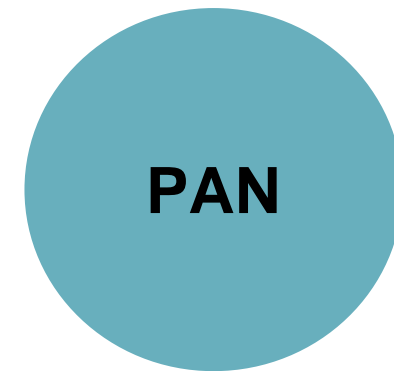


POLIARTERITIS NUDOSA CLÁSICA



POLIARTERITIS NUDOSA

- **Periarteritis nodosa/nudosa**
- **Poliarteritis nodosa/nudosa**
- **Panarteritis nodosa/nudosa**



Sobre el aprendizaje...



Velázquez D

Sobre el aprendizaje...



Escher MC



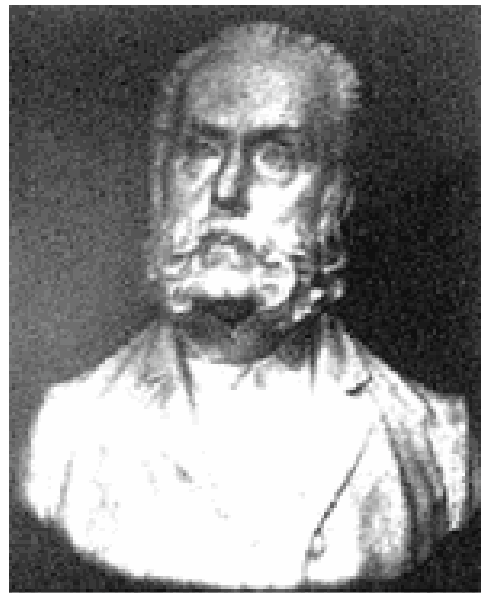
Pollock J

POLIARTERITIS NUDOSA

- El primer caso de PAN fue descrito por Kussmaul y Maier en 1866, y se trataba de un sastre de 27 años llamado Carl Seufarth...



A Kussmaul



R Maier



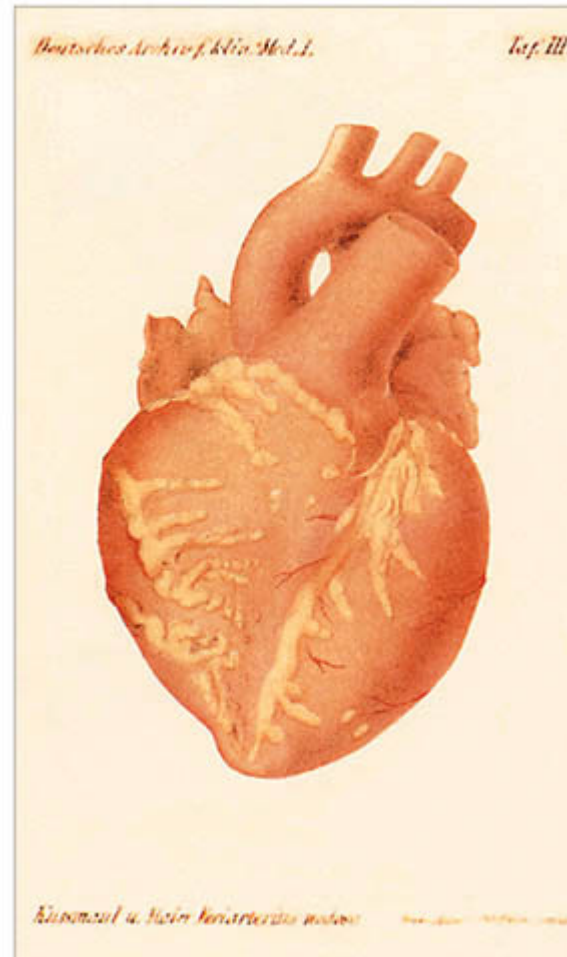
This page of the preliminary account of polyarteritis nodosa (Kussmaul and Maier) is from the *Archiv für Klinische Medicin* 1866, 1866.

POLIARTERITIS NUDOSA

A Small Muscular Artery From Jejunum

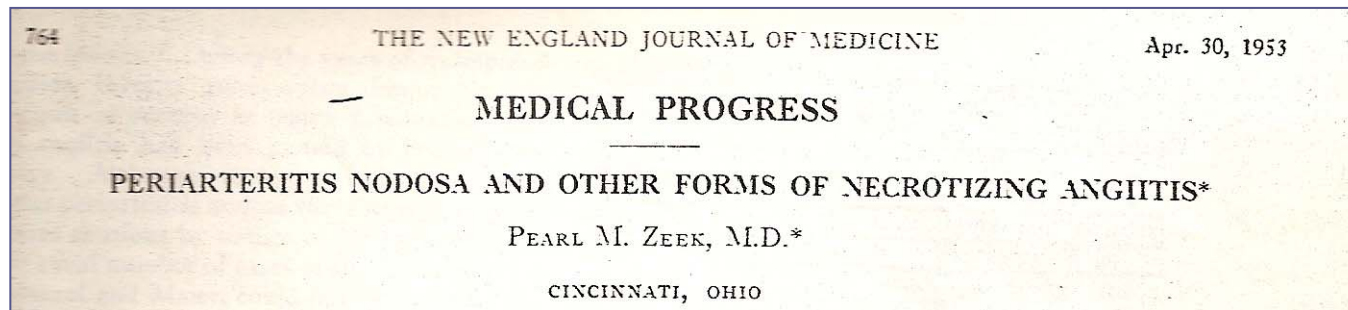


B Nodular Thickening of Coronary Arteries



A Kussmaul R Maier

POLIARTERITIS NUDOSA



- **Periarteritis nodosa**
- Angeitis por hipersensibilidad
- Arteritis reumática
- Angeitis alérgica granulomatosa
- Arteritis de la temporal
- Otras (LES...)

Zeek PM, 52

POLYARTERITIS NODOSA¹

By G. A. ROSE AND H. SPENCER

(From the Medical Unit, St. Mary's Hospital, and the Department of Pathology, St. Thomas's Hospital, London)

¹ Received June 2, 1956

Quarterly Journal of Medicine, New Series XXVI, No. 101, January 1957.

TABLE II

Contrasting Characteristics in Cases of Polyarteritis Nodosa With (Group A) and Without (Group B) Lung Involvement

The percentages in this table are based on the numbers of cases in which the relevant data were available, e.g. with regard to eosinophilia, the number of patients with differential white-cell counts.

Manifestation	Incidence	
	Group A (32)	Group B (66)
1. Clinical		
Specific respiratory illness, usually preceding systemic polyarteritis	100%	0
Blood eosinophilia of 1,500 per c.mm. or more	54%	0
Nasal or middle-ear granuloma	16%	0
2. Pathological		
(a) Lungs:		
Necrotizing lesions (other than typical infarcts and bronchiectasis)	83%	0
Demonstrable pulmonary polyarteritis	54%	0
(b) Other organs:		
Numerous eosinophils in polyarteritic lesions	58%	4%
Giant cells present in polyarteritic lesions	35%	0
Granulomatous polyarteritis	55%	6%
Necrotizing or granulomatous lesions not demonstrably related to arteries	60%	0

THE KIDNEY IN PERIARTERITIS NODOSA¹

By J. DAVSON, J. BALL, AND R. PLATT

(From the Departments of Pathology and Medicine, University of Manchester)

Case Reports, Group A

The 14 cases have been divided into two main groups (A and B) based on the histological findings in the kidneys. In Group A severe and widespread glomerular damage was present, whereas in Group B glomerular changes were not widespread.

Case Reports, Group B

The following five cases of periarteritis nodosa, in contrast with those of Group A, showed no extensive glomerular lesions in the kidneys.

POLIARTERITIS NUDOSA

Polyangiitis Overlap Syndrome

Classification and Prospective Clinical Experience

- Grupo de la PAN:
- PAN clásica
- Granulomatosis alérgica
- Síndrome de superposición (overlap)

- Vasculitis por hipersensibilidad
- Granulomatosis de Wegener
- Granulomatosis linfomatoide
- Arteritis de células gigantes
- Tromboangeitis obliterante
- Síndrome mucocutáneo ganglionar(Kawasaki)
- Miscelánea

RANDI Y. LEAVITT, M.D., Ph.D.
ANTHONY S. FAUCI, M.D.
Bethesda, Maryland

July 1986 The American Journal of Medicine Volume 81 79

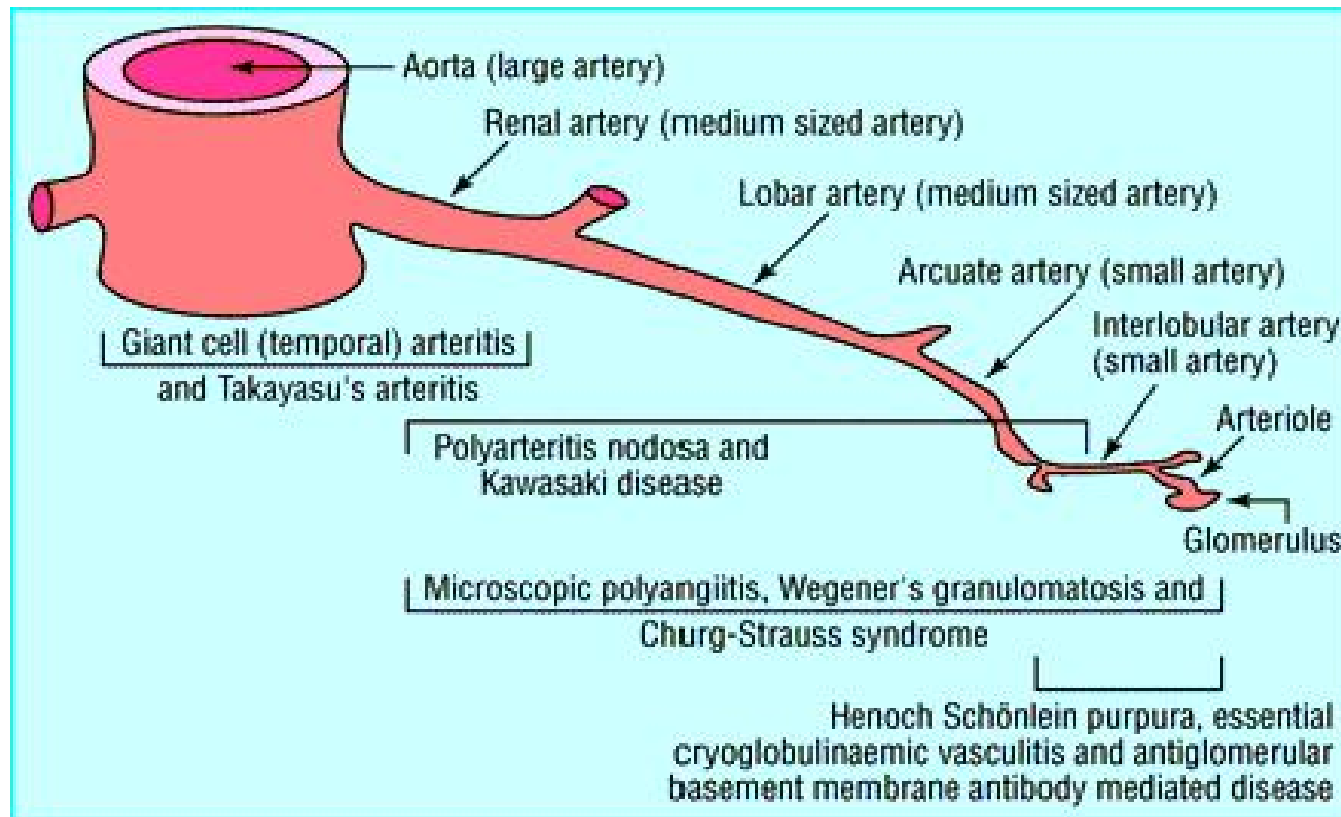
POLIARTERITIS NUDOSA

Clasificación de las vasculitis (basada en la Conferencia Consenso Chapel-Hill 1993)

- **VASO GRANDE**
 - Arteritis de células gigantes
 - Arteritis de Takayashu
- **VASO MEDIANO**
 - **Poliarteritis nudosa**
 - Enfermedad de Kawasaki
- **VASO PEQUEÑO**
 - Granulomatosis de Wegener(*)
 - Poliangeitis microscópica(*)
 - Síndrome de Churg-Strauss(*)
 - Púrpura de Schönlein-Henoch
 - Vasculitis crioglobulinémica
 - Vasculitis leucocitoclástica cutánea

(*)ANCA

POLIARTERITIS NUDOSA



Criterios de clasificación

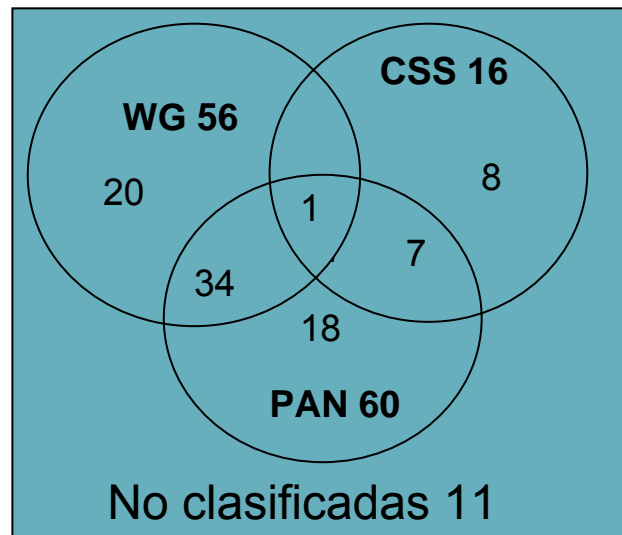
- **ACR 1990**

- Pérdida de >4kg no debido a dieta desde el comienzo de la enfermedad.
- Livedo reticularis.
- Dolor a sensibilidad a la palpación testicular no debido a infección, traumatismo u otra causa conocida.
- Mialgias o debilidad muscular.
- Mono o polineuropatía.
- Desarrollo de hipertensión con TAD >90 mmHg.
- Elevación de Urea o creatinina no debido a obstrucción o deshidratación.
- Serología VHB (Ag o Ac).
- Alteraciones angiográficas. Aneurismas u oclusiones vasculares no debidas a arteriosclerosis o displasias fibromusculares.
- Biopsia arterial mostrando infiltración por neutrófilos y leucocitos mononucleares de la pared arterial.

Para la clasificación debe cumplir 3 ó más criterios (S 82,2% y E 86,6%).

POLIARTERITIS NUDOSA

99 PACIENTES



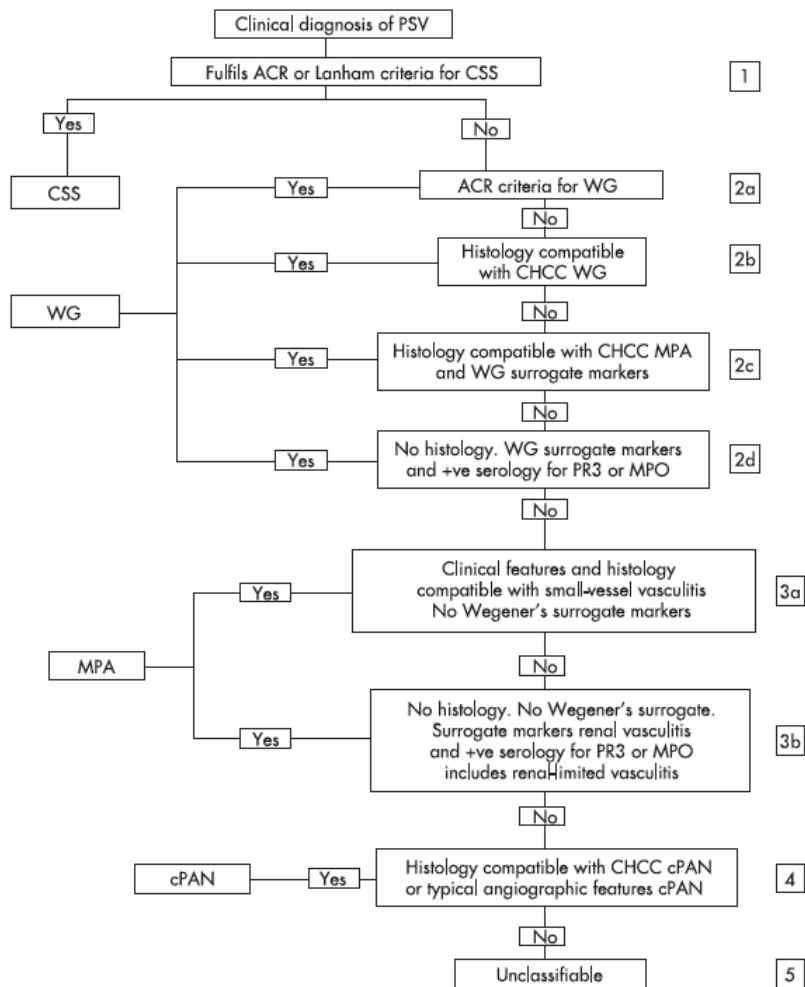
Clasificación ACR



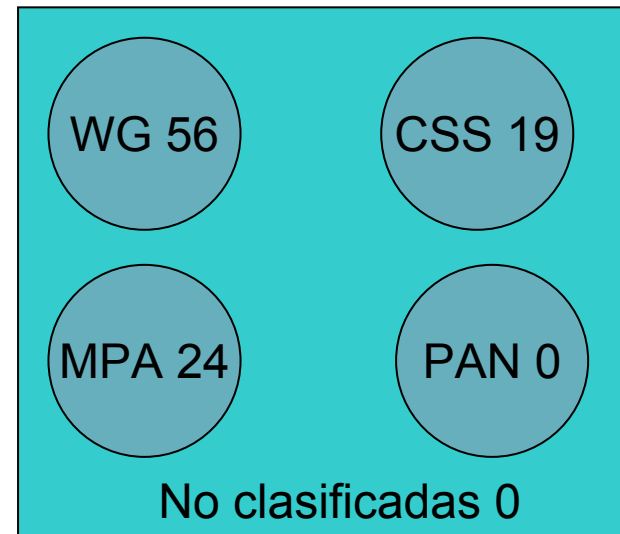
Definición CHCC



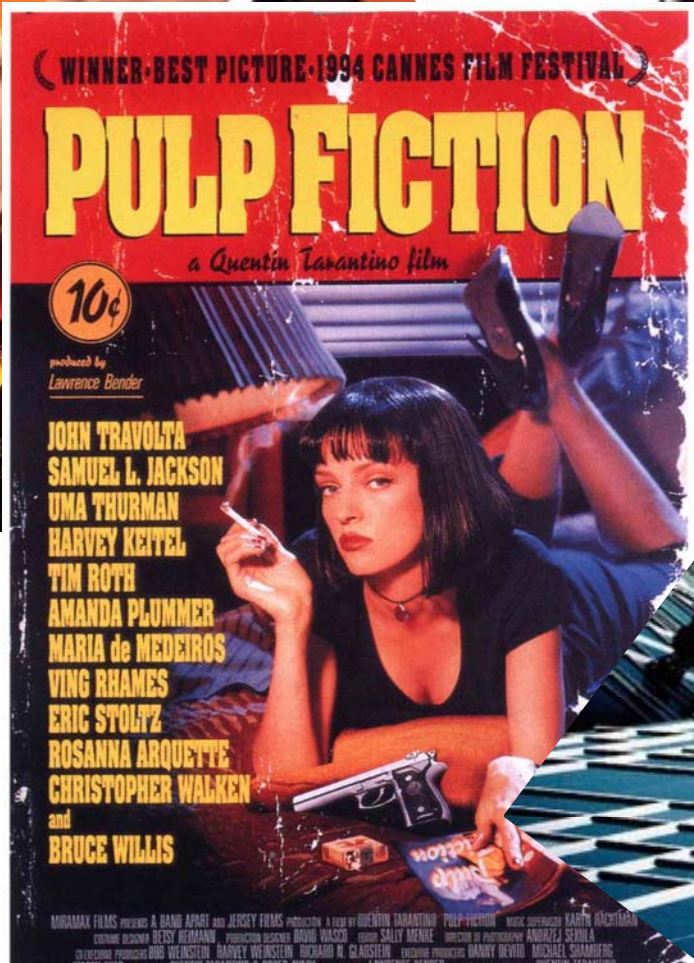
POLIARTERITIS NUDOSA



99 PACIENTES



Algoritmo diagnóstico



Dx	Año	Lugar	Incidencia
PAN	1972-80	UK	4,6
PAN	1951-67	USA	7,0
PAN	1957-71	USA	2,0
PAN(*)	1974-85	ALASKA	77,0
PAN	1976-79	USA	9,0
ACR	1992-96	NORUEGA	6,6
ACR	1990-99	LITUANIA	7,7
ACR	1988-97	UK	8,0
CHCC	1993-96	KUWAIT	16,0
ACR	1988-97	SPAIN	6,6
ACR	1992-96	NORUEGA	6,6
ACR+CHCC	1990-01	SUECIA	1,4
CHCC	1998-02	ALEMANIA	0,4-2,0

ACR
2-9/millón

CHCC
0,5-2/ millón

Watts R,08

Incidencia

VASCULITIS

INCIDENCIA (x millón)

Todas vasculitis sistémicas 1 ^a	13,07
Poliangeitis microscópica	7,91
Granulomatosis Wegener	2,95
Síndrome de Churg-Strauss	1,31
Poliarteritis nudosa clásica	0,90

POLIARTERITIS NUDOSA

¿Corre peligro la poliarteritis nudosa?

PAN

OTRAS VASCULITIS



POLIARTERITIS NUDOSA

- **PAN clásica**
- **PAN secundaria**
 - Asociada a infecciones: VHB, VHC, VIH
 - Asociada a tumores: Tricoleucemia
 - Asociada a conectivopatías: LES, AR, SSj
- **PAN infantil**
- **PAN localizada**

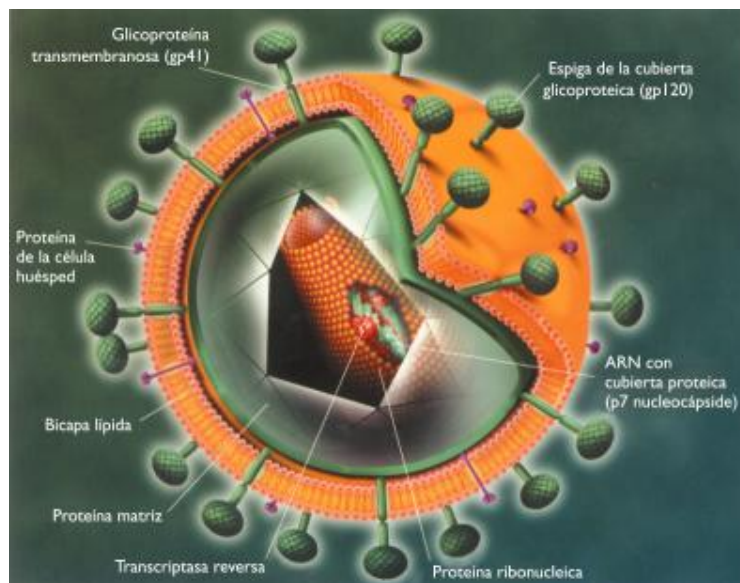
POLIARTERITIS NUDOSA

Vox Sang. 19: 410-411 (1970)

Hepatitis Associated Antigen and Periarthritis Nodosa (PAN)

CH. TREPO and J. THIVOLET

Laboratoire d'Hygiène, Faculté de Médecine (Service du Prof. THIVOLET), Lyon



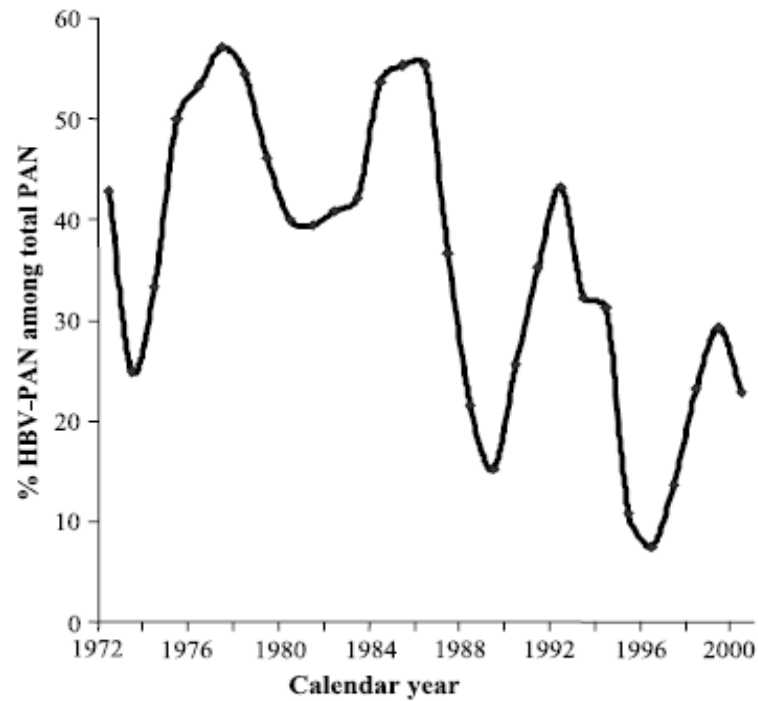
J. clin. Path., 1974, 27, 863-868

The role of circulating hepatitis B antigen/antibody immune complexes in the pathogenesis of vascular and hepatic manifestations in polyarteritis nodosa

CHRISTIAN G. TREPO, ARIE J. ZUCKERMAN, RICHARD C. BIRD, AND ALFRED M. PRINCE

From the University of Lyons, New York Blood Center and Cornell University, and the London School of Hygiene and Tropical Medicine

PAN Y VHB

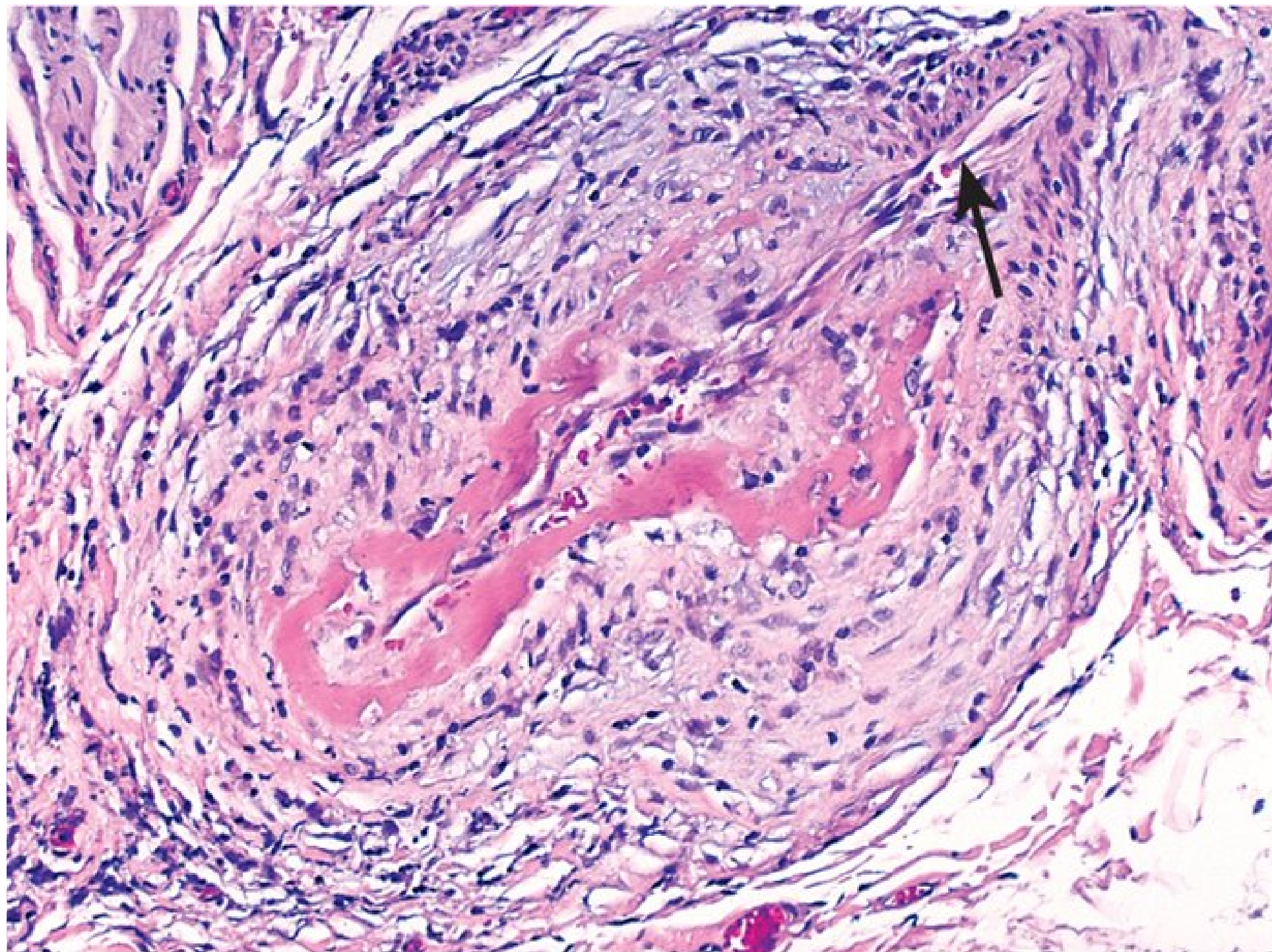


Guillevin L, 2005

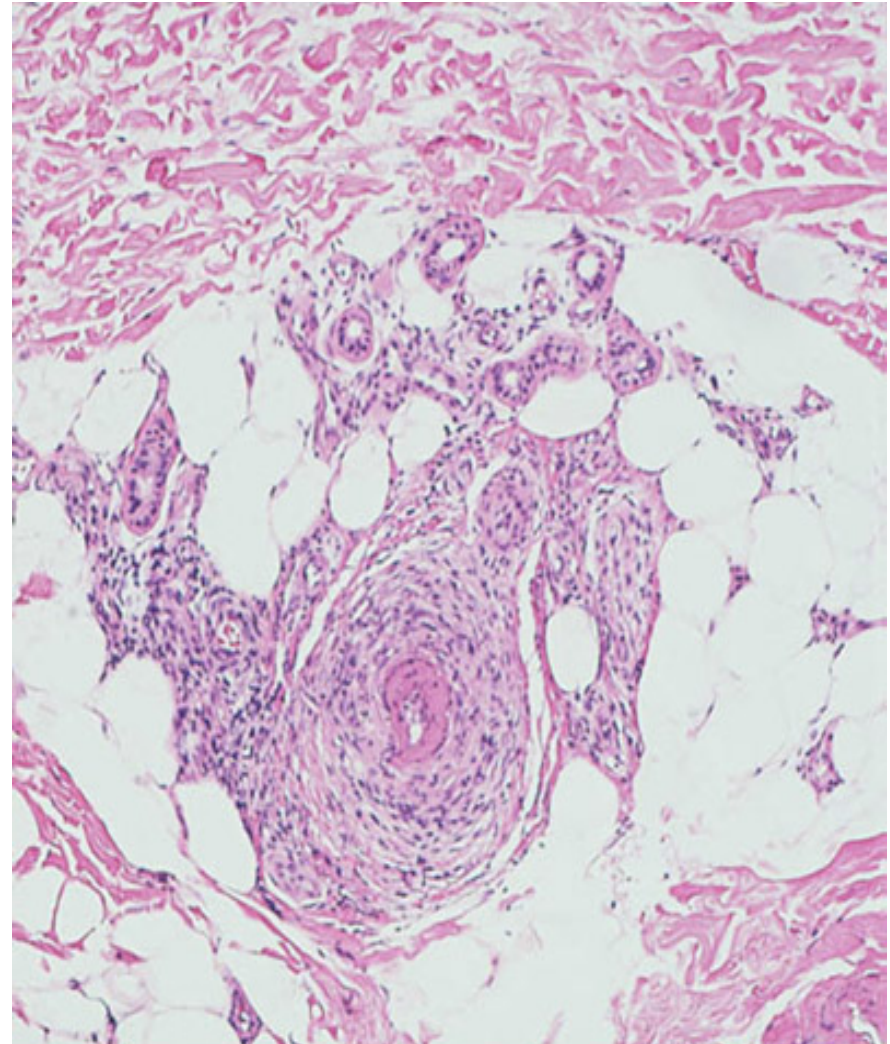
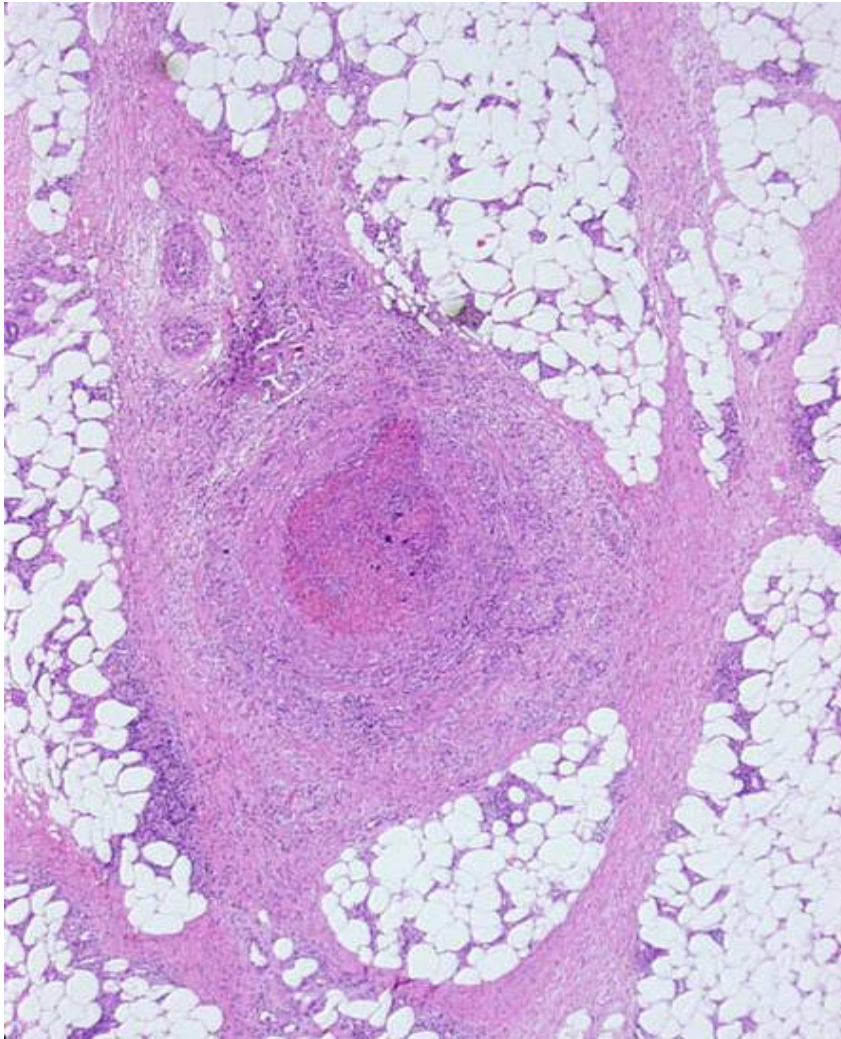
No. of PAN	Period 1972–1979								Period 1980–1989								Period 1990–2002								Total							
HBV	2	0	1	1	1	4	3	1	2	3	5	7	6	6	17	8	6	4	1	2	8	2	6	2	2	0	1	6	3	3	2	115
Non-HBV	0	2	2	2	2	2	3	1	1	5	9	9	8	9	8	8	9	14	17	8	7	7	7	7	8	18	11	15	7	7	13	226

POLIARTERITIS NUDOSA

- Afecta arterias de mediano y pequeño calibre
- Respetada aorta y sus ramas, arteriolas, capilares, vénulas y venas
- Afectación transmural, segmentaria y en puntos de bifurcación y coexistencia de diferentes estadios evolutivos en el mismo ó diferentes tejidos
- Infiltración por PMN y variable número de linfocitos y eosinófilos, leucocitoclasia, necrosis fibrinoide, destrucción de elásticas. La curación se sigue de fibrosis de la pared
- Formación de aneurismas , oclusión de la luz y trombosis



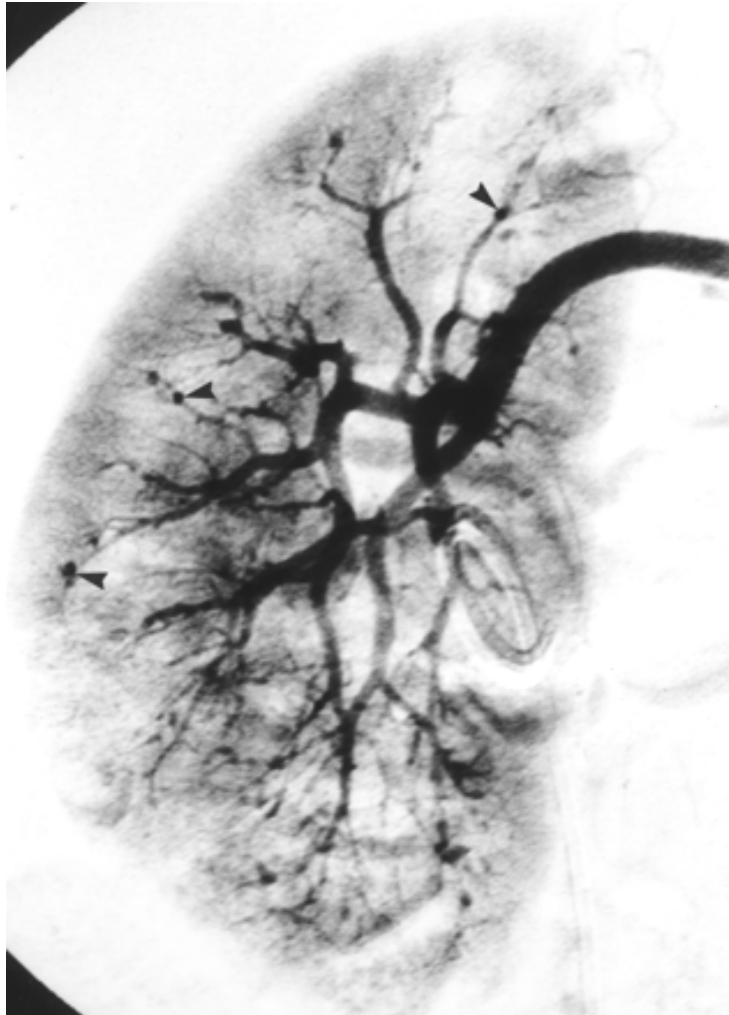
POLIARTERITIS NUDOSA



POLIARTERITIS NUDOSA



POLIARTERITIS NUDOSA



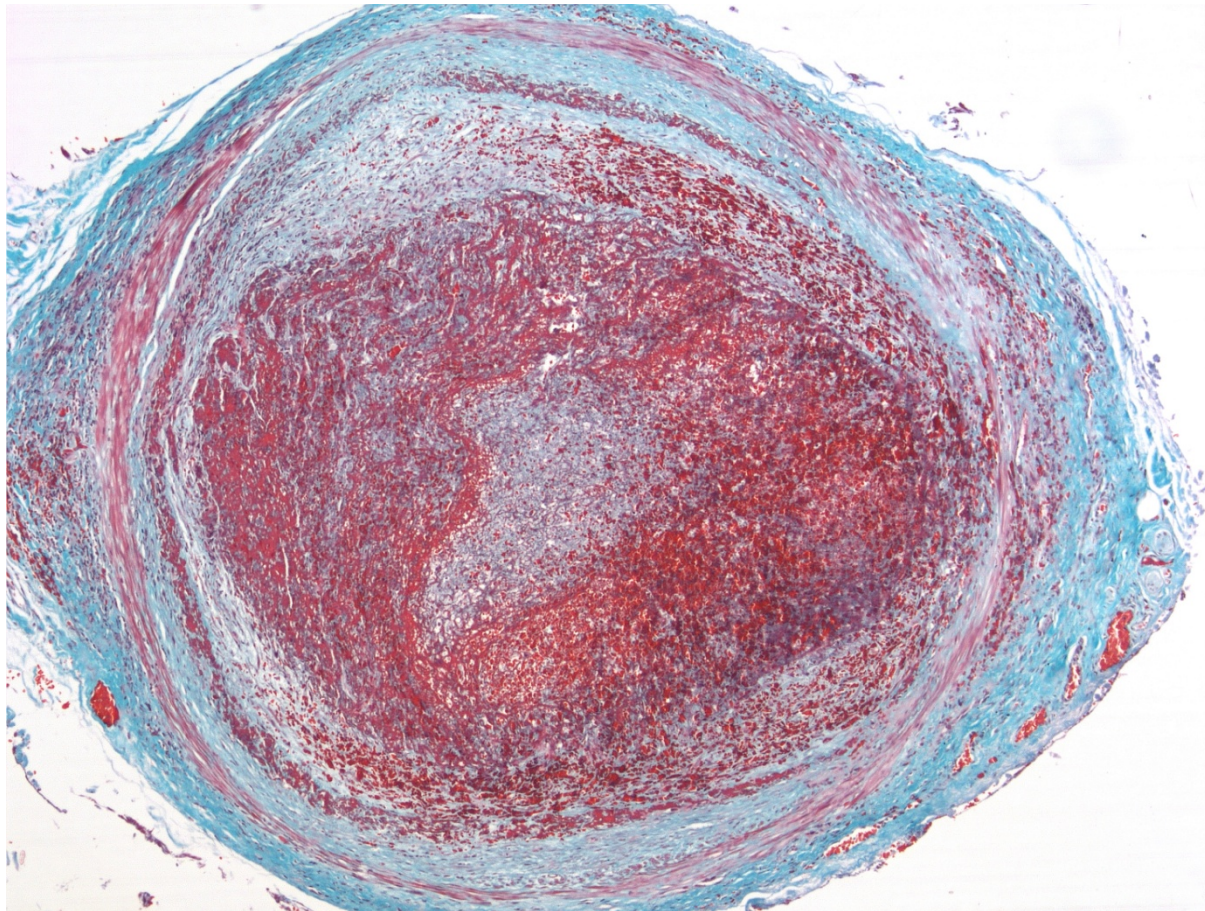
POLIARTERITIS NUDOSA



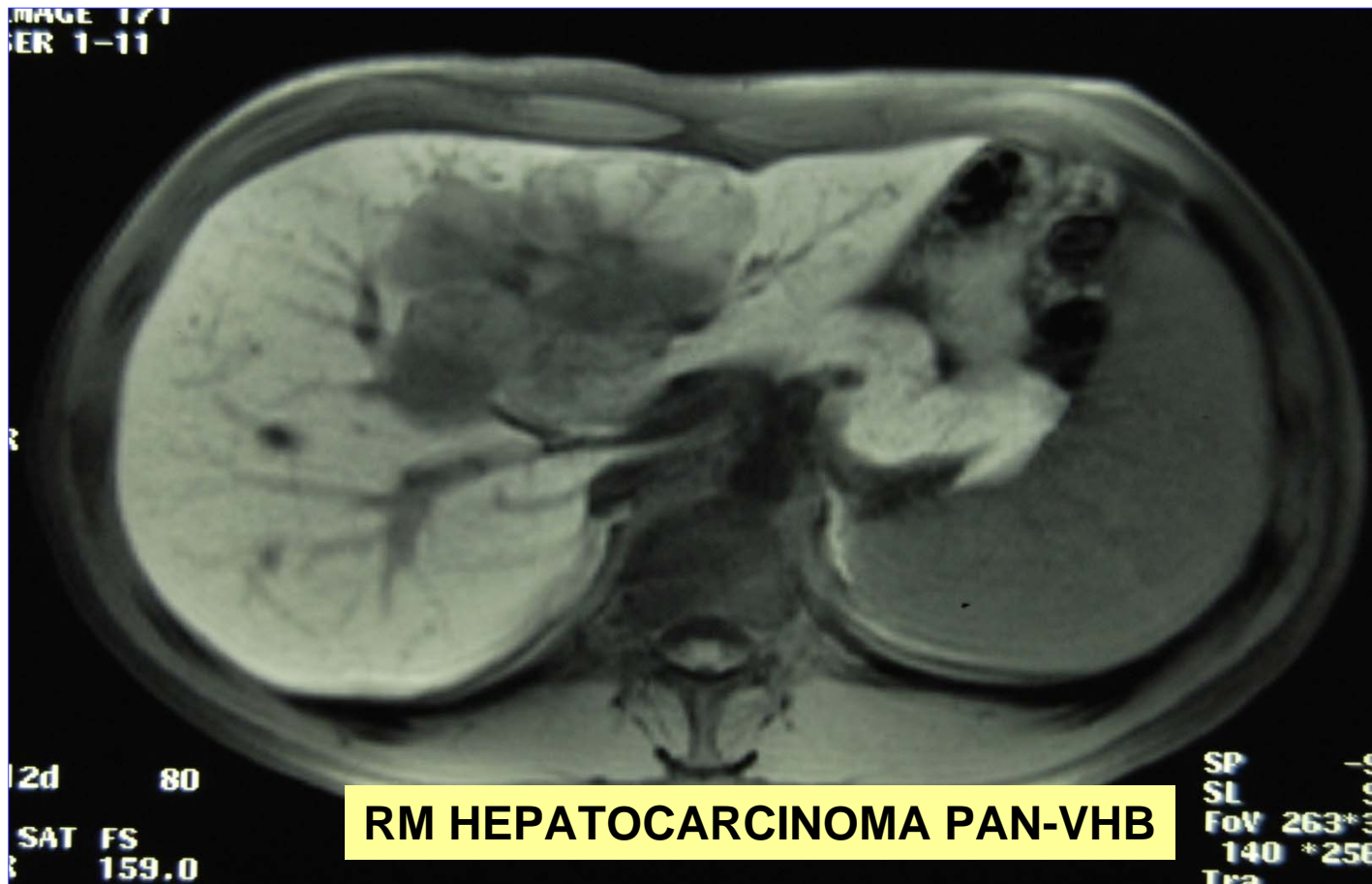
HEMATOMA PERIRENAL EN PAN POR ROTURA DE ANEURISMA



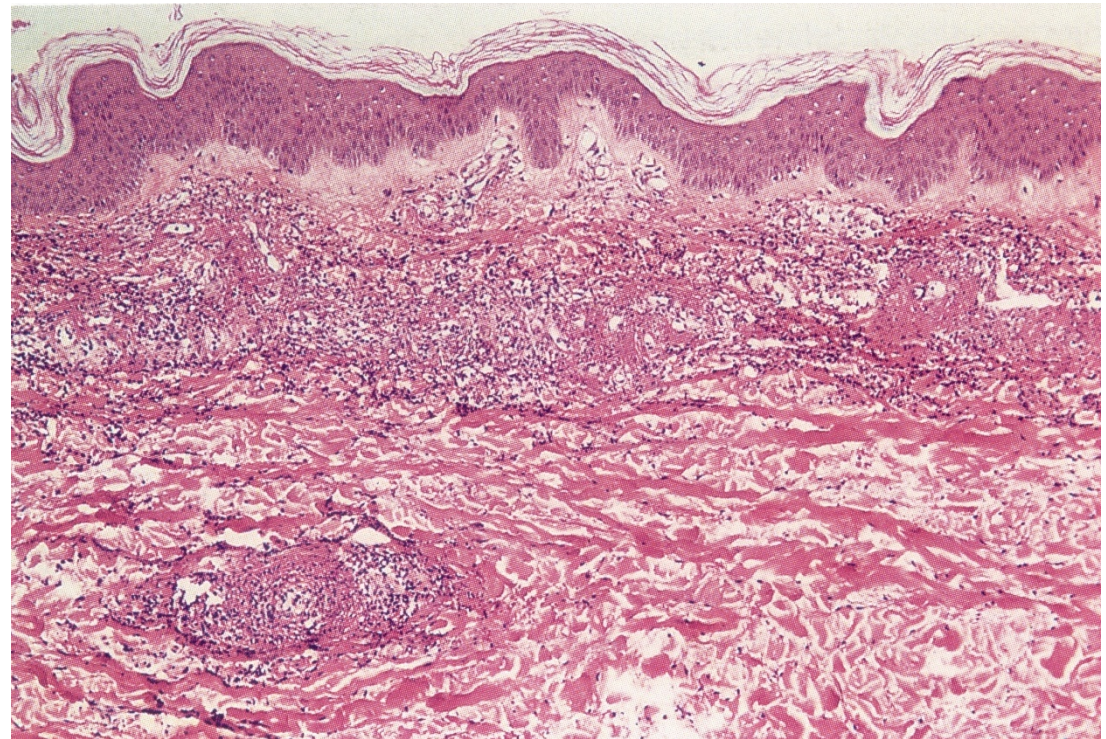
POLIARTERITIS NUDOSA



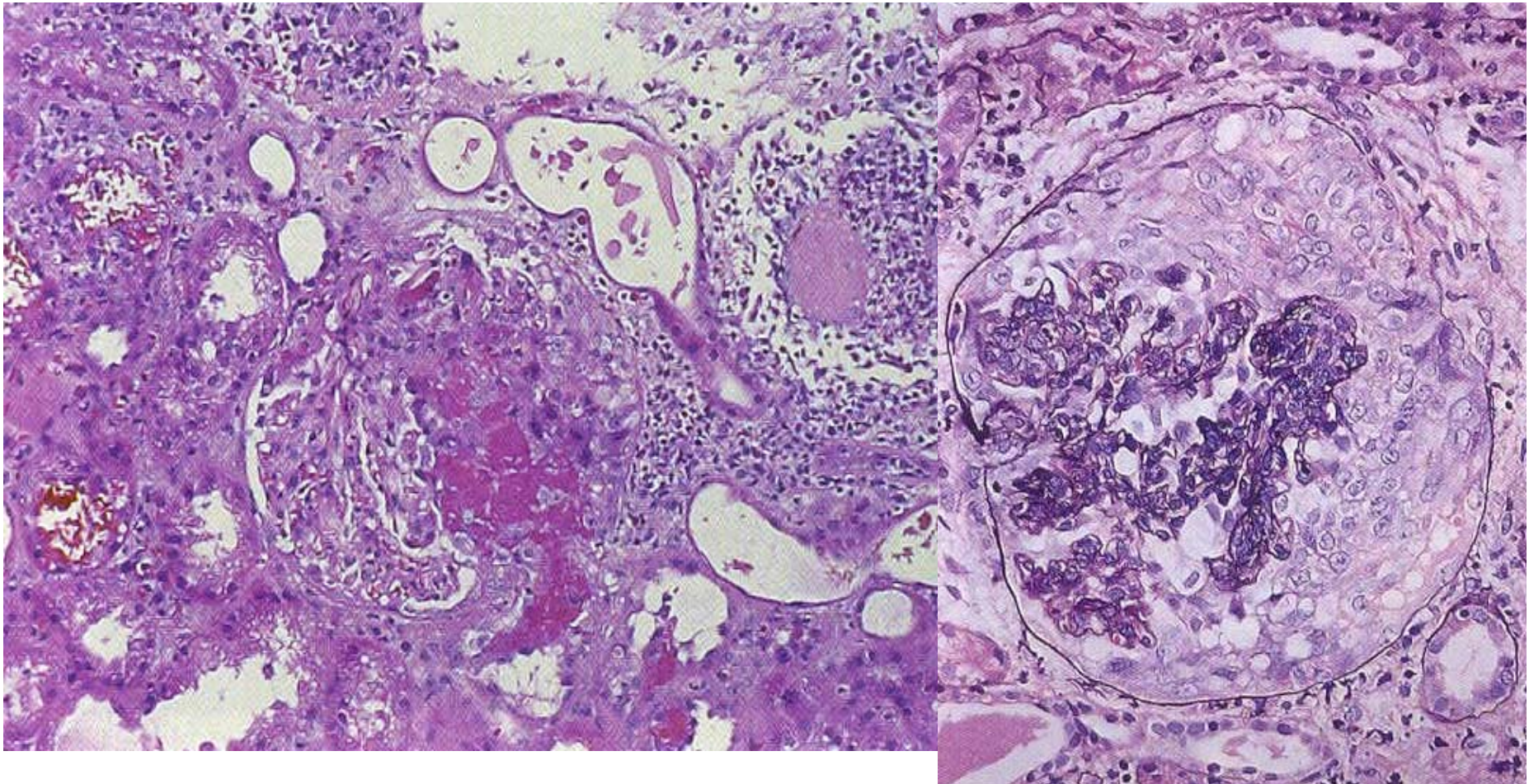
POLIARTERITIS NUDOSA



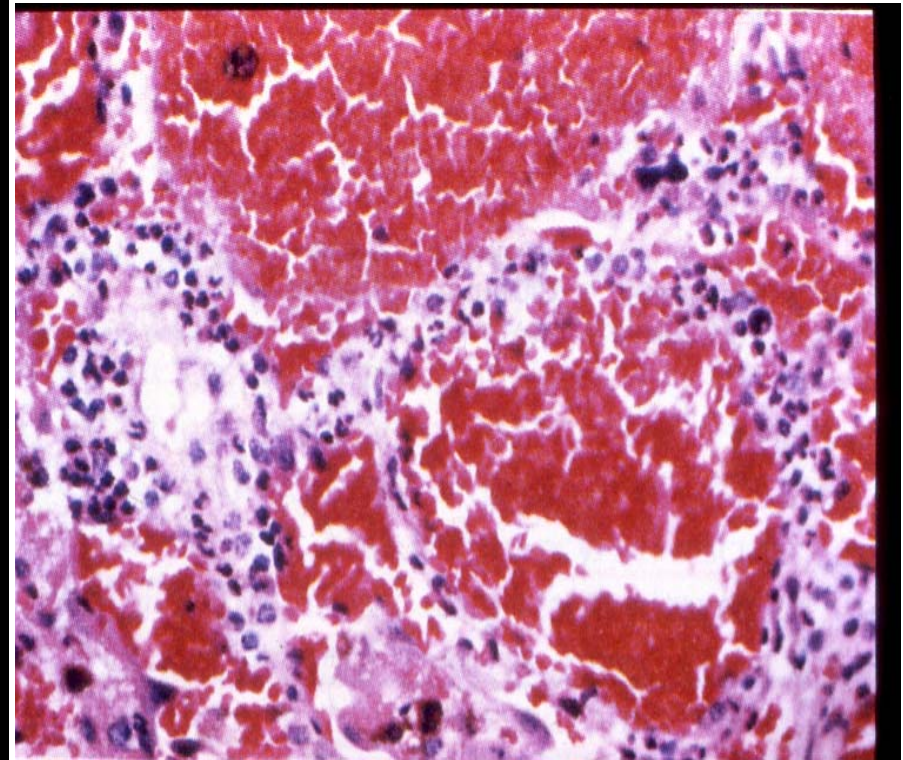
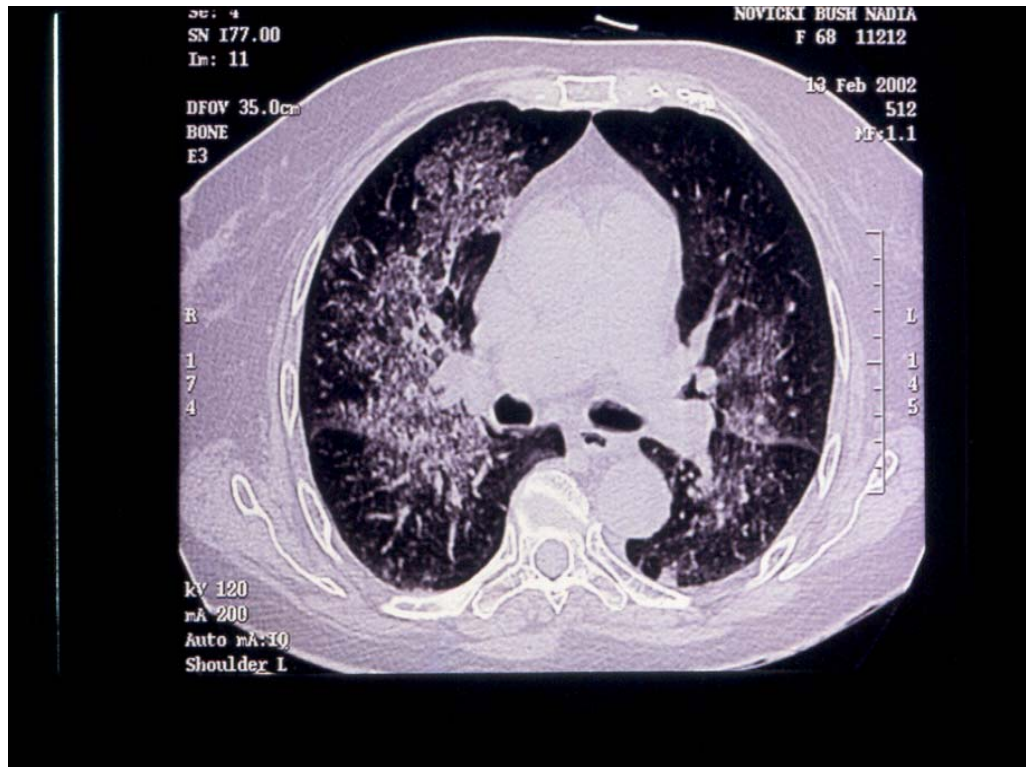
Vasculitis leucocitoclástica



Glomerulonefritis pauciimmune



Poliangeítis microscópica



POLIARTERITIS NUDOSA

ARTHRITIS & RHEUMATISM
Vol 62, No. 2, February 2010, pp 616-626
DOI 10.1092/art.27240
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Clinical Features and Outcomes in 348 Patients With Polyarteritis Nodosa

A Systematic Retrospective Study of Patients Diagnosed Between
1963 and 2005 and Entered Into the French Vasculitis Study Group Database

Christian Pagnoux,¹ Raphaèle Seror,¹ Corneliu Henegar,² Alfred Mahr,¹ Pascal Cohen,¹
Véronique Le Guern,¹ Boris Bienvvenu,³ Luc Mouthon,¹ and Loïc Guillevin,¹ for
the French Vasculitis Study Group

Diferencias clínicas VHB (+) vs VHB (-)

Total 348	VHB(+) 123	VHB(-) 225
N. periférica	87,8	74,2
Orquitis	24,1	13,1
HTA	48,8	27,1
Gastrointestinal	50,4	31,1
Miocardopatía	13	4,4
Afect. cutánea	35	57,8
FFS ≥ 1	52,9	33,3
BVAS (media)	19,1	15,1
Hipertransaminemia	64,2	15,6
Angio mesenterica(+)	71,9	48,9

P<0,05

FVSG, 2010

Diferencias clínicas VHB (+) vs VHB (-)

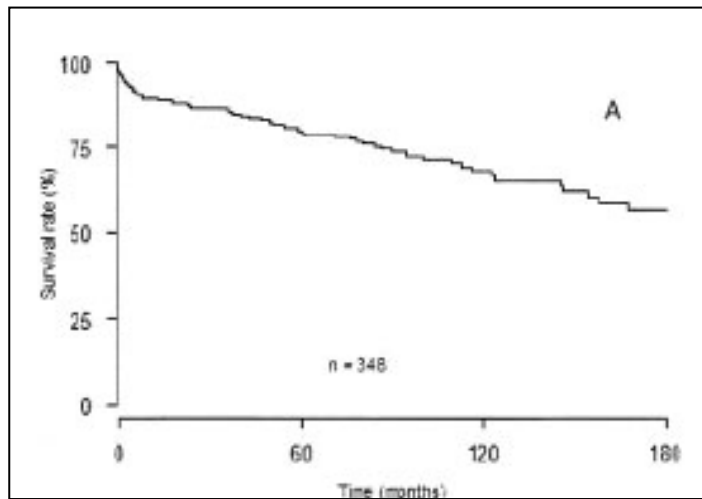
Total 348	VHB(+) 123	VHB(-) 225
Muertes	34,1	19,6
Recaídas	10,6	28(*)

P<0,05

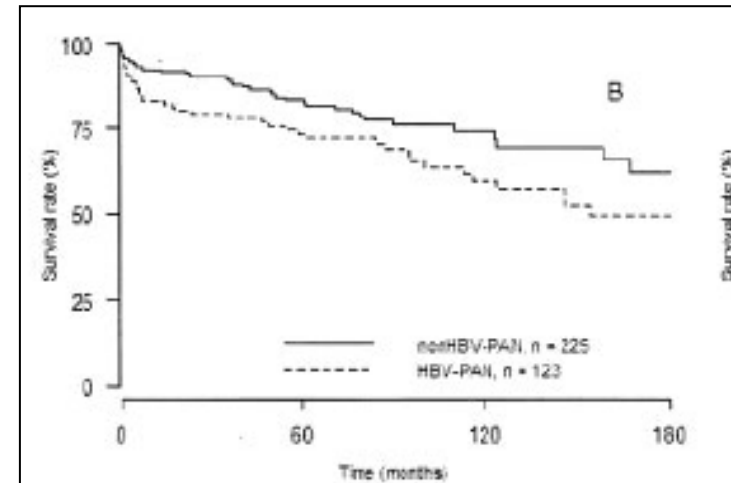
FVSG, 2010

(*)Especialmente los que presentan afectación cutánea

Diferencias clínicas VHB (+) vs VHB (-)



TODOS 75%

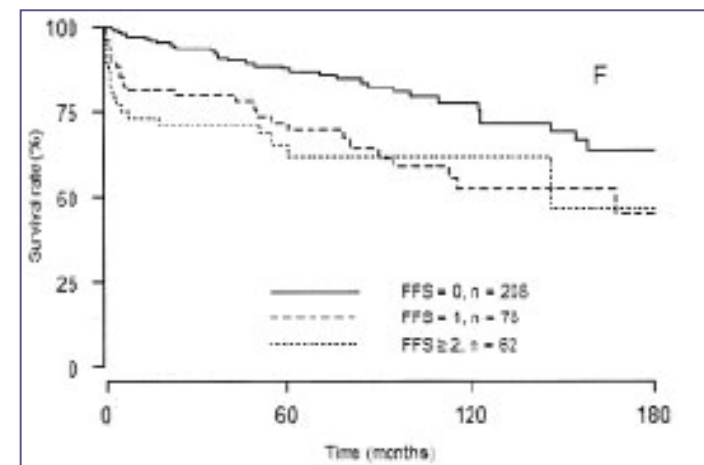
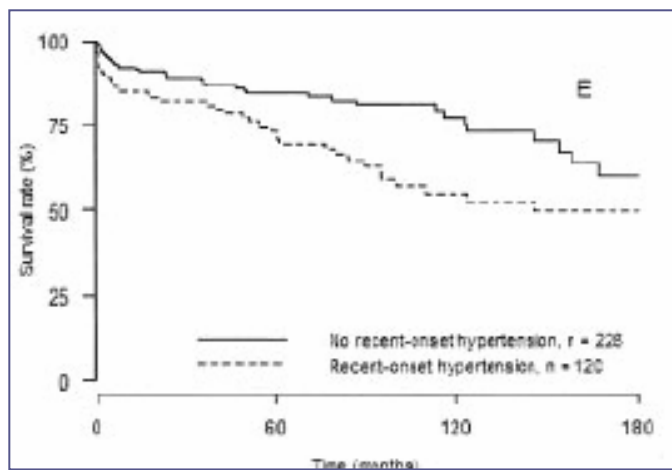
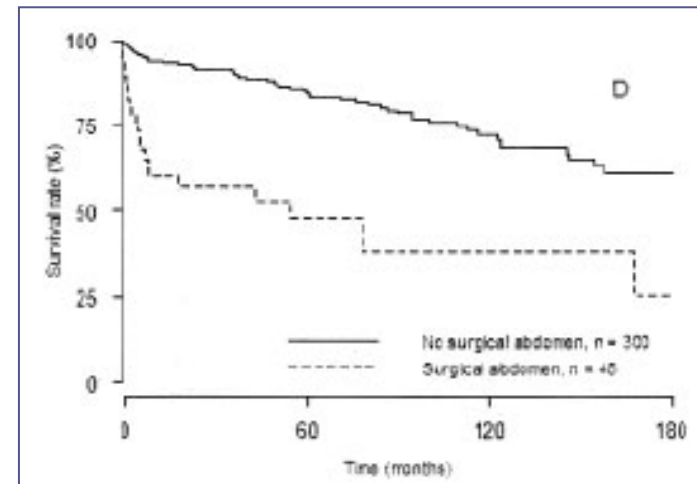
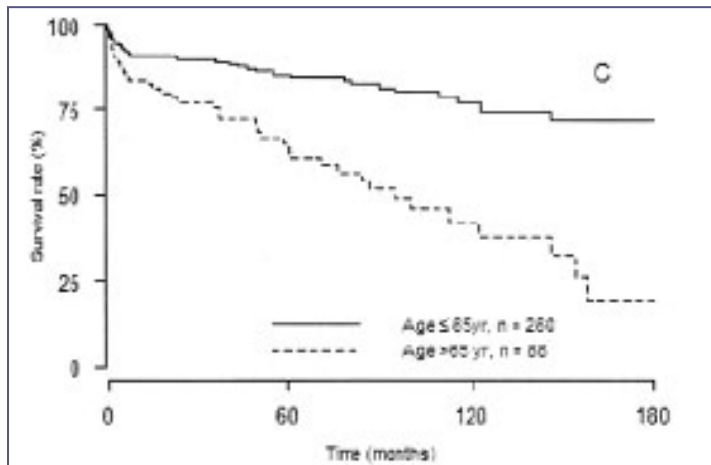


VHB(+) 66% vs VHB(-) 80% (p =0,003)

Seguimiento medio 5 años

FVSG, 2010

Factores pronósticos VHB(+) vs VHB(-)



Tratamiento problemas



- **Muchas publicaciones se basan en la clasificación de Fauci: Grupo PAN:**
 - 1) PAN clásica
 - 2) E. Churg Strauss
 - 3) Overlap
- **Aparece y se mezcla la PAN relacionada con el VHB**
- **No se tiene en cuenta la diferencia establecida en Chapel Hill (1994) entre la Poliarteritis nudosa (PAN) y la Poliangeitis microscópica (PAM)**

Tratamiento

Tratamiento	FROHNERT, 67	Vivos 5 años(%)	LEIB 79	Vivos 5 años(%)	COHEN, 80	Vivos 5 años(%)	FORTIN 95	Vivos 5 años(%)
Sintomático	20	13	8	12	--	--	--	--
Esteroides	110	48	34	53	36	61	13	76
Esteroides +inmuno supresores	---	---	22	80	14	42	22	64

Tratamiento

- 17 pacientes grupo PAN con resistencia a esteroides se les añade ciclofosfamida 2 mg/kg/día vo
- Todos tuvieron remisión completa, 14 viven, 3 fallecen, ninguno recidiva
- Sugiere que pacientes con vasculitis del grupo PAN que tengan afectación renal deben recibir desde el comienzo tratamiento combinado

Factores pronósticos

Variable	p
Proteinuria > 1g/d	<0,001
GI grave	<0,001
Creatinina > 1,5	NS
SNC	NS
Miocardopatía	NS

FFS	Mortalidad	RR
0	11,9%	0,62
1	25,9%	1,35
2	45,9%	2,40

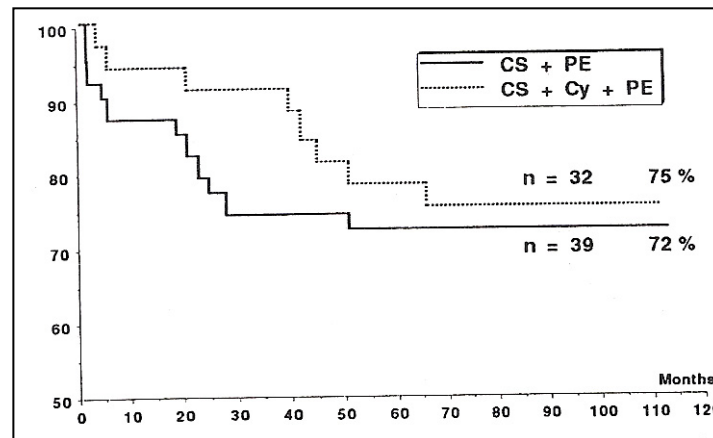
342 pacientes: PAN clásica 208 (VHB- 119 VHB+ 89) PAM 52 Ch-S 82

GI grave: sangrado, perforación, infarto, pancreatitis

Longterm Followup After Treatment of Polyarteritis Nodosa and Churg-Strauss Angiitis with Comparison of Steroids, Plasma Exchange and Cyclophosphamide to Steroids and Plasma Exchange. A Prospective Randomized Trial of 71 Patients

L. GUILLEVIN, B. JARROUSSE, C. LOK, F. LHOTE, J.P. JAIS, D. LE THI HUONG DU, and A. BUSSEL and the Cooperative Study Group for Polyarteritis Nodosa.

followup. Nineteen deaths were reported during the followup period. There was no difference between the 10 year cumulative survival rates of the 2 groups (respectively, 72 and 75%). Thus, the association of cyclophosphamide with corticosteroids and plasma exchanges reduced the incidence of relapses and improved the quality of the clinical response to therapy. (*J Rheumatol* 1991;18:567-74)



Recaídas
Grupo A 38,5%
Grupo B 9,4% (p<0,01)

LACK OF SUPERIORITY OF STEROIDS PLUS PLASMA EXCHANGE TO STEROIDS ALONE IN THE TREATMENT OF POLYARTERITIS NODOSA AND CHURG-STRAUSS SYNDROME

A Prospective, Randomized Trial in 78 Patients

LOÏC GUILLEVIN, OLIVIER FAIN, FRANÇOIS LHOTE, BERNARD JARROUSSE,
DU LE THI HUONG, ANNETTE BUSSEL, and ANNE LEON

Conclusion. Based on our data, we conclude that combined treatment with prednisone and plasma exchange is not superior to treatment with prednisone alone and must not be systematically employed for initial treatment of PAN and CSS. In most cases, cyclophosphamide as second-line treatment is effective and well tolerated.

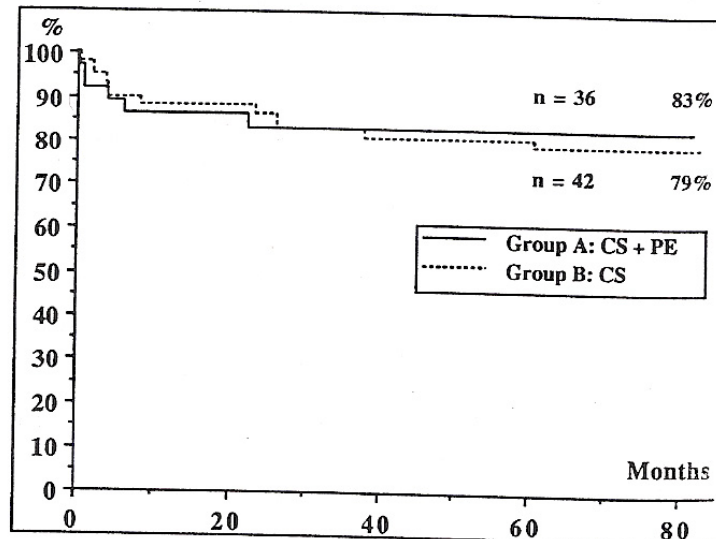


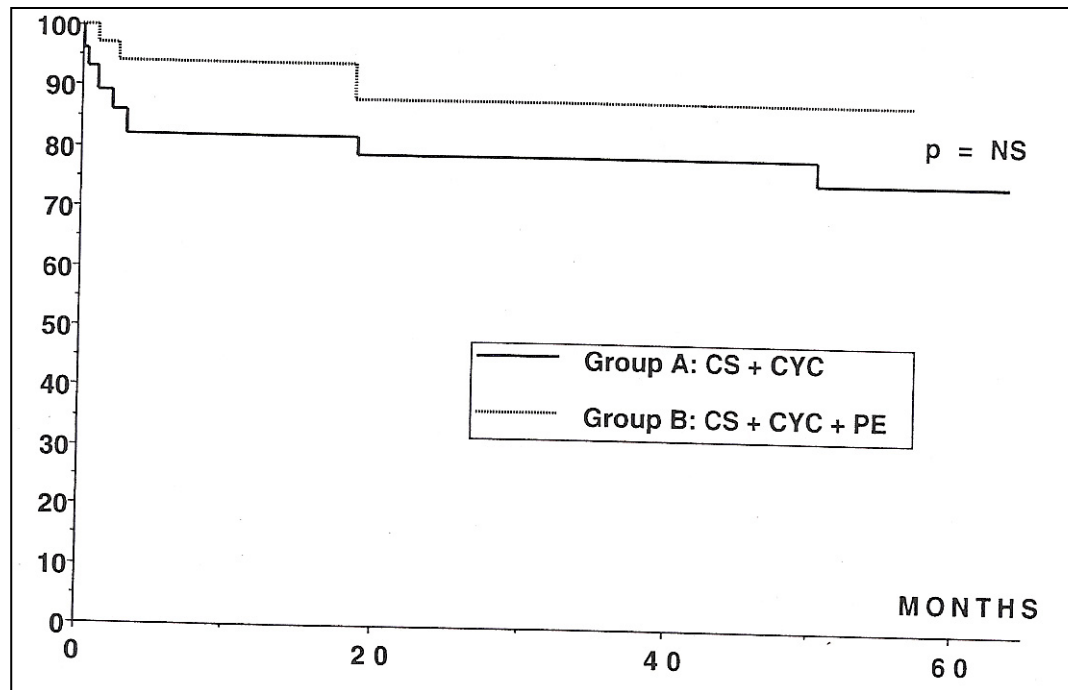
Figure 1. Rates of survival in remission.

Arthritis and Rheumatism, Vol. 35, No. 2 (February 1992)

CORTICOSTEROIDS PLUS PULSE CYCLOPHOSPHAMIDE AND PLASMA EXCHANGES VERSUS CORTICOSTEROIDS PLUS PULSE CYCLOPHOSPHAMIDE ALONE IN THE TREATMENT OF POLYARTERITIS NODOSA AND CHURG-STRAUSS SYNDROME PATIENTS WITH FACTORS PREDICTING POOR PROGNOSIS

A Prospective, Randomized Trial in Sixty-Two Patients

LOÏC GUILLEVIN, FRANÇOIS LHOTE, PASCAL COHEN, BERNARD JARROUSSE, OLIVIER LORTHOLARY, THIERRY GÉNÉREAU, ANNE LÉON, and ANNETTE BUSSEL



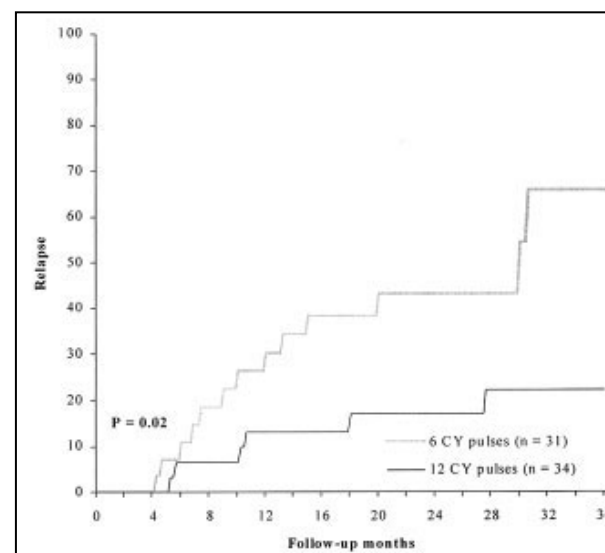
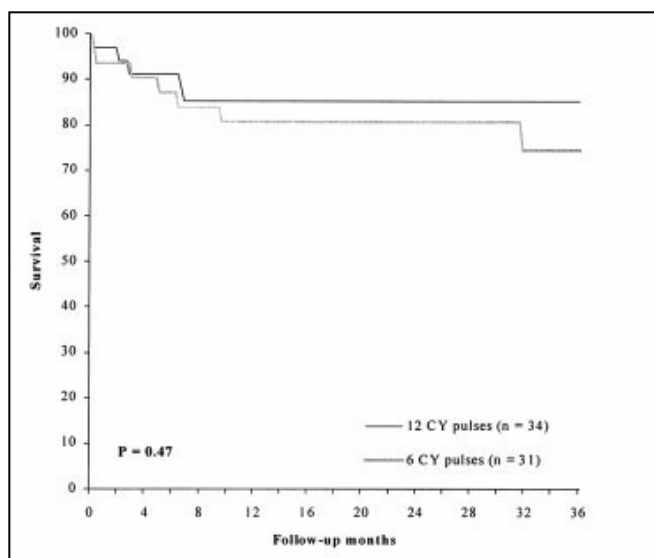
Conclusion. Based on our data, combined treatment with prednisone, cyclophosphamide, and plasma exchanges is not superior to treatment with prednisone and cyclophosphamide alone, and plasma exchanges should not be systematically proposed for initial treatment of severe PAN or CSS.

ARTHRITIS & RHEUMATISM
Vol. 38, No. 11, November 1995, pp 1638-1645
© 1995, American College of Rheumatology

Treatment of Polyarteritis Nodosa and Microscopic Polyangiitis With Poor Prognosis Factors: A Prospective Trial Comparing Glucocorticoids and Six or Twelve Cyclophosphamide Pulses in Sixty-Five Patients

LOÏC GUILLEVIN,¹ PASCAL COHEN,¹ ALFRED MAHR,¹ JEAN-PIERRE ARÈNE,¹ LUC MOUTHON,¹ XAVIER PUÉCHAL,² EDOUARD PERTUISET,³ BRIGITTE GILSON,⁴ MOHAMED HAMIDOU,⁵ PATRICIA LANOUX,⁶ ALAIN BRUET,⁷ MARC RUIVARD,⁸ PHILIPPE VANHILLE,⁹ JEAN-FRANÇOIS CORDIER,¹⁰ AND THE FRENCH VASCULITIS STUDY GROUP

Conclusion. These results suggest that 6 CY pulses are less effective than 12 CY pulses to treat severe PAN and MPA, particularly with respect to the risk of relapses.



Resumen de los 4 ensayos del FVSG

- La CFM asociada a CS frente a CS sólo, no modifica la supervivencia pero disminuye las recaídas en el grupo general y en el grupo con factores de mal pronóstico 12 ciclos de CFM consiguen menos recaídas que 6 ciclos
- La PE asociada a CS+/-CF frente a CS+/- CF sólo, no modifica la supervivencia ni las recaídas en ninguno de los grupos

Long-Term Followup of Polyarteritis Nodosa, Microscopic Polyangiitis, and Churg-Strauss Syndrome

Analysis of Four Prospective Trials Including 278 Patients

Martine Gayraud,¹ Loïc Guillevin,¹ Philippe le Toumelin,¹ Pascal Cohen,¹ François Lhote,²
Philippe Casassus,¹ Bernard Jarrousse,¹ and the French Vasculitis Study Group

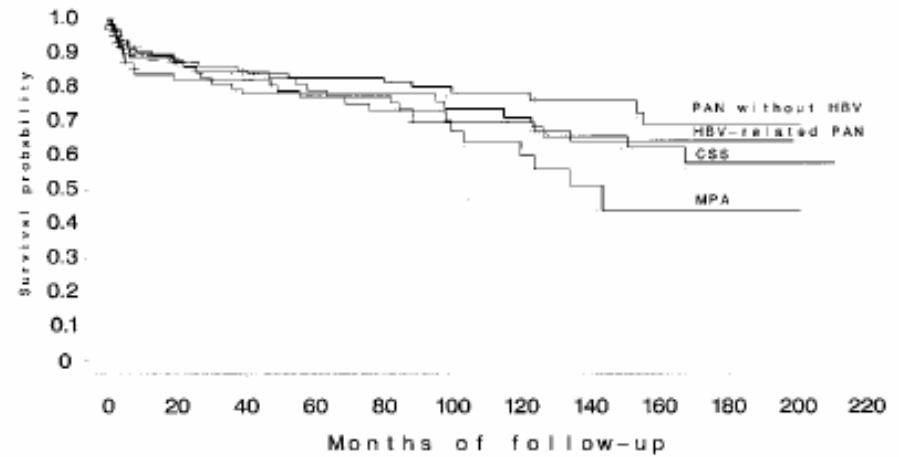
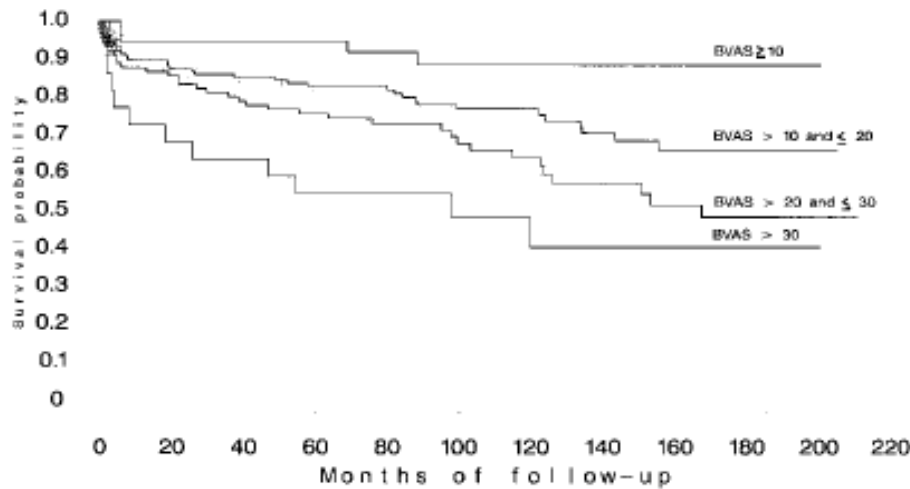
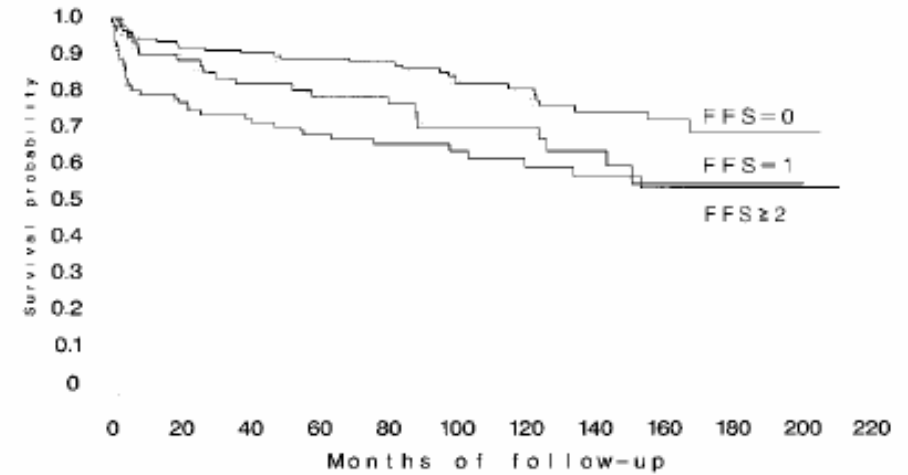
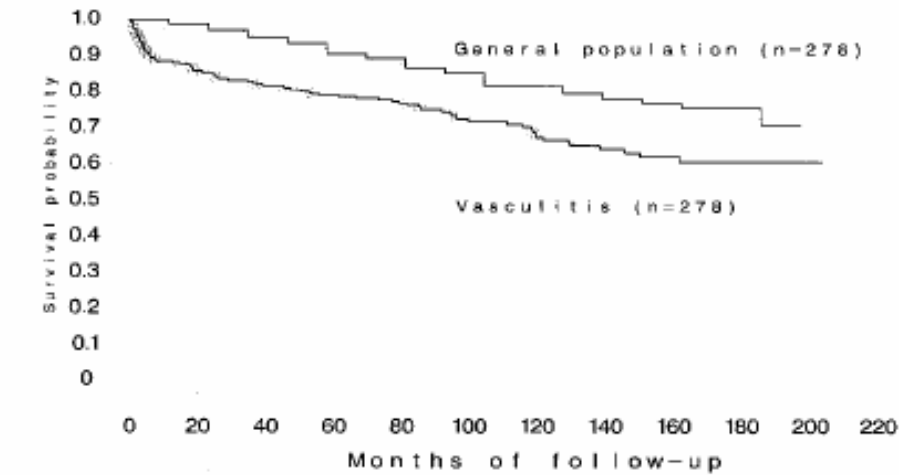
ARTHRITIS & RHEUMATISM
Vol. 44, No. 3, March 2001, pp 666–675
© 2001, American College of Rheumatology



Un maestro ...

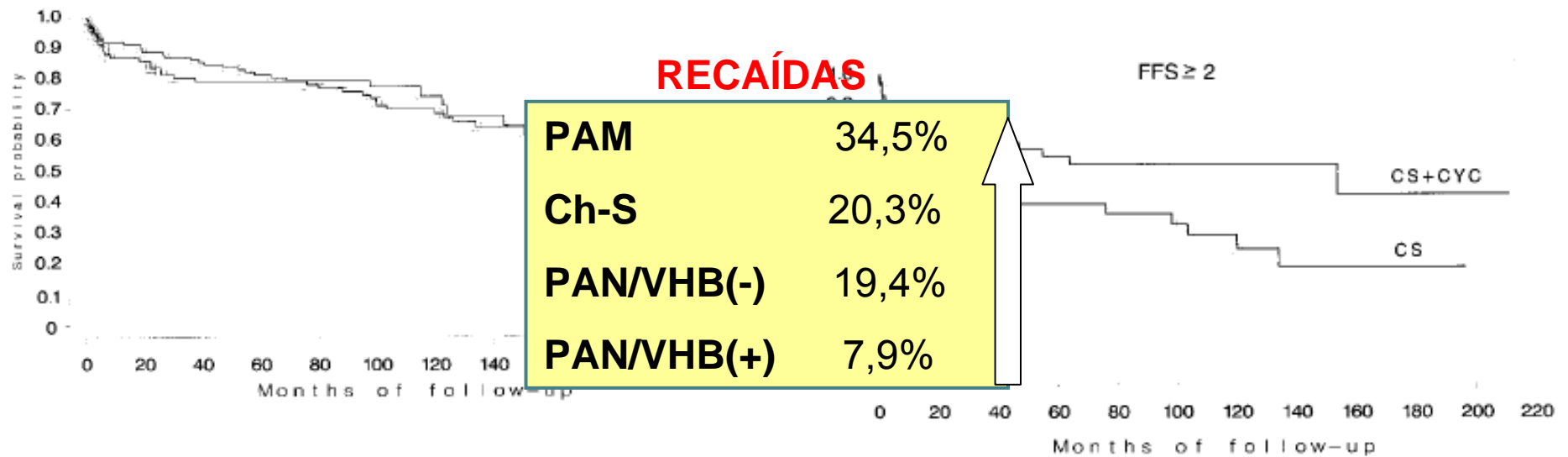
Resumiendo...

278 pacientes: PAN/VHB(-) 93, PAN/VHB(+) 63, PAM 58, ChS 64



Resumiendo...

278 pacientes: PAN/VHB(-) 93, PAN/VHB(+) 63, PAM 58, Ch-S 64

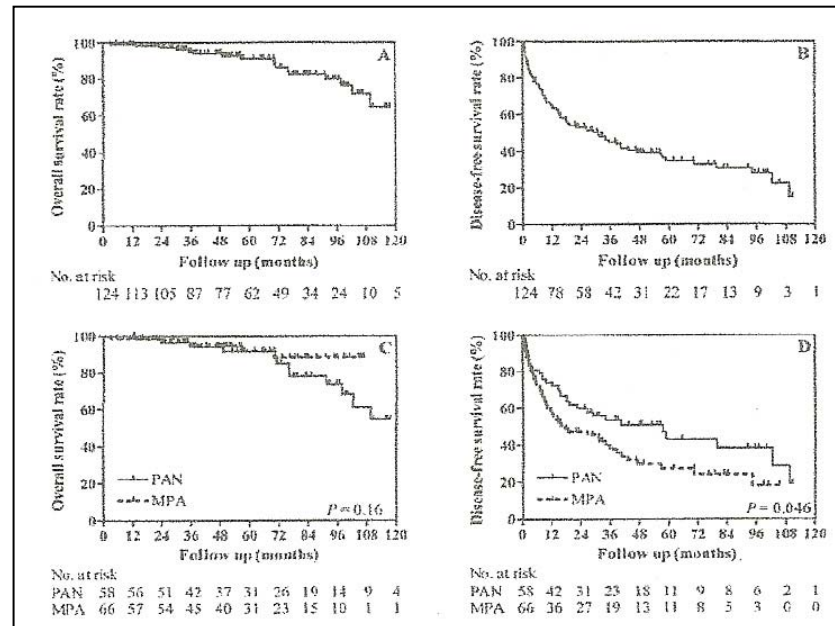


Treatment of Polyarteritis Nodosa and Microscopic Polyangiitis Without Poor-Prognosis Factors

A Prospective Randomized Study of One Hundred Twenty-Four Patients

Camillo Ribi,¹ Pascal Cohen,¹ Christian Pagnoux,¹ Alfred Mahr,¹ Jean-Pierre Arène,¹ Xavier Puéchal,² Philippe Carli,³ Xavier Kyndt,⁴ Claire Le Hello,⁵ Philippe Letellier,⁵ Jean-François Cordier,⁶ and Loïc Guillevin,¹ for the French Vasculitis Study Group

Conclusion. For patients with PAN or MPA with an FFS of 0, overall 5-year survival was good, but first-line corticosteroid treatment was able to achieve and maintain remission in only about half of the patients, and 40% of the patients required additional immunosuppressive therapy. Azathioprine or pulse cyclophosphamide was fairly effective for treating corticosteroid-resistant disease or major relapses.



PAN Y PAM (FFS=0)

Pacientes	124
RC	98(70%)
Fracaso /recaída	74(60%)
Fracaso	26
Recaída	48(grave9)
Supervivencia 1 / 5 a	99% / 92%

Variable	CFM(19)	AZT(20)
RC	13/19	14/20
Recaída	4/13	8/14
Muertes	6	2

TRATAMIENTO PAN VHB(-)

- **PAN leve (FFS 0)**
- Prednisona 1 mg/kg de peso x 4 semanas y descender hasta completar 12 meses
- **PAN moderada/grave(FFS>0) , ó leve no respondiente ó recidivante**
- Prednisona 1 mg/kg de peso x 4 semanas y descender hasta completar 12-18 meses en dosis bajas
- CFM 500-750 mg/m² iv mensual x6 y seguir con AZT 2 mg/kg/día vo hasta completar 18 meses
- **CONSIDERAR** al comienzo MP 500-1000mg iv x3

TRATAMIENTO PAN VHB(-)

Tratamiento adyuvante

IECA ó ARA-II

Calcio+vitaminaD+Bifosfonatos

Trimetrprim-sulfametoxazol

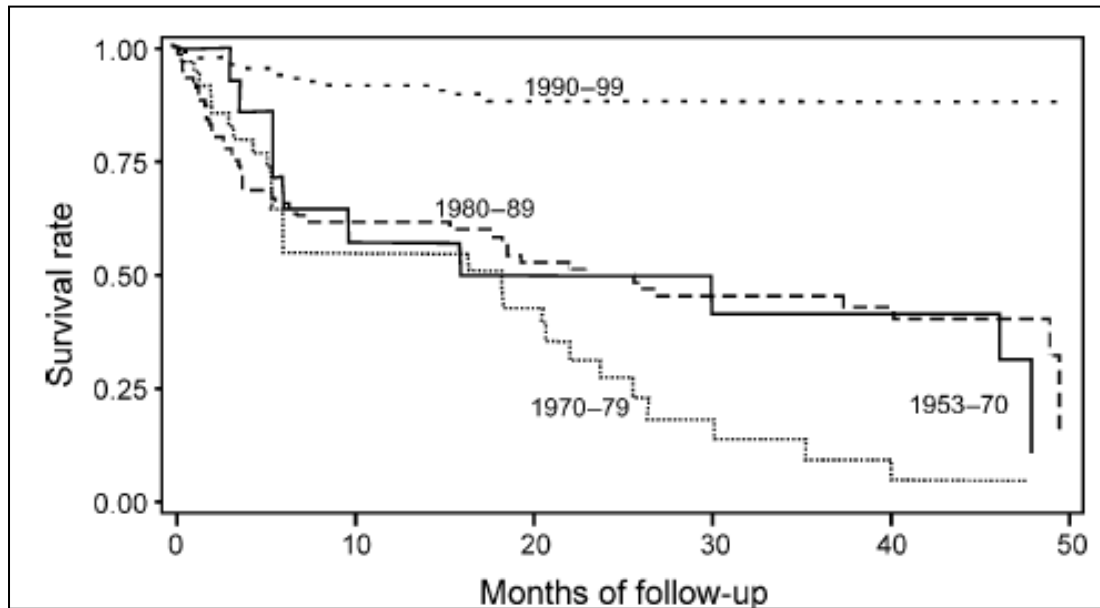
MESNA

Gabapentina ó Pregabalina

Banco de semen ó leuprólido

Cirugía abdominal

Mortalidad general y de 1º año



Time of Diagnosis	Total Population (n = 595)	Deaths	
		Total (n = 145)	1 st Year/Total Deaths (n = 60)
1953-69	23	8/23 (35)	3/8 (38)
1970-79	104	21/104 (20)	7/21 (33)
1980-89	240	85/240 (35)	32/85 (38)
1990-99	228	31/228 (14)	18/31 (58)

*Mortality declined significantly after 1990, compared to 1953-1989 (p < 0.01).

Bourgarit A, 05

Mortalidad general y de 1º año

Causa muerte	<1 AÑO(60)	>1 AÑO(85)	p
Vasculitis activa	58%	37%	<0,05
Digestivo	16	1	
Efectos 2º	26%	7%	<0,005
Infección	13	3	
Miscelánea	16%	56%	<0,001
Cáncer	1	17	
ICC	0	8	

0025-7974/95/7405-0238\$03.00/0
MEDICINE
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Vol. 74, No. 5
Printed in U.S.A.

Polyarteritis Nodosa Related to Hepatitis B Virus

A Prospective Study with Long-Term Observation of 41 Patients

LOÏC GUILLEVIN, M.D., FRANÇOIS LHOTE, M.D., PASCAL COHEN, M.D., FRANÇOISE SAUVAGET, M.D.,
BERNARD JARROUSSE, M.D., OLIVIER LORTHOLARY, M.D., LAURE-HÉLÈNE NOËL, M.D.,
AND CHRISTIAN TRÉPO, M.D., PH.D.

Hepatitis B Virus-Associated Polyarteritis Nodosa *Clinical Characteristics, Outcome, and Impact of Treatment in 115 Patients*

*Loïc Guillevin, MD, Alfred Mahr, MD, Patrice Callard, MD, Pascal Godmer, MD,
Christian Pagnoux, MD, Emmanuelle Leray, MD, and Pascal Cohen, MD,
for the French Vasculitis Study Group**

(*Medicine* 2005;84:313-322)

PAN Y VHB

- **Número 115 pacientes (1972-2002)**
- **Edad 20-80 años (51+/-17)**
- **Raza 110 blancos, 94 europeos**
- **Vía contagio Sexual 15, ADVP 16, Transfusión 12**
- **Periodo incubación (12) 30-1695 días, 7<12 meses**
- **Hepatitis aguda previa 32 (media 7 meses), concomitante 17, en general leve**
- **Elevación ALT/AST 66% (90%<200)**
- **Biopsia hepática revisada (33) Metavir <2: 23; >3: 10**
- **Replicación viral 115(100%)**

PAN Y VHB

EVOLUCIÓN	NÚMERO(%)
Remisión clínica	93(81%)
Seroconversión Tratamiento antiviral Tratamiento inmunosupresor	43(38,7%) 38/77(49%) 5/34 (14,7%)
Recaída Tratamiento antiviral Tratamiento inmunosupresor	9/93(9,7%) 5% 14%
Muerte Tratamiento antiviral Tratamiento inmunosupresor	41/115(35,7%) 30% 48%
Supervivencia 5 años	63(72,5%)

Guillevin L, 2005

PAN Y VHB

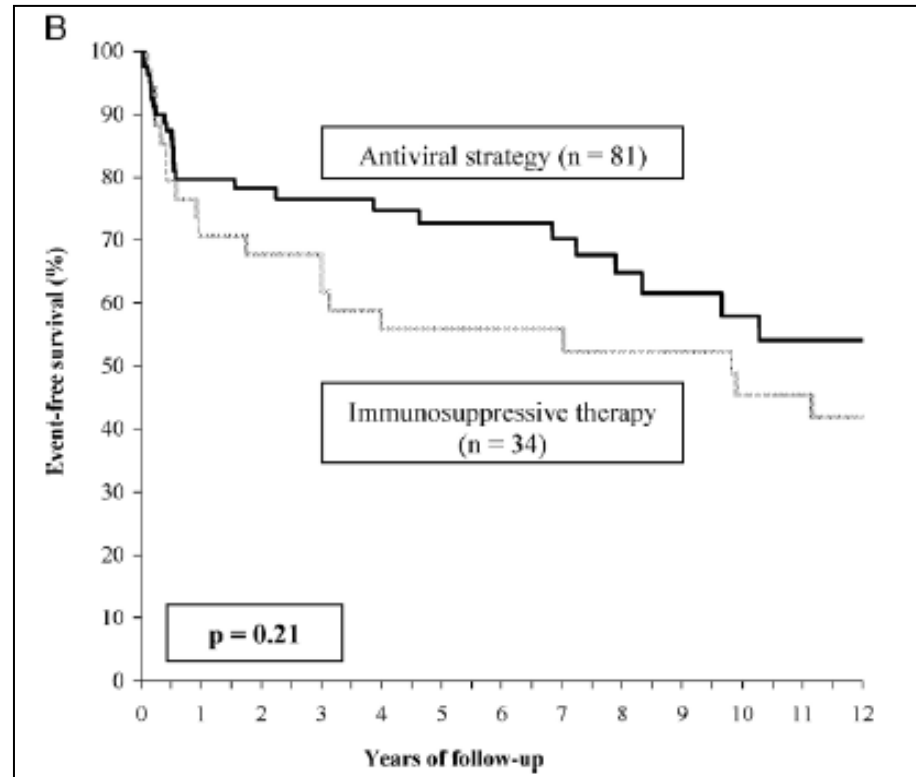
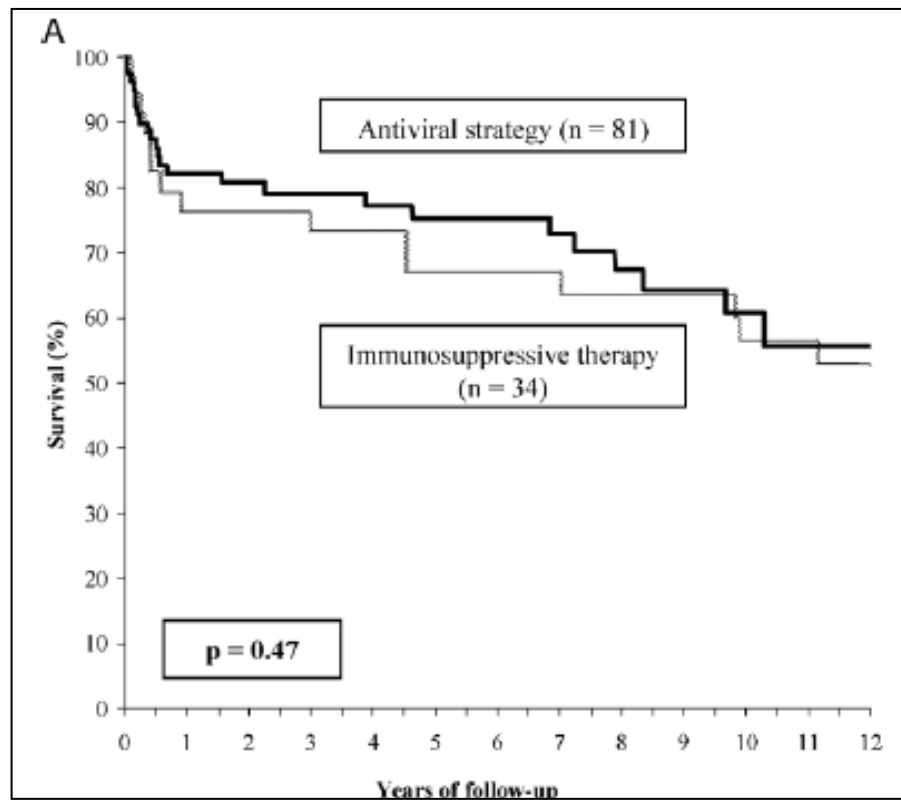
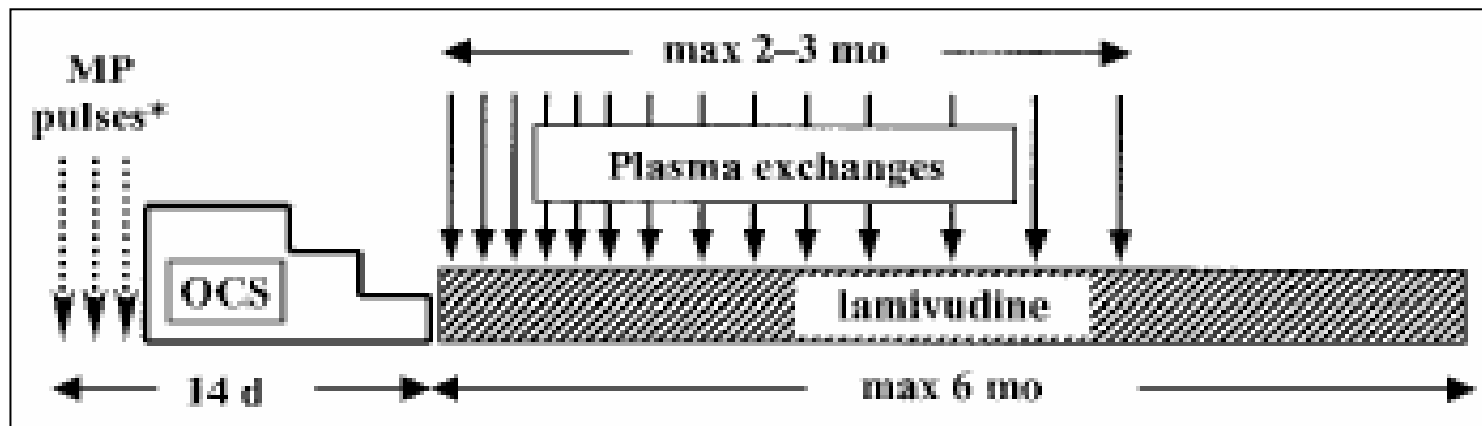


FIGURE 3. Survival (A) and event-free survival (B) curves for 115 patients with HBV-PAN as a function of the initial therapeutic strategy.

Guillevin L, 2005

PAN Y VHB



Trepo C, 2001

El “protá” de la película...



L Guillevin

Sólo una persona entre nosotros puede hacerle sombra...

- Varón
- Caucasiano
- Español, con perdón
- Edad fértil (científica, se entiende)



Manuel Ramos Casals



VASCULITIS

“ To recognize a completed picture is no feat, but to be able to see the missing parts is”

Lie JT, 89

