 80%, lymphocytes 15%, monocytes 6%, and basophiles 2%. The smear showed marked hypochromia. The platelets appeared normal. The reticulocyte count was 2.4%. The serum iron was 7 μg/100 ml, and iron-binding capacity 274 μg/100 ml. Urine specific gravity was 1.015 with a pH of 5.5, albumin 3+, and sugar was negative. Microscopic examination revealed 10 to 15 white blood cells, 25 to 30 red blood cells, and 1 to 2 granular casts/hpf. The blood urea nitrogen (BUN) was 25 mg/100 ml, and the creatinine was 3.6 mg/100 ml. The serum albumin was 3.2, and globulin, 2.7 g/100 ml. The concentrations of sugar, bilirubin, and uric acid were normal. A chest film revealed normal

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THE PRESENCE OF ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODIES IN PERIPHERAL BLOOD[1]

J. J. McPHAUL, JR. AND FRANK J. DIXON

From the Scripps Clinic and Research Foundation, La Jolla, California 92037

Received for publication July 25, 1969

The use of immunofluorescent assay for circulating anti-glomerular basement membrane (anti GBM) antibodies is described. Groups of people studied for the presence of anti-GBM antibody included: a) normals; b) immune-complex glomerulonephritic patients; c) anti-GBM antibody-mediated nephritic patients; d) a hemodialysis-maintained group of kidney disease patients; and e) an allergy clinic group. Anti-GBM antibodies were found in the circulation only in patients with anti-GBM antibody-mediated nephritis. Paired-label isotopic studies to determine the percentage fixation of kidney-fixing antibodies, combined with serial dilution of the same anti-GBM antibody-containing sera, allowed estimation of the sensitivity of the assay to be in the range of 0.1 to 1.0 μg/ml antibody content. Despite the sensitivity of the technique and its specificity, two principal handicaps were encountered: a) only 40% of people known to have anti-GBM antibody-mediated glomerulonephritis were shown to have circulating anti-GBM antibodies, and b) several sera were encountered which fixed with wide anatomical definition to the target substrate and made it difficult to recognize the presence of anti-GBM antibodies in such sera.

Goodpasture Disease

THE ROLE OF ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY IN THE PATHOGENESIS OF HUMAN GLOMERULONEPHRITIS*

By R. A. LERNER, M.D., R. J. GLASSOCK,‡ M.D., and FRANK J. DIXON, M.D.

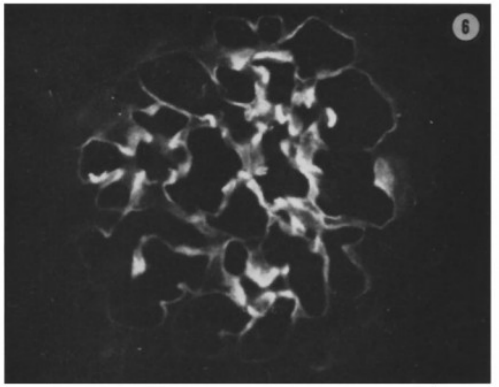
(*From the Department of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California 92037,§ and the Cardiorenal Section, Peter Bent Brigham Hospital, Harvard Medical School, Boston, Massachusetts 02115*‖)¶

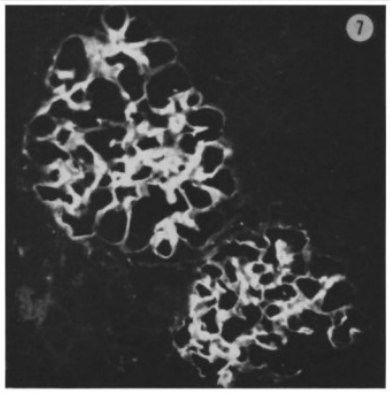
Plates 72–76

(Received for publication 5 July 1967)

The concept that anti-glomerular antibodies might cause glomerulonephritis dates back to the beginning of this century, when Lindemann demonstrated the nephritogenic properties of heterologous anti-kidney antibodies (1). Subsequent work on nephrotoxic serum nephritis has provided precise information concerning the nature and potency of these heterologous nephritogenic antibodies, the location and immunochemical characteristics of the glomerular antigen, and some of the mediators of inflammation activated by the antibody-antigen interaction (reviewed in reference 2). A further step toward implicating this pathogenetic mechanism in nephritis was achieved when it was shown that animals immunized with homologous or heterologous glomerular basement membranes (GBM) could develop glomerulonephritis (3, 4). The demonstration of anti-GBM antibody in the serum and kidneys of such animals and the passive serum transfer of this form of nephritis in sheep (5) and rabbits (6) to normal homologous recipients provided definitive evidence that an animal could, upon appropriate immunization, form nephritogenic anti-GBM antibodies apparently capable of producing an autoimmune glomerulonephritis.

A question still unanswered, however, was whether anti-GBM antibodies were ever formed, particularly in man, in the absence of intentional immunization. While there





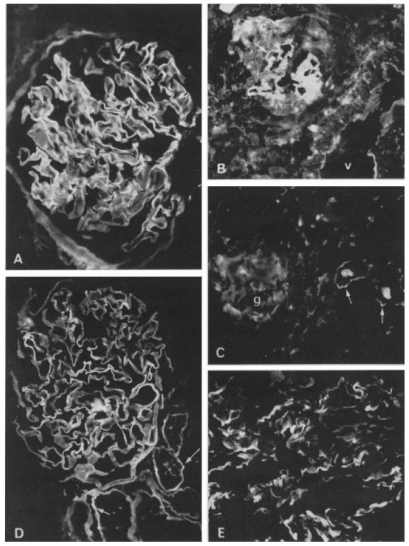
Goodpasture Disease

Anti-glomerular basement membrane antibody-induced glomerulonephritis

CURTIS B. WILSON and FRANK J. DIXON

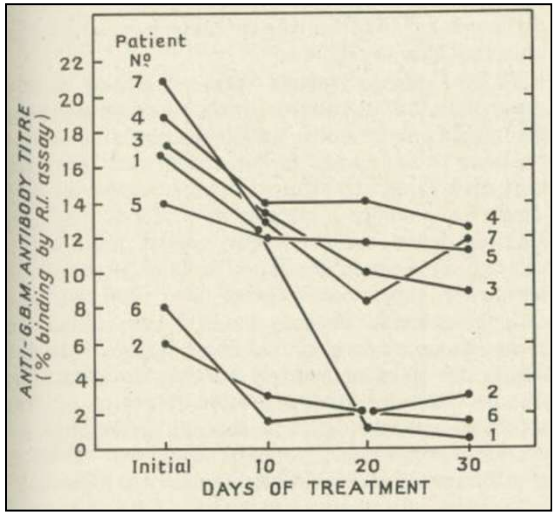
Department of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California

Kidney International, Vol. 3 (1973), p. 74–89



IMMUNOSUPPRESSION AND PLASMA-EXCHANGE IN THE TREATMENT OF GOODPASTURE'S SYNDROME

C. M. LOCKWOOD
A. J. REES
T. A. PEARSON
D. J. EVANS
D. K. PETERS



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Goodpasture Disease

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Symposium on Plasma Exchange in Nephrology - 1982

Plasma exchange and immunosuppressive drugs in the treatment of glomerulonephritis due to antibodies to the glomerular basement membrane

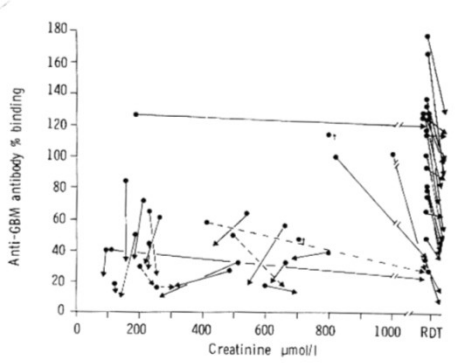
C.D. Pusey, C.M. Lockwood, D.K. Peters

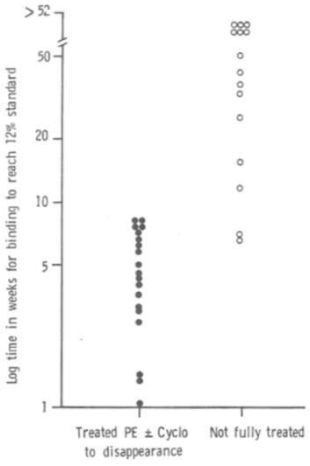
Department of Medicine,
Royal Postgraduate Medical School,
Hammersmith Hospital, Du Cane Road,
London W12 OHS - U.K.

Treatment and Prognosis in Antibasement Membrane Antibody-Mediated Nephritis

D.K. Peters, A.J. Rees, C.M. Lockwood, and C.D. Pusey

NEPHRITIS mediated by antibodies to glomerular basement membrane (GBM) has long been of interest. The induction of nephritis using heterologous antisera[1] could be exerted. The apparent success of this approach has given us a considerable experience of patients with this rare form of nephritis and a number of aspects have emerged.





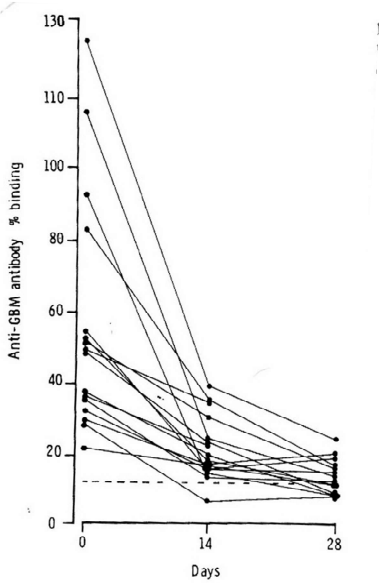


Fig. 2. Short-term effects of treatment on anti-GBM antibody titers.

Table 3. Immunogenetics of Anti-GBM Disease

	Patients	Controls	Relative Risk	Pc
DR2	32/36	24/125	33.7	1.22×10^{-8}
B7	21/36	25/125	5.3	0.33×10^{-3}
A3	15/36	31/125	2.4	0.69

Anti-glomerular basement membrane disease

Rare: 1-2 per million population per year

Bimodal age distribution
Age 20s and 60s
Slight male preponderance

Common in Caucasians and Asians

Relapse uncommon

>80% HLA *DRB15*01*

Aetiological Associations

- Cigarette Smoking
- Hydrocarbon exposure
- Other renal diseases
- Infection
- Medications (Campath, SACT)

The identification of spatial and temporal clustering of cases may support a role for environmental triggers

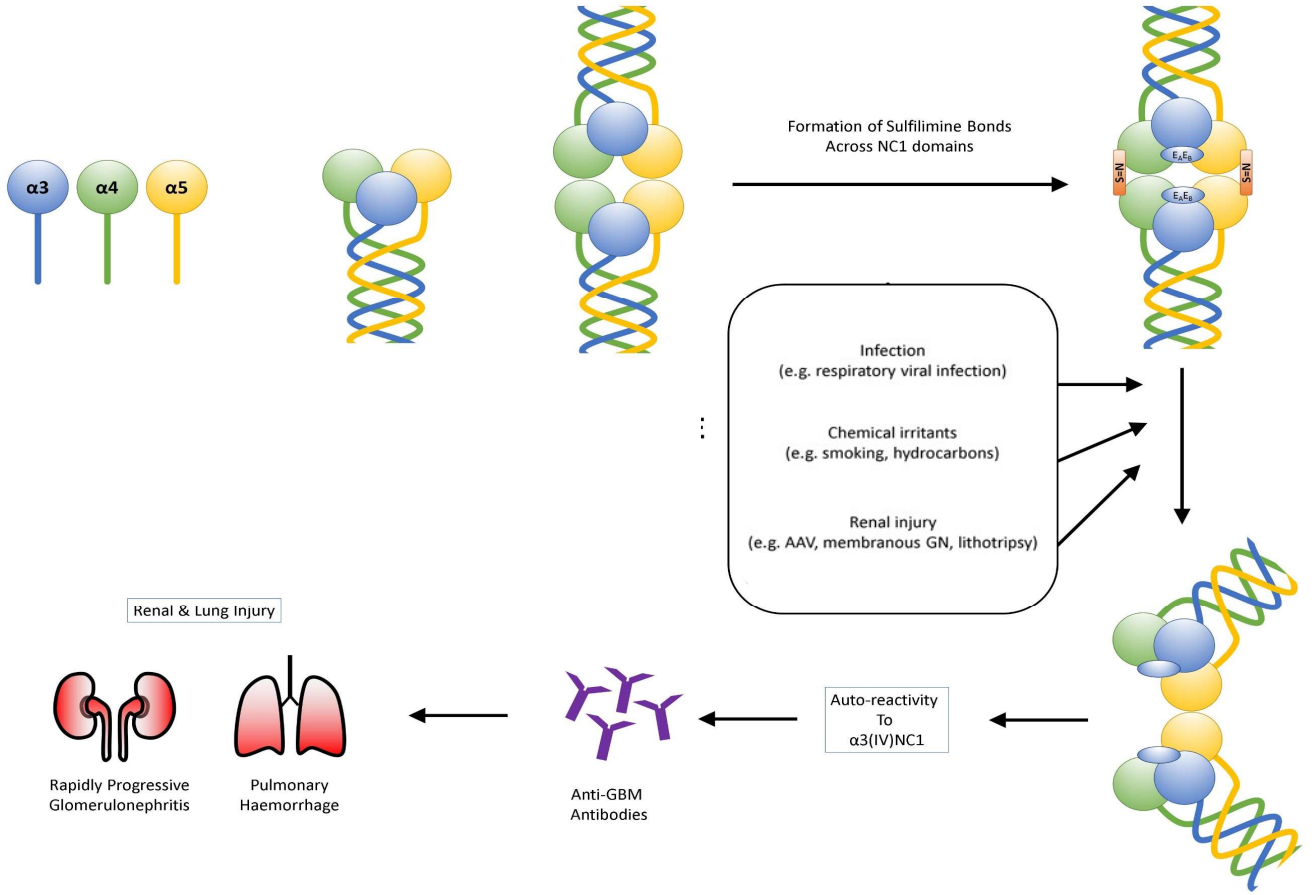
Pathogenesis

‘Typical’ anti-GBM invariably associated with detection of autoantibodies to α3(IV)NC1

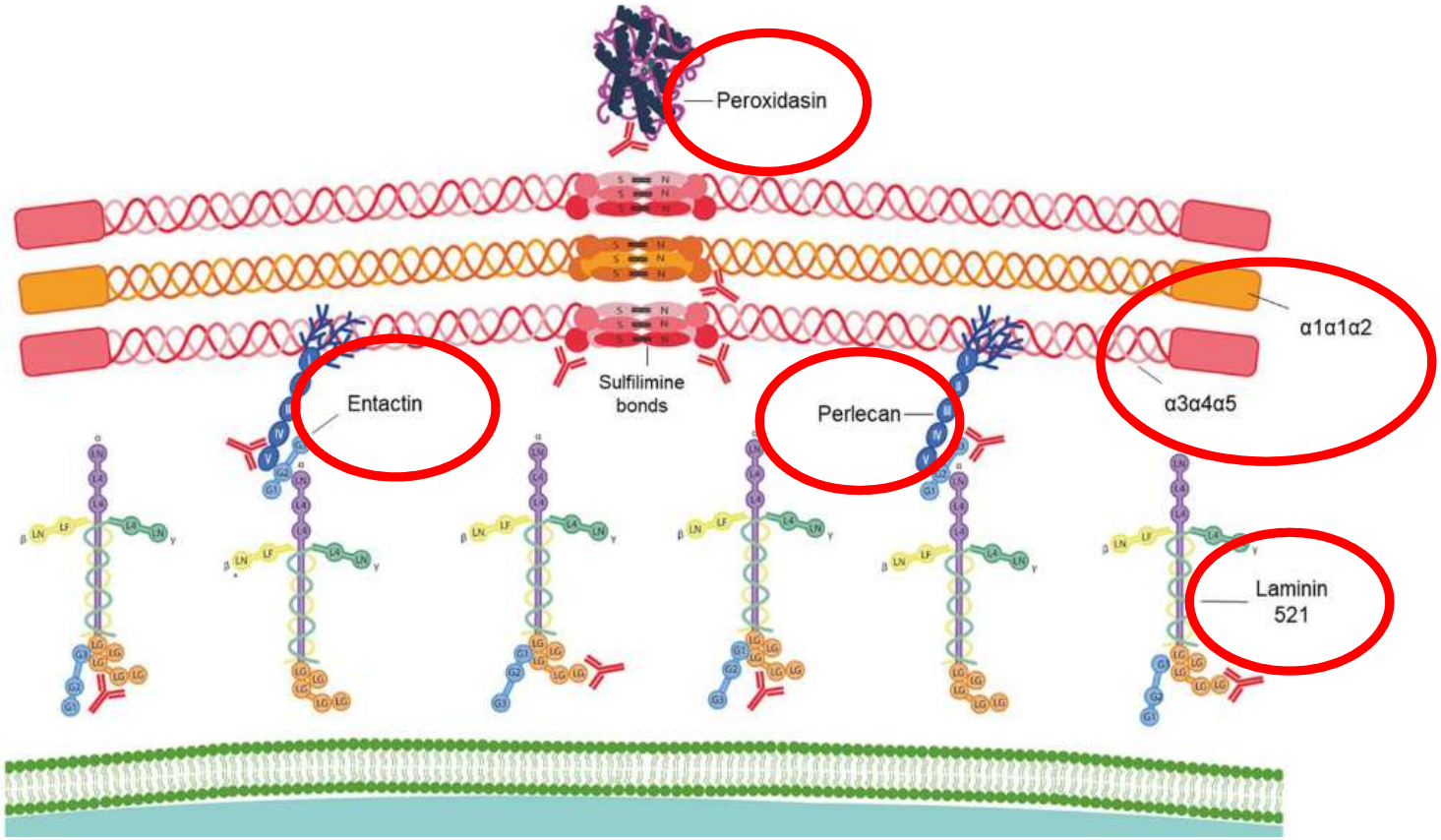
- Transfer experiments confirm directly pathogenic capability
- Disease rapidly recurs in renal allografts if still detectable
- Titre broadly correlates with disease severity at presentation
- Rapid removal by plasma exchange consistently associated with better outcome
- IgG1 and IgG3 predominate

Studies in experimental models suggest a role for directly nephritogenic T cell responses in disease pathogenesis

Pathogenesis



Novel autoantigens in anti-GBM disease



Prendecki, *NDT* 2025

Clinical Presentation & Diagnosis

Presentation

>90% present with rapidly progressive GN

Alveolar haemorrhage in ~50%

A small proportion present with indolent renal disease ('atypical') or isolated lung involvement

Diagnosis

Circulating anti-GBM antibody

and/or

Deposited anti-GBM antibody

and

Renal or Lung injury

Diagnosis

Circulating anti-GBM antibody

Deposited anti-GBM antibody

Renal or Lung injury

Diagnosis

Circulating anti-GBM antibody

Deposited anti-GBM antibody

Renal or Lung injury

Commercially available ELISA or bead-based immunoassays

Optimised to detect IgG to α3(IV)NC1

'False' Negative:

- The 'immunological sink'
- Isotype variants (e.g. IgA, IgG4)
- Epitope variants (e.g. α5(IV)NC1, α1(IV)NC1)
- Alport post-transplant Ab

False Positive:

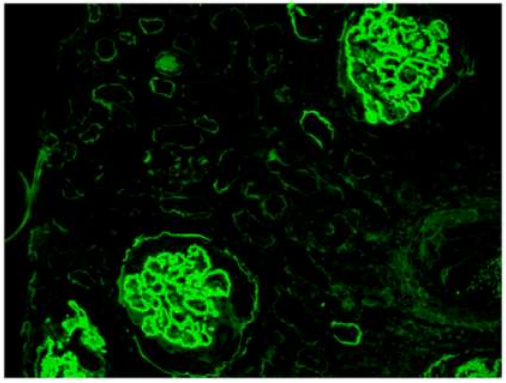
- Polyclonal hypergammaglobulinaemia
- HIV
- Dairy allergy (anti-bovine albumin Ab)

Diagnosis

Circulating anti-GBM antibody

Deposited anti-GBM antibody

Renal or Lung injury



Direct IF on frozen tissue:
Deposited polyclonal IgG +/- C3

IP on paraffin less sensitive

'False positive' linear IgG staining:
- Diabetes
- Dysproteinaemias
- Fibrillary GN

'False negative' staining:
- Loss of glomerular architecture

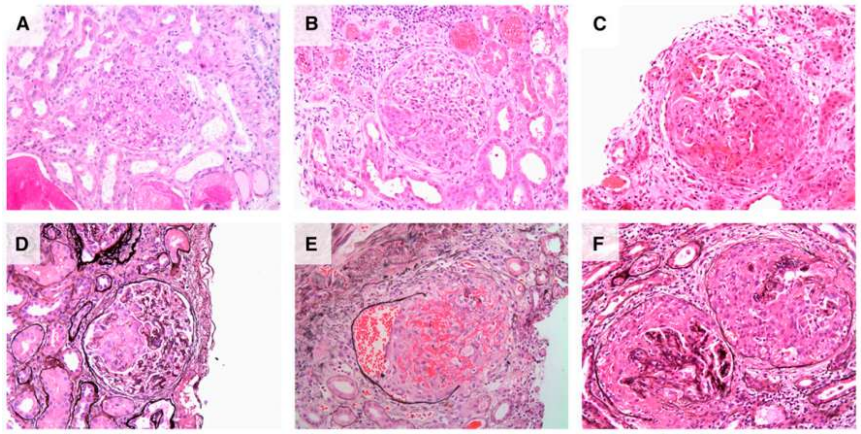
May identify tissue-bound antibody in seronegative cases, even in absence of GN

Diagnosis

Circulating anti-GBM antibody

Deposited anti-GBM antibody

Renal or Lung injury



Disease	Any Crescents (%)	>50% Crescents (%)
Anti-GBM GN	**95**	**81**
Pauci-immune GN	90	48
Lupus nephritis	40	11
HSP	53	5
IgAN	27	5
Post-infection GN	25	3
MCGN	20	3

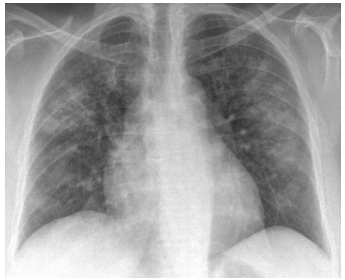
Asynchronous crescents or extra-glomerular arteritis = think concomitant ANCA vasculitis

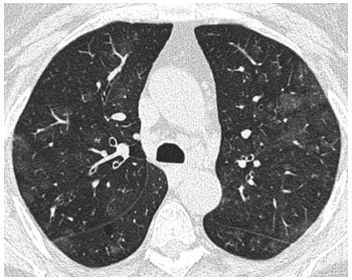
Diagnosis

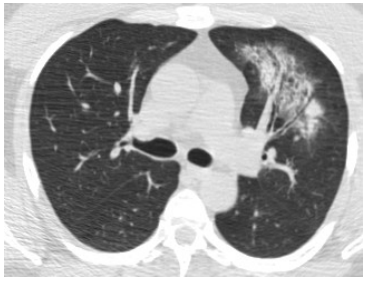
Circulating anti-GBM antibody

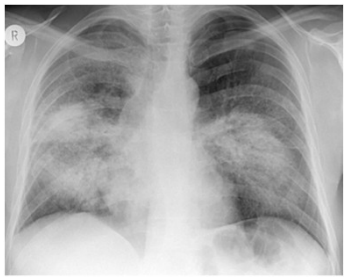
Deposited anti-GBM antibody

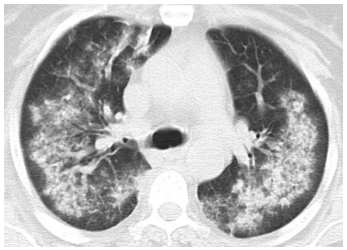
Renal or Lung injury

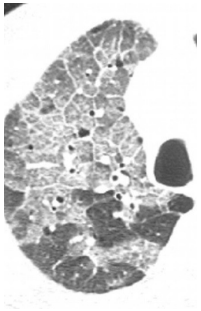


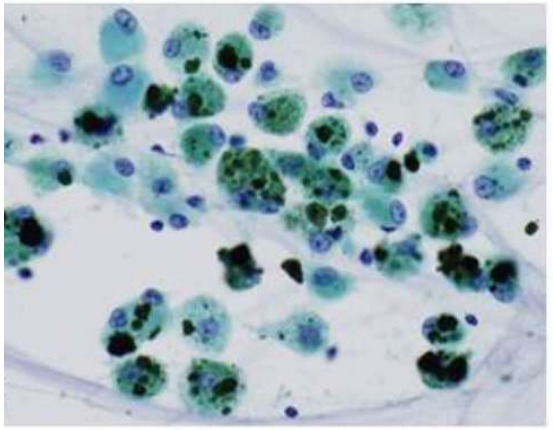












Treatment

Plasma Exchange	Daily 1-1.5 PV exchanges Against albumin or FFP Until circulating anti-GBM negative (~14 days)
Cyclophosphamide	2-3 mg/kg/day PO, typically for 3m Dose adjustment for age and eGFR Limited evidence for pulsed intravenous CyP
Glucocorticoids	Prednisolone 1 mg/kg/day Tapered over 3-6m Limited evidence for role of pulsed intravenous steroids
(Avoid pulmonary irritants	Infection, pulmonary oedema, smoking & vaping)

KDIGO 2021

Treatment

The International Journal Of Artificial Organs / Vol. 6 / S-1 / p.p. 15-18
© by Wichtig Editore srl, 1983

Symposium on Plasma Exchange in Nephrology - 1982

Plasma exchange and immunosuppressive drugs in the treatment of glomerulonephritis due to antibodies to the glomerular basement membrane

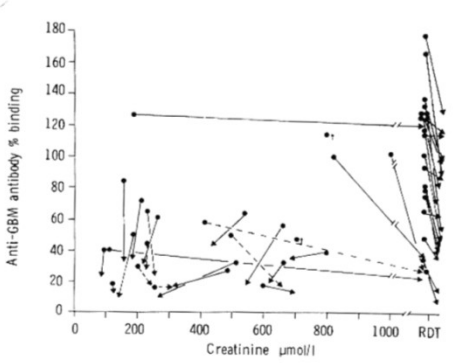
C.D. Pusey, C.M. Lockwood, D.K. Peters

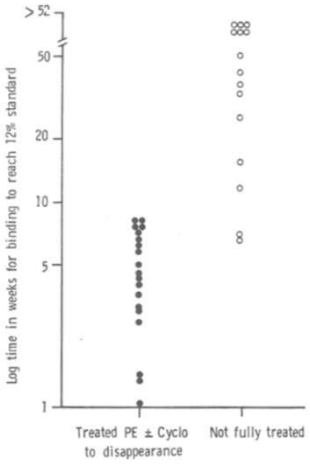
Department of Medicine,
Royal Postgraduate Medical School,
Hammersmith Hospital, Du Cane Road,
London W12 OHS - U.K.

Treatment and Prognosis in Antibasement Membrane Antibody-Mediated Nephritis

D.K. Peters, A.J. Rees, C.M. Lockwood, and C.D. Pusey

NEPHRITIS mediated by antibodies to glomerular basement membrane (GBM) has long been of interest. The induction of nephritis using heterologous antisera[1] could be exerted. The apparent success of this approach has given us a considerable experience of patients with this rare form of nephritis and a number of aspects have emerged.





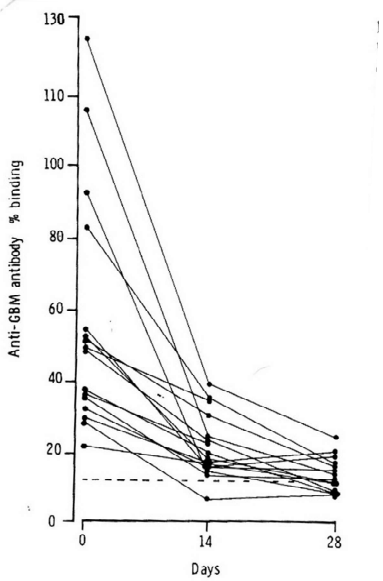


Fig. 2. Short-term effects of treatment on anti-GBM antibody titers.

Table 3. Immunogenetics of Anti-GBM Disease

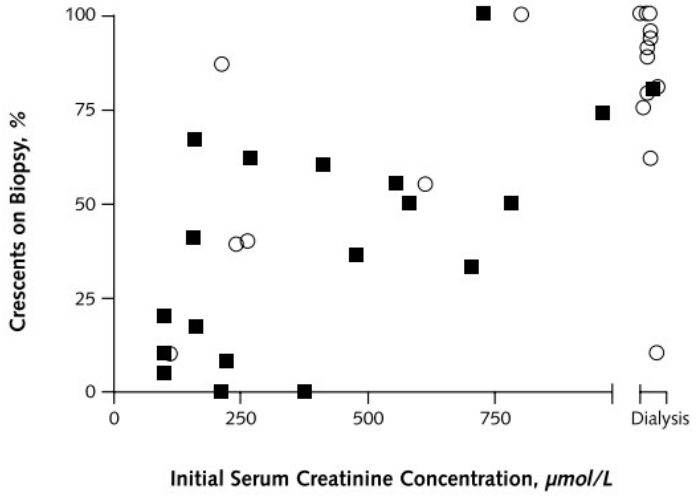
	Patients	Controls	Relative Risk	Pc
DR2	32/36	24/125	33.7	1.22×10^{-8}
B7	21/36	25/125	5.3	0.33×10^{-3}
A3	15/36	31/125	2.4	0.69

Outcome

Study	Cases (n)	RRT at Diagnosis (%)	Alveolar Haemorrhage (%)	Patient survival at 1 year	Renal survival at 1 year	Recovery from RRT (%)
Marques 2019	119	78%	46%	92%	31%	16%
van Daalen 2017	123	56%	35%	83%	34%	9%
McAdoo 2017	78	60%	38%	86%	42%	17%
Canney 2016	79	73%	23%	73%	28%	N/A
Huart 2016	122	68%	77%	86%	38%	2%
Alchi 2015	43	81%	40%	88%	16%	5.7%
Cui 2011	176	N/A	46%	73%	25%	N/A
Hirayama 2008	47	60%	23%	77%	21%	N/A
Segelmark 2003	79	46%	23%	64%	25%	3%
Levy 2001	71	55%	62%	77%	53%	5%
TOTAL		**~50%**	**~50%**	↑	**~30%**	**<10%**

Outcome

	n	Patient Survival (%)	Renal Survival (%)
sCr <500	19	100	95
sCr >500	13	83	82
Dialysis	39	65	8
Total	71	77	53



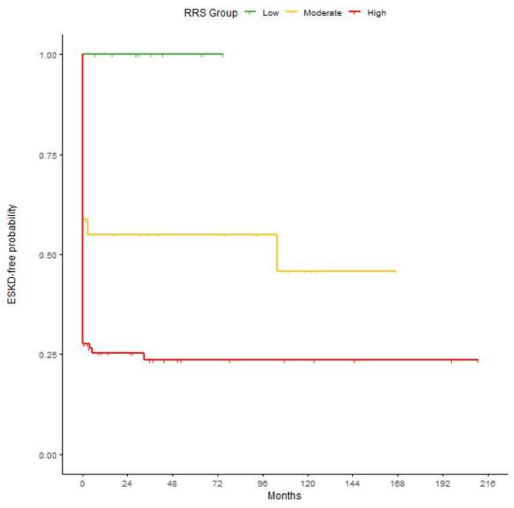
■ No dialysis

○ Dialysis

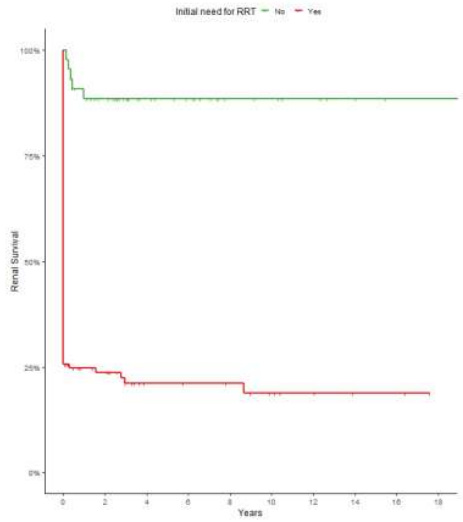
Levy, *Ann Intern Med* 2001

Histopathological Predictors of Outcome

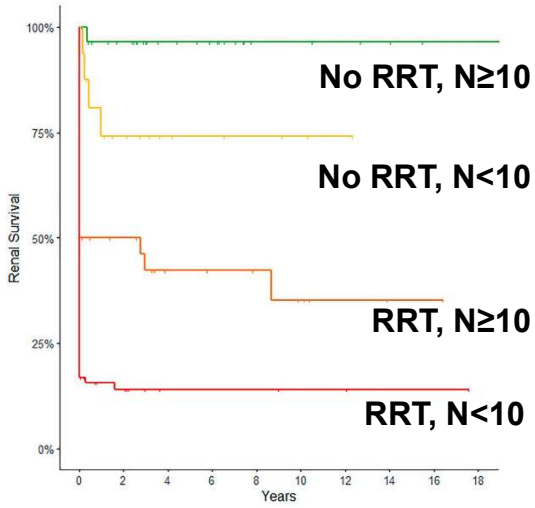
ARRS Class



RRT at baseline



Modified RRS



International study of 174 anti-GBM patients (39% ANCA positive)
36-month renal survival 100%, 62.4%, & 20.7% in low-, moderate-, and high-risk groups
RRT at diagnosis and threshold of 10% normal glomeruli provided best model for prediction

Floyd, *JASN* 2023

Adverse Prognostic Factors & Decisions to Treat

Dialysis-dependence and

- 100% crescents
- >50% glomerulosclerosis
- <10% normal glomeruli
- Oligoanuria

In the absence of lung haemorrhage

Decisions to treat should consider contra-indications to and tolerability of immunosuppression

Initiate treatment in (nearly all) and consider early withdrawal in non-response

Modified immunosuppression may have role in preparing for kidney transplantation

Case 3

60F non-smoker

Asthma diagnosed ~6m previously

3m arthralgia, dyspnoea, wheeze, rash, red eye

Systemic inflammatory response

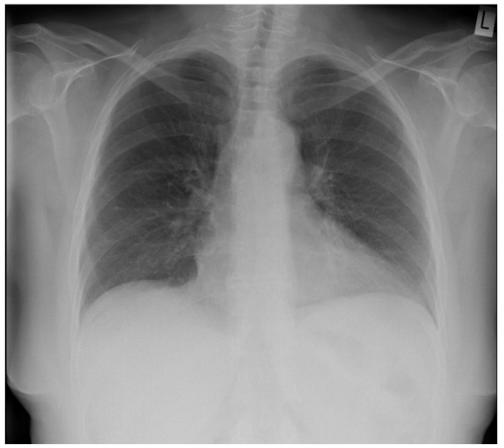
- ESR 45 mm/hr, CRP 28 mg/L

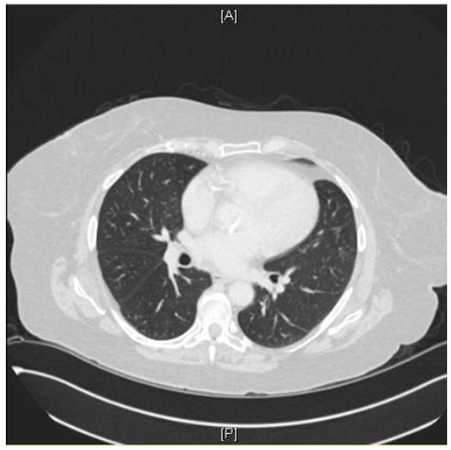
Peripheral blood eosinophilia

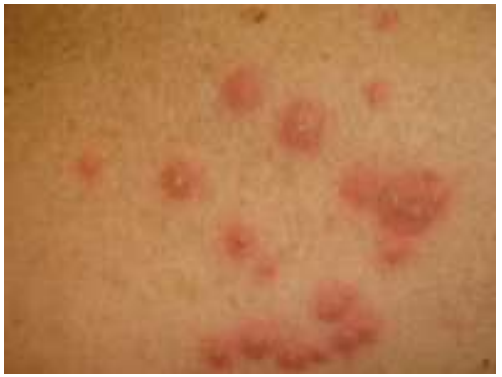
- 1.9 x10^9/L

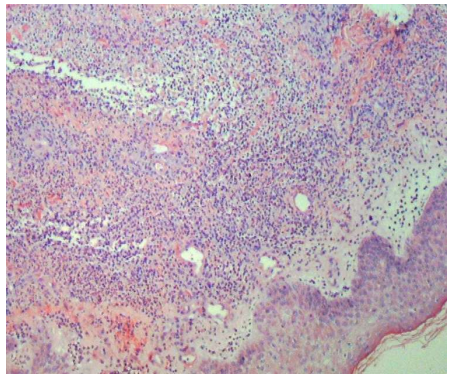
Acute kidney injury

- sCr 184 µmol/L
- uPCR 45 mg/mmol, uRBC >50/cm^3









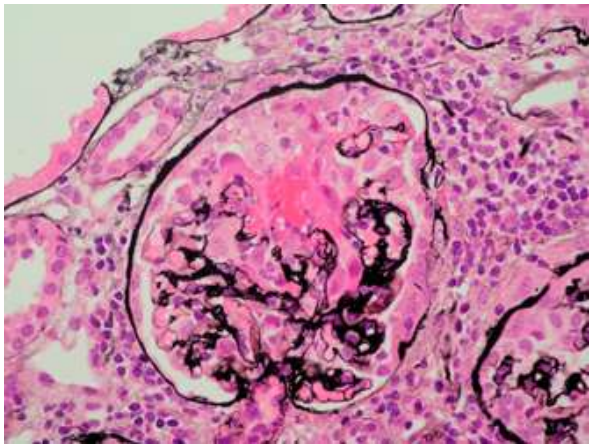
Case 3

Renal biopsy

5/14 necrosis; 4/14 cellular crescents

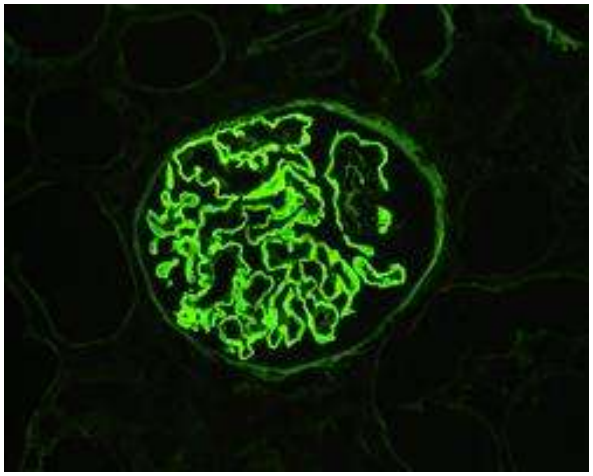
Remainder normal

Minimal tubular atrophy and interstitial scarring



PR3-ANCA 234 iu

Anti-GBM antibody titre: 134 IU



Case 3

Treatment

Plasma Exchange x7

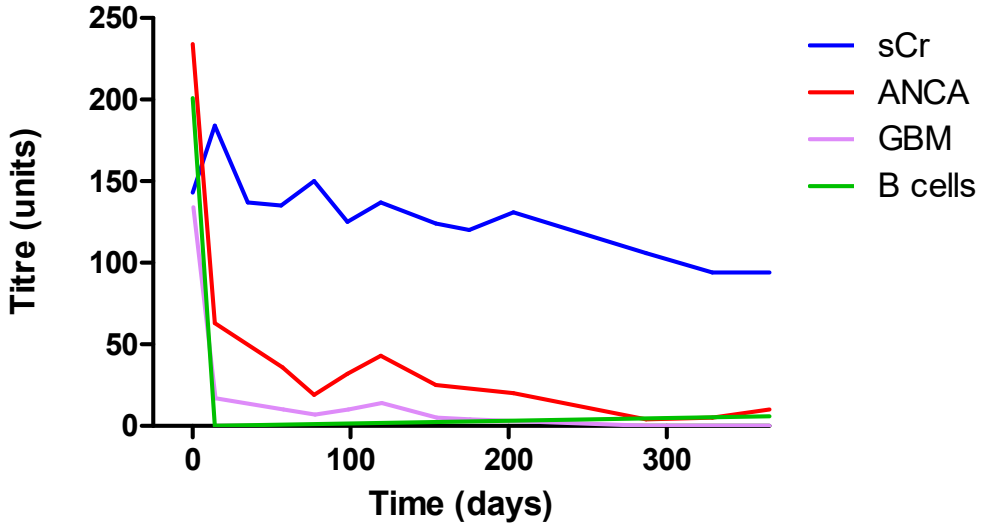
iv Cyclophosphamide 500mg x6

iv Rituximab 1g x2

Oral Prednisolone 60mg od

Azathioprine Maintenance from 3 months

Switched to MMF due to abnormal LFTs



Case 3

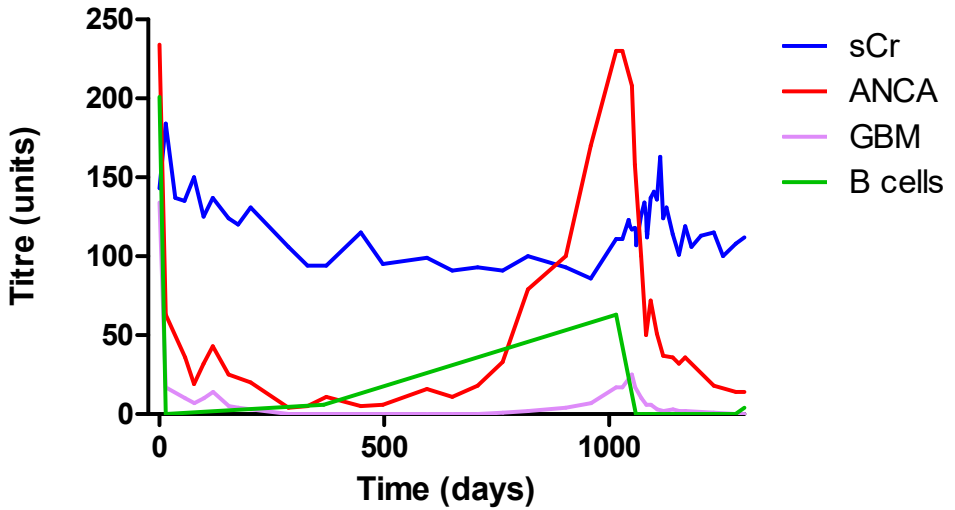
3 years later…

Arthralgia, rash

Deteriorating renal function

- sCr 134 µmol/L, uPCR 41 mg/mmol

cANCA++, PR3-ANCA 230 iu, B cell replete



Repeat Renal Biopsy:

3/15 crescents, 3/15 segmental scars, 7/15 obsolescence

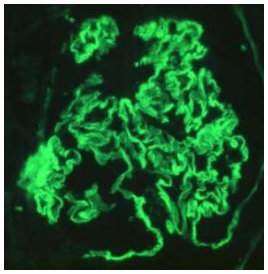
15% tubular atrophy

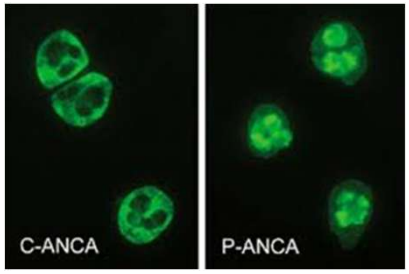
Pauci-immune

Retreatment with ‘Cyclovas’ (without plasma exchange)

Double Positivity

‘Double Positivity’ used to describe patients with co-existent anti-GBM and ANCA antibodies





Incidence of AAV: 20/million/year

Incidence of anti-GBM disease: 1/million/year

Kidney International, Vol. 66 (2004), pp. 1535–1540

Clinical features and outcome of patients with both ANCA and anti-GBM antibodies

JEREMY B. LEVY, TARIG HAMMAD, ANNE COULTHART, TAMMY DOUGAN, and CHARLES D. PUSEY

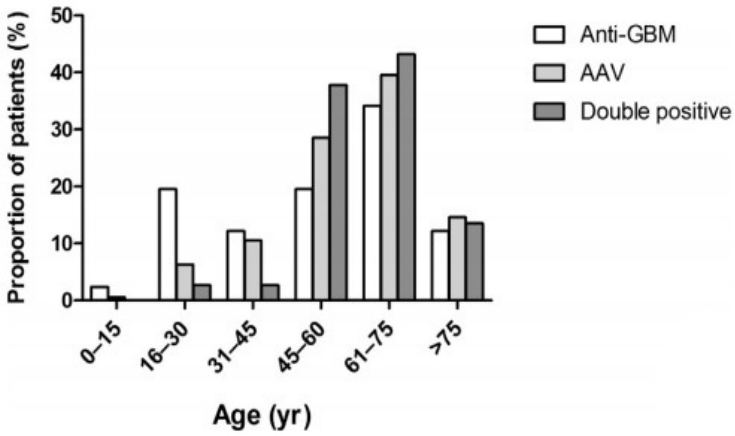
Renal Section, Faculty of Medicine, Imperial College London, Hammersmith Hospital, United Kingdom

>20,000 ANCA and >4000 anti-GBM Ab samples

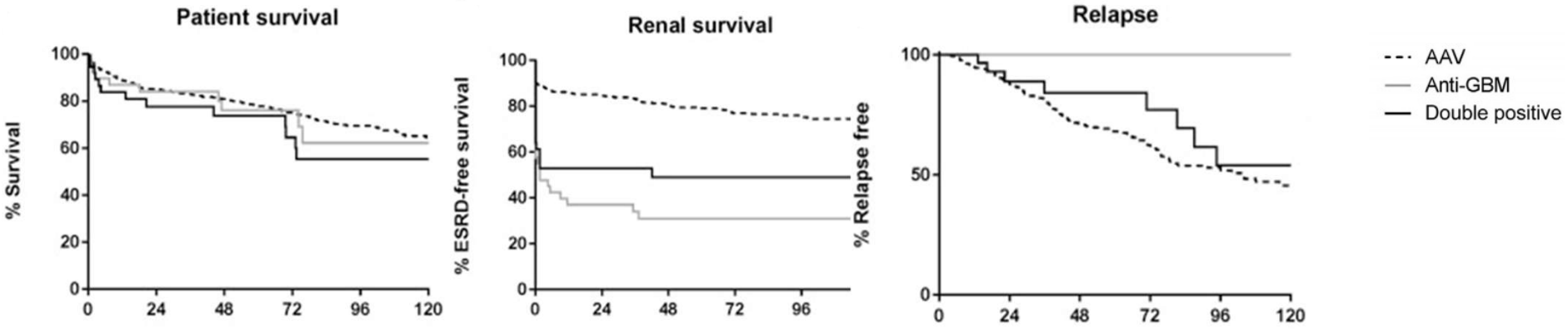
5% of ANCA+ samples also + for anti-GBM Ab

32% of anti-GBM Ab+ samples also + for ANCA

Double Positivity



	AAV	Anti-GBM	Double-Positive
n	568	41	37
Duration of Symptoms, weeks	12	2	10
Dialysis Dependence	23%	63%	57%
Lung Haemorrhage	23%	40%	38%
ANCA Serology	48% MPO 51% PR3	-	70% MPO 27% PR3



McAdoo, *Kidney Int* 2017

Rituximab in anti-GBM disease

Review of published cases, n=67

- First-line 39
- Second-line 28

Age 37 years

Creatinine 426 µmol/L

48% dialysis-dependent

36% DAH

Steroids ~98%

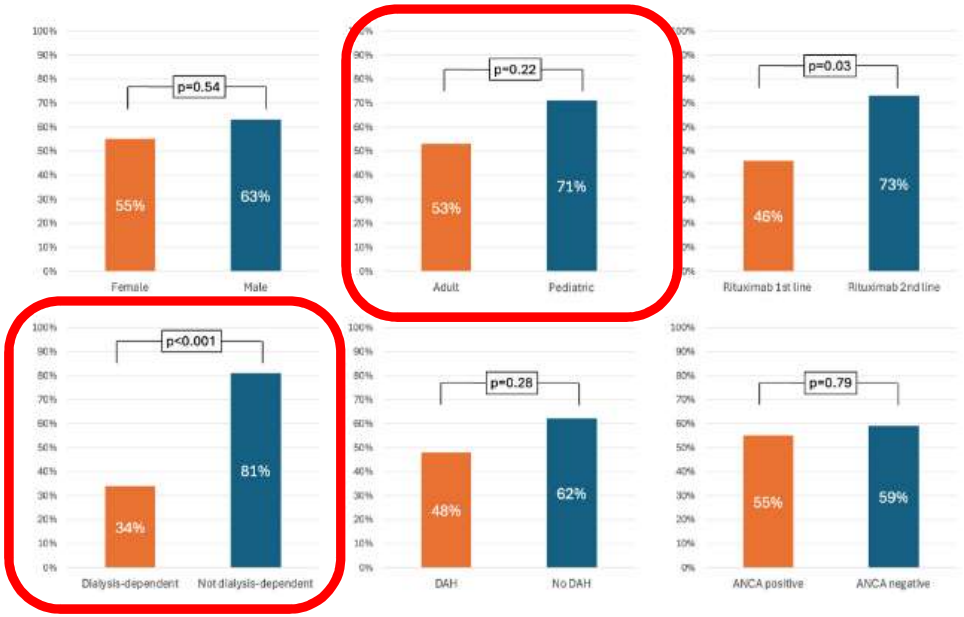
PLEX ~95%

Cyclophosphamide ~50%

Patient survival 91%

Renal Survival 67%

- 53% adults, 71% children
- HD-dep 34%, non-HD-dep 81%



Ivkovic, *Kidney Int Rep* 2025

IMPERIAL

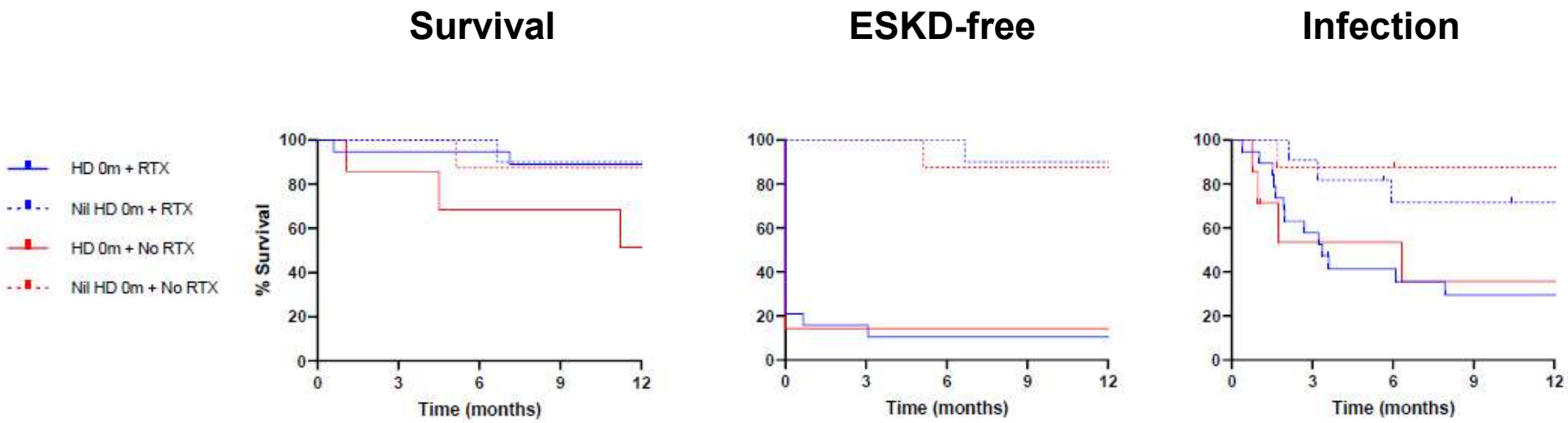
Rituximab in anti-GBM disease

	All	RTX	No RTX
Demographics			
n	45	30	15
Age (years)	62	62	62
Sex, M:F	19:26	12:18	7:8
Disease Features at Baseline			
Creatinine (µmol/L)	647 (314-957)	763 (296-1344)	532 (348-795)
Dialysis	58%	63%	47%
DAH	31%	27%	40%
ANCA +ve	42%	46%	40%

	All	RTX	No RTX
Treatment			
CYC dose (g)	4.0 (3.0-6.1)	3.6 (3.0-4.8)	6.4 (4.2-7.1)
PEX (n)	14 (7-17)	10 (7-14)	19 (15-21)
Time to -ve (months)	1.9 (0.5-5.0)	1.6 (0.2-5.5)	3.1 (1.1-5.0)

Srikantharajah, unpublished

Rituximab in anti-GBM disease



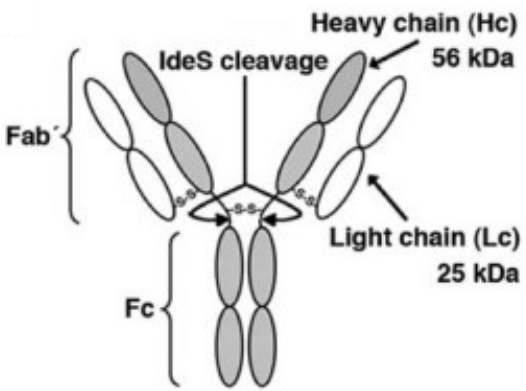
Srikantharajah, unpublished

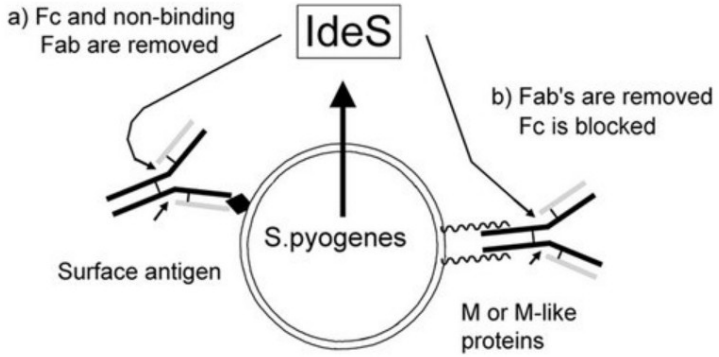
IDES

Immunoglobulin-degrading enzyme of Streptococcus pyogenes

Bacterial cysteine endopeptidase that cleaves human IgG in the hinge region

No effect of IgA or IgM

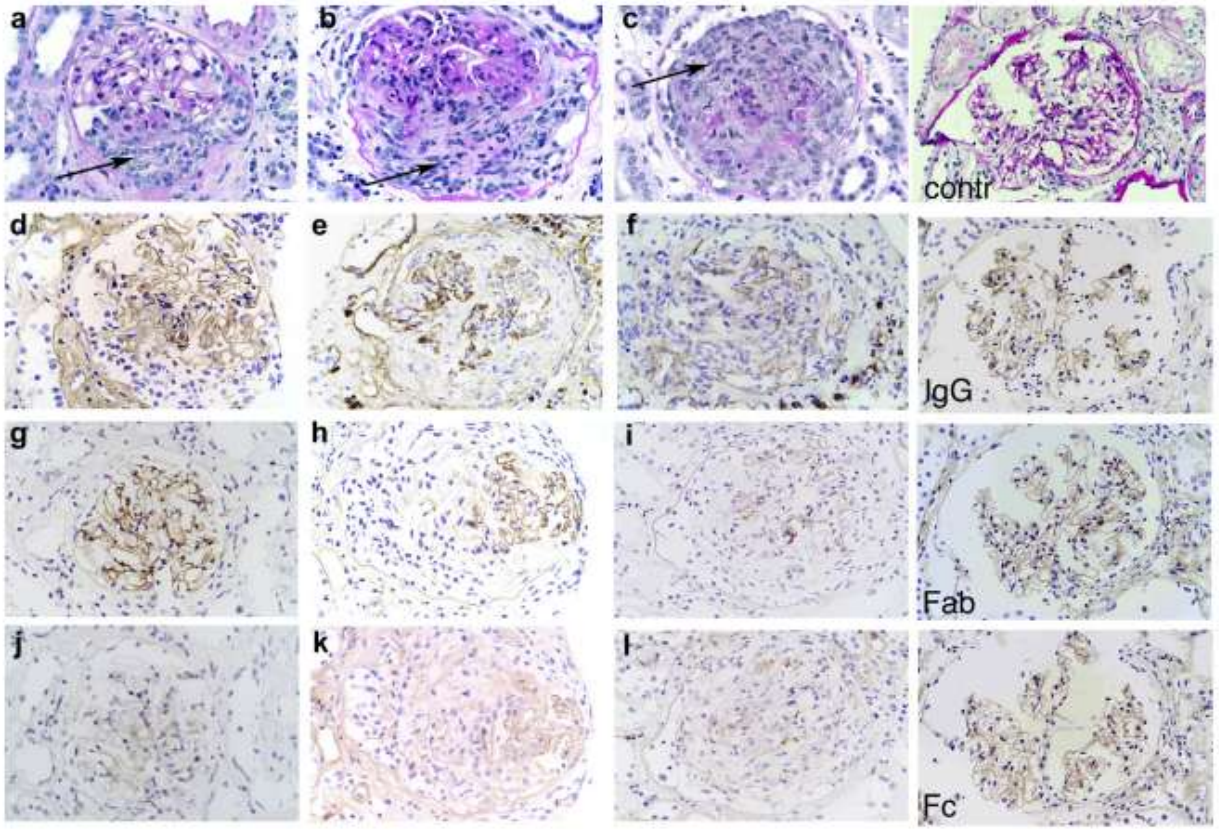




Von Pawel-Rammingen, *EMBO* 2002

IDES in anti-GBM disease

Compassionate use in 3 patients with severe/refractory anti-GBM and poor prognosis



Soveri, *Kidney Int* 2019

GOOD-IDES-01

Open-label Phase 2a study

15 patients with circulating anti-GBM disease

eGFR <15 ml/min/1.73m^2

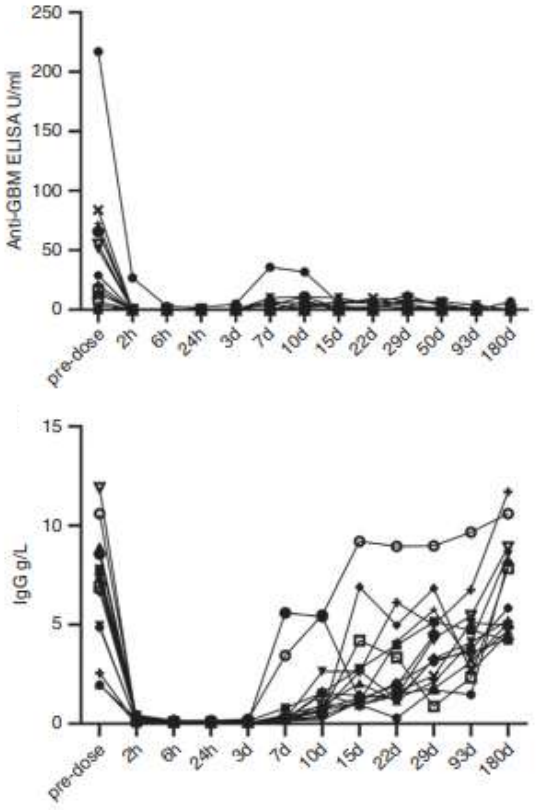
40% ANCA-positive

IDES 0.25mg/kg

Cyclophosphamide

Glucocorticoids

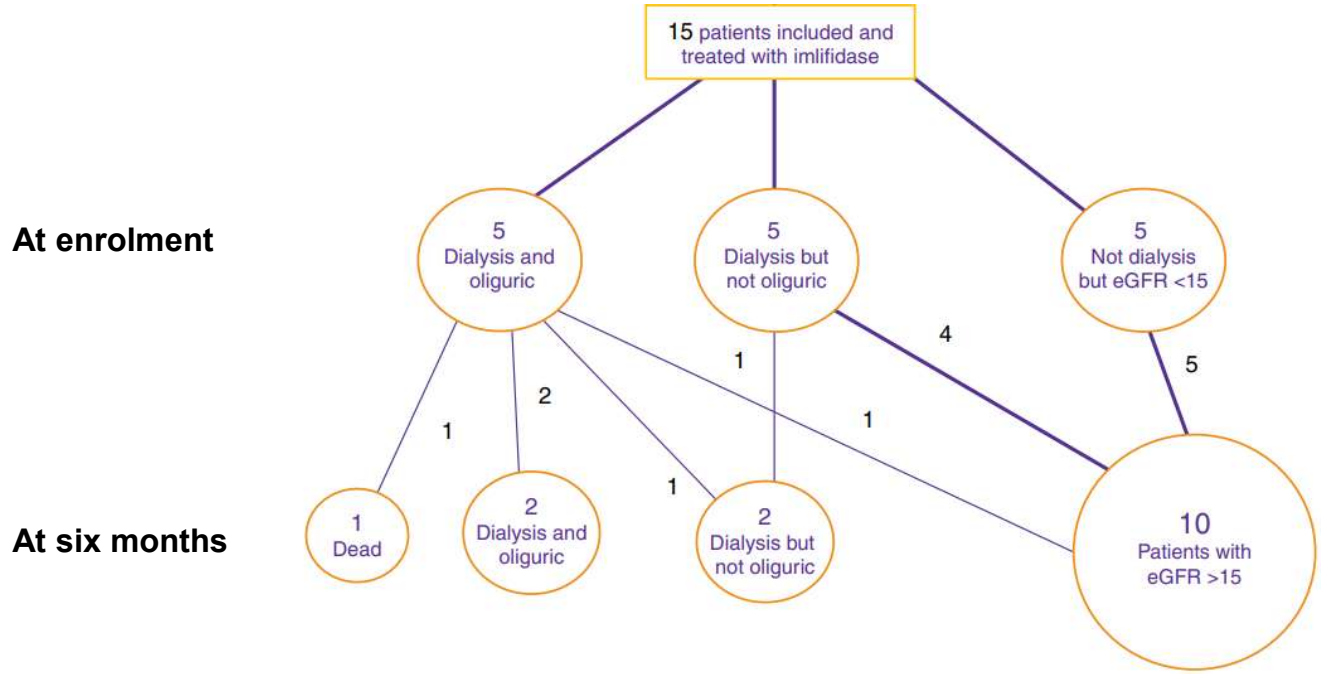
PEX if anti-GBM antibodies detected



Uhlin, *JASN* 2022

IMPERIAL

GOOD-IDES-01



	This Study			McAdoo *et al.*[a]		
	Dialysis at Study Drug	No Dialysis at Study Drug	All	Dialysis at PLEX	No Dialysis at PLEX	All
Total	10 (67)	5 (33)	15 (100)	41 (82)	9 (18)	50 (100)
Dead at 6 months, *n* (%)	1 (10)	0	1 (6.7)	5 (12)	3 (33)	8 (16)
Dialysis at 6 months, *n* (%)	4 (40)	0	[illegible]	29 (77)	4 (43)	[illegible]
Dialysis independent at 6 months, *n* (%)	5 (50)	5 (100)	10 (67)	7 (17)	2 (22)	9 (18)

Uhlin, *JASN* 2022

GOOD-IDES-02

Phase 3 open-label RCT

5 UK, 19 European, 6 USA sites

50 patients

eGFR <20 ml/min/1.73m^2

IDES 0.25 - 0.50 mg/kg

In addition to SOC

Primary end-point: eGFR at 6 months

Recruitment completed

Full results expected Q2/3 2026

Hansa provides update on Pivotal Phase 3 trial in anti-glomerular basement membrane (anti-GBM) disease

16 Dec 2025, 23:07
Regulatory information

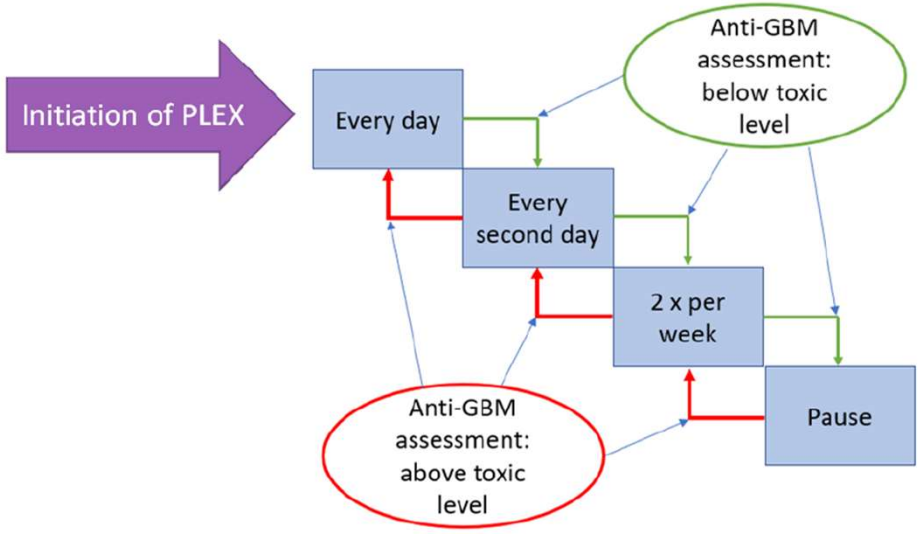
Lund, Sweden, 16 December 2025. Hansa Biopharma AB, "Hansa" (Nasdaq Stockholm: HNSA), today announced that GOOD-IDES-02, a global pivotal Phase 3 trial in anti-glomerular basement membrane (anti-GBM) disease, did not meet its primary endpoint. The endpoint was renal function at 6 months, evaluated by estimated glomerular filtration rate (eGFR).

Approximately 60% of patients treated with imlifidase followed by the standard of care (SoC) protocol defined in the trial did not require dialysis at 6 months, which represented a substantial improvement and clinical benefit compared to what has been observed in historical control cohorts. Outcomes generally observed in these patients reflect only 20-25% who do not require dialysis at 6 months, which also was the basis for powering the trial. However, the treatment response was similar in patients in the control arm treated with the defined SoC alone.

ClinicalTrials.gov Identifier: NCT05679401

IMPERIAL

GOOD-IDES-02



Did not meet primary end-point

~60% did not require dialysis at 6m

Better than anticipated outcome with SoC

Expected 20-25% renal survival

Reduced use of plasma exchange?

Shorter hospital admission?

Reduced blood product use?

Cost-effectiveness?

Intravenous cyclophosphamide?

Removal of non-immunoglobulin mediators by PEX?

ClinicalTrials.gov Identifier: NCT05679401

Case 4

25M, fit & Well

Non-smoker

Ruptured Achilles tendon whilst playing football - tendon repair under GA July 2020

72h later: haemoptysis, dyspnoea on minimal exertion

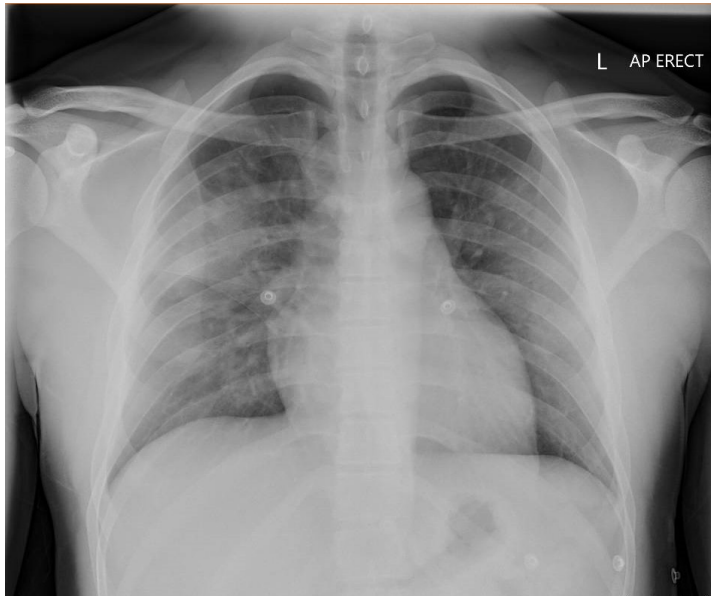
Sats 94% OA, T 37.8C

Hb 14.5 -> 12 g/dL

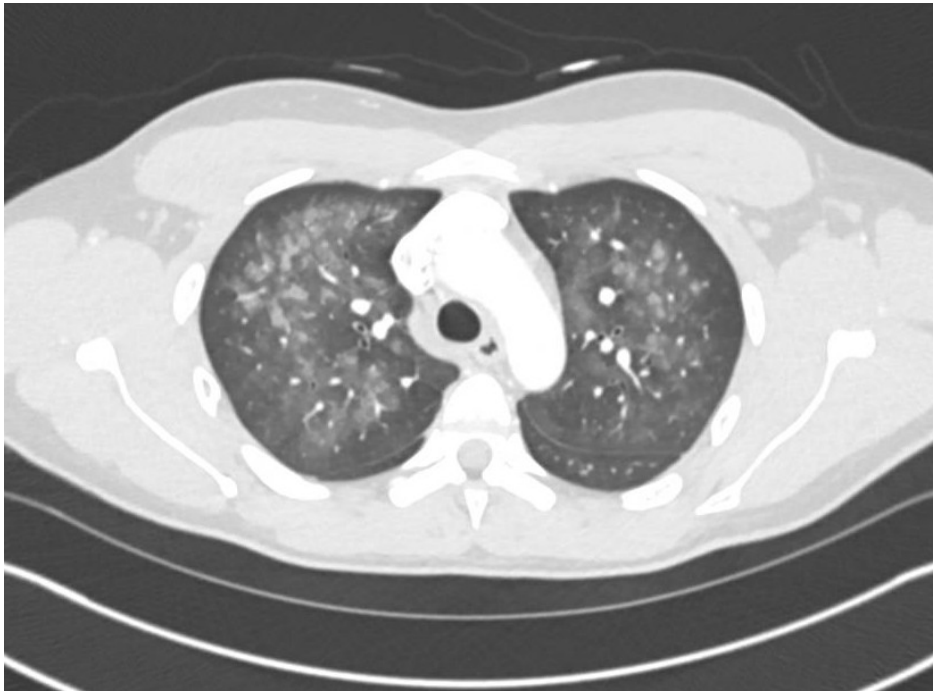
CRP 21.2 mg/L

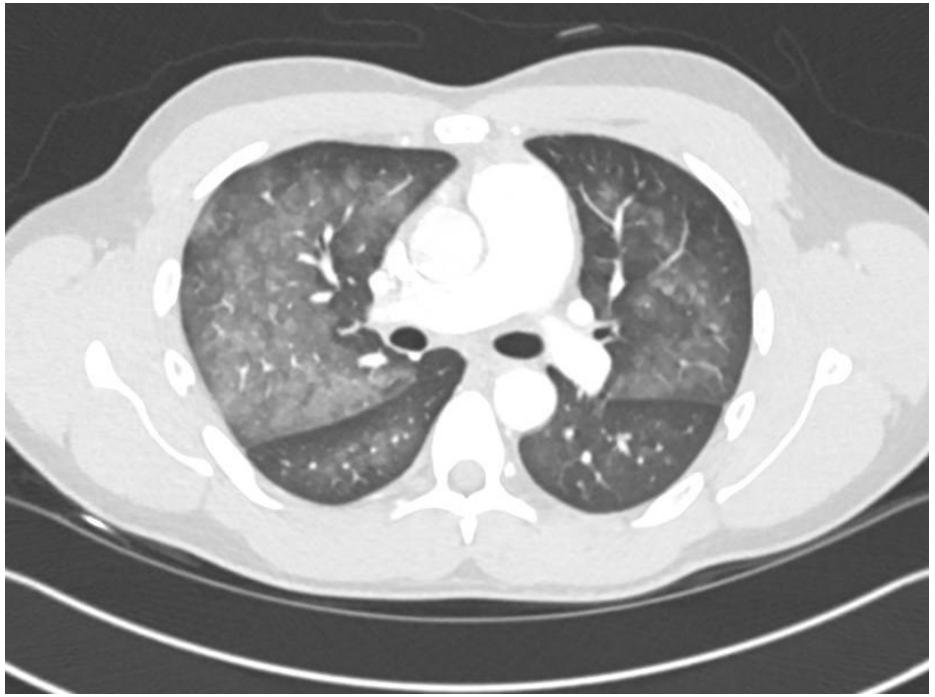
sCr 98 µmol/L, negative urinalysis

SARS-CoV-2 PCR negative x4



Case 4





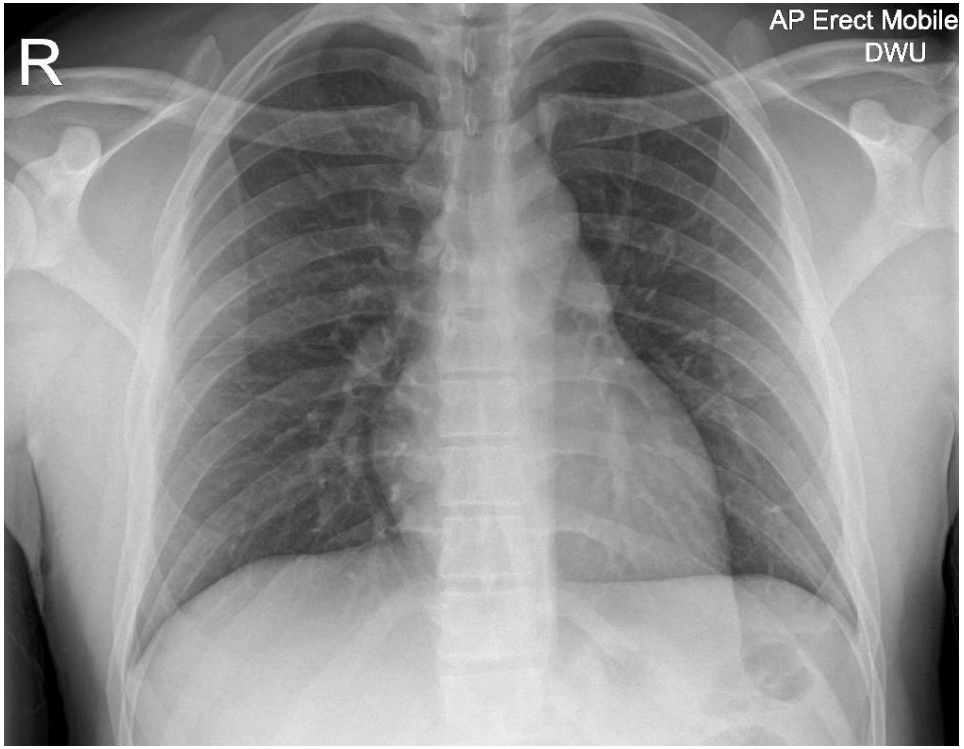
Case 4

Anti-GBM 8.7 iu (NR <3): Confirmed on WB
ANA, ANCA negative
HBV, HCV, HIV negative
No paraprotein
SARS-CoV-2 IgM & IgG negative

BALS:
Haemorrhagic fluid
Microbiology negative
98% macrophages; ~30% haemosiderin-laden cells

No renal biopsy or PFTs

Treated with RTX and Steroids



Case 5

21F, fit & Well

Non-smoker

Haematoproteinuria Feb 2022

sCr 125 umol/L,uPCR 125 mg/mmol

Renal biopsy

25 glomeruli; 8 segmentally scarred, 3 with fibrocellular or fibrous crescents; 4 endocapillary proliferation; 15% IFTA

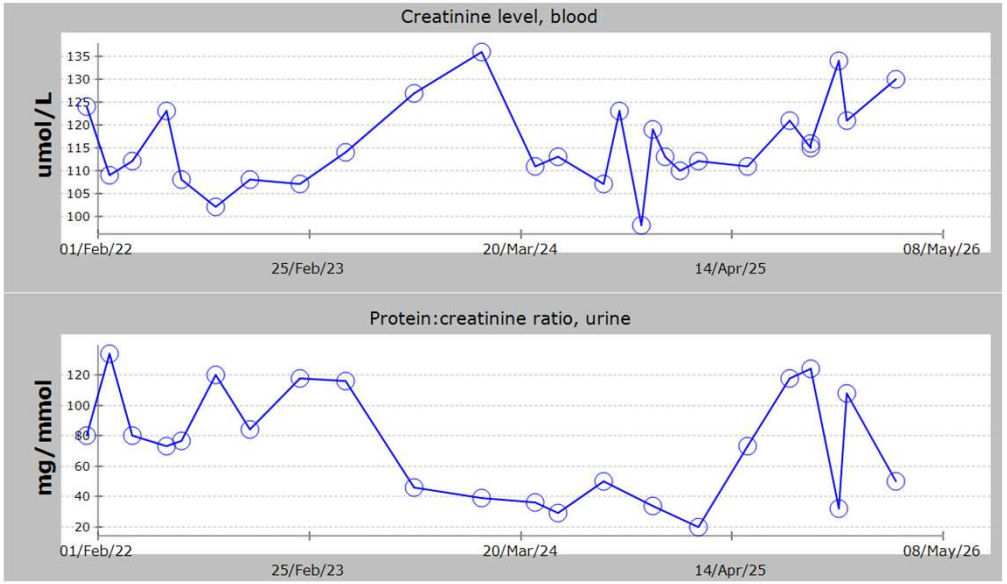
Linear IgA 2+, no LC restriction, no deposits on EM

No circulating antibodies

No paraprotein

Negative virology

Treated with MMF



“Atypical” anti-GBM disease

Uncommon presentations
Isolated lung haemorrhage
With normal kidney function
Relapsing or recurrent disease

With concomitant disease
Membranous GN
IgA nephropathy
Thrombotic microangiopathy

Immunologic variants
Isotype variants (IgA, IgM)
Subclass variants (IgG4)
Epitope variants (α5, α4)

Seronegative cases
With otherwise entirely typical clinical features (RPGN, DAH)

"Atypical" anti-GBM disease

Anti-glomerular basement membrane antibody-induced glomerulonephritis

CURTIS B. WILSON and FRANK J. DIXON

Department of Experimental Pathology, Scripps Clinic and Research Foundation, La Jolla, California

Kidney International, Vol. 3 (1973), p. 74–89

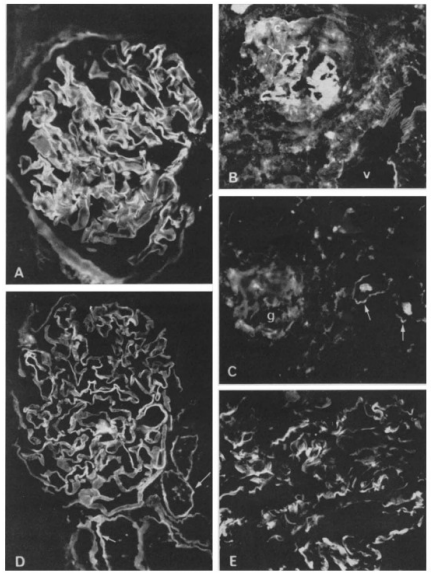
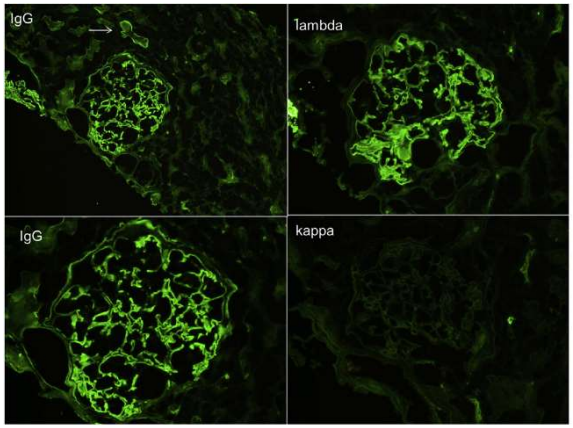


Table 4. Patients with antiGBM antibody-induced glomerulonephritis without Goodpasture's syndrome

Patient	Sex/ age	Diagnosis			Onset to renal failure	Bilateral nephrec-tomy	Immuno-sup-pression	Followup and course
		If	E	Se				
33	M/20	+	+	+	1 mo[a]	yes	no	living 1 yr on dialysis
34	M/42	+	+	+	22 yr[a]	yes	no	died after second Tx (hemorrhage)
35	M/20	+	+	0	9 mo[a]	yes	SA	died 12 mo after unsuccessful Tx (overdose)
36	M/25	+	+	NA	18 mo[a]	yes	S	living 3 yr after Tx
37	M/25	+	+	NA	2 mo[a]	yes	no	living 5 yr after Tx
38	M/13	NA	+	0	1 mo[a]	yes	SA	died after second Tx (cardiac arrest)
39	M/14	+	NA	+	none	no	S	living 1 yr with normal function
40	M/23	+	NA	+	5 mo[a]	yes	no	living 3 yr after Tx
41	M/24	+	NA	+	5 mo[a]	yes	SC	died 9 mo after Tx (sepsis)
42	M/20	+	NA	+	1 mo[a]	yes	no	living 11 mo after Tx
43	M/23	+	NA	NA	2 mo[a]	no	A	living 12 mo on dialysis
44	M/13	+	NA	0	none	no	SA	living 18 mo with normal function
45	M/5	+	NA	0	none	no	SC	living 7 yr with normal function
46	M/29	NA	NA	+	9 yr[a]	yes	no	living 4.5 yr after Tx
47	F/28	+	+	+	2 yr[a]	yes	NA	living 15 mo after Tx
48	F/22	+	+	0	3 mo[a]	yes	A	died 10 mo after Tx (sepsis)
49	F/60	+	+	NA	0.1 mo[a]	yes	A	died after 18 mo on home dialysis (hyperkalemia)
50	F/16	0	+	+	2 mo[a]	yes	no	living 2 mo after Tx
51	F/23	NA	+	+	2 mo[a]	yes	SA	died 8 mo after Tx (sepsis)
52	F/8	NA	+	NA	9 mo[a]	yes	SA	living 5 yr after Tx
53	F/40	+	NA	0	10 yr[a]	yes	NA	died after second Tx (sepsis)

“Atypical” anti-GBM disease

“glomerular disease with idiopathic linear Ig deposition”



NO identifiable circulating Ab

Linear IgG along GBM in the absence of another known cause

Progressive proteinuric CKD, no lung haemorrhage

Histopathology

- Mesangial or endocapillary proliferative GN most common
- Focal crescents and fibrinoid necrosis ~10%
- Secondary focal-segmental glomerulosclerosis common

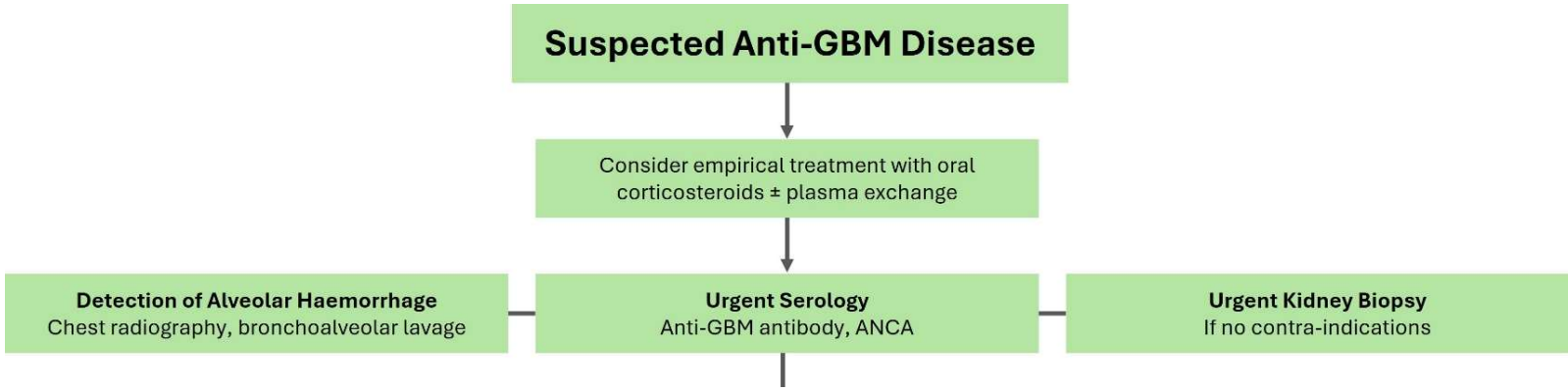
Deposited Ab show light chain restriction in ~50%

Chronic course, relapse and recurrence after kidney transplantation is common

Immunopathogenesis & optimum treatment not clearly defined

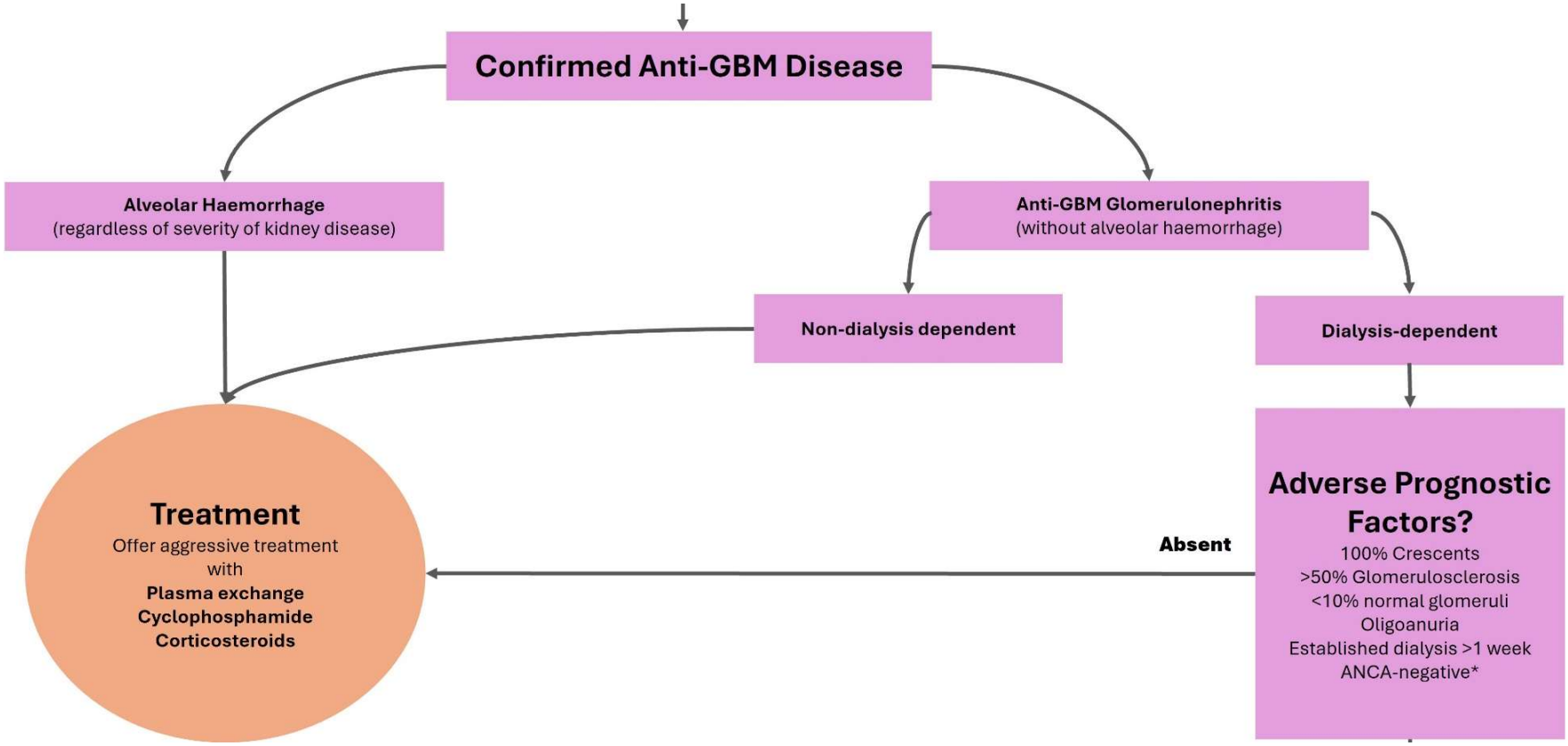
Chauveau, *AJKD* 2024

Treatment Standard



McAdoo, *NDT* 2025

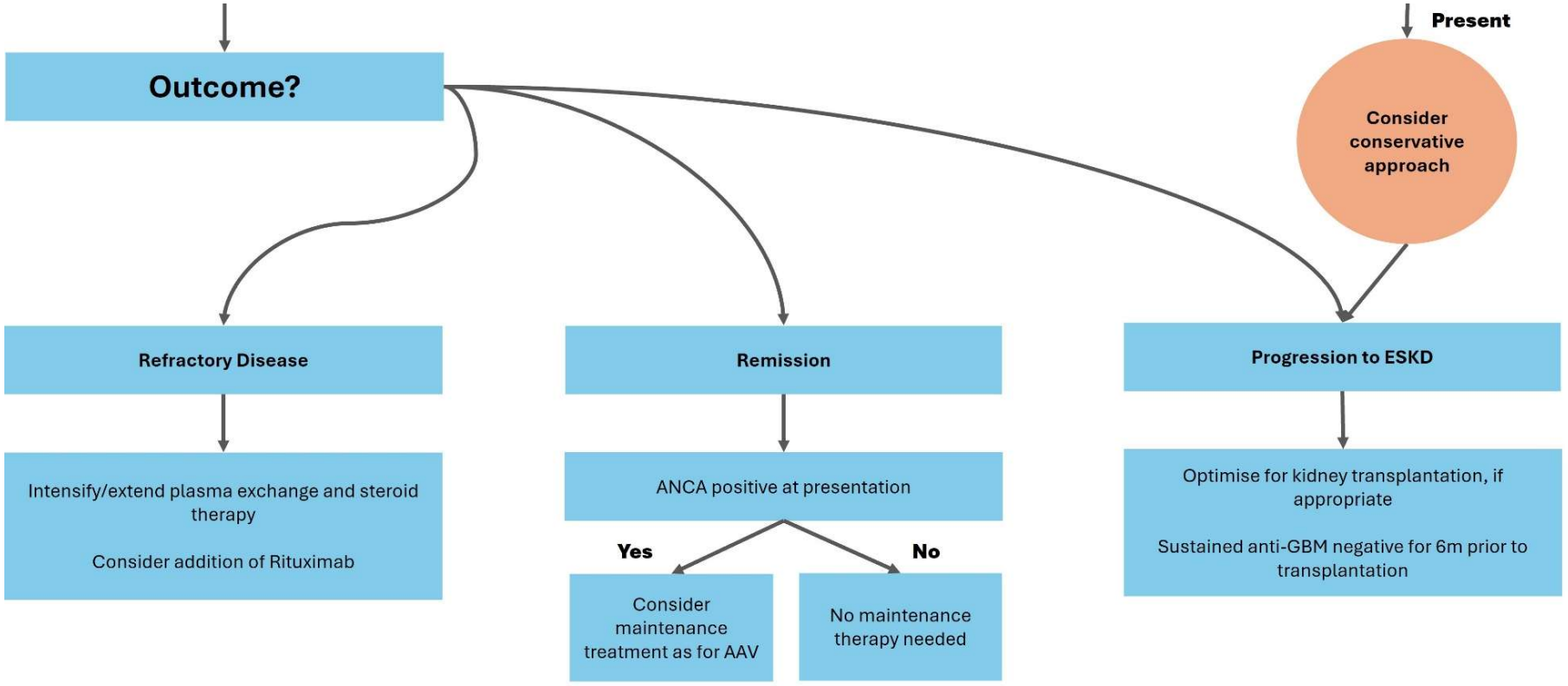
Treatment Standard



McAdoo, *NDT* 2025

IMPERIAL

Treatment Standard



McAdoo, *NDT* 2025

Conclusions

Anti-GBM disease remains a medical emergency where rapid diagnosis and treatment still fundamentally determine outcome

Risk-stratification is important, but avoid therapeutic nihilism

Double-positive disease deserves to be considered a distinct clinical phenotype

Emerging therapeutics such as IDES *may* reshape management of severe disease

Spectrum of disease is more heterogeneous than previously appreciated; more precise classification needed

Acknowledgements

NHS
Imperial College Healthcare
NHS Trust

IMPERIAL

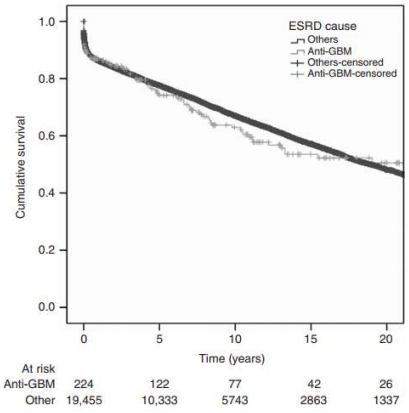
Transplantation after anti-GBM disease

Transplantation in the presence of anti-GBM antibodies is associated with high risk of recurrent disease in the allograft (~50% in historic series)

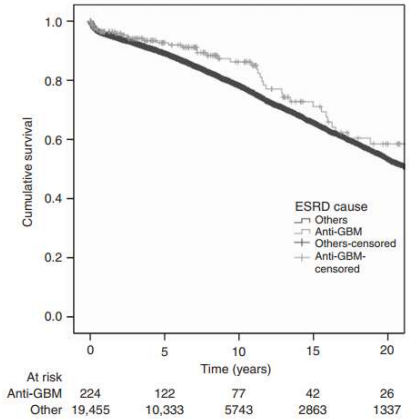
6 months sustained sero-negativity advised before transplantation

ANZDATA Registry Study

- 449 anti-GBM cases, 1963-2010
- 224 received transplant
- Recurrent disease in 6/224 (<3%)



Allograft Survival



Patient Survival

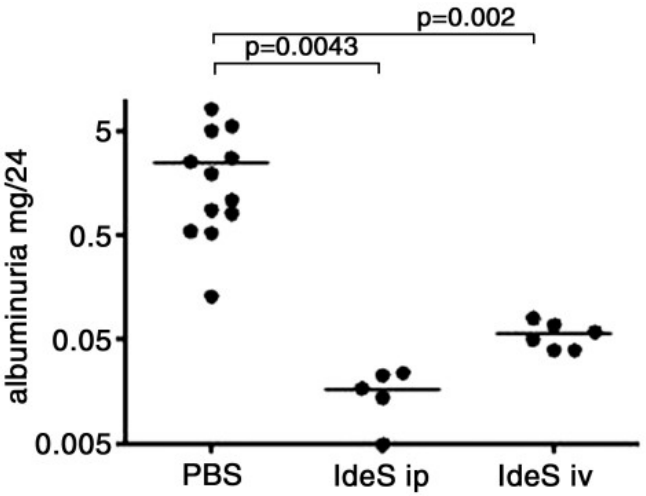
Tang, *Kidney Int* 2013

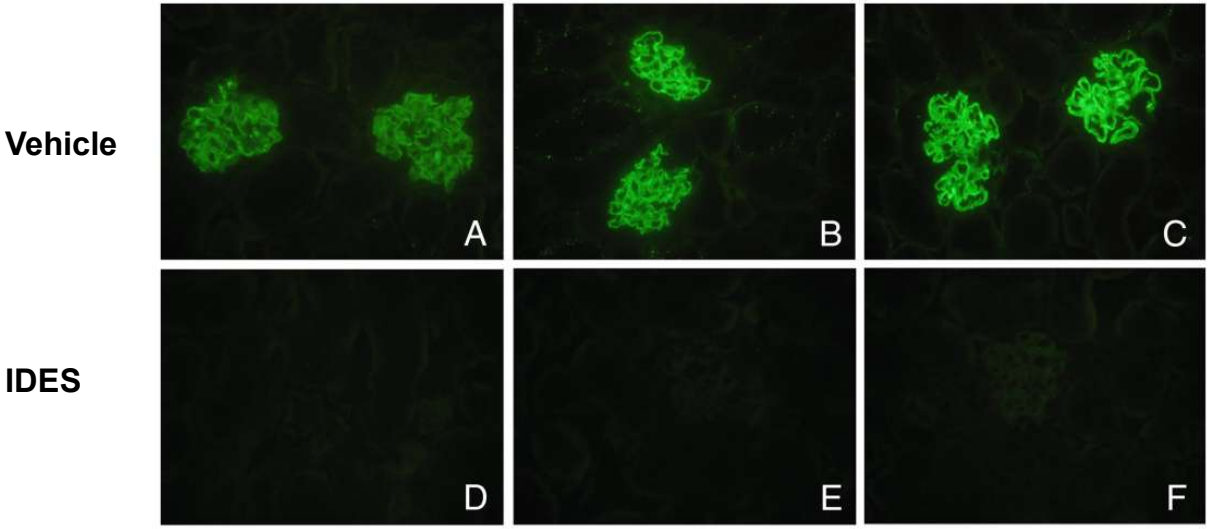
IDES

Immunoglobulin-degrading enzyme of Streptococcus pyogenes

Bacterial cysteine endopeptidase that cleaves human IgG in the hinge region

No effect of IgA or IgM

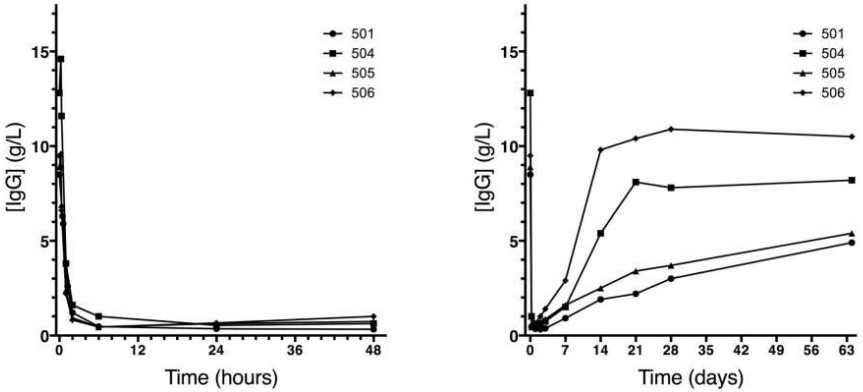




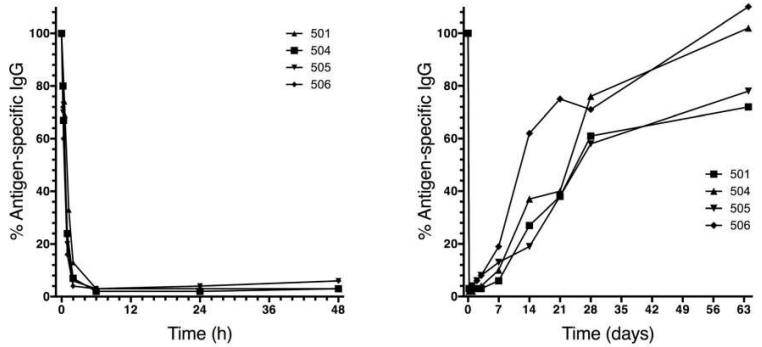
Yang, *NDT* 2010

IDES in healthy human volunteers

Total IgG



Antigen-specific IgG



Winstedt, *Plos ONE* 2015