Clinical Review

Viral Hepatitis

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The three types of viral hepatitis, A, B, and non-A, non-B, differ in many epidemiologic, clinical, prognostic, and preventive aspects. Within the past decade rapid advances have been made in the delineation of the structure of hepatitis viruses A and B, with the subsequent development of commercially available tests that have greatly improved the diagnostic and preventive medicine capabilties of physicians with regard to viral hepatitis. At the present time, non-A, non-B viruses, which have recently been reported to account for 90 percent of posttransfusion hepatitis, 40 percent of chronic hepatitis, and up to one fourth of the cases of sporadic hepatitis, are still diagnosed by exclusion.

The medical literature in the 19th century noted scattered outbreaks of a syndrome that was identified by several names such as epidemic, catarrhal, and infectious jaundice. In studies using human volunteers conducted during World War II, two distinct types of viral hepatitis (subsequently designated A and B) were noted. The lack of cross-immunity between the two types of viral hepatitis suggested the existence of two separate etiologic agents.

In 1964 Blumberg[1] reported the existence of the hepatitis associated (or Australia) antigen, now called hepatitis B surface antigen (HB_sAg), in the sera of patients with hepatitis B. In 1973 Feinstone[2] reported the association of a specific virus-like particle with hepatitis A (HAV) infection. In the same year a second antigen associated with hepatitis B virus (HBV), the hepatitis B core antigen (HB_c) was reported.[3] In 1975 non-A, non-B hepatitis (NANBV) was described.[4]

Occurrence

The prevalence of HBV in the United States has been estimated at 0.2 percent.[5] It is higher among health professionals, male homosexuals, institutionalized patients, intravenous drug users, and people from Africa, Asia, and South and Central America. Because HAV is dependent on fecal-oral spread, the prevalence is inversely related to the standard of living conditions; thus high concentrations of IgG serum antibody to HAV, indicating previous exposure, has varied from 45 percent in the United States[6] to near 100 percent in underdeveloped nations.[7]

Because the responsible viral agents have yet to be characterized, neither the prevalence nor the percentage of the population with immunity to NANBV is known.

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It should be noted that the true incidence of the three types of viral hepatitis is actually much higher than what is reported (approximately 15,000, 30,000 and 8,000 cases of HBV, HAV, and NANBV, respectively, per year[8]) because many cases are mild or subclinical, a number of cases present as nonspecific infections, and physicians often fail to report the disease, even when it is detected.

Epidemiology

There is considerable difference in the epidemiology among the three types of viral hepatitis. Hepatitis B virus was previously known as serum hepatitis because it was believed that it could be transmitted only by the parenteral route. As noted by the demonstration of HB_sAg in various body secretions, however, including oropharyngeal secretions, seminal fluid, urine, and stool,[9,10] HBV can be transmitted by a variety of nonparenteral routes. In addition to posttransfusion hepatitis, random cases due to HBV occur in all age groups. The overall mortality due to HBV varies from 1 to 10 percent in various series, and there is approximately a 10 percent incidence of progression to either a carrier state or chronic hepatitis.[11] About 30 percent of the cases of chronic hepatitis are believed to be due to HBV.[12]

Hepatitis A virus, formerly known as infectious or short-incubation hepatitis, has a mortality less than that of HBV, approximately 0.5 percent. There is no carrier state and probably no chronic state associated with HAV. Thus, transmission of disease depends solely on exposure to the virus from an acutely infected subject. Although the fecal-oral route is the prime route of transmission, HAV can be transmitted by parenteral routes. Unlike HBV, it does not spread through salivary droplets. Hepatitis A virus occurs most frequently in children and young adults. The endemic and epidemic occurrence is determined to a large extent by socioeconomic and environmental factors.[7] This accounts for the point source outbreaks of HAV described in day-care centers[13] and the high incidence of serum antibody to HAV in adults of underdeveloped third world countries. It should also be noted that HAV is one of the enteric infections sexually transmitted among homosexual men,[14] and ingestion of sewage-contaminated shellfish has resulted in several epidemics of HAV.[15]

Non-A, non-B virus can be transmitted by both parenteral and nonparenteral routes. Evidence is accumulating that it may account for up to 40 percent of the cases of chronic hepatitis.[16] Mortality and the existence of a carrier state due to NANBV have yet to be determined. In one study, NANBV has been reported to account for 90 percent of the present cases of posttransfusion hepatitis.[17] Non-A, non-B virus appears to be responsible for 12 to 25 percent of the cases of endemic hepatitis.[18]

Clinical Course

The usual clinical course of HBV begins with an insidious onset following an incubation period that varies from 6 to 26 weeks. The first symptoms are commonly nonspecific and include anorexia, fatigue, and abdominal discomfort. There may also be a striking distaste for cigarettes. One to two weeks later, the usual symptoms and signs of hepatitis are noted (ie, jaundice, light-colored stools, dark foamy urine, and an enlarged tender liver). Joint pains or acute migratory arthritis, along with urticarial or erythematous maculopapular rashes, can be present in HBV infections. Serum transaminase (glutamic-oxaloacetic and glutamic-pyruvic) levels are maximally elevated early in the icteric phase and are usually in the range of 100 to 1000 IU. During the icteric phase itself, the levels start to fall toward normal. Six to 15 percent of patients will have recurrent symptoms and worsening of liver function before recovery from the initial attack is complete.[19] This relapse is usually milder than the original attack and is short-lived.

In contrast to HBV, the onset of HAV is usually acute, following a shorter incubation period of two to six weeks. The illness is usually milder, with lower bilirubin levels and of shorter duration. Patients are no longer infectious 21 days after the illness begins. The symptomatology is the same as that described for HBV, except that joint pain and rashes are uncommon.

The clinical course of NANBV is not so well defined. The severity of the illness has been de-

scribed as moderate, that is, between that of HBV and HAV, whereas the incubation period can resemble that of both HBV and HAV, suggesting the possibility of two types of NANBV.

Diagnosis

The diagnosis of hepatitis from whatever cause is usually made when the elevation of the transaminase enzymes is at least twice that of the upper limit of normal values set by each particular laboratory. Other disease entities to be considered in the differential diagnosis of acute viral hepatitis are listed in Table 1. They can be conveniently divided into those illnesses that can be confused with preicteric or anicteric viral hepatitis (eg, the differential diagnosis of right-sided abdominal pain) and icteric hepatitis. Although this division is arbitrary, and obviously there can be overlap, it is still useful. Gastroenteritis is most commonly confused with preicteric or anicteric acute viral hepatitis. The short self-limiting course and the absence of elevation of liver enzymes are prominent distinguishing features. Acute cholecystitis can usually be differentiated by a history of fatty food intolerance and a nonvisualizing oral cholecystogram. Exudative pharyngitis, lymphadenopathy, and a positive heterophile test help the clinician make the diagnosis of infectious mononucleosis. It should be noted that jaundice occurs in 10 to 20 percent of patients with infectious mononucleosis. Cytomegalic virus is similar in presentation to infectious mononucleosis, but the heterophile test is negative, and the diagnosis is confirmed by a fourfold rise in specific cytomegalic virus titers. Involvement of Glisson's capsule as part of the Fitz-Hugh–Curtis syndrome (gonococcal perihepatitis) can be confused with preicteric or anicteric hepatitis, but the presence of signs of pelvic inflammatory disease and a positive Thayer-Martin culture for Neisseria gonorrhea help distinguish this illness. Although not common, atypical presentations of pneumonitis, acute appendicitis, and acute mesenteric lymphadenitis can be included in the differential diagnosis of preicteric or anicteric hepatitis.

Several other illnesses can often resemble the clinical presentation of icteric viral hepatitis. These illnesses include drug-induced hepatitis, the most common offenders being isoniazid, methyldopa, and anesthesia with fluorinated agents such as halothane and methoxyflurane. A history of exposure is the most helpful distinguishing feature. The diagnosis of alcoholic hepatitis is facilitated by a history of alcohol abuse and physical findings of the stigmata of alcoholism. Increases in alkaline phosphatase, 5-nucleotidase, and conjugated bilirubin suggest biliary tract obstruction due to choledocholithiasis or neoplasm. The diagnosis is confirmed by ultrasound, endoscopic retrograde catheterization of the pancreas, or at the time of surgery. Rigor, polymorphonuclear leukocytosis, and a history of choledocholithiasis distinguish ascending cholangitis from icteric hepatitis. Leptospirosis is usually accompanied by headache, photophobia, and signs of meningeal irritation with abnormal cerebrospinal fluid. Chronic active hepatitis can at times be confused with acute viral hepatitis. The lesions of extrahepatic obstruction, chronic hepatitis, acute alcoholic hepatitis, and active cirrhosis can be distinguished from the changes of acute viral hepatitis on pathologic examination. Therefore, using standard clinical criteria and the serologic tests noted below, if a case of viral hepatitis is atypical, consideration should be given to consultation for a percutaneous liver biopsy.

In the last decade striking advances have been made in the serologic diagnosis and follow-up of

Table 1. Differential Diagnosis of Acute Viral Hepatitis

Preicteric or Anicteric
Gastroenteritis
Acute cholecystitis
Infectious mononucleosis
Cytomegalic virus
Fitz-Hugh–Curtis syndrome
Pneumonitis
Acute appendicitis
Acute mesenteric lymphadenitis
Icteric
Drug-induced hepatitis
Anesthesia with fluorinated agents
Alcoholic hepatitis
Biliary tract obstruction
Leptospirosis

acute viral hepatitis. Many of these tests, which are based on the structural components of the hepatitis virus, are now commercially available for clinical use. The test most familiar to physicians is the HB_sAg, previously known as the hepatitis-associated (or Australia) antigen, which refers to the small spherical and long filamentous forms having an average diameter of 22 nm, found in the sera of patients with HBV. Testing for this antigen has passed through several generations of testing, with each successive generation of tests being more sensitive.

The time sequence of HB_sAg positivity in acute HBV in relation to the clinical course is noted in Figure 1. It is found most frequently during the late incubation and early acute illness phases, lasting an average of three to six weeks. In some patients, however, it may be present for only a few days. Thus if a patient has a negative test for HB_sAg but is strongly suspect clinically of having HBV, not only should it be repeated in one to two weeks, but other serologic testing, which will be discussed shortly, should be considered. In addition, even if the patient improves clinically, tests for HB_sAg should be repeated approximately two to three months after the acute illness to detect a possible carrier or chronic hepatitis state.

The test for the antibody to the hepatitis B core antigen (anti-HB_c), which is antigenically different from HB_sAg and is represented on electron microscopy as the 28-nm diameter electron-dense core of the Dane particle, is clinically available. This antibody is usually detected two to three months after exposure, usually at or close to the time when clinical symptoms and abnormal liver enzymes are present. The anti-HB_c test may be a useful adjunct in the situation described above, when despite a negative HB_sAg, the clinician strongly suspects HBV.

The third commercially available serologic test of HBV is the antibody to HB_sAg (anti-HB_s). Figure 1 shows a rising titer of anti-HB_s in the two months following an acute hepatitis episode as indicative of a recent HBV infection. Thus paired, acute and convalescent phase sera for anti-HB_s titers may serve as a second possible test in the HB_sAg-negative patient with suspected HBV. It is believed that the rise in anti-HB_s titer confers immunity against reinfection by HBV and that failure of its appearance is indicative of either a carrier or chronic state. The detection of anti-HB_s in an

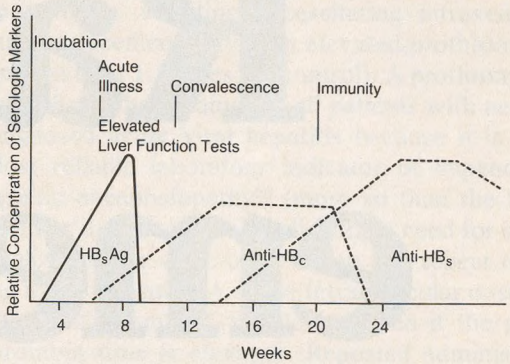

Figure 1. Typical sequence of HBV markers in acute HBV infection with resolution

asymptomatic patient indicates that the patient previously had HBV infection and is probably immune to it. In addition, a recently available test is the e antigen (HB_eAg), a soluble protein present only in HB_sAg positive serum, and its antibody (anti-e), the main value of which has been the identification of those HB_sAg-positive patients with asymptomatic or chronic hepatitis who are most apt to be infectious to others, individuals with HB_eAg being the most infective.[20]

With regard to serologic testing for hepatitis A, two tests, both of which are antibodies to the hepatitis A virus (anti-HAV), are currently commercially available.[21] As noted in Figure 2, by the time most patients are first seen, most no longer have viremia and have stopped secreting HAV in their feces. It is important, therefore, to start sampling at the earliest clinical suspicion. Two methods are available. If a serum specimen obtained in the acute illness phase demonstrates the presence of antibody of the IgM class against HAV (and no anti-HAV of the IgG class), a presumptive diagnosis of HAV infection can be made. In addition, a retrospective diagnosis can be made by noting a greater than fourfold rise in anti-HAV of the IgG class between acute and convalescent sera drawn four weeks apart. A single positive reading using this test does not establish that the recent acute episode was due to HAV.

At the present time there is no test to identify NANVB, although investigators in France have claimed to identify a specific serologic marker.

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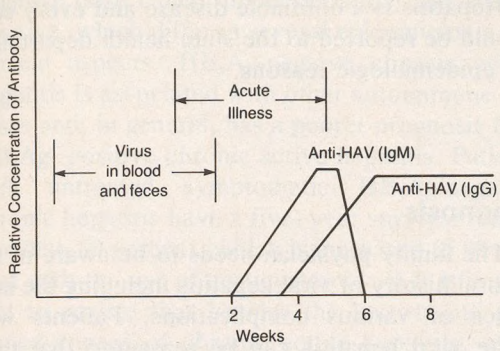

Figure 2. Typical sequence in HAV infection

Thus, the diagnosis of NANBV is one of exclusion. It is applied to cases of acute hepatitis without serologic evidence of HAV, HBV, Epstein-Barr virus, or cytomegalic virus. In addition, cases of posttransfusion hepatitis that are HB_sAg negative are given the diagnosis of NANBV.

A carrier state is defined as a persistently positive serologic test (either HB_sAg and/or anti-HB_c without a rise in anti-HB_s titers) with no symptomatic, biochemical, or histologic evidence of disease. Chronic hepatitis is defined as a chronic inflammatory reaction of the liver continuing without improvement for at least six months. The diagnosis is based on clinical and biochemical criteria plus the definitive microscopic changes seen in liver biopsy. Thus, the main differentiating feature between a carrier state and chronic hepatitis is normal liver function tests in the former and persistently abnormal liver function tests in the latter. Several other important points need to be made. Not all cases of chronic hepatitis are HB_sAg positive, and the diagnosis by liver biopsy has important prognostic and therapeutic implications as well. In addition, a history of hepatitis in the recent or distant past may or may not be obtained in patients with chronic hepatitis.

Management

Most patients with acute viral hepatitis do not have to be hospitalized. The only two indications for hospitalization are dehydration secondary to anorexia or vomiting necessitating intravenous fluid replacement and/or an elevated prothrombin time (at least 1.5 times the control). A prothrombin time should be obtained in all patients with newly diagnosed acute viral hepatitis because it is the most reliable laboratory indicator of impending hepatic encephalopathy[22] (more so than the bilirubin or liver enzymes), indicating a need for hospitalization for close observation and repeat testing if it is elevated. A single intramuscular dose of 20 mg of vitamin K should be given if the prothrombin time is elevated. Repeated administrations are not necessary. Failure of vitamin K to decrease the prothrombin time emphasizes the severity of the underlying parenchymal disease.

The management of patients with acute viral hepatitis, both in the hospital and at home, involves relative bed rest, avoidance of alcoholic beverages, and abstinence from sexual activity until both liver function tests have returned to normal and the patient's symptoms have resolved. A beneficial effect of strict bed rest on the outcome of acute viral hepatitis has not been established. The two controlled prospective studies on this subject were performed in a young, previously healthy military population.[19,23] Strict bed rest had no effect on the course or incidence of sequelae. This has not been well studied in a general population. Diet, in the absence of hepatic failure, should be based on palatability. A high caloric intake (more than 3,000 calories per day) may shorten the course of acute viral hepatitis by a few days,[19] but in most patients this is unreasonable because of the usual symptoms of anorexia and nausea. Abstinence from alcohol and sexual activity is necessary only during the acute phase of the illness. Likewise, birth control pills should be avoided during the acute phase, since they may increase the serum bilirubin, making it more difficult to monitor the disease course. An individual's gradual return to normal activity should be guided by both absence of symptoms and a decline in liver function tests, the latter usually occurring in the one- to two-month convalescent period.

There is no specific therapy for acute viral hepatitis. Immune serum globulins, which are used in prophylaxis, have no value in this regard.[24] Even in severe cases of acute viral hepatitis, three controlled double-blind studies failed to show any beneficial effect of steroid therapy.[25-27] Other aspects of the management of acute viral hepatitis,

including personal hygiene, patient education, and certain techniques of isolation, are more appropriately discussed in the section on prevention. The patient with HBV should be followed after the acute episode with specific serologic tests. In addition, all cases of acute viral hepatitis should be followed monthly with liver function tests until the results have declined to within the normal range. Persistently elevated liver function test results continuing six months after the acute episode are an indication for a liver biopsy and consultation with a gastroenterologist. Management of biopsy-diagnosed chronic hepatitis is a somewhat complex subject but can be summarized by noting that chronic persistent hepatitis requires only careful follow-up whereas chronic active hepatitis, after exclusion of potentially treatable causes, usually requires corticosteroid therapy for only those HB_sAg-negative patients who are symptomatic.[28,29] Although ineffective when used alone, azathioprine has been used in combination with steroids in these patients.[30]

The management of patients with severe hepatocellular dysfunction, such as that which occurs in fulminant hepatitis and some cases of chronic active hepatitis, mainly involves the treatment of hepatic encephalopathy and associated secondary complications. The goal is to sustain life long enough for regeneration of the liver to occur, which usually takes several weeks. Survival is directly related to good supportive care rather than any specific therapy. The components of management of hepatic encephalopathy include restriction of protein from the diet, emptying of the colon with repeated high enemas, avoidance of sedatives, and the administration of oral neomycin (4 g/d) or lactulose (40 to 160 g/d) or both. The physician should also be familiar with the various aspects of prevention and treatment of complications such as secondary bacterial infection, gastrointestinal bleeding, aspiration, hypoglycemia, renal failure, respiratory failure, and hypotension.

Finally, a discussion of the management of the person who is incidentally discovered to be HB_sAg positive is needed. The first step should be to order a second specimen to exclude a laboratory error. If HB_sAg positivity is confirmed, the patient should be followed as described above to determine whether he or she is a carrier, which is the most likely outcome, or possibly has chronic hepatitis.

Hepatitis is a notifiable disease and every case should be reported to the state health department for epidemiologic reasons.

Prognosis

The family physician needs to be aware of the natural history of viral hepatitis including the incidence of various complications. Patients with acute viral hepatitis can be reassured that their disease will most likely resolve without complications. Sequelae are much less common after HAV than after acute viral hepatitis that is due to HBV or NANBV. Approximately 10 percent of the cases of HBV will maintain a carrier state. A carrier state after HAV has not been demonstrated, whereas the incidence of a carrier state due to NANBV has not been determined because of the lack of a specific serologic marker. In most carriers the HB_sAg usually persists for years; in a lesser number it persists for life. Whatever the case, the prognosis for a carrier is excellent.

Chronic hepatitis following HBV infection is more likely to occur early in life or when the immunologic reaction to infection is modified by disease, such as in patients with chronic renal failure or following a renal transplant. Hepatitis B virus presently accounts for 30 percent of the cases of chronic hepatitis, whereas the incidence of chronic hepatitis following HBV is approximately 10 percent. It is currently thought that NANBV accounts for 40 percent of the cases of chronic hepatitis. Hepatitis A virus most likely does not progress to a chronic state. Approximately two thirds of the cases of chronic hepatitis are chronic persistent hepatitis, and the remainder are chronic active (formerly called aggressive) hepatitis.[31] The former is a benign, self-limited disorder that may persist for many years.[32] Twenty to 60 percent of patients with this disorder are HB_sAg positive.[16] Chronic active hepatitis is a much more serious syndrome of progressive hepatocellular dysfunction, which may lead to cirrhosis and hepatic insufficiency. Both HBV and NANBV can result in this complication, but HAV probably does not.

Why some patients develop chronic persistent hepatitis and others develop chronic active hepatitis is still unknown. Chronic active hepatitis can be divided into two distinct syndromes, HB_sAg

negative (also called lupoid hepatitis) and HB_sAg positive, which differ in several epidemiologic and clinical aspects. HB_sAg-negaive chronic active hepatitis is associated with other autoimmune diseases and, in general, has a poorer prognosis than HB_sAg- positive chronic active hepatitis. Patients with untreated symptomatic HB_sAg-negative chronic hepatitis have a five- year survival rate of less than 50 percent, which is increased to 90 percent with the use of corticosteroids.[33] It is important to realize that besides the known and presumed causes of chronic active hepatitis, other diagnosable and potentially treatable causes include a variety of medications (ie, methyldopa,[34] isoniazid,[35] and nitrofurantoin[36]), Wilson's disease,[37] and several autoimmune disorders.[38]

A dreaded early complication of acute viral hepatitis is fulminant hepatitis. It occurs in less than 5 percent of the cases associated with HBV but may also occur with NANBV or even HAV.[39] Adults do not do as well as children. The level of coma is the best indicator for prognosis; with deep coma the survival rate is less than 20 percent. In patients who do survive, complete recovery without a residual cirrhosis is usually the rule.

Prevention

The four major components of hepatitis prevention are personal hygiene, patient education, certain techniques of isolation, and passive prophylaxis with specific immune globulins.

All HB_sAg positive patients, whatever their status (acute, chronic, or carrier), should be instructed to maintain excellent personal hygiene. This includes not only thorough handwashing but also careful disposal of blood-contaminated articles and the avoidance of sharing personal items (eg, towels, razors, toothbrushes) with others. In addition, because all patients who are HB_sAg positive are considered infectious to others, they should be told never to donate blood. Health care professionals who are HB_sAg positive should double-glove during surgical procedures and observe the highest standards of surgical technique.

Sexual activity should be avoided in patients with acute hepatitis, but this is not necessary in patients who are carriers or have chronic hepatitis.

It is not necessary to isolate all patients with acute viral hepatitis in a private room, whether at home or in the hospital. The presence of fecal incontinence and a bleeding diathesis are the only indications for isolation of patients with acute viral hepatitis. Since most infants are incontinent of stool, children of this age with viral hepatitis should be isolated in a private room. In addition to the usual "needle precautions," the only other precautions needed are the use of gloves in the handling of bedpans and the use of gowns when there is direct contact with blood or feces. Masks are needed only when there is danger of blood or feces being splattered. All specimens from hepatitis should be conspicuously labeled as such in order to alert laboratory personnel.

Specific circumstances in which prophylaxis in persons exposed to HBV is indicated are listed in Table 2.[40] Prophylaxis consists of pooled hepatitis B immune globulin (HBIG), which is comprised of anti-HB_s. All patients exposed to HBV should first be tested for the presence of HB_sAg and anti-HB_s. If either test is positive, the administration of HBIG is not warranted, since in the first instance the patient has previously been infected, and in the latter the patient is already immune. An intramuscular dose of .06 mL/kg of HBIG should be given, if needed, within 48 hours of exposure and repeated in one month.[41] Because testing for anti-HB_s may be delayed in many local primary care hospitals, for practical purposes the first injection of HBIG is given if the patient is HB_sAg negative; if the anti-HB_s returns as positive, the second injection in one month is not needed.

Another important indication for HBIG administration is for infants born to mothers who are HB_sAg positive at the time of delivery, regardless of her hepatitis status (ie, acute, chronic, or carrier).[42] The appropriate dose is .13 mL/kg given within two to seven days of birth and repeated in one month.

Prophylaxis against symptomatic HAV is well established and consists of standard immune globulin in a single intramuscular injection of .06 mL/kg.[42] Prophylaxis against HAV can be divided into two categories: pre-exposure and postexposure. Pre-exposure prophylaxis is reserved for those persons whose anti-HAV status is either negative or not known and who are planning to reside in a Third World country for at least two weeks. Postexposure prophylaxis is indicated in epidemic situations and in household, close per-

Table 2. HBV Prophylaxis

Situation	Prophylaxis Recommended	Prophylaxis Not Recommended
Needle puncture or laceration, abrasion, ingestion, or mucous membrane contact with urine, blood, saliva, pus, or stool	Contact HB_sAg positive *and* patient HB_sAg and anti-HB_s negative	Contact HB_sAg negative, unknown, or cannot be located *or* patient either HB_sAg or anti-HB_s positive
Sexual contact	Contact HB_sAg positive with acute hepatitis *and* patient HB_sAg and anti-HB_s negative	Contact HB_sAg positive carrier or chronic hepatitis *or* patient either HB_sAg or anti-HB_s positive
Infants born to HB_sAg positive mothers	Mother HB_sAg positive at time of delivery	Mother not HB_sAg positive at time of delivery

sonal, or institutional contacts of sporadic cases. The latter does not include hospital, office, or school contacts. Pooled gamma globulin provides protection against HAV for a period lasting from four to six months, decreasing the clinical attack rate by seven- to eightfold.[43]

Immunoprophylaxis of NANBV is not so well established. However, a recent study has shown that standard immune globulin may decrease the severity of NANBV after parenteral exposure.[44] Because of this, some authorities recommend intramuscular injection of 5 mL of immune serum globulin for (1) a needle-stick exposure in which the contact was known or suspected to have acute or chronic NANBV, (2) sexual contact of known or suspected acute NANBV, and (3) newborn infants of mothers with known or suspected NANBV (.13 mL/kg).[42] It should be realized that at the present time NANBV is still a diagnosis of exclusion, and these recommendations, therefore, are not so solid as for the other two forms of viral hepatitis.

Other aspects of viral hepatitis prevention include HB_sAg testing of blood component recipients prior to transfusion and HB_sAg screening of certain groups known to be at high risk both for accidental exposure to HBV and transmission of disease. These groups include operating personnel, patients and staff in renal dialysis units, laboratory technicians, personnel of blood bank and blood donor stations, and primate animal handlers.[45]

No vaccine is currently available for active immunization against any type of hepatitis. However, limited human trials have shown that purified HB_sAg, inactivated with formalin, is effective as a protective vaccine when administered intramuscularly as a 40-μg dose three times over a six-month period. Of 1,083 high-risk homosexual men who received the vaccine, 96 percent developed high anti-HB_s titers with a subsequent 90 percent decrease in new HBV infections.[46] After further clinical testing, this vaccine will be available for use in high-risk populations.

A final note on prevention is the current risk of posttransfusion hepatitis given the present methods of testing volunteer blood donors for HB_sAg. For less than 15 units of blood, the risk is approximately 2 to 3 percent. For massive transfusions requiring more than 15 units of blood, the risk increases to 6 percent.[47]

Family Factors

The adjustment in lifestyles of all family members, when one or more have viral hepatitis, can be considerable, with resultant stress on the family unit as a whole. In addition, an important psychosocial aspect to consider is the need to avoid social isolation in these patients, not only in those with

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acute viral hepatitis but also, more importantly, in those who have been diagnosed as carriers or having chronic hepatitis. Despite this, a thorough review of the literature on viral hepatitis reveals little information on family factors and psychosocial aspects. The available studies deal almost exclusively with genetic and epidemiologic aspects. For example, it has been noted that among relatives of HB_sAg-positive blood donors, serologic evidence of HBV was 10 times more frequent than in relatives of HB_sAg-negative blood donors.[48] Epidemiologic studies of HAV among family members have shown that most household cases occur one or more incubation periods after the index case, thus suggesting that the patient with HAV is most infectious about the time of onset of symptoms.[49,50] The only studies that have dealt with any of the psychosocial aspects of viral hepatitis are those that have addressed the problem of inappropriate reactions to transmission risks among HB_sAg carriers.[51,52] They recommend routine screening of these individuals and the provision of appropriate counseling if indicated.

Conclusion

Within the past decade striking advances have been made in the delineation of type A and B viral structure, with subsequent development and commercial availability of serologic testing, greatly improving all aspects of medical care of viral hepatitis, including diagnosis, management, and prevention. Obviously, the characterization of the responsible viral agent for NANBV, at the present time a diagnosis of exclusion, would be another large step forward. Primary care research can contribute to this rapidly developing body of knowledge in the still rather unexplored areas of the risks and psychosocial effects of viral hepatitis on the family unit.

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