

**WHITE LETTER:**

**Liver Diseases in Viet Nam:**

**Screening, Surveillance, Management and Education**

*A Five-Year Plan and Call to Action*

**Viet Nam Coauthors:**

**Hanoi Medical University:** President Nguyen Duc Hinh, MD, PhD  
Dao van Long, MD, PhD  
Nguyen Thi Kim Chuc, Pharm, PhD

**Hue Medical University:** President Cao Ngoc Thanh, MD, PhD  
Tran Van Huy, MD, PhD  
Nguyen Vu Quoc Huy, MD, PhD

**HCM Medical University:** President Vo Tan Son, MD, PhD  
Bui Huu Hoang, MD, PhD  
Nguyen Hoang Bac, MD, PhD

**CanTho Medical University:** President Pham Van Linh, MD, PhD  
Tran Ngoc Dung, MD, PhD  
Pham Thi Tam, MD, PhD

**Bach Mai Hospital-Hanoi:** Director Nguyen Quoc Anh, MD, PhD  
Vu Truong Khanh, MD, MSc

**Cho Ray Hospital-HCMC:** Director Nguyen Truong Son, MD, PhD  
Le Thanh Ly, MD, PhD

**Australia Coauthor:**

Stephen Locarnini, MD, PhD, FRC VIDRL, Melbourne, Australia

**United States Coauthors:**

Bui Duy Tam, MD, PhD	San Francisco, California
Jessica A. Clarke, MD, PhD	University of Washington
Anthony M. Cosentino, MD	St. Mary's Medical Center
Do Tuong Son, MD	Plano, Texas
Robert G. Gish, MD	California Pacific Medical Center
Le Loc, MD	Baltimore, Maryland
Le Duc Truong Sinh, MD	Fountain Valley, California
Paul Martin, MD, FACP	University of Miami, Miller School of Medicine
Nguyen Thanh Chau, MD	San Jose, California
Christine Nguyen, MD	California Pacific Medical Center
Nguyen Tien Duc, MS, PhD	Long Beach, California
Nguyen Anh Huy, MD, AGAF	San Jose Gastroenterology MC
Tran Thuy Tram, MD	Cedars Sinai Medical Center
Trinh Ngoc Huy, MD, AGAF	San Jose Gastroenterology MC
Gary Vong, MD	San Francisco, California

# BẠCH THƯ'

CÁC BỆNH GAN Ở VIỆT NAM:

*Sàng lọc, theo dõi, điều trị và giáo dục*

*Kế hoạch 5 năm và kêu gọi hành động*

*Đã được các đồng tác giả đồng thuận ký*

*kết*

*với sự chứng kiến của Bộ Y Tế*

*(GS.TS.Thứ Trưởng Trịnh Quân Huân và*

*TS.BS.VụTrưởng Trần Thị Giáng Hương)*

**Các đồng tác giả phía Việt Nam :**

**Bộ Y Tế**

GS.TS Trịnh Quân Huân, Thứ Trưởng

TS.BS Trần Thị Giáng Hương, Vụ Trưởng Vụ hợp tác quốc tế

**Đại Học Y Hà Nội:**

PGS.TS Nguyễn Đức Hình- Hiệu Trưởng

PGS.TS Đào Văn Long

PGS.TS Nguyễn Thị Kim Chúc

**Trường Đại Học Y Dược Huế:**

PGS.TS Cao Ngọc Thành - Hiệu Trưởng

PGS.TS Trần Hữu Dàng- Phó Hiệu Trưởng

PGS.TS Trần Văn Huy

PGS.TS Nguyễn Vũ Quốc Huy

**Trường Đại Học Y Dược TP Hồ Chí Minh:**

PGS.TS Võ Tấn Sơn-Hiệu Trưởng

TS BS Bùi Hữu Hoàng

TS Nguyễn Hoàng Bắc

**Trường Đại học Y Dược Cần Thơ:**

PGS.TS Phạm Văn Linh- Hiệu Trưởng

TS.BS Trần Ngọc Dung

TS.BS Phạm Thị Tâm

**Bệnh Viện Bạch Mai- Hà Nội:**

TS. BS Nguyễn Quốc Anh-Giám Đốc

ThS. BS Vũ Trường Khanh

**Bệnh Viện Chợ Rẫy-TP HCM:**

TS. BS Nguyễn Trường Sơn- Giám Đốc

BSCCKII. Hoàng Hoa Hải

TS. BS Lê Thành Lý

---

**International Coauthors:**

Nguyen Trong Hau, MD

Bui Duy Tam, MD, PhD

Jessica A. Clarke, MD, PhD

Anthony M. Cosentino, MD

Do Tuong Son, MD

Robert G. Gish, MD

Le Trong Loc, MD

Le Duc Truong Sinh, MD

Stephen Locarnini, MD, PhD

Paul Martin, MD

Medicine

Nguyen Thanh Chau, MD

Christine Nguyen, MD

Nguyen Tien Duc, MS, PhD

Nguyen Anh Huy, MD, AGAF

Tran Thuy Tram, MD

Trinh Ngoc Huy, MD, AGAF

Garen Vong, MD

The Atlantic Philanthropies

San Francisco, California

University of Washington

St. Mary's Medical Center

University of Texas Southwestern

California Pacific Medical Center

Woodholme Gastroenterology Ass.

Fountain Valley, California

VIDRL Melbourne, Australia

University of Miami, Miller School of

San Jose, California

California Pacific Medical Center

Long Beach, California

San Jose Gastroenterology MC

Cedars Sinai Medical Center

San Jose Gastroenterology MC

San Francisco, California

**SIGNATURES OF CO-AUTHORS**

**Viet Nam Coauthors:**

**Bô Y Tế**

GS.TS Trịnh Quân Huân, Thứ Trưởng

---

TS.BS Trần Thị Giáng Hương, Vụ Trưởng Vụ hợp tác quốc tế

---

**Hanoi Medical University:**

Nguyen Duc Hinh, MD, PhD



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Dao van Long, MD, PhD



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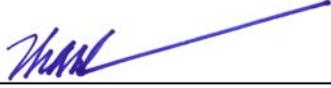
Nguyen Thi Kim Chuc, Pharm, PhD



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**Hue Medical University:**

Cao Ngoc Thanh, MD, PhD



---

Tran Huu Dang, MD, PhD



---

Tran Van Huy, MD, PhD



---

Nguyen Vu Quoc Huy, MD, PhD



---

**HCM Medical University:**

Vo Tan Son, MD, PhD



---

Bui Huu Hoang, MD, PhD



---

Nguyen Hoang Bac, MD, PhD



---

**CanTho Medical University:**

Pham Van Linh, MD, PhD

---



Tran Ngoc Dung, MD, PhD

---



Pham Thi Tam, MD, PhD

---



**Bach Mai Hospital-Hanoi:**

Nguyen Quoc Anh, MD, PhD

---



Vu Truong Khanh, MD, MSc

---



**Cho Ray Hospital-HCMC:**

For Nguyen Truong Son, MD, PhD

Hoang Hoa Hai, MD

---



Le Thanh Ly, MD, PhD

---



**International Coauthors:**

Nguyen Trong Hau, MD, MPH, The Atlantic Philanthropies



---

Bui Duy Tam, MD, PhD, San Francisco, California



---

Jessica A. Clarke, MD, PhD, University of Washington



---

Anthony M. Cosentino, MD, St. Mary's Medical Center



---

Do Tuong Son, MD, University of Texas Southwestern



---

Robert G. Gish, MD, California Pacific Medical Center



---

Le Trong Loc, MD, Woodholme Gastroenterology Assoc.



---

Le Duc Truong Sinh, MD, Fountain Valley, California



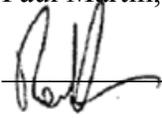
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Stephen Locarnini, MD, PhD, VIDRL, Melbourne, Australia



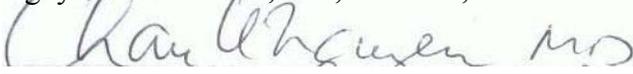
---

Paul Martin, MD, University of Miami, Miller School of Medicine



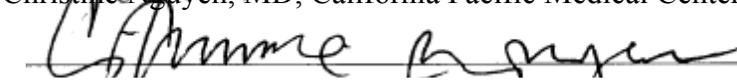
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Nguyen Thanh Chau, MD, San Jose, California



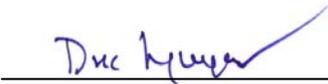
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Christine Nguyen, MD, California Pacific Medical Center



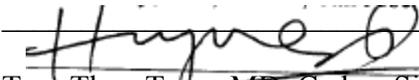
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Nguyen Tien Duc, MS, PhD, Long Beach, California



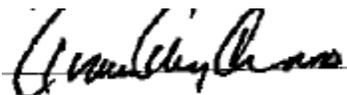
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Nguyen Anh Huy, MD, AGAF, San Jose Gastroenterology MC



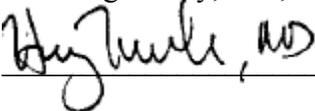
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Tran Thuy Tram, MD, Cedars Sinai Medical Center



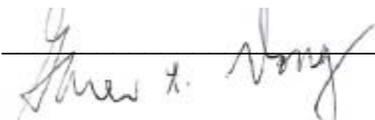
---

Trinh Ngoc Huy, MD, AGAF, San Jose Gastroenterology MC



---

Garen Vong, MD, San Francisco, California



---

**Australia Coauthor:**

Stephen Locarnini, MD, PhD, FRC (Path), VIDRL, Melbourne, Australia



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## INTRODUCTION

There is a high prevalence of liver disease in Viet Nam, much of which results from preventable causes, including chronic infection with hepatitis viruses, as well as high consumption of alcohol among men. Chronic infection with hepatitis viruses, including hepatitis B virus (HBV) and hepatitis C virus (HCV), can lead to cirrhosis (liver damage) and liver cancer, the risk of which is substantially increased in the absence of appropriate treatment. Long-term high-volume consumption of alcohol can also lead to cirrhosis. When such alcohol consumption is combined with viral infections, the risk of cirrhosis and cancer can be doubled. A recent nationwide study found that liver cancer is the most common cause of cancer death in Viet Nam.<sup>1</sup>

One large study has predicted an enormous liver disease burden in Viet Nam over the next fifteen years from chronic hepatitis B (CHB) alone.<sup>2</sup> That CHB liver disease burden includes the loss of many years of healthy life due to the complications of liver failure, liver cancer, and death in many people as well as all the monetary costs associated with the disease. The overall liver disease burden will be greatly increased by the addition of substantial numbers of people living with other forms of the disease, including chronic hepatitis C (CHC), alcoholic liver disease, and non-alcoholic fatty liver disease. Without proper intervention, the combination of all of these will affect substantial numbers of people in Viet Nam, and could make the ultimate costs to both individuals and society quite staggering.

Despite ample evidence showing the high number of Vietnamese people living with infections or other conditions that are highly likely to result in serious liver disease, there is no systematic nationwide screening in Viet Nam of at-risk individuals, and no nationwide comprehensive response to the disease. Unfortunately, people may live with advancing liver disease for many years while remaining symptom-free until late disease stages. There is a general lack of understanding by both the general public and healthcare providers about the major risk to health that liver disease represents in Viet Nam. Many things contribute to the lack of informed awareness about liver disease, including cultural misconceptions, misinformation and mythology about the disease, inadequate access to care, and a lack of educational programs about liver disease directed to the Vietnamese population and to health care professionals, including nurses, physicians, public health professionals, and pharmacists.

What we propose here is development of a comprehensive integrated approach to liver disease in Viet Nam that includes the following:

- (1) Education and training for healthcare providers, health educators, and the public about the various forms of liver disease;
- (2) Expansion of nationwide screening for HBV and HCV followed by, as appropriate, HBV vaccination or treatment and/or HCV treatment;

- (3) Education about alcoholic liver disease and non-alcoholic fatty liver disease, with identification of resources to address these;
- (4) In patients with identified liver disease, long-term surveillance for liver cancer;
- (5) Reduction of infection transmission related to medical, commercial, and personal re-use of contaminated needles, syringes, sharp instruments, razors, and inadequately sterilized medical equipment; and
- (6) Ongoing collection and analysis of data about the prevalence of all forms of liver disease and the results of the expanded screening, vaccination, and treatment programs.

We believe that this type of comprehensive nationwide approach to liver disease could substantially reduce the morbidity and mortality from this disease and greatly lessen the burden in terms of both lives lost and health care costs.

Currently in Viet Nam there is an excellent example of the type of systematic approach to a disease that we believe is needed for liver disease. A comprehensive nationwide, government-supported approach to HIV/AIDS, a disease that affects far fewer people, is already in place. In March of 2004 the Vietnamese government released the National Strategic Plan on HIV/AIDS Prevention and Control for 2004-2010 with a Vision to 2020. The strategy described in this plan provides a framework for a comprehensive national response to the epidemic, and calls for mobilization of government, party and community-level organizations across multiple sectors. Since then, the Vietnamese government has provided broad support for addressing HIV/AIDS, including passage of the June 2006 Law on HIV/AIDS Prevention and Control and, at the proposal of the Minister of Health, the Government's Decree No. 108/2007/ND-CP of June 26, 2007, which details the implementation of the law. These legal documents provide guidelines for many aspects of addressing HIV/AIDS, including for the distribution of medicine, condoms, and clean needles and syringes free of charge. With such government support in place, a broad-based response to HIV/AIDS has been developed. Currently, resources for HIV/AIDS programs in Viet Nam are being provided by approximately 30 international non-governmental organizations (NGOs), seven government-sanctioned local NGOs, nine United Nations organizations, five major bilateral agencies, and the Global Fund to Fight HIV/AIDS, TB, and Malaria.

There are an estimated 280,000 people living with HIV/AIDS in Viet Nam (an estimated overall prevalence of 0.53%)<sup>3</sup> compared to the estimated 10 to 15 million people living with CHB alone (an estimated overall prevalence of approximately 12%). Adding the additional people living with CHC, alcoholic liver disease, and non-alcoholic liver disease equals a population of people with liver disease that is vastly larger than that of HIV/AIDS, and that certainly warrants at least as substantial a level of support. We believe that a comprehensive, science-based approach to liver disease is urgently needed in Viet Nam and with this white letter we call for that.

## CHRONIC HEPATITIS B VIRUS INFECTION

Chronic infection with HBV is a major public health problem estimated to affect 400 million people worldwide<sup>4,5</sup>. Modeling the burden of CHB worldwide, the Centers for Disease Control and Prevention (CDC) conservatively estimated that in the year 2000, 620,000 persons died from HBV-related causes, with 580,000 (94%) from CHB-related cirrhosis and hepatocellular carcinoma (HCC).<sup>6</sup> HBV has particularly high prevalence in Asians and Pacific Islanders (API), many of whom become chronically infected at birth or in early childhood.<sup>7</sup> It is estimated that API constitute more than half of the global reservoir.<sup>6</sup>

Viet Nam has one of the highest rates of HBV infection in the world. The majority of people have been exposed to the virus, with an estimated prevalence of anti-HBc (+) that ranges from 51.8% in Thai Nguyen province<sup>8</sup> to 68.2% in Thai Binh province<sup>9</sup> to 79.2% in Thanh Hoa province.<sup>10</sup> It is estimated that 10 to 15 million people in Viet Nam are currently living with CHB. This means that at least one in eight people in this country are living with this chronic infection that can lead to serious liver disease. The prevalence in major cities is high, with estimates of 10-14% in Ho Chi Minh City and Hanoi.<sup>11,12</sup> There is an even higher estimated prevalence in some rural areas, with an estimated 18.8% in Thanh Hoa province<sup>10</sup> and 19% in Thai Binh province,<sup>9</sup> and a somewhat more modest though still high 8.8% in Thai Nguyen province.<sup>8</sup> As would be expected, the prevalence of CHB in patients with liver disease is even higher. In two studies of liver disease patients in Ho Chi Minh City, the prevalence has been reported to be 31.2%<sup>11</sup> to 47%.<sup>13</sup>

Without medical monitoring and treatment of CHB, the risk of developing cirrhosis and HCC with sequelae of liver failure and death is 25-30%.<sup>14-18</sup> Using age-specific HBV prevalence rates from Vietnamese community-based studies, it has been projected that by the year 2025, CHB could result in 58,650 patients with cirrhosis, 25,000 patients with HCC, and 40,000 deaths.<sup>2</sup>

One of the problems with public awareness of the extent of CHB in the population and the widespread need for treatment is that for many years it can be a silent disease. Most people with CHB will remain symptom-free and unaware that they are infected until a late disease stage when they develop clinically apparent liver cancer, most commonly hepatocellular carcinoma (HCC), and/or the signs of more advanced cirrhosis. Standard blood tests may not point to the disease since liver enzymes may be in the normal range for lengthy periods. The disease spectrum of CHB is highly variable. At one extreme, some people experience inactive infection (no hepatitis) throughout a lifetime while at the other some develop cirrhosis and HCC during childhood. Between these extremes are many intermediates where there are irregular cycles of disease activation (“flares” in hepatic enzymes with liver inflammation, injury and fibrosis) and inactive disease. However, the general lack of symptoms until late disease stages keeps people from an awareness of the disease’s effects.

In addition, many people in the general public have no real understanding of the risks and long-term consequences of untreated infection. Even worse, many healthcare providers

lack this understanding, as well. In some cases, neither the person living with CHB nor their physician is aware that there are safe and effective treatments. In a country with a low per capita income, there are also many people for whom treatment is simply not affordable. When antiviral drugs are available and affordable, CHB can be effectively treated, suppressing the virus and substantially reducing the risk of disease progression. With long-term effective antiviral treatment, preferably initiated in a relatively early disease stage, the ultimate progression to cirrhosis and HCC may be prevented in many patients.

Because safe and effective vaccines and therapies exist, there is an obvious need to identify, follow and treat people with existing CHB, while also vaccinating those who are susceptible in order to prevent transmission. For Viet Nam to effectively address HBV disease there is an urgent need to systematize this task by moving forward with a nationally supported program that includes education, screening, vaccination, and treatment. The overall goals for improving the approach to HBV in Viet Nam should include raising awareness among healthcare providers about the high existing prevalence of HBV infection, the need for screening and vaccination to prevent the spread of infection, the need to identify people with CHB, and the consequences of failure to treat CHB properly and, thus, the importance of effective management of CHB. The latter should include treatment, where appropriate, as well as liver cancer surveillance.

This education of healthcare providers should be combined with raising awareness in the community that HBV infection is preventable through vaccination and, when active, is treatable with safe, effective antiviral agents. It will be important to correct common misperceptions about HBV infection, vaccination and treatment among both healthcare providers and the general public. It will be very important to educate both healthcare providers and patients about the importance of long-term treatment adherence (properly taking medicine exactly as prescribed) to prevent development of viral resistance.

### ***Reducing Transmission of HBV***

The acquisition of HBV could be greatly limited by addressing the major risk factors for infection. Perinatal transmission—vertical transmission from an HBV-infected mother to her child at birth—can be prevented in up to 95% of cases by prompt neonatal vaccination and infusion of hepatitis B immune globulin (HBIG).<sup>19</sup> In the United States (US), the universal neonatal HBV vaccination that was introduced in 1991 has resulted in immunity in a high proportion of young children.<sup>20</sup> Although Viet Nam's Expanded Program on Immunization (EPI) began the introduction of HBV vaccine in 1997, neonatal HBV vaccination had only been implemented in approximately 70% of the provinces by 2004.<sup>21</sup> It will be very important to ensure that all hospitals and clinics have in place a written policy for newborn hepatitis B vaccination, and that healthcare providers are knowledgeable about this standard of care. The potential utilization of HBIG as part of a perinatal HBV transmission protection program can be evaluated as part of this five-year initiative.

A recent study in four provinces in Viet Nam identified several factors that affected birth-dose timeliness and coverage, including family perceptions, perceived contraindications, community-based pregnancy tracking practices, and relationships of the vaccination program with both private maternity services and large urban hospitals.<sup>22</sup> Addressing all the factors that have so far prevented neonatal HBV vaccination from becoming truly universal could greatly reduce vertical transmission.

In addition, an effective catch-up vaccination program could provide protection for children and adolescents who were not infected at birth and were not successfully vaccinated as newborns. Because the prevalence of HBV is so high in Viet Nam, screening should be done prior to vaccination of children. It is important for healthcare providers to be aware that vaccination without screening children is inappropriate.

A significant percentage of the children who might be included in a mass vaccination program carried out without screening could already have the disease. If they are vaccinated without screening, they and their parents may believe that they are protected. The end result will be that they may never be properly screened and, thus, will not receive needed follow up and treatment, and will not be aware that they are carrying an infectious virus that could be transmitted to others. The children born to mothers with CHB who receive neonatal vaccination should still be screened between ages one and five since 5-10% of infants will become infected despite the vaccination.

Horizontal transmission, passing the infection from one person to another, can also be prevented by vaccination which is highly effective<sup>23</sup> and unequivocally safe. Important components of Viet Nam's approach to liver disease prevention would be to raise awareness among the general public that HBV infection is preventable through vaccination, and to establish effective approaches to screening nationwide in order to identify and increase vaccination rates among those who are susceptible, while also identifying and informing individuals with immunity and those who are infected, referring the latter for assessment and treatment, where indicated. To ensure the highest possible success for vaccination programs, it will be crucial to provide free or low-cost vaccination for all those at risk.

It will also be very important to educate both the general public and healthcare providers about all the risk factors for transmission of HBV. It will be important to teach both the public and all healthcare providers about the ways in which HBV is spread: when blood, semen, or other body fluids infected with the virus enter the body of a person who is not infected. Thus, it must be taught that in addition to infection at birth, people can become infected:

- (1) During unsafe sex with an infected partner;
- (2) Through exposure to blood via re-use of syringes, needles or sharp instruments (including not only in the healthcare setting but also in the home or when used for tattoos or in traditional medicine practices);

- (3) Through use of inadequately sterilized medical equipment (such as dialysis equipment in hospitals);
- (4) Through sharing items such as razors or toothbrushes with an infected person;
- (5) Through direct contact with the blood or open sores of an infected person; and
- (6) Among drug users, through sharing needles, syringes, or other drug-injection equipment previously used by an HBV-infected person.

These practices and habits and behaviors must be eliminated through education and institutional standard of care protocols.

In one recent study, household contact with a person with liver disease, sharing of razors, and reuse of syringes were all identified as major risk factors for HBV infection,<sup>9</sup> and clear education about such risks needs to be part of any Vietnamese program aimed at reducing transmission. In a study of 309 injection drug users in northern Viet Nam, the prevalence of HBV infection was 80.9%.<sup>24</sup> As is discussed further below, outreach programs to educate drug users about this risk and various interventions suggested by experts in the field, including needle/syringe exchange programs might reduce this risk.

Education about sexual transmission is also needed, both within schools and for the general public. Viet Nam is becoming a country that is less conservative in terms of sexual practices than was once the case, and education about sexual transmission of infectious diseases and prevention with safe-sex practices is importantly needed.

Conversely, viral hepatitis B and C are not spread by hugging or shaking hands or sharing meals together in the home or workplace, and prejudice about this disease in the workplace, home and society also needs to be eliminated.

As part of Viet Nam's nationwide approach to screening, it will be important to identify and address any barriers to screening in order to improve the overall success of the program. Confidential databases can be used to track and follow individuals who test positive for HBV on screening, while also collecting data on CHB prevalence, and the results of screening and treatment programs.

Transmission of HBV in the health care setting via contaminated needles, syringes, and inadequately sterilized hospital equipment also occurs much too frequently. Recent studies have shown that major risk factors for HBV infection in Viet Nam include a history of hospitalization and a history of acupuncture,<sup>9</sup> as well as a history of surgery.<sup>8</sup> As discussed further below, this absolutely must be addressed nationwide to reduce infection rates of both HBV and HCV.

## ***HBV Screening Assays***

The principal screening assay for acute hepatitis B and CHB, as well as for the screening of blood and organ donors, is detection of the HBsAg in serum.<sup>25</sup> The typical serological profiles found in active or past HBV infection are shown in Table 1.

**Table 1. Significance of a positive HBV test:**

HBsAg	Infected and infectious
Anti-HBs	Immune (in the absence of HBV DNA)
Anti-HBc IgM IgG	Exposed Recent or acute infection Historical exposure (with possible current infection) or false positive or low level carrier
HBeAg	High replication
Anti-HBe	May indicate low replication or presence of precore/BCP mutant
HBV DNA qualitative	Presence of HBV DNA, sensitive
HBV DNA quantitative	Presence of HBV DNA and level of replication
Anti-HD	Recent or current infection with Delta Hepatitis
Delta antigen/HDV RNA	Replication of Delta hepatitis

As part of the HBV-specific medical education directed to healthcare providers, it will be important to provide simplified guidelines for proper use and interpretation of these tests. As already mentioned, even in the US 30%-55% of healthcare providers would order the wrong test to screen for HBV infection.<sup>26</sup> Inexpensive screening for chronic hepatitis B can take place with HBsAg and anti-HBs with a reflex to HBV DNA by PCR for HBsAg-positive patients and vaccination for those HBsAg-negative and anti-HBs-negative.

## ***Treatment of CHB***

Although there is no current cure for CHB, it can be effectively treated by suppression of the virus through long-term use of antivirals, a growing number of which are available, some in inexpensive generic versions. Effective treatment can reduce liver damage and substantially decrease the risk of progression to cirrhosis and liver cancer.<sup>27</sup> The oral antiviral drugs currently approved for the treatment of CHB are the nucleoside analogues lamivudine (Epivir-HBV, Zeffix, or Heptodin), entecavir (Baraclude), and telbivudine (Tyzeka or Sebivo); and the nucleotide analogues adefovir dipivoxil (Hepsera) and tenofovir (Viread). The injectable drugs that are approved for treatment of CHB are two types of interferon-alpha, the older standard version of interferon-alpha (Intron A) and

the more recently approved pegylated form of interferon-alpha (Pegasys) which is now the preferred choice of interferons.

As part of the total approach to CHB in Viet Nam, it will be very important to initiate treatment in all appropriately identified individuals and provide long-term affordable treatment. It will be important to monitor patients' treatment success. Treatment will be considered successful (1) if in individual patients, HBV DNA is negative on therapy and there is a durable response off therapy; and (2) if there is an overall decrease in liver cancer, cirrhosis, end-stage liver disease, and the need for liver transplant, long term.

Where there is failure in individual patients, it will be important to identify whether it is due to viral resistance or lack of compliance (failure to always properly take medications, as prescribed).

To improve treatment outcomes it will be very important to ensure adequate HBV-related training of physicians and other health care workers who provide primary care to people in Viet Nam, including the provision of current information on hepatitis B therapies. Lack of knowledge among primary care physicians about treatment and proper monitoring of patients is a major problem in Viet Nam today that must be addressed to improve patient outcomes.

Patients should also be given educational materials that describe available treatments for active hepatitis B and contain information on effectiveness, side effects, and the importance of long-term adherence (taking the medications exactly as instructed) to prevent viral resistance, and healthcare providers should ensure that they understand these materials.

Failure to treat in a timely manner can result in an ever increasing liver disease burden nationwide and, for the individual, may ultimately lead to the advanced disease stage when liver function is so severely impaired that liver transplant may be the only remaining option. [A specific action plan for the initiation of liver transplantation will be outlined in a separate document.]

### ***Coinfection and Cofactors in CHB Disease Progression***

Coinfection with HCV, Delta infection and HBV and/or human immunodeficiency virus (HIV) may accelerate liver disease progression, as may alcohol consumption.<sup>28</sup> In one study in Ho Chi Minh City, coinfection with HBV and HCV was found in 8% of liver patients.<sup>13</sup> HBV/HIV coinfecting individuals are likely to have higher serum HBV DNA levels and experience faster progression to cirrhosis and liver cancer.<sup>29</sup> There is substantial observational data that supports that HIV/HBV-coinfecting people have a 3- to 6-fold increased risk of developing chronic HBV, an increased risk of fibrosis and cirrhosis, and a 17-fold increased risk of death compared to HBV-monoinfecting people, and that earlier use of HBV-active antiretroviral regimens leads to a reduction in liver-related disease.<sup>30</sup>

When a person with HBV is identified, a medical professional should ask screening questions to identify those at risk for HIV and HCV so that subsequent testing can be ordered, if indicated. It is important to be aware of fears about the possible consequences of testing HIV-positive where stigma still exists, and to assure the patient that absolute confidentiality about testing results will be maintained.

In those who are identified as HIV/HBV-coinfected, it will be very important to follow up-to-date guidelines on proper treatment since a number of the drugs approved for treatment of HBV also have activity against HIV. Using a single agent known to have activity against both viruses would lead to rapid selection of medication-resistant HIV strains since this would be equivalent to antiretroviral monotherapy. Because of the high level of cross-resistance with many antiretrovirals and the need for effective nucleoside analogues as the backbone for most HIV treatment regimens, this could leave the patient with few options for durable HIV suppression. It is also recommended that coinfecting patients in need of HIV suppression not be treated with less than two agents with anti-HBV activity in order to slow development of HBV resistance and to limit the risk of a clinically significant hepatitis flare in the setting of treatment-induced immune reconstitution.

The most recent recommendation from the World Health Organization is that in all HIV/HBV-coinfected individuals who require treatment for their HBV infection, a highly active antiretroviral therapy (HAART) regimen be started to suppress HIV, regardless of CD4 count or WHO clinical stage.<sup>30</sup> WHO strongly recommends a starting antiretroviral regimen that contains tenofovir (Viread) with either lamivudine (Epivir) or emtricitabine (Emtriva), along with the addition of the other antiretroviral agents required to create an effective anti-HIV regimen.

## **CHRONIC HEPATITIS C VIRUS INFECTION**

Chronic hepatitis C (CHC) is estimated to affect 130 to 170 million people worldwide.<sup>31,32</sup> Data on the overall prevalence of HCV infection in Viet Nam are less clear since there has been no nationwide study to assess this. Studies have reported intermediate prevalence in patients without liver disease in Hanoi (4%).<sup>12</sup> In Ho Chi Minh City, in patients without liver disease the reported prevalence has ranged from 2%<sup>11</sup> to 9%.<sup>12</sup> A much lower prevalence of only 1.0 % in patients without liver disease has been reported in rural northern Viet Nam<sup>33</sup> and rural Dalat City.<sup>13</sup> As would be expected, the prevalence in patients with liver disease has been reported to be higher. In one study, 23% of liver disease patients in Ho Chi Minh City were reported to be seropositive for HCV antibodies, with detectable HCV RNA in 61% of these.<sup>13</sup> In another Ho Chi Minh City study, the prevalence of HCV in liver disease patients was 19.2%.<sup>11</sup>

A 1994 study found that the prevalence of HCV was particularly high in Ho Chi Minh City in drug users (87%) and patients who required medical treatment that potentially exposed them to this blood-borne virus through contaminated medical devices or blood products, including patients on maintenance hemodialysis (54%) and those with

hemophilia (29%).<sup>12</sup> It has been shown that in intravenous drug users in Hanoi, HCV is acquired relatively quickly after the onset of injection, with a prevalence of 30% in heroin users with ten or fewer months of injection risk and 70% in those with 30 or more months of injection risk.<sup>34</sup> In a study of 309 intravenous drug users in northern Viet Nam, HCV prevalence was 74.1%.<sup>24</sup>

The high prevalence of HCV in drug users and others exposed to contaminated syringes or medical equipment is not surprising. It is estimated that illicit use of injectable drugs accounts for 40% or more of HCV infections in developing countries worldwide.<sup>35</sup> In addition, nosocomial transmission of HCV is high in developing countries because too often contaminated syringes and needles are re-used in medical, paramedical and dental procedures.<sup>36,37</sup> Re-use of needles in the community for tattoos is also common. In one study of patients without liver disease, the two main risk factors associated with HCV acquisition were hospital admission and tattoos.<sup>33</sup> As discussed further below, addressing these sources of infection will be very important for decreasing HCV infection in Viet Nam.

Approximately 25% of people with chronic HCV will eventually develop cirrhosis,<sup>38</sup> and a substantial percentage will subsequently develop HCC. Coinfection with HCV and HBV and/or human immunodeficiency virus (HIV) may accelerate liver disease progression, as may alcohol consumption.<sup>28</sup> As with CHB, most people with CHC will remain symptom-free and unaware that they are infected until a late disease stage when they develop obvious signs of cirrhosis or HCC. Thus, screening to allow for early and accurate diagnosis is essential for the best outcomes.

### ***Screening for HCV infection***

Screening for HCV infection is more complex and more expensive than the simpler screening for HBV infection. CHC is generally diagnosed when anti-HCV is present and serum aminotransferase levels remain elevated for more than six months. However, PCR testing for HCV RNA is needed to confirm the diagnosis by detection of viremia (the presence of the virus in the bloodstream). Diagnosis may be problematic in patients with anti-HCV who have another form of liver disease that might be responsible for liver damage such as CHB, alcoholic liver disease, iron overload, or autoimmunity. In such patients, the presence of anti-HCV might represent previous HCV infection, a false-positive reaction, or mild hepatitis C that is present along with other serious liver conditions that may be the more significant source of damage to the liver. Again, HCV RNA testing can help confirm that CHC is present and contributing to the liver disease.

Diagnosis is also more difficult in patients who have immune dysfunction as the result of disease or drugs. They may test negative for anti-HCV despite having HCV infection because they may not be capable of producing enough antibodies for detection. Thus, even in patients who have tested negative with anti-HCV testing, HCV RNA testing may be required when they are HIV/HCV coinfecting, have a solid-organ transplant, are on dialysis, are taking corticosteroids, or have agammaglobulinemia.

Since the prevalence of HCV infection is suspected to be higher than 2% overall, HCV broad-based testing should take place in the initial sites for HBV screening. Based on the data for the first 5000 patients screened for HBV and HCV, a decision can be made on whether to call for nationwide HCV screening or to focus on high-risk groups only.

### ***Treatment of CHC***

CHC is treatable and in some cases curable with the combination of interferon and ribavirin. The current standard of care for treatment of CHC is the combination of peginterferon alfa-2a + ribavirin (Pegasys + Copegus) or peginterferon alfa-2b + ribavirin (PegIntron + Rebetol). However, with the most common genotypes in Viet Nam, including genotype 6, the likelihood of sustained virological response is less likely. In addition, the combination of subcutaneous pegylated interferon with oral ribavirin, continued for 24-48 weeks (depending on genotype), is expensive. It is also the cause of side effects (especially flu-like symptoms and depression) which can lessen some patients' willingness to complete the treatment series.

Proper medical management, including dose reductions, can lessen side effects and allow most patients to complete the full series of treatments. Thus, it is very important for patients to be monitored by physicians who are highly knowledgeable about HCV treatment. It is also important to confirm patient willingness as well as the certainty that a full course of treatment can be provided and is affordable by that patient.

## **ALCOHOLIC LIVER DISEASE**

Alcoholic liver disease (ALD) is another major contributor to the overall burden of liver disease in Viet Nam. Mortality from alcoholic liver disease is closely tied to per capita alcohol consumption.<sup>39</sup> A recent study which collected data from nine rural Health and Demographic Surveillance System (HDSS) sites located in five Asian countries found very high rates of alcohol consumption by men in Viet Nam.<sup>40</sup> In fact, of the nine rural HDSS sites assessed, the two sites in Viet Nam had by far the highest rates of male at-risk drinkers, defined as men who consumed five or more standard drinks per day. These sites were the FilaBavi site, a field lab located in the Ba Vi district in Ha Tay province in northern Viet Nam which collects data from 11,000 households with 55,000 inhabitants; and the CHILILAB site, a field lab located in the Chi Linh District of Hai Duong province in the Red River Delta of northeastern Vietnam which collects data from 16,689 households with 57,161 inhabitants in three townships (Sao Do, Pha Lai, and Ben Tam) and four communes (An Lac, Le Loi, Van An, and Hoang Tien).

Heavy consumption of alcohol was found in 31.4% of men in the FilaBavi site (where the mean level of alcohol consumption was 5.3 standard drinks per day) and 17.3% in the CHILILAB site. Another 53.2% of men in the FilaBavi site and 68.5% of men in the CHILILAB site were rated as moderate drinkers, defined as men who consumed four or

fewer drinks per day. Although women generally drink much less than men in Asian countries and rates of at-risk drinkers among women were very low in Viet Nam, the highest proportion of moderate drinkers (those who consumed fewer than four drinks per day) among women was found in the CHILILAB site (29.1%). In the FilaBavi site, 14.0% of women were moderate drinkers.

Cultural factors may influence alcohol consumption in Viet Nam where at special events drinking and sharing alcohol are considered a means for strengthening friendship. In addition, home-brewed alcohol is very popular in Vietnam, and is produced and consumed in a large percentage of households, particularly in rural areas and by those with lower income. The total production of this type of alcohol has been estimated to be over a quarter million liters per year. Unfortunately, this home-brewed alcohol is made in a traditional and primitive way and often contains poisonous substances, making its consumption very risky.

In earlier stages of alcoholic liver disease, there may be few if any symptoms. In more advanced stages, symptoms experienced by the person with alcoholic liver disease may include anorexia (appetite loss), nausea and vomiting (sometimes with blood), abdominal pain and tenderness, jaundice, ascites (fluid accumulation) which may cause very noticeable abdominal swelling, mental confusion, fatigue, thirst, dry mouth, pale appearance, lightheadedness, and unexpected rapid weight gain. Such symptoms may worsen after binge drinking. Diagnostic tests may include blood tests (liver enzymes), ultrasound, and liver biopsy.

Complete abstinence from alcohol is the most effective treatment for alcoholic hepatitis, although a message of moderation would be at least a first step to decrease unhealthy consumption of alcohol. With less advanced disease, abstinence may allow reversal of liver damage. With more advanced disease, abstinence may at least help prevent disease progression. Without abstinence from alcohol, the majority of people with alcoholic hepatitis will eventually develop cirrhosis. When alcoholic liver disease is apparent, it is appropriate for healthcare workers to refer patients to counseling and alcohol support groups, where available. Other treatments may include:

- Nutritional therapy to reverse the malnutrition that is common with ALD and that may contribute to liver damage. A nutrient-rich diet may help liver cells regenerate. Reducing dietary fat may also be helpful because alcohol interferes with the normal metabolism of fatty acids, leading to alcoholic fatty liver. Medium-chain triglycerides (MCT's) may be recommended since they provide a good source of calories and may help reduce the buildup of harmful fats in the liver. Coconut oil is an easily available source of MCT's in Viet Nam. Supplementation of the vitamins and minerals that are often depleted by excessive alcohol consumption is advisable, particularly of the vitamins B-1, B-2 and B-6 and the minerals calcium and iron.
- Smoking cessation should be advised since smoking may increase the rate of cirrhosis development in people with alcoholic hepatitis,

- Avoidance of other illicit drugs should be advised since they could further worsen liver damage.
- In advanced stages with severe alcoholic hepatitis, drug treatments that may be considered include the short-term use of corticosteroids (only in rare cases) to reduce inflammation, as well as treatment with drugs that may reduce liver inflammation by inhibiting tumor necrosis factor-alpha, including pentoxifylline.
- Antioxidant nutrient supplements may be helpful because free radicals and other reactive oxygen species cause damage to liver cells in ALD. Countering this with antioxidant nutrients that boost glutathione production in the liver, including N-acetyl-cysteine and alpha-lipoic acid, may be useful.
- Liver transplant may be the only remaining option when liver function is severely impaired. A specific action plan for the initiation of liver transplantation will be outlined in a separate document.

## **NON-ALCOHOLIC FATTY LIVER**

In the least problematic and most common form of nonalcoholic fatty liver disease, simply termed nonalcoholic fatty liver, excess fat develops in the liver, but there are generally no complications. In the much less common form called nonalcoholic steatohepatitis (NASH), the excess fat causes significant inflammation in the liver, impairing liver function and leading to complications that may include cirrhosis, liver cancer, and liver failure. Risk factors for development of nonalcoholic fatty liver disease include:

- Certain medications
- Hyperlipidemia, including both elevated cholesterol and elevated triglycerides
- Malnutrition
- Metabolic syndrome
- Obesity
- Rapid weight loss
- Exposure to toxins and chemicals, including pesticides
- Type 2 diabetes
- Wilson's disease

In the last two decades in Viet Nam, there has been an increase in some of these risk factors, including heart disease and diabetes,<sup>41</sup> possibly presaging a coming increase in fatty liver disease. Nonalcoholic fatty liver disease is often asymptomatic. When symptoms do occur, the most common are fatigue, pain in the upper right abdomen, and weight loss. Diagnostic procedures can include liver enzyme and liver function tests, imaging tests, including ultrasound, computerized tomography (CT) scan and magnetic resonance imaging (MRI), and liver biopsy. In Viet Nam today, there is a movement

toward replacing liver biopsy with non-invasive tests such as Fibroscan. There are no specific treatments for nonalcoholic fatty liver disease. Rather, any risk factors that appear to be possible contributors to the problem are addressed.

## LIVER CANCER

Liver cancer includes many tumor types, with HCC being the most common, and cholangiocarcinoma occurring much more rarely. A recent large nationwide study found that liver cancer is the most common cause of cancer death in Viet Nam.<sup>1</sup> This study collected cancer mortality data from almost all (94.6%) of the 10,769 commune health stations which provide health services in Viet Nam.<sup>1</sup> Over the two full years in which data were collected (2005-2006), liver cancer caused 25,410 deaths, accounting for 27.1% of all cancer deaths (31.04% of deaths in men and 19.91% of deaths in women). It is thought that over 90% of these liver cancer deaths reflected the high prevalence of hepatitis B virus (HBV) infection in Viet Nam.<sup>42</sup> In people with CHB, the risk of developing HCC sharply increases with advancing age.<sup>43</sup> HCV infection also contributes to the risk of liver cancer. In one study, of 100 patients diagnosed with HCC in Hue City, the majority had evidence of CHB (85% were HBsAg+; HBV DNA was detected in 65.5%); almost one in seven patients had evidence of HCV infection (anti-HCV was detected in 19% and HCV RNA in 14%).<sup>44</sup>

The death rate for HCC patients depends on treatment availability, with an estimated 80% annual death rate in industrialized nations, and a 90% rate in developing countries.<sup>32</sup> Liver transplantation and occasionally surgery are the only current cures for HCC. Other treatments (most commonly some type of ablative therapy) are generally only palliative and in general have only short-term survival benefits. Ablative therapy includes embolization, chemoembolization, radiofrequency ablation, alcohol injection and destroying cancerous tissue by freezing or heating tumors.

For prevention of liver cancer in Viet Nam, the first long-term focus should be to vaccinate all uninfected individuals for HBV, thus effecting primary prevention of all liver cancers that are directly related to this virus. In addition, for liver cancer prevention it will be important to use the best available treatments to profoundly suppress HBV and HCV in those with chronic infection. As discussed above, without proper treatment of CHB, the risk of developing cirrhosis and HCC with sequelae of liver failure and death is 25-30%.<sup>14-18</sup> Long-term suppression of HBV with effective antivirals can substantially reduce this risk.

HCV-infected patients with advanced fibrosis or cirrhosis are likely to develop HCC if they do not previously succumb to complications of cirrhosis. Effective and timely treatment of HCV has the possibility of eliminating the infection before the disease has reached the stage where there is a high risk of development of HCC. Even when the infection is not eliminated, there are apparent benefits to treatment that may ultimately lower the risk of HCC, although not eliminating it completely. Another important part of a strategy to reduce liver cancer in Viet Nam is to address alcoholic liver disease and

fatty liver disease well before they reach the stage that can lead to cancer. Research is needed concerning nutrient, herbal and other therapies that may decrease the risk of liver cancer.

Another important focus for preventing liver cancer deaths is the use of the best available screening and surveillance protocols to help diagnose patients at earlier stages of their cancer, thus bringing more patients to liver transplantation and other forms of treatment when smaller, more “curable” tumors are present. Proper utilization and interpretation of imaging tests should be emphasized in order to decrease both false positive and false negative rates.

## **OVERCOMING CHALLENGES**

There are many challenges that exist in Viet Nam related to providing the type of total integrated approach to liver disease that could substantially decrease both morbidity and mortality. This is a developing country with a relatively low annual per capita income (approximately \$1024 USD)<sup>45</sup> and very limited annual per capita spending on health care (according to WHO, approximately 264 international dollars, 2006). Consideration of the current barriers to prevention and management of liver disease in Viet Nam and approaches to overcoming these challenges is a crucial part of our liver disease project.

### ***Barriers to Effective Prevention and Control of Hepatitis Viruses***

In early 2010, the Institute of Medicine (IOM) in the US released an in-depth report entitled *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*<sup>46</sup> which noted the urgent need to address these diseases and discussed three major factors currently impeding efforts to prevent and control them: (1) lack of knowledge and awareness about these diseases among health-care and social-service providers; (2) lack of knowledge and awareness about these diseases among high-risk populations, as well as the general public and policy-makers; and (3) insufficient knowledge of the extent and seriousness of liver diseases resulting in inadequate public resources being devoted to prevention, control, and surveillance programs.

Although this report was related to the situation with hepatitis virus infection and liver cancer in the US, the same factors impede efforts to prevent and control these problems in Viet Nam. An effective, integrated response to liver disease in Viet Nam requires increased awareness by healthcare professionals, policy makers, and the general public about the importance of targeted screening and testing for infection. Educational programs thus need to be directed toward all these groups, with a particular need for medical education directed to healthcare providers, as emphasized by recent surveys showing that even in the US 30%-55% of healthcare providers would order the wrong test to screen for HBV infection<sup>26</sup>. In addition, it will be very important to educate the general public on the risks of untreated HBV infection, and the major benefits of HBV screening, including vaccination to provide lifelong protection, prompt evaluation and

treatment of people with active hepatitis and/or incipient liver failure, and early identification and treatment of HCC.

### ***Medical Care Limitations and Resources for Education, Screening, Vaccination and Treatment***

Approximately 70-75% of Viet Nam's 84 million people dwell in rural and mountainous regions where medical care is substantially limited compared to that which is available in the cities. As a result of this and the asymptomatic nature of earlier disease stages, many patients infected with HBV and/or HCV are only seen when they reach the very advanced stage of liver disease when effective treatment is no longer likely.

The commune health centers in Viet Nam could be a valuable resource for addressing this, providing education on HBV and HCV infection and on CHB and CHC, as well as carrying out screening for both viruses, providing HBV vaccination, and providing treatment, where indicated. The commune health centers are at the base of the four levels into which the public health care system is divided in Viet Nam (central, provincial, district and commune). Because these commune health centers already have information flowing to and from the Ministry of Health (the national level), the Provincial Health Bureaus (the provincial level), and the District Health Divisions (the district level), a national mandate to improve liver disease education, screening, vaccination, and treatment could efficiently reach the local commune level. According to a 2005 report on the human resources for healthcare in Viet Nam, almost all of the 10,769 communes have a health center where commune health workers provide both primary health care and most preventive health care activities.<sup>41</sup>

However, the report points out that there are major disparities in the quality of health care available in different parts of the country. There are medical doctors working in more than 80% of the commune health centers in the Red River Delta region, the Southeast region, and the Mekong River Delta region. There are medical doctors in only a bit more than half of the commune health centers in the Northeast region (52.7%), the North Central Coast region (51.0%), the South Central Coast region (54.9%), and the Central Highlands (52.7%). In the Northwest Region, only 22.8% of the commune health centers have medical doctors. However, other healthcare workers, including assistant physicians, nurses, midwives, and village/ward health workers, provide services in the centers. Providing the commune health centers with simple accurate guides on proper screening and vaccination procedures for HBV, screening for HCV, and treatment for those with CHB and CHC, could reach a substantial proportion of the population nationwide.

However, not all people use the services of the public commune health centers. Private health care services having been officially recognized in Viet Nam in 1989, a community-based survey conducted in 30 of the 160 communes in Hung Yen found that at least in this rural area there were more private providers (11.5) per 10,000 population than public providers (6.7 per 10 000).<sup>47</sup> Unfortunately, 11 percent of the private providers had no professional qualifications. In order to determine the quality of health

care provided by both the public commune health centers and the private providers, the survey looked at the services provided, the medical equipment and pharmaceuticals that were available, the quality of health personnel in terms of their medical training, and the quality of professional performance of the health care providers related to diagnosis and treatment of selected common health problems.

The overall quality of services by both the public providers and the private providers was determined to be of relatively low quality, falling below Viet Nam's national standard, although the quality provided by public providers was rated as significantly better than that of the private providers. However, both private providers and commune health center staff scored poorly in the area of chronic disease. It could be much more difficult to reach the private providers to try to enlist them in the campaign to improve HBV-related services since this survey found that fewer than one in five had registered their practice with the government system.

In addition, less than two-thirds of private facilities (61%) have any Western healthcare workers (medical doctors, assistant doctors, or nurses); only about one in three has a medical doctor; approximately one in four has only an assistant doctor.<sup>41</sup> Traditional practitioners (those who practice the traditional folk medicine of Viet Nam) make up 17% of the private practitioners. It may be possible to enlist the help of traditional practitioners and others not trained in Western medicine for improving hepatitis and liver disease-related services, as has been successfully done in Africa for HIV/AIDS prevention and care.<sup>48</sup>

Other particularly valuable resources for an effective campaign against HBV and HCV infection are the non-profit health organizations and non-governmental organizations (NGOs) that provide health care in Viet Nam, especially for the poor. In particular, the Viet Nam Red Cross Society plays an important role in providing primary health care at the commune level. All provinces and almost all communes (95.7%) have a Red Cross Society branch that provides services including free health checks for the poor and other vulnerable groups, including children, the elderly, and women.<sup>41</sup> Enlisting the Red Cross Society's help in the campaign against liver disease might be invaluable.

Regardless of the healthcare setting, one of the largest obstacles to overcome is healthcare providers' current lack of awareness about the extent of liver disease in Viet Nam and lack of knowledge about appropriate screening, treatment, and monitoring of patients. There are not enough hepatologists (liver specialists) to treat liver disease throughout Viet Nam. Unfortunately, among primary care physicians there is too often greatly inadequate knowledge about treatment of both HBV and HCV, as well as inadequate knowledge about non-alcoholic fatty liver and alcoholic liver disease and appropriate monitoring for liver cancer. The result is inadequate and inappropriate patient care in far too many cases. This categorically must be addressed in order to improve treatment outcomes for patients with liver disease.

It will be crucially important to ensure adequate training of physicians and other health care workers who provide primary care to people in Viet Nam, including in particular the

provision of current information on screening, vaccination, and treatment of HBV; screening and treatment of HCV; diagnosing and addressing non-alcoholic fatty liver disease and alcoholic liver disease; and the prevention, early detection and case management of liver cancer. Educational programs on these topics which are directed to health care professionals, including nurses, physicians, public health professionals, and pharmacists, are urgently needed. As discussed under Task 1, below, a combination of approaches for improving medical education in this regard could be one of the most important components of an integrated approach to liver disease in Viet Nam.

### ***Infection Transmission in Healthcare Settings***

Re-use of contaminated needles, syringes, and inadequately sterilized medical equipment is another major challenge that must be addressed to counter transmission of the hepatitis viruses that lead to a large proportion of liver disease in Viet Nam. In general, in many developing countries, the risk of healthcare-associated transmission of HCV, HBV, and other pathogens is high because of the re-use of contaminated syringes and needles in medical, paramedical and dental procedures.<sup>36,37</sup> It is estimated that worldwide in the year 2000, injections with contaminated syringes and needles in healthcare settings caused two million HCV infections, 21 million HBV infections, and 260,000 HIV infections, accounting for 40% of new HCV infections, 32% of new HBV infections, and 5% of new HIV infections.<sup>49</sup> Southeast Asia is one of the three regions in the world identified as having the highest reported rate of re-use of contaminated needles, along with the Middle East and Western Pacific.<sup>37</sup>

As is mentioned above, in Viet Nam, recent studies have shown that major risk factors for HBV infection include a history of hospitalization and a history of acupuncture,<sup>9</sup> as well as a history of surgery.<sup>8</sup> A 1994 study found that the prevalence of HCV was particularly high in Ho Chi Minh in patients who required medical treatment that potentially exposed them to this blood-borne virus through contaminated medical devices or blood products, including patients on maintenance hemodialysis (54%) and those with hemophilia (29%).<sup>12</sup> It is particularly troubling to consider that the failure to address the use of contaminated medical equipment and contaminated blood products could leave patients with such chronic conditions as kidney disease and hemophilia with only the terrible choice of remaining untreated, or being treated but at the risk of acquiring a very serious infection.

Education on the risks and absolute unacceptability of re-using needles and syringes and of inadequate sterilization measures related to hospital equipment will be very important to counter this avenue of infection, preferably combined with governmental initiatives and mandates against these vectors of infection. Such education and mandates should extend to the traditional medicine practices, as well. Traditional medicine practitioners clearly need to be educated on the risks of re-using needles or unsterilized knives. Currently, there are no clear-cut policies and a lack of standardization related to medical equipment sterilization in hospitals, health care centers, and medical and dental offices. Government regulation to prevent re-use of needles and syringes and to mandate

appropriate standards on sterilization of medical equipment is a very important component of an overall approach to reducing liver disease in Viet Nam. As is discussed further below, the cost effectiveness of such measures has been clearly shown.

Another risk in the healthcare setting is the possibility of transmission of infections (HBV, HCV, or HIV) from a healthcare provider to a patient and vice versa. In general, universal precautions—the consistent and proper use of protective barriers such as gloves, gowns, masks, and protective eyewear—are presumed to provide protection for healthcare workers by preventing parenteral, mucous membrane, and non-intact skin exposures of healthcare workers to bloodborne pathogens. However, there is not always perfect consistency in the use of universal precautions by healthcare workers. It is important that clear guidelines on universal precautions always be given to all healthcare workers and that hospitals, clinics and physician’s offices consistently maintain high standards on this. Infection control committees at hospitals and clinics should set standards on this, and institute the policies and procedures necessary to enforce the standards that are needed to protect healthcare workers.

Conversely, although the risk for transmission from an infected provider to a patient during the provision of routine healthcare is quite low, the risk increases with higher viral loads (the amount of virus circulating in the bloodstream) in the infected person. Updated guidelines regarding the management of healthcare workers who are infected with HBV, HCV, and/or HIV have recently been released by the Society for Healthcare Epidemiology of America (SHEA).<sup>50</sup> The complete guidelines are available online at: <http://www.journals.uchicago.edu/doi/full/10.1086/650298> or at: [http://www.shea-online.org/Assets/files/guidelines/BBPathogen\\_GL.pdf](http://www.shea-online.org/Assets/files/guidelines/BBPathogen_GL.pdf)

The guidelines note that restriction from working as a healthcare provider is not justified when these conditions are well managed and the provider practices in a safe, competent way. However, specific recommendations for additional precautions are given based on the presence of infection and the viral load of any provider. Specifically, the guidelines recommend the routine use of double-gloving for all invasive procedures, for all contact with mucous membranes or non-intact skin, and for all instances in patient care for which gloving is recommended for any provider in the following categories:

- (1) HBV-infected providers who test either positive for HBV “e” antigen or test negative for it but who have an HBV viral load equal to or greater than 10<sup>4</sup> genome equivalents (GE) per milliliter (mL) of blood;
- (2) HCV-infected providers who have circulating HCV viral burdens of greater than or equal to 10<sup>4</sup> GE/mL;
- (3) HIV-infected providers who have circulating HIV viral burdens of greater than or equal to 5 x 10<sup>2</sup> GE/mL.

In addition, the guidelines specify that providers in any of those categories should not perform Category III activities associated with a risk for provider-to-patient transmission of bloodborne pathogens despite the use of appropriate infection prevention procedures.

The Category III restricted procedures include general surgery, oral surgery, cardiothoracic surgery, open head and neck surgery involving bones, neurosurgery, open resuscitation efforts, obstetrical or gynecological surgery, orthopedic procedures, plastic surgery, transplantation surgery, trauma surgery, and lengthy open surgical procedures. The guidelines also recommend that infected healthcare providers not interact with violent or seizure-prone patients who might bite them. Education based on these guidelines should be provided for all healthcare workers in Viet Nam. The guidelines should be made available to healthcare facilities nationwide.

Last but not least, there remains in many healthcare settings the possibility of transmission of HBV or HCV via blood transfusions and other blood products. It is now widely known that the safest source of blood is from regular and repeat voluntary unpaid blood donors. Paid, family and replacement donors are all higher risk groups than voluntary unpaid blood donors. According to the World Health Organization (WHO), Viet Nam has made substantial progress on this, increasing the rate of voluntary blood donations from less than 15% in 1994 to more than 65% currently.<sup>51</sup> These increases were in large part the result of intensive campaigns in Viet Nam's largest cities. However, the country still suffers from a chronic shortage of blood, and more funding and staffing is needed to improve donor recruitment.

Screening for HIV, HBV, HCV, malaria and syphilis is compulsory for all blood donations. Both "rapid" and ELISA tests are used and these have greatly reduced the risk to patients of infection transmission. Utilizing the latest and most sensitive tests alongside nucleic acid tests is of the utmost importance. In order to further reduce transfusion risks, WHO reports that there is an urgent need to develop quality assurance systems in blood centers and blood banks nationwide.<sup>51</sup> WHO recommends the creation of a national blood service in Viet Nam in order to improve coordination in the sector, unify practices, build upon developing blood bank networks, and maximize the use of limited resources combined with parallel development of a national blood policy that would define the roles and responsibilities within such a national blood service.

### ***Injecting Drug Users***

Re-use of contaminated needles and syringes by injecting drug users (IDUs) is another substantial contributor to transmission of hepatitis viruses in Viet Nam. It is estimated that illicit use of injectable drugs accounts for 40% or more of HCV infections in developing countries worldwide.<sup>35</sup> The prevalence of HCV has been shown to be extremely high (87%) in IDUs in Ho Chi Minh<sup>12</sup> and in northern Viet Nam (74.1%).<sup>24</sup> The prevalence of HBV among IDUs in northern Viet Nam has also been shown to be extremely high (80.9%).<sup>24</sup> Among IDUs in Hanoi, it has been shown that HCV is acquired relatively quickly after the onset of injection, with a prevalence of 30% in heroin users with ten or fewer months of injection risk and 70% in those with 30 or more months of injection risk.<sup>34</sup> Researchers who have studied this population in Viet Nam have strongly recommended interventions that target new heroin users, including

interventions that improve the users' understanding of viral transmission, that promote alternative strategies for drug sharing, and that delay initiation of injection.<sup>34</sup>

Outreach harm reduction programs to educate IDUs about risks, generally combined with needle/syringe exchange programs, have been used in other countries to successfully reduce the risk of infection in this population. To date in Viet Nam, most such efforts have focused on reducing HIV infection rates since the majority of HIV infections in this country (52%) are estimated to come from injection drug use.<sup>52</sup> However, as discussed above, there is also an extremely high risk of acquisition of both HBV and HCV from needles and syringes re-used by IDUs.

A 1998 study indicated the feasibility of establishing needle/syringe exchange programs in Viet Nam.<sup>53</sup> The researchers reported that the key requirements for success with such programs are: (1) recruitment and training of ex-user outreach workers; (2) workshops with key community members, including the local police, to increase community acceptance of the program; (3) use of outreach services to distribute clean syringes/needles; and (4) use of appropriate methods to collect used injection equipment.

The Vietnamese government has supported harm reduction through needle/syringe exchange. In 2002, the Vietnamese Ministry of Health initiated a national community-based outreach program for IDUs that includes referrals to pharmacy-based syringe and needle access services, using a modified version of WHO's *Training Guide for HIV Prevention Outreach to Injection Drug Users*.<sup>54</sup>

In January 2007, Viet Nam's Law on HIV/AIDS Prevention and Control came into effect, providing the legal foundation for substantially expanded harm reduction services.<sup>52</sup> This law specifically calls for the implementation of harm reduction, including promotion of clean needles and syringes (as well as condoms) and medically assisted addiction treatment.

A number of international donors have provided substantial funding for expanding needle/syringe exchange in Viet Nam, including the Asian Development Bank, the Canadian International Development Agency (CIDA), the United Kingdom's Department for International Development (DFID), the German Agency for Technical Cooperation (GTZ), the Australian Agency for International Development (AusAID), and the Ford Foundation.<sup>52</sup> The funds go to various components of harm reduction programs, including training, technical assistance, employing peer outreach workers to distribute sterile injection equipment, funding clinics, and providing IDUs with vouchers for new needles/syringes which are redeemable at pharmacies.

The use of pharmacies to deliver clean needles/syringes may be the most efficient way to carry out this aspect of harm reduction. In a 2006 study carried out in two districts in Hanoi, pharmacies succeeded in delivering twice as many syringes as the peer educators employed by district needle/syringe exchange programs.<sup>52</sup>

A recent study of a harm reduction, needle/syringe exchange program in northern Viet Nam found that it contributed to a shift toward safe injecting practices by IDUs, as well as safe disposal of used needles and syringes.<sup>55</sup> Advocacy activities promoting a public health approach to IDUs were used to address initial resistance to the program by local government officials and members of the community.

The resulting reduced community discrimination encouraged IDUs to participate in the free needle/syringe exchange program, as well as other project services provided by peer educators. The safe disposal component of the program not only reduced the potential for harm within the community (from accidental exposure to contaminated injection equipment), it also positively influenced community attitudes.

The most clearly identified obstacle to the potential success of this northern Viet Nam needle/syringe exchange program was the periodic action of police against IDUs. The researchers noted that for the program to be successful would require gaining the support of law enforcement officials, and that this would require ongoing sustained efforts. The same problem has been identified nationwide in Viet Nam where police crackdowns have made many IDUs reluctant to use exchange services for fear of being arrested.<sup>52</sup>

Despite all the funding and the government's support for harm reduction that includes needle/syringe exchange, the overall access to clean syringes/needles nationwide is still quite limited. A 2007 study in Viet Nam found that in the previous half year, 90% of IDUs in seven provinces had no access to sterile injection equipment.<sup>52</sup> Additional work is clearly needed in this area to reduce the risk of infection with HBV, HCV, and HIV through re-use of contaminated needles/syringes.

### ***Commercial Re-Use of Needles and Razors: Tattoo Artists and Barbershops***

Although tattoos and body piercing were once scorned in Viet Nam as being the province of only criminals or gang members or ex-soldiers, they have become much more popular in recent years. There are many tattoo artists nationwide whose customers range from well-known entertainers to urban youth who think of the tattoos as a form of art or a fashion statement. Unfortunately, it is not uncommon for needles and sometimes knives to be re-used in tattoo shops. In one study, one of the two main risk factors associated with HCV acquisition was having tattoos.<sup>33</sup>

The re-use of razors in barber shops could be a risk factor for HBV transmission. In one recent study, household sharing of razors was identified as a major risk factor for HBV infection,<sup>9</sup> and the same risk would apply to commercial re-use. As part of a total approach to preventing liver disease, educating barbers and tattoo shop personnel about the risks inherent in re-use of needles, knives, or razors is very important.

## *Language and Literacy Limitations*

The difficulty of providing education to all of Viet Nam's people on the need for screening and HBV vaccination is increased by the fact that there are at least 54 ethnic groups throughout the country, each with its own language. Although the majority of the people are the Vietnamese (Kinh, also called Viet, approximately 85.73% of the population) whose native language is Vietnamese, there are significant numbers of people whose native tongue is that of one of the ethnic minorities. The largest ethnic minorities in Viet Nam, in descending order of population size, are: the Tày, 1.97% of the population; the Thái, 1.79%; the Mường, 1.52% ; the Khmer Krom, 1.37%; the Hoa (Chinese), 1.13%; the Nùng, 1.13%; the H'Mông, 1.11%; and the Dao (the Yao people, also known as Mien), just under 0.5%.<sup>45</sup> Just these eight minority groups include over nine million people (over 10 percent of the population). There would be no possibility of providing completely effective nationwide educational outreach on liver disease without reaching the minority groups.

Although developing educational materials in all the languages spoken in Viet Nam might be overwhelming difficult, for the best educational outreach, it would be important to at least develop them in the languages spoken by the largest minority groups where a significant part of the population may only be truly fluent in their native language.

- An estimated 1.7 million Tày people live in Viet Nam, mostly in the northern Viet Nam provinces of Cao Bang, Lang Son, Bac Kan, Thai Nguyen, and Quang Ninh, with some also in parts of Bac Ninh and Bac Giang provinces. Their native language is Tày.
- The second largest minority group in Viet Nam, numbering approximately 1.5 million, are the Thái whose native language is Thai.
- Another language spoken by a sizable minority in Viet Nam is Mường, primarily spoken by the approximately 1.3 million Mường people who live in the mountainous regions of the northern Vietnamese provinces of Hòa Bình, Thanh Hóa, Vinh Phúc, Yên Bái, Sơn La, and Ninh Bình.
- There are an estimated 1.2 million Khmer Krom people in Viet Nam, living mostly in the Mekong Delta region in the provinces of Trà Vinh and Sóc Trăng, who speak their Khmer Krom dialect of Khmer.
- There are an estimated 970,000 Hoa (ethnic Chinese) people in Viet Nam, living mostly in Ho Chi Minh City, Can Tho, Bac Lieu, Da Nang, Kien Giang, and Quang Ninh. Although the younger generation of Hoa in Viet Nam tends to speak both Vietnamese and Cantonese, the native language of most Hoa people (and the only language spoken by many in the older generation) is either Cantonese or Teochew (Chaozhou).
- There are also an estimated 970,000 Nùng people in Viet Nam. They are located mostly in the provinces of Bac Giang, Bac Kan, Cao Bang, Lang Son, Thai Nguyen, and Tuyen Quang.

- There are an estimated 950,000 H'Mông people in Viet Nam whose native language is H'Mông.

The provision of effective educational materials may be particularly problematic in areas where there are multiple ethnic groups, some of whom may speak only their own language. For example, in Lào Cai province, with its high estimated prevalence of HBV, the ethnic minority groups include the H'Mông, Tày, and Dao people. Thus, to fully educate the people in this area, it would be important to provide educational materials in not only Vietnamese but also in Tày, H'Mông, and the Iu Mien language spoken by the Dao people (an estimated 350,000 of whom live in Viet Nam). In any of the areas where sizable minority populations reside, it will be important to have educational resources that use the languages of those ethnic minorities.

Literacy rates are another problem related to educating people on the need for screening and vaccination. Although in Viet Nam as a whole, literacy rates are high, a report issued by the Ministry of Education and Training in 2008 estimated that there are still approximately 1.7 million illiterate people nationwide. Even in large cities, there are a substantial number of people who cannot read, including 235,000 in Ha Noi City, 90,000 in HCM City, and 60,000 in Long An. According to the report, literacy rates are the lowest in people over 36 years old who live in the northern mountainous provinces, Tay Nguyen (the Central Highlands) and the Cuu Long (Mekong) River Delta.

Literacy rates are particularly low among ethnic minorities. According to UNESCO National Committee General Secretary Pham Sanh Chau, only 77 per cent of ethnic minority people can read and write. In some minority groups, literacy rates are particularly low. For example, among Tày people, the largest ethnic minority, literacy in their own language is thought to be probably around 5% or less. This does not obviate the need for written materials in the Tày language, but it adds the additional need for educators fluent in Tày who can present the information orally, either in community settings or via video. The same need for speakers fluent in the local language will be true for any area where the literacy rate is low.

### ***The Costs of Addressing Liver Disease***

The costs associated with any program of education, screening, vaccination, and treatment may present a serious problem in a country with very low per capita health care expenditure. It may even be difficult to obtain funding for educational programs, much less for the more expensive parts of a truly comprehensive integrated approach to liver disease. However, the cost effectiveness of treating liver disease, as discussed further below, should absolutely be considered.

In addition, a large percentage of people in Viet Nam do not have any type of health insurance or other health care coverage and even those who do may not have full coverage. Thus, much of the expense of vaccination, screening tests, and any treatments will generally be paid by patients or their families, a considerable obstacle in this country

with an estimated per capita income of only approximately \$1024 USD (2008).<sup>45</sup> It will be important to consider the cost effectiveness of providing free vaccination nationwide, as well as free or low-cost treatment, where needed, as part of a strategy to reduce the impact that low income has on successful prevention of liver disease.

## **COST EFFECTIVENESS**

In simple terms, looking at the cost effectiveness of a program to prevent liver disease in Viet Nam means looking at the costs of screening, vaccination, treatments, and other interventions that could ultimately help prevent liver disease and comparing those up-front costs to the potential benefits down the line from the disease prevention versus the outcome if there is no intervention. In looking at outcomes, cost effectiveness studies incorporate loss of quality of life as well as actual loss of years of life by using what is called the disability-adjusted life year (DALY), with one DALY equal to the loss of one healthy year of life.

According to the World Health Organization, an intervention is defined as “cost effective” when each DALY averted costs between one and three times the GDP per capita. An intervention is defined as “very cost effective” if each additional DALY is prevented at a cost less than the per capita gross domestic product (GDP).<sup>56</sup> As already discussed, in Viet Nam today, the estimated per capita GDP is \$1024 USD.<sup>45</sup>

A major review of studies of the cost effectiveness of hepatitis B vaccination found that in areas of low, intermediate and high endemicity, universal vaccination is generally cost effective.<sup>57</sup> A cost-effectiveness analysis of universal childhood HBV immunization in low-income countries with intermediate endemicity found it to be very cost-effective.<sup>58</sup> In terms of CHB prevention efforts in Viet Nam, a cost effectiveness analysis might include many variables, including the cost of the HBV vaccine; the vaccine’s effectiveness (about 95 percent); vaccine compliance rates; likely infection, disease and mortality rates with and without the intervention; and the cost of treatment and other health care costs for HBV-infected and uninfected people over their lifetimes, based on current health-care costs in Viet Nam.

Although a national study to assess the cost effectiveness of a nationwide program to prevent CHB in Viet Nam has not yet been done, a recent study in China gives strong support for the likelihood that it would be very cost effective. In this study, it was shown that if China spent \$423 million to provide free “catch-up” vaccination to an estimated 150 million unvaccinated children (all children ages 1 to 19 who were not vaccinated at birth), it would produce a net return in the economy of \$840 million from lower health-care costs.<sup>59</sup> Their model also predicted that the vaccination program would prevent 8 million infections along with 65,000 deaths.

Thus, the initial monetary costs of the program would be greatly outweighed by the costs savings from avoiding the need to treat millions of people for CHB for many years, and ultimately preventing the need for very expensive late-stage liver disease treatments

when people develop cirrhosis and liver cancer. In addition, there would be huge savings in terms of preventing loss of quality of life and actual loss of years of life in a very large number of people. The program in China would meet the international standard for being judged cost effective when judged in terms of per capita gross domestic product (currently \$2459 USD in China).<sup>60</sup>

Studies have also shown the cost effectiveness of substituting safe injection practices in health care settings for the re-use of syringes and needles that currently leads to inadvertent transmission of multiple infections, including HBV, HCV, and HIV.<sup>61,62</sup> One large study by the World Health Organization showed that in all regions of the world studied, policies for the safe and appropriate use of injections would be highly cost effective.<sup>61</sup>

Overall, it is highly likely that the costs of a proactive approach to liver disease that includes institution of safe injection practices, nationwide neonatal and catch-up HBV vaccination, nationwide screening for HBV infection with follow up that includes vaccination or treatment, appropriate screening for HCV with follow up that includes assessment and, where possible, treatment, and monitoring for liver cancer combined with education on liver disease for both the public and healthcare providers would be very cost effective when compared to the ultimate costs of failing to address liver disease and allowing millions of people to progress toward cirrhosis, liver cancer, and death.

## **FIVE-YEAR PLAN**

It is both timely and extremely urgent to create a scientifically based project that addresses the fast-growing problem of liver disease among the Vietnamese population. A comprehensive approach should combine updated public health methods (including health education, health economics, health administration, epidemiology, health information, biostatistics, health systems, health planning, and health policy) with a state-of-the-science medical approach that includes screening, immunization, detection, and treatment. With the looming threat of a rapidly growing liver disease burden in Viet Nam, this program needs to be strategically planned and effectively implemented as soon as possible.

We propose here a five-year plan to address liver disease in Viet Nam. The project will include the design and implementation of a comprehensive health promotion program to educate the Vietnamese public, to train health professionals, and to provide screening, vaccination, and treatment services to the Vietnamese population. Integration with current health systems in Viet Nam will be an essential part of this program development. In order to achieve the goal of culturally sensitive and competent health systems, our proposed five year project includes the ten major tasks discussed below.

### ***Task 1: Education of the Vietnamese Population***

One of the most important parts of our project will be educating the Vietnamese public about liver disease, with particular emphasis on education related to HBV screening, vaccination, and treatment, HCV screening and treatment, and the contribution to the overall burden of liver disease from alcohol consumption and non-alcoholic fatty liver disease. This program will apply three major communication channels, including person-to-person, group education, and mass media. Structured interviews, surveys, and focus groups will identify the best educational intervention strategies, the most efficient messages, the most cost-effective messengers, and the most effective materials.

The strategies will be selected and applied depending on the educational targets, including patients, the public, health professionals, and health policy makers. The strategies used will depend on the targets' educational levels. We will test and use a variety of resources for educational messages. For example, celebrity endorsement, dramatic interaction, documentary, or factual presentation formats might be selected for video spots. The actual approaches for each medium will be assessed by focus groups in order to review and decide on the most effective presentation approaches to communicate with the targeted audience. In general, what is called the Shoemaker's four-stage approach will be applied to provide knowledge and create awareness of the population (Stage 1), to convince people to change attitudes and behaviors (Stage 2), to lead people to make decisions about changing (Stage 3), and to help people confirm and continue the changes (Stage 4). Stages 1 and 2 are usually relatively easy to achieve, but Stages 3 and 4 can be very difficult.

As discussed above, the commune health centers in Viet Nam could be an extremely valuable resource for achieving success with Task 1. Because these commune health centers already have information flowing to and from the academic and hospital community, the Ministry of Health, the Provincial Health Bureaus, and the District Health Divisions, a national mandate to improve HBV education, screening, vaccination, and treatment could efficiently reach the local commune level. Since almost all of the 10,769 communes have a health center where commune health workers already work to provide both primary health care and most preventive health care activities, they could be trained both to provide education on HBV infection and CHB and to carry out screening, followed by vaccination and treatment, where indicated. In addition, the District Health Divisions already have teams that provide education and assistance in specific areas (such as Hygiene and Epidemiological). Thus, these health workers at both the commune and district levels could be an invaluable resource for this project when properly educated about screening, vaccination, and treatment.

Where necessary, additional health educators can be selected and trained in health education on liver disease, so that they can perform person-to-person health education activities in such settings as policy makers' offices, health centers, physicians' offices, pharmacies, barber shops, and hair salons, as well as group education sessions at gathering points such as waiting rooms in hospitals, churches, temples, senior centers, community centers, schools, universities, music performance, health fairs, and food markets. In addition, the mass media can promote awareness via articles in Vietnamese or

English language newspapers and magazines, posters, pamphlets, flyers, and television or radio talk shows.

### ***Task 2: Training of Health Providers***

This program will include both regular classroom educational seminars and online CME courses. With the collaboration of expert consultants, we will design and conduct CME seminars to update and improve the knowledge base of medical professionals regarding all aspects of liver disease in Viet Nam. While the classroom setting continues to be a popular format for CME, research indicates that it results in a significantly lower level of behavior change than the computer-based CME approach, often referred to as internet or e-learning CME. Because time available to physicians for CME is so limited, the approach must be flexible, permitting physician learners to re-review the materials as frequently as desired.

Online CME courses will consist of a series of e-learning modules for health professionals focusing on screening, vaccination, and treatment of HBV; screening and treatment of HCV; and the prevention, early detection and case management of liver cancer. There will also be CME courses to provide education on the risks and absolute unacceptability of re-using needles and syringes and of inadequate sterilization measures related to hospital equipment. In addition, there will be a CME course on guidelines for healthcare providers who are infected with HBV, HCV, and HIV; the guidelines on this recently released by the Society for Healthcare Epidemiology of America (SHEA) can be used as the basis for this CME.<sup>50</sup> The complete guidelines are available online at: [http://www.shea-online.org/Assets/files/guidelines/BBPathogen\\_GL.pdf](http://www.shea-online.org/Assets/files/guidelines/BBPathogen_GL.pdf). Additional CME courses will provide information on treating and preventing alcoholic liver disease and non-alcoholic fatty liver disease. These internet CME courses will be available to all health professionals nationwide, including physicians, public health professionals, pharmacists, and nurses.

### ***Task 3: Data Collection and Analysis***

We will create a comprehensive nationwide hepatitis B and C surveillance system. There will be targeted active surveillance to collect and monitor data on incidence and prevalence of hepatitis B and C virus infection, as well as capturing data on other liver diseases such as alcoholic liver disease and non-alcoholic fatty liver disease. As part of this, the program will include conducting scientific samples of the population, using the medical records of hospitals and health centers, to collect and analyze data on the incidence and prevalence of all of these liver diseases. Both a Health Information System and Health Information Technology will be established to build reliable and valid databases on hepatitis, liver diseases, and liver cancer in the Vietnamese population. Electronic Medical Record (EMR) and Personal Health Record (PHR) systems will be partially established.

#### ***Task 4: Screening and Vaccination***

Another crucial part of our project is to expand screening for HBV. Screening for HBV will be performed at the Commune Health Centers and at the gathering points indicated in Task 1. After the screening, recommendations will be made to individuals with negative results who are not immune to do the vaccination series either at the Commune Health Center or at the office of their primary care physician. Three vaccination shots are required within a six-month period. Patients with test results that show that they have chronic infection with HBV will be referred to the Commune Health Centers, to primary care physicians, or to physician specialists for assessment. In addition, as part of this task we will work to help ensure that all hospitals and clinics have in place a written policy for newborn hepatitis B vaccination, and that healthcare providers are knowledgeable about this standard of care.

As is discussed above, since the prevalence of HCV infection is suspected to be higher than 2% overall, HCV screening should also take place in the initial sites for HBV screening. Based on the data for the first 5000 patients screened for HBV and HCV, a decision can be made on whether to call for nationwide HCV screening or to focus on high-risk groups only.

#### ***Task 5: Treatment of CHB and CHC and Linkage to Care***

As is discussed above, CHB can be effectively treated in a way that leads to durable viral suppression and reversal of liver disease, substantially decreasing the risk of progression to cirrhosis, liver cancer, death, or the need for liver transplantation. [A specific action plan for the initiation of liver transplantation is outlined in a separate document.] CHC is also treatable and in some cases curable. Educational programs and materials will be developed to help ensure that up-to-date information on treating CHB and CHC is available to Commune Health Centers, primary care physicians, physician specialists, and private health care providers so an appropriate treatment program can be recommended to patients who are screened and found to have chronic infection with one or both viruses.

#### ***Task 6: Alcoholic Liver Disease and Fatty Liver Disease***

As is discussed above, alcoholic liver disease (ALD) is another major contributor to the overall burden of liver disease in Viet Nam. ALD in combination with CHB, CHC and/or fatty liver is an even more serious disease. In addition, non-alcoholic fatty liver disease is rapidly emerging as a serious liver disease in all developing countries. Counseling about healthy eating will be one key to decrease the weight trajectory that we see in all countries that can contribute to the development of fatty liver. In addition, it will be important to educate both the public and health professionals about the need to address other risk factors for the development of fatty liver, including type 2 diabetes, heart disease, exposure to pesticides, and malnutrition. Educational materials on alcoholic liver disease and non-alcoholic fatty liver disease and resources available for addressing

them will be developed as part of this project. In addition, we will look into setting up a consultation network concerning alcoholic liver disease and non-alcoholic liver disease.

### ***Task 7: Liver Cancer Toolbox***

We will develop, test and evaluate an educational toolbox of medical interventions and educational materials to inform and educate the Vietnamese public and their health care providers about the relationship between HBV and liver cancer. We will use a variety of assessment tools to determine the most effective intervention strategies and the best educational messages.

The toolbox will incorporate Vietnamese culture and medical ethics, particularly the Ethics for Vietnamese Health Professionals by Hai Thuong Lan Ong, a Vietnamese physician in the 18<sup>th</sup> century. Briefly, Hai Thuong Lan Ong listed the 8 “Do’s” for physicians, including concern for others, brightness, intelligence, virtue, generosity, honesty, modesty, studiousness, and the 8 “Do Not’s” for physicians, including laziness, stupidity, immorality, narrow-mindedness, cruelty, lying, stinginess, and eagerness for money. As we go forward with our project, we will pledge to uphold the highest standards of medical ethics, as expressed in The World Medical Association Declaration of Geneva in 1948 and the International Code of Medical Ethics in 1949. Key principles of these codes that we pledge to follow include "respect and gratitude to the teachers," "extreme confidentiality to the patients," "brotherhood between colleagues," and "honor to the noble traditions of the medical profession."

### ***Task 8: Training of Health Educators***

We will include as part of our project approaches to improving the knowledge, awareness, attitude and behavior of health educators related to the high risk of HBV and HCV, and the need for screening for both viruses, vaccination against HBV, and treatment for CHB and CHC. We will select, train and manage educators and messengers who can plan and perform effective intervention tasks, either in community health centers or in outreach activities.

The goal will be to increase screening, testing and, for HBV, vaccination rates, followed by treatment of CHB and/or CHC, where appropriate, ultimately leading to reduction of illness and death rates from these infections. As more fully discussed above, the health educators that are part of the current health system will play an important role in carrying out this task.

In addition, where needed, additional health educators may be selected among health professionals (such as nurses, pharmacists, physicians, public health educators, and social workers) as well as other people who regularly come in contact with the public such as musicians, singers, teachers, hair stylists, and barbers. Health educators will be tested for qualification and performance and then will be trained in health education, counseling,

health behavior, and cultural adaptation. Assessment of existing educational materials and development and testing of new materials will be performed to select materials that can be effectively used within the constraints of the Vietnamese language, behavior, and culture. Website material delivery will be applied to satisfy on-demand printing and the quick download of digital audio-visual and preformatted educational tools.

### ***Task 9: Cost and Health Care Quality***

As part of this project, we will work to design and promote methods which can manage costs while maintaining quality. Quality must be controlled using quality assurance and quality improvement methods including practice guidelines, criteria, Joint Commission standards, and indicators. Costs must be considered and justified by analyses showing cost effectiveness.

We will use the World Health Organization definitions of cost effectiveness, as discussed above, and will calculate the disability-adjusted life year (DALY) for Viet Nam in order to incorporate loss of quality of life as well as actual loss of years of life in our cost effectiveness analyses. Based on such assessments, decisions can be made about which approaches are the worst and the best values.

### ***Task 10: Reducing Infection Transmission Related to Medical, Commercial, and Personal Re-Use of Contaminated Needles, Syringes, Sharp Instruments, Razors, and Inadequately Sterilized Medical Equipment***

As is discussed above, a key step for countering liver disease in Viet Nam will be to address the current high risk of infection with hepatitis viruses from re-use of contaminated needles, syringes, and inadequately sterilized medical equipment in healthcare settings, including not only in both public and private hospitals, clinics, and physician's offices but also in traditional medicine practices. As part of this project, we will seek to work in partnership with the Ministry of Health, the National Institute of Hygiene and Epidemiology, and other government entities in Viet Nam which provide guidance on infection control.

We will also seek to cooperate with other organizations already working in this area, including PEPFAR (the US President's Emergency Plan For AIDS Relief). Currently, in collaboration with the Ministry of Health's Vietnam Administration for HIV/AIDS Control (VAAC) and the World Health Organization (WHO), PEPFAR is helping develop national injection safety guidelines, providing training related to dissemination of these guidelines, and procuring sharps disposal equipment for eight focus provinces. As part of our project, we will assess what we may contribute to these efforts.

We will also assess how we may contribute to the development and nationwide dissemination of guidelines for proper sterilization of medical equipment such as that used for dialysis. The goal will be to help ensure that healthcare providers nationwide will have clear guidance on the risks and absolute unacceptability of re-use of contaminated needles, syringes, and inadequately sterilized medical equipment, and that all healthcare settings will adhere to the guidelines for injection safety and proper disposal of injection equipment, as well as to guidelines for proper sterilization of medical equipment. Within this task, we will also assess how to best reach traditional medicine practitioners with clear information on these risks, and training on properly following injection safety guidelines.

As part of this task, we will also assess how we might provide additional resources to help expand the success of harm reduction projects, including needle/syringe exchange programs. Although, as previously discussed, most such efforts to date have focused on reducing HIV infection rates, there is also an extremely high risk of acquisition of both HBV and HCV from needles and syringes re-used by IDUs. As discussed above, the recent peer educator-based syringe/needle exchange program carried out in northern Viet Nam showed both the feasibility of carrying out such programs, and their potential to reduce unsafe injection practices while providing safe disposal of used injection equipment, thus protecting community members from accidental exposure to contaminated equipment. As part of our task we will reach out to the ongoing programs working in this area to see how we might contribute.

It will also be important to address the risk of infections from commercial re-use of needles and other sharp instruments in tattoo parlors, and of razors in barbershops. As part of this task, we will investigate the best approaches for reaching out to these commercial enterprises in order to provide guidance on eliminating unsafe practices by barbers and tattoo artists nationwide.

### ***Task 11: Project and Performance Evaluation***

An expert evaluation team will perform process evaluation for each of the tasks defined here, as well as outcome evaluation for the entire project. Both qualitative information and quantitative data will be collected, analyzed, and reported by the evaluators for adjustment under formative evaluation and for final report under a formal/summative evaluation. Convenient samples of patients in commune health centers, selected clinics, and selected pharmacies who have been screened or vaccinated for hepatitis B will be statistically analyzed for effectiveness. Samples of people at the gathering points will be selected for pre-post knowledge, attitude, and practice changes. Evaluation forms at health education training meetings and health professionals' training sessions will be analyzed to assess training effectiveness and trainers' performance. Evaluation reports will be submitted during and after the project life to indicate the achievement of project goals and objectives.

## CONCLUSION

The combined results of an integrated approach to liver disease in Viet Nam are highly likely to significantly help to turn the tide against this disease, preventing HBV infection of the uninfected, providing effective treatment of all the causes of liver disease, to the greatest extent possible, substantially lowering the risk of liver cancer and the death rate due to acute and chronic liver disease, and substantially decreasing the future need for liver transplantation, thus generally improving the lives of affected individuals while greatly reducing the associated healthcare burden.

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