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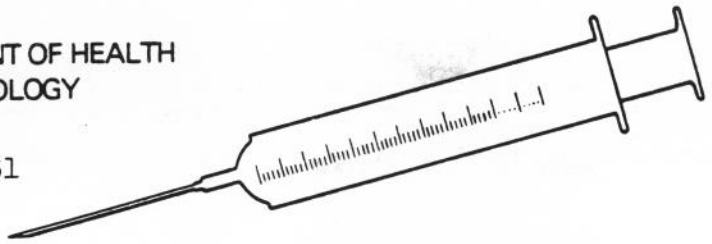

EPIDEMIOLOGY BULLETIN

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RECOMMENDATIONS OF THE PUBLIC HEALTH SERVICE IMMUNIZATION PRACTICES ADVISORY COMMITTEE

Immune Globulins for Protection against Viral Hepatitis (Part II)

HEPATITIS B

Hepatitis B is caused by the hepatitis B virus (HBV), a 42-nm, double-shelled DNA (deoxyribonucleic acid) virus. Several well defined antigen-antibody systems have been associated with HBV infection. HBsAg, formerly called "Australia antigen" or "hepatitis associated antigen," is an antigen found on the surface of the virus and on accompanying 22-nm spherical and tubular forms. HBsAg can be identified in serum 30-60 days after exposure to HBV and persists for variable periods. The various subtypes of HBsAg provide useful epidemiologic markers. Antibody against HBsAg, i.e., anti-HBs, develops after a typically resolved infection and is responsible for long-term immunity.

The frequency of chronically carrying HBsAg apparently relates both to age and immunologic competency. As many as 10% of HBV infections result in chronic carriage of HBsAg. The carrier state can be completely asymptomatic or, less commonly, associated with active liver disease. HBsAg carriers play an important role in the continuing transmission of hepatitis B, even though they show varying degrees of infectivity.

The hepatitis B e antigen (HBeAg) and antibody (anti-HBe) are distinct from HBsAg and anti-HBs. The potential infectivity of a carrier is higher if the HBeAg is present and lower if anti-HBe is present.

Routes of transmission of HBV include 1) direct percutaneous inoculation of infective serum or plasma by needle or transfusion of infective blood or blood products; 2) indirect percutaneous introduction of infective serum or plasma, such as through minute skin cuts or abrasions; 3) absorption of infective serum or plasma through mucosal surfaces, such as those of the mouth or eye; 4) absorption of other potentially infective secretions such as saliva or semen through mucosal surfaces, as might occur following sexual (heterosexual or homosexual) contact; and 5) transfer of infective serum or plasma via inanimate environmental surfaces or, possibly, vectors. Experimental data indicate that fecal transmission of HBV does not occur and that airborne spread is not epidemiologically important.

The onset of hepatitis B is generally insidious. Clinical symptoms and signs include various combinations of anorexia, malaise, nausea, vomiting, abdominal pain, and jaundice. Arthralgias and arthritis can also occur. Overall fatality rates for hospitalized patients generally do not exceed 1%. The incubation period of hepatitis B is long--45-160 days (average 60-90). Cirrhosis and primary hepatocellular carcinoma are closely associated with chronic HBV infection.

IMMUNE GLOBULINS AND HEPATITIS B

IG and HBIG contain different amounts of anti-HBs. IG is prepared from plasma that is not preselected for anti-HBs content. Since 1977, all lots tested have contained anti-HBs at a titer of at least 1:100 by radioimmunoassay (RIA). HBIG has an anti-HBs titer of>1:100,000 by RIA. (Currently, the price of a dose of HBIG is more than 20 times that of IG.)

Recent studies have shown that immune globulins can prevent up to 75% of hepatitis B cases in certain settings (10,11). What has been difficult to determine is the concentration of antibody that would be effective under various conditions of exposure, because studies differed in experimental design and in the immune globulins tested (12-19).

The studies generally indicated that: 1) HBIG is effective when given after percutaneous (needle stick) or mucous membrane exposure to blood containing HBsAg; 2) IG appears to have some effect in preventing clinical hepatitis; and 3) an immune globulin is most effective if given immediately after exposure.

It can be agreed further that HBIG is preferable to IG when there is bona fide percutaneous or mucous membrane exposure to blood known to contain HBsAg. However, because IG does contain anti-HBs, it remains an important alternative to HBIG whenever HBIG is unavailable, its cost is prohibitive, or a truly significant exposure to HBV may not have occurred.

Post-Exposure Prophylaxis:

Acute exposure to blood that might contain HBsAg: Percutaneous (needle stick) or mucous membrane exposure to blood that might contain HBsAg calls for a prompt decision about giving an immune globulin. In deciding whether to give a globulin and, if so, whether it should be IG or HBIG, one must recognize that the need is relative and depends on the kind of exposure. In the hospital, risk of clinical hepatitis B following exposure to blood known to contain HBsAg is approximately 1 in 20. If the blood is of unknown HBsAg status, the risk is 100 times lower, only about 1 in 2,000. This latter risk increases, however, in direct proportion to the likelihood that the blood is HBsAg positive.

Recommendations on prophylaxis can, thus, be categorized as to 1) whether the source of blood is known or unknown and 2) whether the HBsAg status of the source blood is known or unknown. The following outline and summary table (Table 2) are based on these categories. Management of each exposure must be individualized in view of the number of contributing factors. Furthermore, it is important to emphasize that for greatest effectiveness, globulin should be given promptly (its value beyond 7 days of exposure is unclear).

A. Source known, HBsAg status positive.

HBIG (0.06 ml/kg) should be given immediately, ideally within 24 hours of exposure. A second identical dose should be given 1 month later. (If HBIG is not available, IG should be used in the same dose and schedule.)

B. Source known, HBsAg status unknown.

Two decisions are involved here: whether to test for HBsAg and which immune globulin to give. Because these decisions relate both to the relative probability that the source will be HBsAg positive and to the inherent delay in testing, the following operational guidelines are suggested:

1. High risk that the source is HBsAg-positive--such as associated with patients with acute, unconfirmed viral hepatitis; patients institutionalized with Down syndrome; patients on hemodialysis; persons of Asian origin; male homosexuals; users of illicit, intravenous drugs.

If HBsAg test results can be known within 7 days of the exposure, IG (0.06 ml/kg) should be given immediately, certainly within 24 hours. If test results are positive, HBIG (0.06 ml/kg) should be given at that time and again 1 month later.

TABLE 2. Summary of postexposure prophylaxis of acute exposures to HBV*

Exposure	HBsAg Testing	Recommended prophylaxis
HBsAg positive		**HBIG (0.06 ml/kg) immediately and 1 month later**
HBsAg status unknown		
Source known:		
High Risk†	**Yes‡**	**IG (0.06 ml/kg) immediately, and if –TEST POSITIVE– HBIG (0.06 ml/kg) immediately and 1 month later or if –TEST NEGATIVE– Nothing**
Low Risk†	**No**	**Nothing or IG (0.06 ml/kg)**
HBsAg status unknown		
Source unknown	**No**	**Nothing or IG (0.06 ml/kg)**

* Important details are in the text.
† Characterized in text.
‡ If results can be known within 7 days of exposure.

If HBsAg test results cannot be known within 7 days of the exposure, the decision to use IG or HBIG must be based on the clinical and epidemiologic characteristics of exposure and the availability of globulin, remembering the importance of characterizing the source and giving globulin as soon after exposure as possible.

2. Low risk that the source is HBsAg-positive--such as associated with the average hospital patient.

Prophylaxis is optional; HBsAg testing is not recommended. If an immune globulin is to be used, IG (0.06 ml/kg) should be given promptly, certainly within 24 hours. No further action is necessary.

C. Source unknown, HBsAg status unknown.

Prophylaxis is optional. If an immune globulin is to be used, IG (0.06 ml/kg) should be given promptly, certainly within 24 hours. No further action is necessary.

Exposure of the newborn: Infants born to HBsAg-positive mothers (especially mothers who are HBeAg positive) are at risk of being infected with HBV and becoming chronic carriers. Recent studies have shown that the carrier state can be prevented in about 75% of such infections if newborns are given HBIG immediately after birth (20). (IG was not included in the protocol.)

All infants born to HBsAg-positive mothers should be given HBIG, total dose 0.5 ml intramuscularly, as soon after birth as possible (no later than 24 hours). The same dose (0.5 ml) should be repeated 3 months and 6 months later.

Sexual contact with persons with hepatitis B: In only 1 study has there been any evaluation of the value of immune globulin for sexual contacts of patients with acute hepatitis B (21). Although results suggest protection with HBIG, additional studies comparing IG, HBIG, and placebo groups are needed before specific recommendations can be made.

Pre-Exposure Prophylaxis:

Staff and patients of hemodialysis units: Routine passive immunization against hepatitis B is not recommended for staff and patients of hemodialysis units. Instead, precautions such as serologic screening of patients and staff, segregation of carriers, and environmental hygiene should be encouraged. In the rare event that such measures fail to interrupt transmission, prophylaxis with an immune globulin may be considered. Because carefully controlled studies have failed to demonstrate an advantage of HBIG over IG in this setting, IG (0.05-0.07 ml/kg) every 4 months is recommended for patients and staff (22).

Staff and patients of institutions for custodial care of the developmentally disabled: HBV is commonly endemic in institutions for the developmentally disabled, but passive immunization is not routinely recommended for staff or clients unless it is shown that hepatitis B cannot be controlled by environmental measures alone. Then IG may be administered in the same dose and at the same intervals as for patients and staffs of hemodialysis units.

HEPATITIS NON A/NON B AND HEPATITIS-NONSPECIFIC

Without accurate tests for diagnosing non A/non B viral hepatitis, the value of prophylaxis with immune globulins cannot be determined. No specific recommendation can be made, but as with hepatitis that cannot be specifically diagnosed (hepatitis-nonspecific), it is reasonable to apply the recommendations for prophylaxis against hepatitis A.

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Reference: MMWR, September 4, 1981/Vol. 30/No. 34

MONTH: August, 1981

DISEASE	STATE					REGIONS				
						THIS MONTH				
	THIS MONTH	LAST MONTH	TOTAL TO DATE 1981	TOTAL TO DATE 1980	MEAN 5 YEAR TO DATE	N.W.	N.	S.W.	C.	
CHICKENPOX	61	57	1601	372	784.0		18	7		35
MEASLES	1		7	299	1366.0					
MUMPS	6	29	118	56	110.4					
PERTUSSIS	3	1	6	6	9.2					
RUBELLA	1	1	7	40	259.2			1		
MENINGITIS – ASEPTIC	81	14	134	96	83.0	11	6	59	1	4
BACTERIAL	31	12	159	127	96.6	3	5	4	3	16
ENCEPHALITIS – INFECTIOUS	10	2	29	17	15.4	2	1	4		3
POST-INFECTIOUS	1		3	3	6.2					
HEPATITIS A (INFECTIOUS)	38	11	144	205	195.0	5	8	9	3	13
B (SERUM)	68	24	336	362	241.8	6	18	11	16	17
SALMONELLOSIS	264	179	1086	766	554.6	31	33	44	70	86
SHIGELLOSIS	60	64	1041	79	91.4	6	5	11	36	6
TUBERCULOSIS – PULMONARY	33	44	356	332						
EXTRA-PULMONARY	9	7	70	72						
SYPHILIS (PRIMARY & SECONDARY)	49	65			369.0	6	8	10		19
GONORRHEA	2568	1677	461	376	15,902.8					
ROCKY MOUNTAIN SPOTTED FEVER	39	28	95	70	87.8	4	11	9	4	11
RABIES IN ANIMALS	28	7	70	12	16.2	20	6	2		
MENINGOCOCCAL INFECTIONS	8	5	73	44	44.2	2	1		1	6
INFLUENZA	26	4	4878	762	4540.8	1		23	1	1
MALARIA	8	1	20	48	20.6		5		2	
OTHER: Hepatitis Unspecified	29	12	126	108	111.8		7	5	2	13

COUNTIES REPORTING ANIMAL RABIES: Bedford-1 bat; Clarke - 1-raccoon; Culpeper-3 rac.; Page-1 skunk; Fauquier-6 rac.; Roanoke-1 bat; Rockingham-2 skunks, 2 rac.; Warren-2 rac. Charlottesville-3 bats; Loudoun-5 rac., 1 red fox.

OCCUPATIONAL ILLNESSES:

Occupational pneumoconioses 9, Occupational dermatitis 8, Occupational hearing loss 7, Asbestosis 14

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