

MEDICAL GRAND ROUNDS

The University of Texas Health Science Center at Dallas
Southwestern Medical School

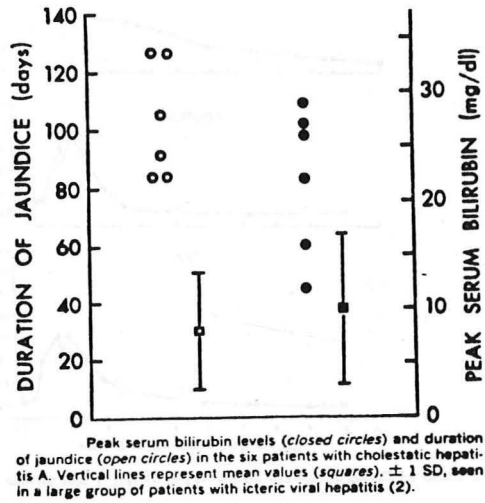
March 19, 1987

EXTRAHEPATIC MANIFESTATIONS OF VIRAL HEPATITIS

Burton Combes, M.D.

Less Well Recognized Features of Hepatitis A Infection

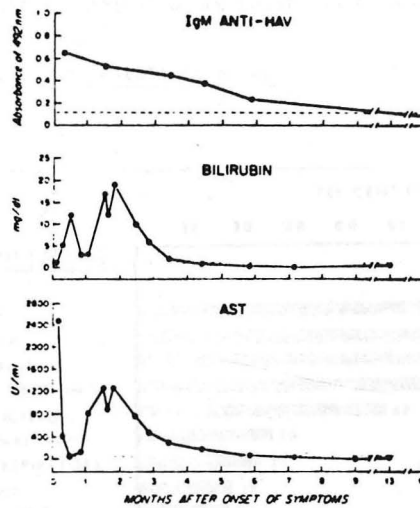
1. Prolonged intrahepatic cholestasis



From Gordon et al, Ann. Intern. Med. 101:635, 1984

Gordon, S. C., Reddy, K. R., Schiff, L. and Schiff, E. R. Prolonged intrahepatic cholestasis secondary to acute hepatitis A. Ann. Intern. Med. 101:635-637, 1984.

2. Pattern of remission and exacerbation of symptoms and liver tests



Laboratory data for case 1. Dashed line (---) indicates normal cut-off for each test.

From Jacobsen et al, J. Med. Virol. 16:163, 1985

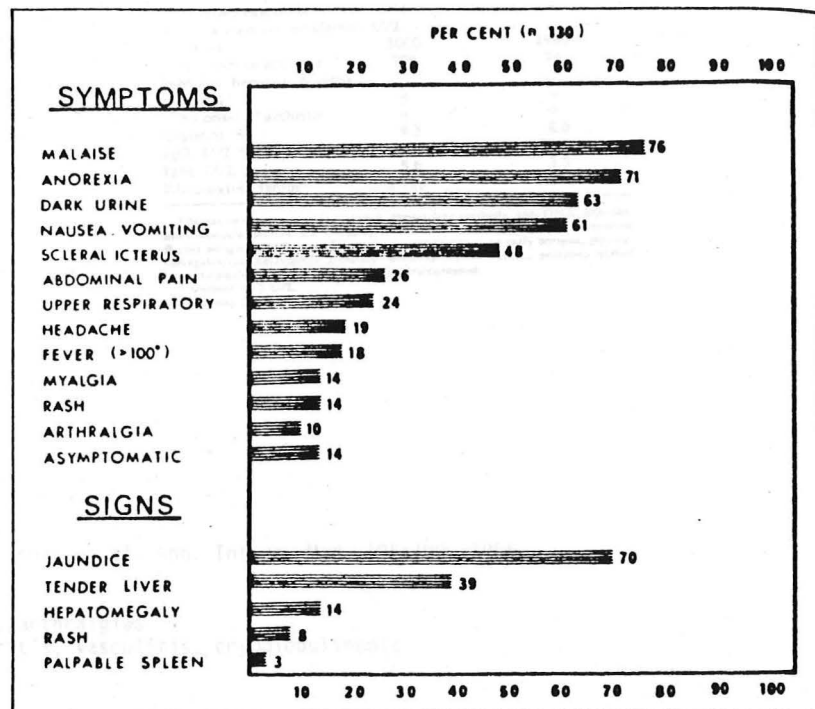
Jacobson, I. A., Nath, B. J. and Dienstag, J. L. Relapsing viral hepatitis type A. J. Med. Virol. 16:163-169, 1985.

3. Serum enzyme elevations may persist for months, rarely for as long as a year, but they always appear to resolve

Routenberg, J. A., Dienstag, J. L., Harrison, W. O., et al. Foodborne outbreak of hepatitis A: clinical and laboratory features of acute and protracted illness. Am. J. Med. Sci. 278:123-131, 1979.

Kao, H. W., Ashcavai, M., and Redeker, A. G. The persistence of hepatitis A IgM antibody after clinical acute hepatitis A. Hepatology 4:933-936, 1984.

4. Extrahepatic manifestations occur



Clinical features of acute hepatitis A virus infection among 130 Naval recruits (percent).

From Routenberg et al, Am. J. Med. Sci. 278:123, 1979

Clinical and Laboratory Features of Patients with Hepatitis-A-Related Arthritis*

	Patient 1	Patient 2
Age, yrs	26	26
Sex	F	F
Interval from onset of hepatitis to arthritis, mos	4.5	4.0
Tender hepatomegaly	+	+
Sites of arthritis	Knees, ankles	Ankles, subtalar joints, metatarsal-phalangeal joints
Cutaneous vasculitis	+	-
Aspartate aminotransferase, U/L		
Initial	3000	1980
At onset of arthritis	708	74
IgM anti-hepatitis A virus		
Initial	+	+
At onset of arthritis	+	+
Cryocrit, %	4.3	8.6
IgG, U/L †	31.8	20.7
IgM, U/L ‡	5.6	3.5
Rheumatoid factor	1:160	1:640

* Negative or normal tests included antinuclear antibody, anti-DNA, anti-Sm, anti-ribonucleoprotein, C3, CH₅₀, IgA, hepatitis B surface antigen, anti-hepatitis B core antigen, anti-Epstein-Barr virus capsid antigen and early antigen, anti-cytomegalovirus, heterophile antibody, antistreptolysin, VDRL, protime, partial thromboplastin time, serum copper, and ceruloplasmin.

† Normal, 14.2 U/L.

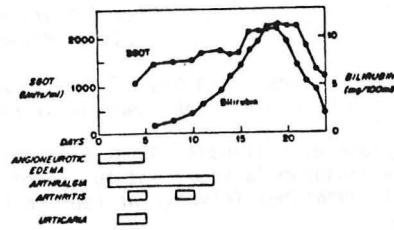
‡ Normal, 3.2 U/L.

From Inman et al, Ann. Intern. Med. 105:700, 1986

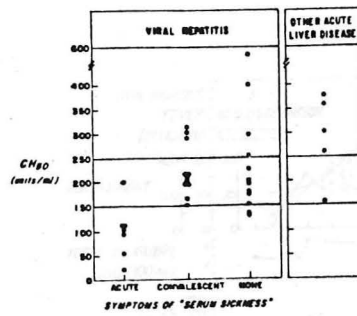
Rash, arthralgias
Arthritis, vasculitis, cryoglobulinemia

Inman, R. D., Hodge, M., et al. Arthritis, vasculitis and cryoglobulinemia associated with relapsing hepatitis A virus infection. Ann. Intern. Med. 105:700-703, 1986.

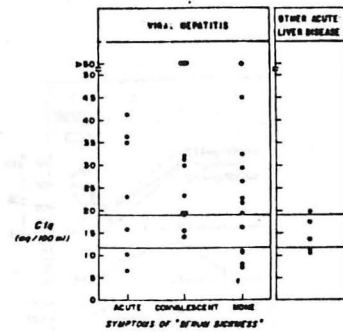
Arthritis-Dermatitis Prodrome



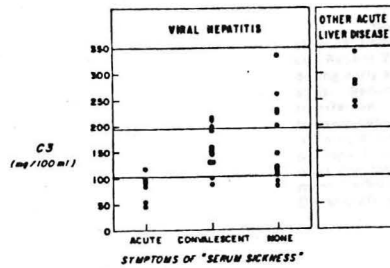
Features of Serum Sickness in the Prodrome of Viral Hepatitis (E.A., July, 1967).
The shaded area indicates the normal range here and in other figures.



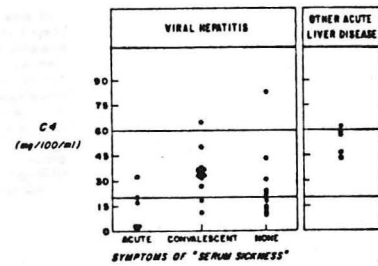
CH₅₀ Levels in Patients with Acute Hepatitis.



C1q Serum Concentration in Patients with Acute Hepatitis.



C3 (β1C/β1A) Serum Concentrations in Patients with Acute Hepatitis.



C4 (β1E) Serum Concentration in Patients with Acute Hepatitis.

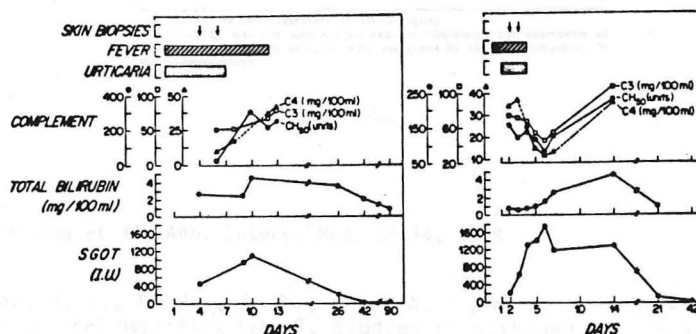
From Alpert et al, New Engl. J. Med. 285:185, 1971

Alpert, E., Isselbacher, K. J. and Schur, P. H. The pathogenesis of arthritis associated with viral hepatitis: Complement-component studies. *New Engl. J. Med.* 285:185-189, 1971.

Onion, D. K., Crumpacker, C. S. and Gilliland, B. C. Arthritis of hepatitis associated with Australia antigen. *Ann. Intern. Med.* 75:29-33, 1971.

Schumacher, H. R. and Gall, E. P. Arthritis in acute hepatitis and chronic active hepatitis. Pathology of the synovial membrane with evidence for the presence of Australia antigen in synovial membranes. *Am. J. Med.* 57:655-664, 1974.

Wands, J. R., Mann, E., Alpert, E. and Isselbacher, K. J. The pathogenesis of arthritis associated with acute hepatitis-B surface antigen-positive hepatitis. Complement activation and characterization of circulating immune complexes. *J. Clin. Invest.* 55:930-936, 1975.



Serial clinical and biochemical findings in Patient 1 (left) and Patient 2 (right) with urticaria during early acute type-B viral hepatitis. Serum aspartate aminotransferase (glutamic oxalacetic transaminase, SGOT) is given in international units (IU). Normal complement levels are 150 to 250 units for total hemolytic complement (CH50), 55 to 120 mg/dl for C3, and 20 to 50 mg/dl for C4.

From Dienstag et al, *Ann. Intern. Med.* 89:34, 1978.

Findings Consistent with Immune-Complex Disease in Two Patients with Urticaria and Acute Hepatitis B

	Patient 1	Patient 2
Skin morphologic findings	Cutaneous necrotizing vasculitis	Cutaneous necrotizing vasculitis
Complement levels	↓ CH50, ↓ C3, ↓ C4	↓ CH50, ↓ C3, ↓ C4
Alternative complement activation	+	+
Detection by immunofluorescence in involved cutaneous vessels	IgM, C3, fibrin, HBsAg*	IgM, C3, fibrin, HBsAg
Cryoprecipitable circulating immune complexes	IgG, HBsAg (20-nm spheres), anti-HBs	HBsAg (Dane particles, 20-nm spheres, 20-nm tubules), anti-HBs†

* Inadequate tissue remained to test specificity.

† Anti-HBs was not detected by radioimmunoassay, but aggregates of HBsAg surrounded by antibody were visualized by electron microscopy in the cryoprecipitate.

From Dienstag et al, Ann. Intern. Med. 89:34, 1978

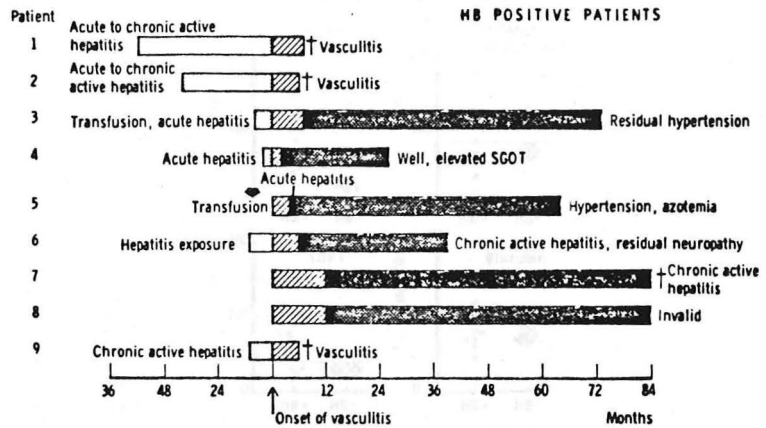
Dienstag, J. L., Rhodes, A. R., Bhan, A. K., et al. Urticaria associated with acute viral hepatitis type B. Studies of pathogenesis. Ann. Intern. Med. 89:34-40, 1978.

Clinical features of acute viral hepatitis

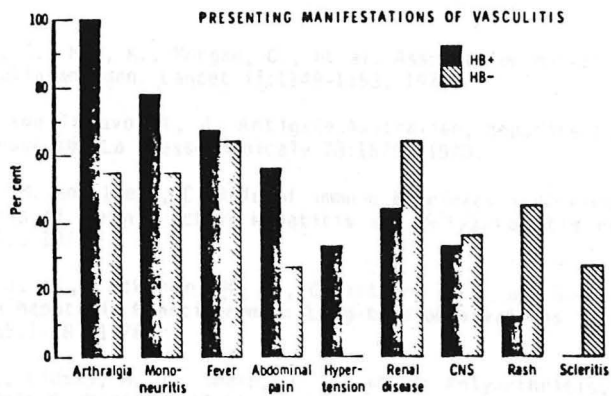
	Fever (%)	Arthralgia (%)	Rash (%)
A	27	11	1
B	5	7	7
NANB	27	18	5

From Bamber et al, Gut 24:561, 1983

Periarteritis-Vasculitis

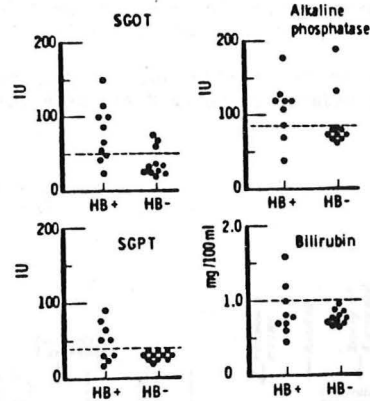


Summary of course of hepatitis B positive patients with vasculitis. Lightly stippled bars (▨) indicate known antecedent liver disease. Diagonally hatched bars (▧) indicate the periods of clinically active vasculitis. Dark stippled bars indicate the duration of follow-up after recovery from vasculitis. + denotes death.



From Sergent et al, Medicine 55:1, 1976

LIVER FUNCTION TESTS (ADMISSION)



Hepatic enzyme studies on admission in patients with generalized necrotizing vasculitis. IU = international units.

From Sergent et al, Medicine 55:1, 1976

Gocke, D. J., Hsu, K., Morgan, C., et al. Association between polyarteritis and Australia antigen. Lancet ii:1149-1153, 1970.

Trepo, C and Thiovolet, J. Antigene Australien, hepatitis A virus et periarterite noueuse. La Presse Medicale 78:1575, 1970.

Prince, A. M. and Trepo, C. Role of immune complexes involving SH antigen in pathogenesis of chronic active hepatitis and polyarteritis nodosa. Lancet i:1309-1312, 1971.

Sergent, J. S., Lockshin, M. D., Christian, C. L. and Gocke, D. J. Vasculitis with hepatitis B antigenemia: Long-term observations in nine patients. Medicine 55:1-18, 1976.

Duffy, J., Lidsky, M. D., Sharp, J. T., et al. Polyarthrititis, polyarteritis and hepatitis B. Medicine 55:19-37, 1976.

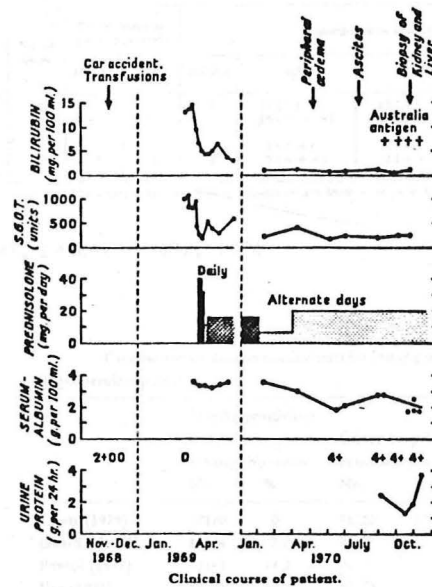
Fye, K. H., Becker, M. J., Theofilopoulos, A. N., et al. Immune complexes in hepatitis B antigen-associated periarteritis nodosa. Detection by antibody-dependent cell-mediated cytotoxicity and the Raji cell assay. Am. J. Med. 62:783-791, 1977.

Michalak, T. Immune complexes of hepatitis B surface antigen in the pathogenesis of periarteritis nodosa. A study of seven necropsy cases. *Am. J. Pathol.* 90:619-632, 1978.

Inman, R. D., McDougal, J. S., Redecha, P. B., et al. Isolation and characterization of circulating immune complexes in patients with hepatitis B systemic vasculitis. *Clin. Immunol. Immunopathol.* 21:364-374, 1981.

Gupta, R. C. and Kohler, P. F. Identification of HBsAg determinants in immune complexes from hepatitis B virus-associated vasculitis. *J. Immunol.* 132:1223-1228, 1984.

Renal Disease in Hepatitis



Clinical course of patient.
Prednisolone therapy was administered daily at first, and later 2 days' therapy was administered at one time in the morning on alternate days.

From Combes et al, *Lancet* ii:234, 1971

Combes, B., Stastny, P., Shorey, J., et al. Glomerulonephritis with deposition of Australia antigen-antibody complexes in glomerular basement membrane. *Lancet* ii:234-237, 1971.

Myers, B. D., Griffel, B., Naveh, D., et al. Membrano-proliferative glomerulonephritis associated with persistent viral hepatitis. *Am. J. Clin. Pathol.* 59:222-228, 1973.

Vos, G. H., Grobbelaar, B. G. and Milner, L. V. A possible relationship between persistent hepatitis B antigenaemia and renal disease in Southern African Bantu. *S. A. Med. J.* 47:911-912, 1973.

Knieser, M. R., Jenis, E. H., Lowenthal, D. T., et al. Pathogenesis of renal disease associated with viral hepatitis. *Arch. Pathol.* 97:193-200, 1974.

SERUM HB_sAg AND ANTI-HB_c AND GLOMERULAR HB_sAg-IMMUNE COMPLEXES IN 32 CASES OF G.N. IN CHILDREN

Histological diagnosis of G.N. type	No. of cases	Serum samples (no. of positives)		Kidney-biopsy specimens (no. of positives)				
		HB _s Ag	anti-HB _c	HB _s Ag	IgG	IgM	IgA	β ₂ C
Endocapillary proliferative ..	13	2	2	2	13 (+)	13 (+)	7 (+)	13 (+)
Membranoproliferative ..	15	10	12	12	15 (+-+ +)	15 (+-+ +)	15 (+)	15 (+ +)
Endo and extracapillary proliferative ..	2	2	2	2	2 (+ +)	2 (+ + +)	2 (+-+ +)	2 (+ +)
Membranous ..	2	2	2	2	2 (+ + +)	2 (+ + +)	2 (+ +)	2 (+ +)

The approximate amount of deposit ranges from + to + + +.

From Brzosko et al, *Lancet* ii:477, 1974

Comparison of data on routine tests for HBsAg positivity in glomerulonephritis.

	HBsAg positivities sera		kidney biopsies	
	examined/positive		examined/positive	
	No.	%	No.	%
Conte [1975]	71/0	0	71/22	31
Guardia [1975]	105/8	7.8	N. D.	
Powell [1977]	21/3	14.2	N. D.	
Vos [1973]	182/37	20.3	N. D.	
Brzosko [1974]*	32/16	50.0	32/18	56.2
Lagrue [1974]*	161/10	6.8	N. D.	
Nagy [1978]*	196/32	16.3	196/33	16.8

N. D. = not done

* Only cases of immune complex glomerulonephritis were considered.

From Nagy et al, *Clin. Nephrol.* 12:109, 1979

**IMMUNOFLUORESCENT ANTIBODIES* IN GLOMERULI OF
PATIENTS WITH MEMBRANOUS NEPHROPATHY**

Patient no.	IgG	IgA	IgM	β IC	Fibrinogen	HBsAg
1	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
2	++	-	±	-	±	-
3	+++	-	-	+	-	-
4	++	-	-	+	-	-
5	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
6	+	+	+	±	-	-
7	+++	-	-	++	-	-
8	++	-	-	+	-	-
9	++	-	-	+	-	-
10	+++	+	-	++	-	-
11	++	+	±	-	-	-

*The reactions are graded—to+++.
N.D.=not done.

From Takekoshi et al, Lancet ii:1065, 1978

**Immunofluorescence in the Kidney of the Two
Patients with the Nephrotic Syndrome in Whom Pathological
Examination Showed Membranous Glomerulonephritis.**

CASE No.	GRANULAR DEPOSITION ALONG GLOMERULAR CAPILLARY WALLS DETECTED BY IMMUNOFLUORESCENCE						
	IgG	IgA	IgM	β IC	HBsAg*	HBsAg†	HBsAg‡
1	+++	+	-	++	+++	-	-
2	++	+	Trace	++	+++	-	-

*HBsAg was stained by the specifically purified human antibody against small molecular (free) HBsAg conjugated with fluorescein isothiocyanate.

†HBsAg was stained by the rabbit anti-HBs. & HBsAg by the human anti-HBs labeled with fluorescein isothiocyanate. ‡

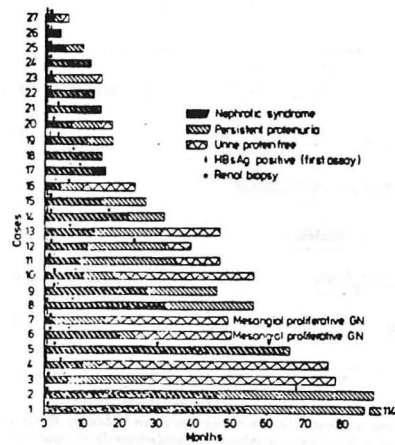
From Takekoshi et al, New Engl. J. Med. 300:814, 1979

**Immune Complexes of Hepatitis B Virus Antigens in Kidney Biopsies From Children
With Nephrotic Syndrome and/or Glomerulonephritis**

Glomerulonephritis form	HBsAg + HBcAg			Total
	HBsAg	HBcAg	HBsAg + HBcAg	
Diffuse membranous glomerulopathy	7/23*	8/23	6/23	21/23
Diffuse membranoproliferative glomerulonephritis	1/3	0/3	0/3	1/3
Diffuse mesangial proliferative glomerulonephritis	2/11	0/11	0/11	2/11
Diffuse extracapillary glomerulonephritis	0/3	0/3	0/3	0/3
Focal proliferative and sclerosing glomerulonephritis	0/16	0/16	0/16	0/16
Different glomerulonephritis forms in				
Systemic lupus	0/2	0/2	0/2	0/2
Schönlein-Henoch's purpura	0/3	0/3	0/3	0/3
Alport's syndrome	0/1	0/1	0/1	0/1
Minimal glomerular change	0/36	0/36	0/36	0/36
Total	10/98	8/98	6/98	24/98

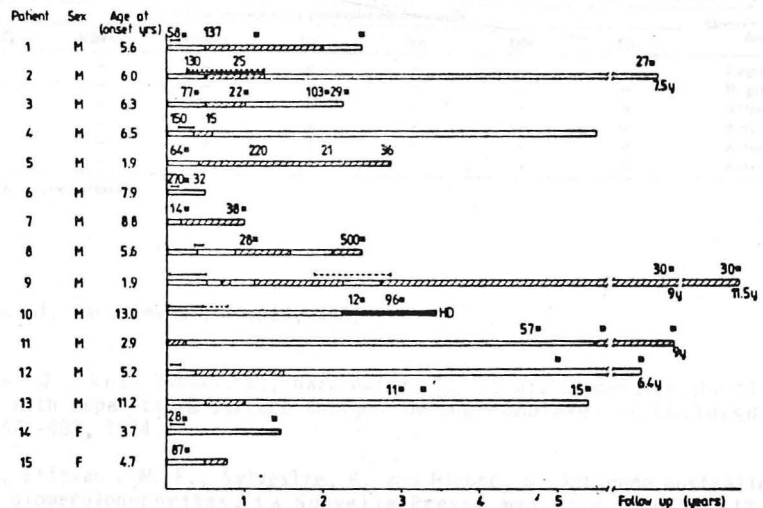
* Number of cases positive/number of cases tested.

From Slusarczyk et al, Am. J. Pathol. 98:29, 1980



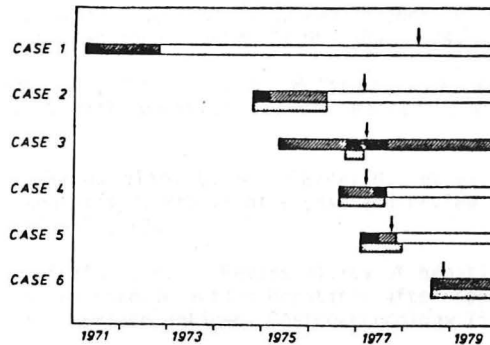
Course of hepatitis B virus associated glomerulonephritis.

From Wiggelinkhuizen et al, Arch. Dis. Child. 58:488, 1983



Clinical evolution of each patient. ■ Nephrotic syndrome; ▨ proteinuria; □ complete remission; renal failure. HD: hemodialysis. — steroid therapy; - - - immunosuppressive therapy. * detection of HBs Ag. The numbers above the bars representing each patient indicate the values of serum transaminases (normal values < 40 iu).

From Kleinknecht et al, J. Pediatr. 95:946, 1979



Clinical courses of six children with membranous glomerulonephritis. ■, period of nephrotic syndrome; ▨, abnormal proteinuria, and □, no urinary abnormalities; ▤ (under the main columns), period of abnormal liver function tests. Arrows indicate the time of the renal biopsy that was evaluated in the present study.

IMMUNOPATHOLOGY IN GLOMERULI OF PATIENTS WITH MEMBRANOUS GLOMERULONEPHRITIS*								
Patient no.	Granular deposits along glomerular capillary walls							Electron microscopic findings
	HBsAg	HBcAg	HBsAg	IgG	IgA	IgM	β1C	
1	-	-	-	+	-	-	-	Regression
2	-	-	-	-	-	-	-	Regression
3	+	-	+	+	-	+	+	Active
4	-	-	+	+	-	+	+	Active
5	-	-	+	+	-	+	+	Active
6	-	-	+	+	-	+	+	Active

* Symbols: +, present; -, not present.

From Ito et al, Lab. Invest. 44:214, 1981

Brzosko, W. J., Krawczynski, K., Nazarewicz, T., et al. Glomerulonephritis associated with hepatitis-B surface antigen immune complexes in children. Lancet ii:477-482, 1974.

Laguer, G., Etievant, M. F., Sylvestre, R. and Hirbec, G. Antigene Australie (Hg-HB) et glomerulonephrites. La Nouvelle Presse medicale 3:1870-1872, 1974.

Kohler, P. F., Cronin, R. E., Hammond, W. S., et al. Chronic membranous glomerulonephritis caused by hepatitis B antigen-antibody immune complexes. Ann. Intern. Med. 81:448-451, 1974.

Blaeker, F., Hellwege, H. H., Kramer, U. and Thoenes, W. Membranous nephropathy and hepatitis-B antigen. *Lancet* ii:955-956, 1974.

Ozawa, T., Levisohn, P., Orsini, E. and McIntosh, R. M. Acute immune complex disease associated with hepatitis. *Arch. Pathol. Lab. Med.* 100:484-486, 1976.

Hirschel, B. J., Benusiglio, L. N., Favre, H., et al. Glomerulonephritis associated with hepatitis B. Report of a case and review of the literature. *Clin. Nephrol.* 8:404-409, 1977.

Knecht, G. L. and Chisari, F. V. Reversibility of hepatitis B virus-induced glomerulonephritis and chronic active hepatitis after spontaneous clearance of serum hepatitis B surface antigen. *Gastroenterology* 75:1152-1156, 1978.

Takekoshi, Y., Tanaka, M., Shida, N., et al. Strong association between membranous nephropathy and hepatitis-B surface antigenaemia in Japanese children. *Lancet* ii:1065-1068, 1978.

Takekoshi, Y., Tanaka, M., Miyakawa, Y., et al. Free "small" and IgG-associated "large" hepatitis B e antigen in the serum and glomerular capillary walls of two patients with membranous glomerulonephritis. *New Engl. J. Med.* 300:814-819, 1979.

Nagy, J., Bajtai, G., Brasch, H., et al. The role of hepatitis B surface antigen in the pathogenesis of glomerulopathies. *Clin. Nephrol.* 12:109-116, 1979.

Silver, M. M., Rance, C. P., Middleton, P. J. and Huber, J. Hepatitis B-associated membranous glomerulonephritis in a child. *Am. J. Clin. Pathol.* 72:1034-1039, 1979.

Kleinknecht, C., Levy, M., Peix, A., et al. Membranous glomerulonephritis and hepatitis B surface antigen in children. *J. Pediatr.* 95:946-952, 1979.

Slusarczyk, J., Michalak, T., Nazarewicz-de Mezer, T., et al. Membranous glomerulopathy associated with hepatitis B core antigen immune complexes in children. *Am. J. Pathol.* 98:29-44, 1980.

Levy, M. and Kleinknecht, C. Membranous glomerulonephritis and hepatitis B virus infection. *Nephron* 26:259-265, 1980.

Ito, H., Hattori, S., Matusda, I., et al. Hepatitis B e antigen-mediated membranous glomerulonephritis. Correlation of ultrastructural changes with HBsAg in the serum and glomeruli. *Lab. Invest.* 44:214-220, 1981.

Rashid, H., Morley, A. R., Ward, M. K., et al. Hepatitis B infection in glomerulonephritis. *Br. Med. J.* 283:948-949, 1981.

Hirsch, H. Z., Ainsworth, S. K., DeBeukelaer, M., et al. Membranous glomerulonephritis in a child asymptomatic for hepatitis B virus. Concomitant seropositivity for HBsAg and anti-HBs. *Am. J. Clin. Pathol.* 75:597-602, 1981.

Maggiore, Q., Bartolomeo, F., L'Abbate, A. and Misefari, V. HBsAg glomerular deposits in glomerulonephritis: Fact or artifact? *Kidney Intern.* 19:579-586, 1981.

Furuse, A., Hattori, S., Terashima, T., et al. Circulating immune complex in glomerulonephropathy associated with hepatitis B virus infection. *Nephron* 31:212-218, 1982.

Iida, H., Nakamoto, Y., Kobayashi, K., et al. Hepatic glomerulonephritis. Role of hepatitis B surface antigen (HBsAg). *Virchows Arch. Pathol. Anat.* 392:55-62, 1981.

Wiggelinkhuizen, J., Sinclair-Smith, C., Stannard, L. M. and Smuts, H. Hepatitis B virus associated membranous glomerulonephritis. *Arch. Dis. Child.* 58:488-496, 1983.

Hsu, H.-C., Lin, G.-H., Chang, H.-H. and Chen, C.-H. Association of hepatitis B surface (HBs) antigenemia and membranous nephropathy in children in Taiwan. *Clin. Nephrol.* 20:121-129, 1983.

Collins, A. B., Bhan, A. K., Dienstag, J. L., et al. Hepatitis B immune complex glomerulonephritis: Simultaneous glomerular deposition of hepatitis B surface and e antigens. *Clin. Immunol. Immunopathol.* 26:137-153, 1983.

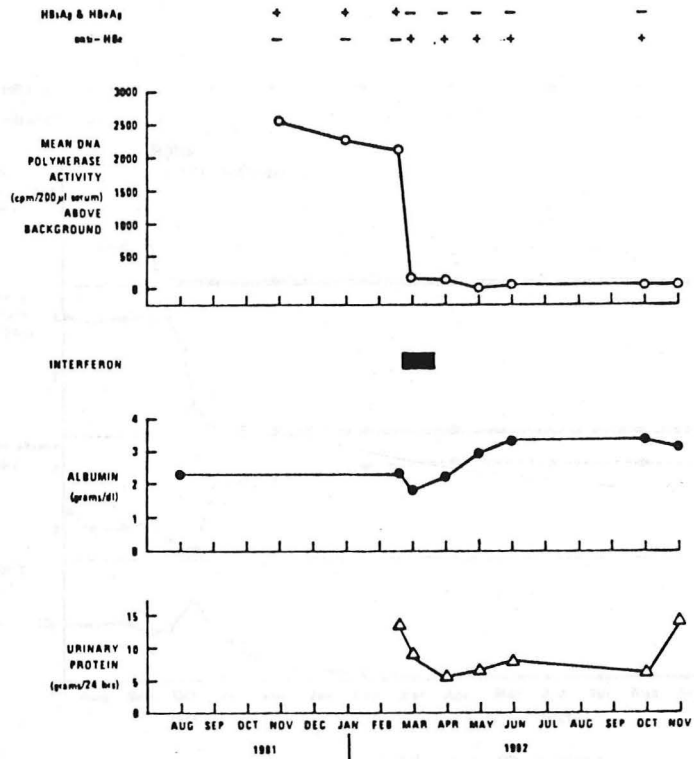
Hirose, H., Udo, K., Kohima, M., et al. Deposition of hepatitis B e antigen in membranous glomerulonephritis: Identification by F(ab')₂ fragments of monoclonal antibody. *Kidney Intern.* 26:338-341, 1984.

Seggie, J., Nathoo, K. and Davies, P. G. Association of hepatitis B (HBs) antigenaemia and membranous glomerulonephritis in Zimbabwean children. *Nephron* 38:115-119, 1984.

Cardobbi, P., Bortolotti, F., Zacchello, G., et al. Hepatitis B virus replication in acute glomerulonephritis with chronic active hepatitis. *Arch. Dis. Child.* 60:583-585, 1985.

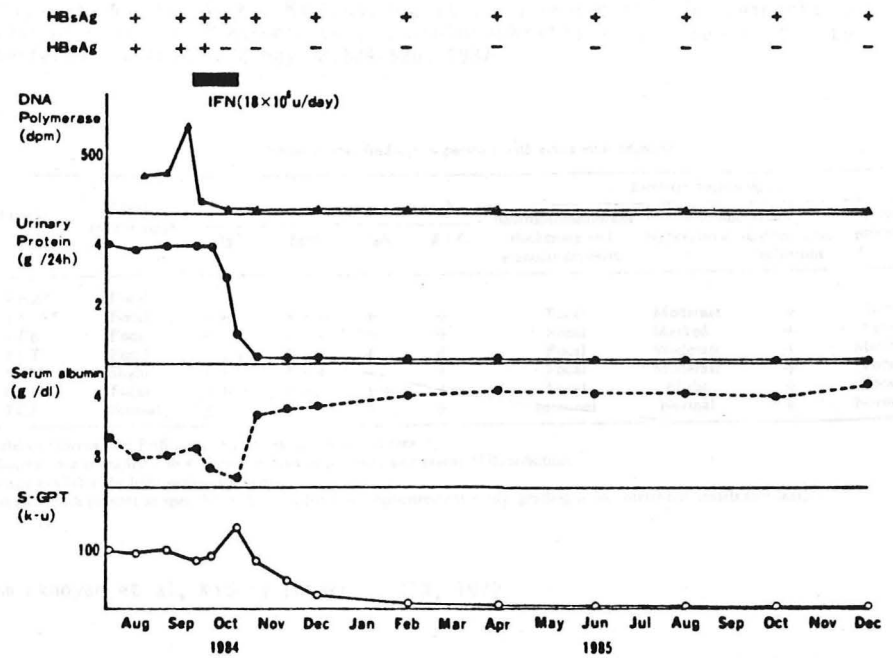
Yoshikawa, N., Ito, H., Yamada, Y., et al. Membranous glomerulonephritis associated with hepatitis B antigen in children: a comparison with idiopathic membranous glomerulonephritis. *Clin. Nephrol.* 23:28-34, 1985.

Southwest Pediatric Nephrology Study Group, Dallas, Texas. Hepatitis B surface antigenemia in North American children with membranous glomerulonephropathy. *J. Pediatr.* 106:571-578, 1985.



Clinical course of Case 1. Human leukocyte interferon was given during the indicated period.

From Garcia et al, Hepatology 5:317, 1985



Clinical course of the patient. IFN, interferon.

From Mizushima et al, Gastroenterology 92:524, 1987

From Mizushima et al, Arch. Pathol. Lab. Med. 103:101, 1979

Garcia, G., Scullard, G., Smith, C., et al. Preliminary observation of hepatitis B-associated membranous glomerulonephritis treated with leukocyte interferon. *Hepatology* 5:317-320, 1985.

Esteban, R., Buti, M., Valles, M., et al. Hepatitis B-associated membranous glomerulonephritis treated with adenine arabinoside monophosphate. *Hepatology* 6:762-764, 1986.

Mizushima, N., Kanai, K., Matsuda, H., et al. Improvement of proteinuria in a case of hepatitis B-associated glomerulonephritis after treatment with interferon. *Gastroenterology* 92:524-526, 1987.

Renal biopsy findings in patients with acute viral hepatitis

Patient	Light microscopy ^a	Immunofluorescent microscopy ^b				Electron microscopy			
		IgG	IgM	IgA	β 1-C	Basement membrane thickening and granular deposits	Endothelial cell Hyperplasia	Cytoplasmic inclusions	Foot process fusion
1 KZ ^c	Focal								
2 MW ^d	Focal	++	+++	+	+	Focal	Moderate	+	Focal
3 BB	Focal	++	+++	+	+	Focal	Marked	+	Focal
4 CT	Focal	+++	+++	+	+	Focal	Moderate	+	Minimal
5 FMc	Slight	++	+++	+	+	Focal	Moderate	+	Focal
6 RM	Focal	++	++	++	++	Focal	Slight	+	Focal
7 CJ	Minimal	±	±	-	±	Minimal	Normal	+	Normal

^a Refers to increase in PAS-positive material in mesangial area.

^b Fluorescence is graded 1 to 4+ on the basis of intensity and extent of distribution.

^c Tissue available for light microscopy only.

^d No glomeruli present in specimen submitted for immunofluorescent study, grading is for interstitial vessels (see text).

From Eknoyan et al, *Kidney Intern.* 1:413, 1972

Immune Deposits in Kidney Glomeruli in HBV Positive and HBV Negative Patients			
Liver Pathology	Total	HBsAg- ^a Positive Cases: Ig + C3 (With HBsAg in Glomeruli)	
		HBsAg- ^a Negative Cases: Ig + C3	
Acute fatal hepatitis, fulminant hepatitis, and subacute hepatitis	14/89	12(9)/37	2/22
Chronic aggressive hepatitis	10/16	8(4)/8	2/8
Liver cirrhosis	8/24	8(3)/10	0/14
Total	32/99	28(16)/55	4/44

^aHBsAg indicates hepatitis B surface antigen.

From Morzycka et al, *Arch. Pathol. Lab. Med.* 103:38, 1979

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Extrahepatic Detection of Hepatitis B Virus or Related Components

Prevalence of HBV-DNA in saliva, urine, and seminal fluid. Figures are proportions of patients (and %)

	Saliva	Urine	Seminal fluid	Serum
Group 1	13/15 (86.6)	9/15 (60)	8/15 (53.3)	15/15 (100)
Group 2	2/2 (100)	3/7 (42.8)	5/6 (83)	8/8 (100)
Total	15/17 (88.2)	12/22 (54.5)	13/21 (61.9)	23/23 (100)
Controls	0/3	0/3	0/3	0/3

From Karayiannis et al, Br. Med. J. 290:1853, 1985

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Aplastic Anemia

Over 200 cases of aplastic anemia following hepatitis. Relatively few have had complete serological studies for hepatitis viruses.

In best studied group, non-A, non-B agents were probably involved in at least 13 of the 16 cases studied.

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Clinical and Laboratory Features of Patients with Aplastic Anemia Following Hepatitis

Patient Number	Age (yr)	Sex	Time between Hepatitis and Aplasia (wk)	Bilirubin* (mg/dl)	ALT† (IU/liter)	Alkaline Phosphatase‡ (U/liter)	Hepatitis B Virus			Hepatitis A Virus		Anti-CMV§
							HBsAg	Anti-HBc	Anti-HBs	IgM	IgG	
U95	3	M	7	1.6	22	99	-	-	+	-	+	-
SG	15	M	20	0.9	212	104	-	-	-	-	-	-
023	24	M	4	7.6	208	103	-	-	+	-	+	-
066	27	M	18	1.8	217	30	-	-	-	-	+	-
055	12	M	3	1.4	5	82	-	+	+	-	+	-
005	26	M	26	1.4	20	15	-	+	+	-	+	-
112	17	M	13	0.8	14	77	-	+	+	-	+	-
014	18	M	3	1.5	35	89	-	-	-	-	+	-
097	11	M	0	0.4	920	209	-	-	-	-	+	-
170	19	M	12	1.0	26	107	-	-	-	-	+	-
212	7	M	8	0.9	40	144	-	-	-	-	+	-
228	29	M	0	1.2	900	101	+	+	-	-	+	-
021	40	M	32	0.7	5	49	-	-	+	-	+	-
041	19	M	16	1.3	10	115	-	-	-	-	-	-
066	21	M	24	0.7	49	56	-	-	-	-	-	-
AR	21	M	5	1.0	66	73	-	-	-	-	+	-

* Bilirubin; normal <1.2 mg/dl.

‡ Alkaline phosphatase; normal <105 units/liter.

† Alanine aminotransferase; normal <36 IU/liter.

§ Cytomegalovirus complement fixation titer.

Clinical and Serologic Studies of Patients with Aplastic Anemia without Hepatitis

Patient Number	Age (yr)	Sex	HBsAg	Hepatitis B Virus		Anti-HBs	Hepatitis A Virus		Anti-CMV*
				Anti-HBc			IgM	IgG	
036	25	F	-	-		-	-	+	-
065	16	M	-	-		+	-	+	-
110	29	M	-	-		-	-	-	-
111	67	M	-	-		-	-	+	-
102	31	M	-	-		-	-	-	+
056	7	F	-	-		+	-	+	-
034	48	M	-	+		+	-	+	+
088	16	M	-	-		-	-	+	-
057	56	M	-	-		+	-	+	+
064	16	M	-	-		-	-	-	-

* Cytomegalovirus complement fixation titer.

From Zeldis et al, Am. J. Med. 74:64, 1983

From Zeldis et al, Am. J. Med. 74:64, 1983

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