TRAINING MANUAL FOR TREATMENT ADVOCATES: 
Hepatitis B, Hepatitis C, & Coinfection with HIV
This Manual was collaboratively developed by the Treatment Action Group (TAG) and the Thai AIDS Treatment Action Group (TTAG). It is written by Tracy Swan, Lei Chou, Karen Kaplan, and Paisan Suwannawong. The authors gratefully acknowledges the extraordinary contributions of the following people:

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This Manual is also available in Thai.

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The purpose of this manual is to help you get access to care and treatment for viral hepatitis, for yourself, and your community. The information here is written for people who are not medical specialists. It is designed to help you understand the background to hepatitis B and C and HIV coinfection issues.

This manual is organized into short sections, and each section can be shared with a small group of people in less than one hour. There are discussion points at the end of some sections that may be useful for people to start talking about the issues they face in the community, and provide an opportunity for people to find solutions together.

Foreword by the Thai AIDS Treatment Action Group:

As Thai people living with HIV have demonstrated, using information to inspire action, for example in the fight for universal access to antiretroviral therapy, can be very successful. It’s time to start thinking about co-infection issues and ensure our CCC centers are able to provide the HBV and HCV services we need.

HBV and HCV/HIV co-infection is a serious issue in Thailand, especially among people who inject drugs. Studies show that up to 96% of people who inject drugs are living with HCV. We believe knowledge = power, so with this manual we begin the road to knowledge about HBV, HCV and HIV. We start with basic knowledge so you can understand your body and help your friends do the same.

Ultimately, we want to fight for the highest standard of prevention, care and treatment for HBV, HCV and HIV coinfection in Thailand.
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Section 1: About Hepatitis
Hepatitis means swollen liver

Hepatitis is a general term for swelling (inflammation) of the liver (hepa is the Greek word for liver, and itis means swollen). Many things can cause your liver to become swollen, including:

- Drinking a lot of alcohol;
- Taking certain medications or herbs;
- Inhalng toxic fumes
- Viral hepatitis infections, or
- Other kinds of infections such as leptospirosis.

Viral Hepatitis

There are five different viruses that can get into the liver (infection) and cause disease: Hepatitis A, B, C, D, and E. These viruses were named alphabetically, in the order that they were discovered. Each of these viruses causes disease differently, and most people don’t know they are infected, because there are usually no symptoms.

**Hepatitis A (HAV)**
HAV infection is usually not serious, but sometimes it can make people feel very ill. There are no treatments for HAV because the body usually clears the virus by itself, and people recover without treatment. It rarely causes liver damage, and HAV is very rarely fatal.

**Hepatitis B (HBV) & Hepatitis C (HCV)**
HBV and HCV are the two most serious hepatitis viruses. Some people can clear HBV and HCV without treatment, but HBV and HCV can also become chronic (lifelong) infections. There are different treatments available for chronic HBV and HCV, and some people can even be cured. Although not everyone with chronic HBV or HCV will need treatment, some people will develop serious liver damage, liver cancer and liver failure without treatment. Most deaths from liver disease are caused by chronic HBV and HCV.

**Hepatitis D (HDV)**
HDV only occurs in people who already have HBV, who may have been infected at the same time. A person cannot get HDV unless they have hepatitis B. Some people can clear HDV without treatment, but it can also cause sudden liver failure. HDV can become chronic, and can make HBV worse.

**Hepatitis E (HEV)**
HEV can have symptoms but will go away on its own. It is usually not serious, but can become life threatening during pregnancy, particularly in the third trimester.
Viral Hepatitis can Cause Serious Liver Disease

Chronic HBV and HCV are “silent” illnesses that usually do not have symptoms until the liver becomes seriously damaged, or complications such as liver cancer have developed, years after people got infected. Many deaths from serious liver disease could have been prevented by people getting diagnosed with chronic HBV or HCV earlier, so that they could have started treatment when they needed it. Learning more about viral hepatitis and sharing the information with your community can help save many people’s lives.

Viral Hepatitis Vaccines can Prevent Infection

There are vaccines to prevent HAV and HBV, but there is no vaccine to prevent hepatitis C, although researchers are working to develop one. People can become infected with more than one hepatitis virus at the same time, and they can also be coinfected with HIV. Coinfection with more than one virus can make you sicker, which is why people who have chronic HCV and/or HIV should be vaccinated against HBV and HAV.

Advocacy Exercise: This section of every chapter is provided to help community educators and advocates help their peers and communities to see the importance of HIV/viral hepatitis education and advocacy. The questions below are intended as sample questions, and you can come up with your own additional questions to invite discussion about HIV and viral hepatitis in your communities.

Discussion Questions:
1. Do you know someone who died from liver disease?
2. Can deaths from liver diseases be prevented?
3. What can you do to help prevent liver disease for your and your community?

Action Steps:
1. Are people interested in learning more about viral hepatitis?
2. Do you know others who might be interested?
3. How can you use this training manual to share information about viral hepatitis with others in your community?
Hepatitis A

Virus found in: Feces (stool; shit)

You can get hepatitis A when: Feces from a person with hepatitis A virus gets into your mouth, such as:

- Drinking water containing sewage (when a sewage pipe breaks, or during flooding);
- Eating food handled by someone with HAV who didn’t wash their hands;
- Eating raw shellfish or fish from contaminated water;
- Unprotected sex – rimming (licking someone’s asshole; mouth to anus).

You cannot get hepatitis A from: casual contact (kissing, shaking hands, sharing glasses or eating utensils).

You can only get infected with HAV once.

- Most people in Thailand have already gotten HAV during childhood. HAV has become less common in Thailand as sanitation has improved.

You can protect yourself against hepatitis A by: getting vaccinated, although it is expensive.

Symptoms: Most children don’t feel sick at all; some adults have symptoms, including: nausea, vomiting, diarrhea, fever, fatigue, rash, jaundice (yellow skin and eyes), liver pain, dark brown urine.

Hepatitis A: is not a chronic (lifelong) infection: it goes away by itself, usually within two months.

You can find out if you have already had hepatitis A by: getting blood tests that tell if you have already been infected, or if you need the vaccine.

Treatment: There is no treatment for HAV; Almost everyone can clear the virus on their own.

Outcome: VERY rarely life-threatening, but people with HCV are at risk for liver failure if they get HAV.
Hepatitis B

Virus found in: Blood, semen, and vaginal fluid (very small amounts of HBV have also been found in breast milk and saliva).

You can get hepatitis B: Mostly the same ways as HIV.

- Sharing drug use or tattoo equipment: including needles, water, cooker, cotton, measuring syringes, and tattoo ink and inkwells;
- Unprotected anal or vaginal sex with a person who has HBV;
- Mother-to-child during birth;
- Sharing personal care items that may have blood on them, such as razors and toothbrushes.

You cannot get hepatitis B from: casual contact (kissing, shaking hands, sharing glasses or eating utensils).

You can only get infected with HBV once.

- About 5% to 10% of people in Thailand have chronic (life-long) HBV; most were infected during birth.

You can protect yourself against hepatitis B by: getting vaccinated

- Since 1992, the hepatitis B vaccine has been included in Thailand’s universal childhood vaccination program.

Symptoms: most children do not have symptoms; some adults (30-50%) have symptoms during the first few months after getting HBV (also called the acute phase): nausea, vomiting, appetite loss, fever, fatigue, abdominal and joint pain, liver swelling, and jaundice (yellow skin and eyes). In very rare cases symptoms may be very severe and can be fatal (called fulminant hepatitis).

Hepatitis B can become a chronic (life-long) infection: in less than 5% of healthy adults. Hepatitis B is more likely to become chronic in people infected at birth or during childhood (90%), and in HIV-positive people.

You can find out if you have hepatitis B by: getting blood tests; they can tell if you cleared hepatitis B without treatment, if you just got it, or if you have chronic hepatitis B.

Treatment: Chronic Hepatitis B can be treated with pegylated interferon, or oral antiviral drugs. Treatment can suppress HBV, but less than 10% are able to clear it. When people stop HBV treatment, hepatitis B usually comes back, so treatment with oral antiviral drugs is usually life-long. Once HBV treatment has begun, it is important to talk to your doctor before stopping or switching medications, to avoid risk of HBV flare-ups, which can be life-threatening.

Outcome: If untreated, about 25% of people with chronic HBV will develop cirrhosis, liver cancer and/or end-stage liver disease. Hepatitis B is worse in people who are coinfected with hepatitis C.

HIV Coinfection: All HIV positive people should be screened for HBV.

HIV makes HBV worse; it is more likely to become chronic, progresses more quickly and is harder to treat. Some HIV drugs are active against both HIV and HBV, such as: lamivudine (3TC), emtricitabine (FTC), and tenofovir (Viread).
Hepatitis C

Virus found in: Blood (very small amounts have been found in semen and vaginal fluid).

You can get hepatitis C when: blood from a person with HCV infected person enters your body. Hepatitis C is a much smaller virus than HIV, so there is more of it in a drop of blood. Bleach doesn’t kill it. Up to 90% of IDUs have hepatitis C.

- Sharing drug use or tattoo equipment – including needles, measuring syringes, water, cookers, cotton, and tattoo ink and inkwells;
- Unprotected sex (especially if you have a sexually transmitted infection such as herpes, syphilis, or HIV) that involves blood: rough anal or vaginal sex, fisting, etc are riskier;
- Mother-to-child during birth;
- Sharing personal care items that may have blood on them, such as razors and toothbrushes.

You cannot get HCV from: casual contact (kissing, shaking hands, sharing glasses or eating utensils).

You can get hepatitis C more than once, even if you already cleared it with treatment or, by your own immune response.

You can protect yourself against hepatitis C by: using clean injection equipment, getting checked and treated for other sexually transmitted infections, using condoms for vaginal and anal sex and gloves for fisting. There is no HCV vaccine (but researchers are working on preventive and therapeutic vaccines).

Symptoms: most people have no symptoms when first infected; about 20% will experience nausea, abdominal pain, appetite loss, fatigue, jaundice (yellow skin and eyes), and dark urine.

Hepatitis C: becomes chronic (lifelong) in 55-85% of people; the rest clear the virus without treatment.

You can find out if you have hepatitis C by: blood tests. They can tell you if you cleared hepatitis C without treatment, if you just got it, or if you have chronic hepatitis C.

Treatment: hepatitis C can be treated—and cured—with a combination of pegylated interferon and ribavirin, but HCV treatment does not always get rid of the virus, and the side effects can be severe. New therapies are currently in development.

Outcome: 20-30% of chronically infected people will develop cirrhosis (serious liver scarring) over decades. Each year, 1-5% of people with cirrhosis develop liver cancer. Hepatitis C is worse in people who are coinfected with hepatitis B.

HIV Coinfection: All HIV positive people should be screened for HCV.

HIV makes HCV worse: it is more likely to be chronic, progresses more quickly, and is harder to treat.
Section 2: About the Liver
The liver is a very important organ in the body that has many critical functions. When the liver is damaged (such as by chronic viral hepatitis), it cannot work properly. Liver damage can lead to life-threatening complications, such as cirrhosis, liver cancer and liver failure.

The Liver Performs Many Important Functions

The liver is the biggest organ inside the human body, found on the right side, underneath the rib cage. Your liver works as a filter and processing plant for your body. Anything you eat, drink, and inhale passes through the liver. Your liver also breaks down drugs—whether or not they are legal—and herbal remedies, and vitamins.

Each day, your liver
• filters waste from the blood;
• stores vitamins, minerals, and iron;
• changes food into energy;
• makes bile (a liquid that your body uses to digest fat);
• helps balance sugar and hormone levels;
• makes cholesterol; and
• creates the hormone that helps to produce platelets (which stop bleeding by clotting blood)

Immune Response to Viral Hepatitis Infection Causes Liver Damage

HBV and HCV do not directly cause liver damage—the way a person’s immune system responds to the infection is what causes the liver to become damaged. The immune system tries to get rid of infected liver cells by surrounding them and walling them off, and this creates scarring in the liver. Although the liver grows new cells, they cannot become unscarred. As the scarring worsens, the liver hardens, making it harder for blood and other important fluids to pass through it. These fluids, which are usually filtered by the liver, can build up to toxic levels in the bloodstream when the liver is too damaged to function.
Liver damage from HBV and HCV happens slowly, usually over decades. It can take from 15 to 50 years for an HIV-negative person who has chronic viral hepatitis to develop cirrhosis.

Some things cause liver damage from viral hepatitis to happen faster.

- Being HIV-positive—especially if you got HBV or HCV after you became HIV-positive;
- Being coinfected with HBV and HCV;
- Drinking alcohol;
- Age over 40;
- Being male (but researchers don’t understand why);
- The amount of time you have had chronic hepatitis—the longer a person has been infected, the more likely he or she is to develop liver damage.

Having chronic HBV or HCV does not always mean that you will have serious liver damage, or that you need treatment. Some people live with viral hepatitis for many years, and will never have liver damage; they will die from other, unrelated causes.

Some people develop mild liver scarring, called fibrosis. Having HBV or HCV and being overweight can cause fat to build up in the liver, a condition called steatosis. People with steatosis are at higher risk for liver damage.

Serious liver scarring, called cirrhosis, happens over decades. Compensated cirrhosis means the liver is still able to function even though it is scarred. People with compensated cirrhosis are at risk for liver failure and other serious complications. Liver failure, also called decompensated cirrhosis, or end-stage liver disease (ESLD), means that the liver can no longer do its job, and a liver transplant is necessary.

Liver cancer (also called hepatocellular carcinoma, or HCC) is very serious. It is very difficult to treat, especially if it is not caught early.

Preventing the development of liver damage and disease by suppressing HBV and getting rid of HCV are the primary goals of HBV and HCV treatment.

Liver Health

Alcohol can be Harmful to the Liver

Alcohol is hard for the liver to break down, even in people who don’t have viral hepatitis. In people with hepatitis, alcohol hurts the liver by increasing inflammation and scarring (cirrhosis). Heavy drinkers with viral hepatitis are more likely to develop cirrhosis.
Drinking Less Alcohol is Good for the Liver

Even though experts have not agreed on a safe amount of alcohol, they do agree that the less that a person with hepatitis drinks, the better. Some studies found that men who drink 50 grams (4-5 mixed drinks, or shots of lao khao, or glasses of wine, or small bottles of beer) of alcohol a day or more, and women who drink 30 grams (2-3 servings) of alcohol a day or more are at higher risk for liver damage than people who drink less, or not at all.

Quitting or cutting down on drinking can be very difficult, but drinking less—or not at all—may be the most important thing a person with hepatitis can do to prevent liver damage. Drinking lots of water can help flush out alcohol and other toxins from your system, It helps your liver to drink as much water as possible, especially if a person also drinks alcohol.

HCV Treatment can be Harder When People Also Drink Alcohol

Some experts think that hepatitis treatment does not work as well for people who drink alcohol. One reason for this may be that people who are heavy drinkers often have more hepatitis C virus in their blood than non-drinkers. Many doctors will not treat people for their hepatitis C if they are drinking alcohol, either because they don’t think treatment will work, or they are concerned that a person won’t be able to take medication on a regular basis.

Drug Use

People who are regular users of heroin and methamphetamine may not be getting enough sleep or eating well, and may be under a great deal of stress. People who don’t have access to clean injection equipment are at risk for HIV, HBV, HCV, as well as other infections. For these reasons, drug use—especially on a daily basis—can have a negative impact on a person’s health. However, there is not enough information to say whether or not drugs actually cause or worsen liver damage in people with chronic hepatitis.

Street Drugs and the Liver

Since heroin and methamphetamine are illegal, there is very little research or information on whether or not these drugs cause liver damage in people with chronic hepatitis. Most research on street drugs has been done in vitro, which means in a test tube, not in vivo (in the human body). What happens inside the human body is often very different than what happens in a test tube, so it is hard to know how the results from an in vitro study relate to what actually happens in a person’s body.

The purity of “street drugs” (illicit drugs) varies. The other substances that are added to street drugs may be harmful to the liver, although the drug itself may not be. This makes it more difficult to know if using street drugs has an effect on chronic hepatitis.
Regular use of marijuana (one joint or more per day, over several years) can cause fibrosis faster in people with chronic HBV and HCV, but occasional use of marijuana has not been found to be harmful.

**Prescription Drug Use**

Some people use prescription drugs to get high. This can be risky because they may interact with other medications, causing lowered or increased drug levels in a person’s body. If drug levels are too low, medications may stop working, and in some cases—such as HIV medications and antibiotics—resistance can develop. Drug levels that are too high can also be dangerous, since they can increase drug toxicity and side effects, or cause an overdose.

For example, midozolam interacts with alcohol, caffeine, sleeping pills, some antidepressants and anti-anxiety drugs, hormonal contraception (birth control pills), some of the drugs used to treat TB, fungal infections, high blood pressure, heart problems and even cold medication (among others).

Benzodiazepines, a family of drugs that includes midozolam, diazepam, rohypnol and xanax are addictive. Withdrawal symptoms seizures, psychosis, and the “rebound effect”, where insomnia or anxiety return, and are worse than what someone experienced before they started using these drugs.

**Drug Overdose**

The risk of overdosing on certain prescription drugs (alprazolam, diazepam, midozolam, triazolam, fentanyl and lidocaine) may be higher in people with cirrhosis (serious liver scarring) from chronic hepatitis, since some drugs are broken down by the liver.

**Other drugs**

Some antibiotics, traditional medicines, herbs, and certain food supplements can be hard on the liver. Discuss anything that you are taking with your doctor.
Section 3: Epidemiology (Who has it) of HBV, HCV & HIV Coinfection
GLOBAL HBV PREVALENCE:
Worldwide, there are 400 million people living with chronic Hepatitis B.

GLOBAL HCV PREVALENCE:
Worldwide, at least 130 to 170 million people have been infected with hepatitis C.
Source: World Health Organization (WHO) 1999

GLOBAL HIV PREVALENCE:
Worldwide, there are more than 33 million HIV-positive people.
GLOBAL PREVALENCE OF HIV/HBV and HIV/HCV COINFECTION

Two to four million people are HIV and HBV coinfected.
Four to five million people are HIV and HCV coinfected.

HIV, HBV, and HCV in Thailand

In Thailand, UNAIDS estimates that 580,000 people are HIV-positive. According to the World Health Organization (WHO), 5% to 15% of the people in Southeast Asia have chronic HBV. The WHO also estimates 32.3 million people in Southeast Asia have been infected with HCV. A small study of drug users in Northern Thailand reported that 86% had hepatitis C.

Coinfection with HIV and HBV is common, since both viruses can be passed on in the same ways. One large study found that 8.7% of HIV-positive people in Thailand also have HBV.

At least 50% of injection drug users (IDUs) in Thailand are HIV-positive, and up to 90% of Thai injection drug users have HCV. Since both HIV and HCV are found in blood, and passed easily by injection drug use with shared, unsterilized equipment, most people who got HIV from injecting drugs are coinfected with HCV. In fact, 88-96% of HIV-positive current and former Thai IDUs are coinfected with HCV.
Section 4.1: HBV Transmission & Prevention
Hepatitis B virus can be spread through blood, semen, and other body fluids (very small amounts of HBV have been found in breast milk and saliva). HBV is much smaller, and is 100 times more infectious than HIV. HBV can survive outside of the body for up to 7 days.

The most common ways HBV can be passed on are:

- From mother to infant during birth;
- Having unprotected anal or vaginal sex with someone who has HBV;
- There is also a low risk with unprotected oral sex;
- Sharing drug injection equipment, including needles, cookers, ties, cotton, straws, water and even measuring syringes;
- Sharing personal care items that may have blood on them, such as razors or toothbrushes;
- Getting a tattoo with any shared, unsterilized equipment, such as needles, ink, and inkwells;
- Getting a contaminated blood transfusion;
- Accidental needle-stick injuries or other occupational hazards.

You cannot get hepatitis B from casual contacts such as kissing, shaking hands, sharing glasses or eating utensils.

**HBV Prevention**

**HBV Vaccine**

Unlike HIV or HCV, there is an effective vaccine against HBV. The HBV vaccine is safe and more than 90% effective. The vaccine works by stimulating your immune system to fight off HBV.

There are two different schedules, one is 3 shots over a 6-month period, the other is 4 shots over a 12-month period. Ask the clinic or doctor when you should return to complete your vaccine series.

**Who should get it?**

Since 1992, HBV vaccination for newborns has been part of Thailand’s National Expanded Program of Immunization. In addition to infants, people who are at risk for HBV, such as people who have a family member with HBV, healthcare workers, people with end-stage renal disease who are on kidney dialysis, people with hemophilia (a hereditary blood clotting disease), HIV positive people, people at high risk of sexual exposure (such as gay men, other men who have sex with men, and sex workers), IV drug users, and people who have chronic liver disease, should all be vaccinated according to various recommendations.
Adults born before 1992 in Thailand who are at risk for HBV should get a blood test to find out if they need to be vaccinated.

**How long does it work?**

The protective effect of the HBV vaccine may also wear off over time, so if you were vaccinated more than ten years ago, it is a good idea to ask your doctor to do a test (called an AntiHBs immunizing antibodies titer) to see if you need a booster shot (another shot of the vaccine) to keep up the protection.

**HBV Vaccine and HIV**

The HBV vaccine does not work as well for HIV positive people who have lower CD4 cell counts (< 200). HIV treatment can boost CD4 cell count, but some people have a low CD4 cell count even when they are on treatment. Sometimes boosters, or a higher dose of HBV vaccine will work for HIV-positive people with lower CD4 cell counts.

**Mother-to-Child Transmission**

HBV can be easily passed from mother to infant. The majority of people with HBV were infected at birth.

**Prevention for Infants**

Since mother-to-child transmission of HBV can be prevented, it is important for all pregnant women to be screened for HBV. Mothers with HBV can protect their babies by making sure the first dose of HBV vaccine is given to the newborn within 12 hours of birth.

Two to three more shots (depending on which vaccine schedule is used) are needed to complete the series over the first year. Ask your doctor how many more shots your baby will need and when you should come back to get them.

Infants can also get a shot of hepatitis B immune globulin (HBIG; a product made from blood plasma that contains antibodies that protect against HBV) for additional protection, especially if the mother has a very high HBV viral load. HBIG is very expensive and it may not be available where you live. One study in Thailand has shown that 85% of infants born to mothers with HBV can avoid the infection with just the vaccine.

Mothers who are HIV/HBV coinfected should be on HIV treatment (See HBV treatment section for more information). This will help prevent the transmission of HIV to the baby.
Breastfeeding

HBV has been found in breast milk, but studies have shown that it is safe to breast feed when the baby is vaccinated against HBV at birth. However, HIV can be passed from mother to infant from breast milk. Breastfeeding is not recommended for HIV positive mothers.

Some important considerations about the use of ARVs for prevention

Sometimes people are given ARVs to prevent HIV, such as when someone is accidentally exposed to HIV (non-occupational HIV post-exposure prophylaxis, or nPEP), or for pregnant mothers with high CD4 counts to prevent HIV transmission to her baby.

One of the ARVs used for prevention in these circumstances is 3TC (lamivudine), which is also an HBV treatment. It is very important to test for HBV before giving anyone lamivudine or tenofovir to prevent HIV. People who have HBV need to avoid using these two drugs for HIV prevention, because stopping them can cause serious, possibly life-threatening HBV flares. Other ARVs can be used instead.

Advocacy Exercise:

Discussion Questions:

1. Do people in my community know how to protect themselves against HBV?
2. Can people get free condoms and clean injection equipment?
3. Have you been vaccinated against HBV? Do you know where to get vaccinated? Is it free?

Action Steps:

1. What can we do to teach others about HBV prevention?
2. How can we increase access to condoms and injection equipment?
3. How can we make sure people who need HBV vaccine can get it for free?
4. How can we make sure people living with HIV can get screening for HBV and vaccination, if necessary, covered under the national health care system?
Section 4.2: Natural History of HBV
(What happens to people infected with HBV?)
Hepatitis B virus infects cells in the liver and can cause serious liver disease. The virus itself is not harmful to liver cells. Liver damage can happen when the body’s immune system recognizes and attacks HBV-infected liver cells. Over time, this causes liver scarring that can gradually make it harder for the liver to function. Liver scarring is a slow process that can take many years to decades. HBV can also cause liver cancer.

**HBV Infection at Birth**

The course of HBV disease differs, depending on when someone is infected. Babies infected at birth usually have no symptoms, but 90% will develop chronic (lifelong) HBV. There is usually no liver damage for many decades, because the immune system does not recognize HBV infection until people infected at birth are older (35-40 years).

**HBV Infection in Adults**

When an adult gets HBV, the body’s immune system can fight off HBV on its own in a majority of people. Only about 6% of people infected as adults will develop chronic disease. Liver damage can develop faster in people who get HBV as adults than people infected at birth.

**Acute HBV**

Some (30-50%) will have symptoms in the first few months (this first stage is also described as acute infection). Acute HBV infection usually lasts between one to three months. Symptoms can include nausea, vomiting, appetite loss, fever, fatigue, abdominal and joint pain, liver swelling, and jaundice (yellow skin and eyes). In very rare cases, these symptoms can become very severe (fulminant hepatitis) and potentially fatal.

**Chronic HBV**

Usually, people with chronic HBV do not have any symptoms for many years to decades, so they don’t know that they are infected. Although most people with chronic HBV do not need treatment, about 25% will develop liver scarring (cirrhosis) and liver cancer. Liver damage happens very slowly, and people don’t feel sick until it is serious, and too late for treatment. Timely HBV treatment can help prevent cirrhosis and liver cancer. In Thailand, most people do not find out they have HBV until they already have liver cirrhosis and/or liver cancer.
Blood Tests for Different Types of Chronic HBV

Chronic HBV is a very complicated disease, and the pattern of the disease and treatment can be different depending on:

- Early or late stage chronic HBV; and
- Strains of the HBV virus.

There are two blood tests that are needed to determine which type of chronic HBV someone has and how to treat it.

1. HB e antigen (HBeAg):

This test looks for a small piece of the hepatitis B virus, called the “e” antigen that can be found in the blood when HBV is making copies of itself during the earlier phase of chronic HBV (HBeAg Positive). But in some people, over time, HBV can still reproduce without making HBeAg (HBeAg Negative). Because the pattern of chronic HBV disease is different between people who are HBeAg Positive and those who are HBeAg Negative, finding out your HBeAg status is important for making treatment decisions.

People who are HBeAg positive are in an earlier phase of chronic HBV, and most of them are generally younger (under age 35). Some people who are HBeAg positive can have a high viral load and no liver damage. This is because the immune system is not yet reacting to HBV and treatment is not needed. However, the immune system will activate in some people who are HBeAg positive, and treatment will be needed to control the virus. If treatment is effective, HBeAg positive people may be able to stop treatment 6-12 months once the virus is under control.

People who are HBeAg negative are in a later phase of chronic HBV. Most are older (over age 35) and HBV has mutated and no longer makes HBeAg when it is making more copies of the virus. People who are HBeAg negative can have inactive disease and won’t need treatment, but some can have low viral loads and still have active liver damage. Current treatments are highly effective in controlling the virus. Unfortunately, HBV will come back in most HBeAg negative people if treatment is stopped, so they will likely need to stay on treatment for life.

2. HBV Genotype:

This test checks to see which strain—or genotype—of HBV a person has. There are eight different HBV genotypes (from type A to H). In Asia, the most common genotypes are B and C. People who have genotype C tend to have more severe liver disease and are at higher risk of developing liver cancer than genotype B, but it is not clear if treatment should start earlier in people with genotype C. Although this information can be useful, genotype testing is very expensive and very few people have access to it outside of clinical trials.
HIV/HBV Coinfection: Impact of HIV on Hepatitis B

HBV is more likely to become chronic in HIV positive people; 30 to 90% develop chronic HBV, because their immune system is weakened by HIV and cannot clear the virus. It is important for HIV positive people to find out if they have HBV for several reasons. Chronic HBV is more serious in HIV positive people. HIV/HBV coinfected people have more hepatitis B virus in their blood (called viral load) than people with HBV alone. A higher viral load makes HBV harder to treat. HIV can speed up development of liver damage and liver cancer, especially in people with low CD4 cell counts (< 200).

Advocacy Exercise:

Discussion Questions:

1. Why is it important to find out if you have chronic HBV?
2. Do HIV positive people in your community know about HBV coinfection?

Action Step:

1. What can we do to educate others about chronic HBV and prevention of serious liver disease and cancer?
Section 4.3: HBV Diagnostic Tests
The first step in finding out if someone has HBV is by taking a blood screening test. The test looks for either small pieces of HBV called antigens, or antibodies produced by the immune system to fight off HBV. The test looks for three things:

**HBV surface antigen (HBsAg):** Small proteins on the surface of HBV.

**HBV surface antibody (anti-HBs):** Antibody targeting the surface antigen.

**HBV core antibody (anti-HBc):** Antibody targeting the core antigen.

### HBV Screening Test Results

<table>
<thead>
<tr>
<th>HBsAg</th>
<th>anti-HBs</th>
<th>anti-HBc</th>
<th>What it means</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
<td>The person has never been infected, and needs to get the HBV vaccine.</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive or Positive</td>
<td>Negative</td>
<td>The person has been vaccinated, or has successfully fought off an earlier infection and is now protected against HBV. This person cannot spread the virus to others and does not need the vaccine.</td>
</tr>
<tr>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
<td>Unclear, the person may have “occult” HBV or recovering from acute HBV infection, will need other tests (HBV DNA) to confirm.</td>
</tr>
<tr>
<td>Positive</td>
<td>Negative or Positive</td>
<td>Negative</td>
<td>The person has recently been infected, or may have chronic HBV. The person can spread the virus to others, and needs further testing.</td>
</tr>
</tbody>
</table>

In Thailand, tests used for screening for HBV may be different depending on where you get your tests done and your health insurance. Some clinics and hospitals might only test for the HB surface antigen and not for the antibodies.

### Chronic HBV Test

If the first test comes back positive for HB surface antigen (HBsAg +), the doctor will test again in six months. If the result comes back positive the second time, it means the person has chronic HBV.

### Regular Monitoring Tests for Chronic HBV

Because there are no symptoms for chronic HBV, it is very important for people to get regular blood tests to monitor disease progression, and so they know if and when they need to start treatment to prevent liver damage and liver cancer. Doctors will check for two main indicators to monitor chronic HBV: inflammation of the liver (by measuring the level of a liver enzyme [ALT]), and activity of the virus (by measuring the amount of HBV in the blood [HBV DNA]). Because both of these can fluctuate (go up and down), they need
to be repeated regularly (every three to six months) in order to show the current pattern of a person’s chronic HBV disease.

1. Liver Enzyme Testing to Monitor Liver Inflammation: ALT (alanine aminotransferase), also known as SGPT

This test measures ALT in the blood. ALT is an enzyme that is normally contained inside the liver. ALT is released from the liver into the bloodstream when liver cells are inflamed. Liver cells can become inflamed when the immune system recognizes HBV infection in liver cells and tries to kill off these infected cells.

ALT is measured in U/L (Units per Liter). Normal ALT levels are different between men and women, and liver inflammation is indicated by ALT above the upper limit of normal (ULN):

- Normal ULN for Male: ALT = 30 U/L
- Normal ULN for Female: ALT = 19 U/L

However, an ALT test alone is not enough to decide if someone needs treatment:

- An elevated ALT level does not always mean HBV treatment is needed (the liver might be inflamed due to other causes, such as alcohol or drugs & herbs).
- A normal ALT level doesn’t always mean the liver is healthy, there might be existing liver damage but no elevated ALT because there is no current inflammation (25% of people with normal ALT may have liver fibrosis).

To get a better picture of chronic HBV disease in addition to ALT, people will also need another important indicator: the HBV DNA, or viral load.

2. HBV DNA Quantitative PCR (Viral Load) Testing to Monitor the Activity of the Virus

This test finds and measures the amount of HBV in the blood. Viral load can range between undetectable (not enough to show up on the test) to very high (measured in the billions). This test can be very expensive and might not be available at local hospitals.

A high viral load means the virus is actively making more copies of itself. Viral load levels are different depending on the phases of chronic HBV disease.

- A viral load greater than 20,000 International Units (IU/mL) or 100,000 copies/ml is considered high in people in the earlier phase of disease (HBeAg positive);
- A viral load greater than 2,000 IU/mL or 10,000 copies/ml is high for people in the later phase (HBeAg negative).
Putting These Results Together for Treatment Decisions

Doctors don’t all agree on when treatment should be started, but they generally consider treatment for people with a high viral load AND an ALT above two times the upper limits of normal. People with chronic HBV need to monitor their disease progression with both ALT and viral load tests every six months. People who have persistently high viral loads but normal ALT will need to be monitored more often (every three months) before starting treatment. People with low viral load but high ALT will need additional testing to find other potential causes of liver damage.

- Some doctors will want to perform a liver biopsy, to get more information on the amount of liver damage before recommending HBV treatment.
- A person’s age can also influence treatment decisions, because men over age 40 and women over age 50 are at higher risk for serious liver disease.
- Gender should also be considered when making treatment decisions. Men can develop serious liver disease earlier in life than women.

Regular Screening for Early Signs of Liver Cancer

People with chronic HBV are at high risk of developing liver cancer, sometimes even without any liver damage. Therefore it is very important to regularly (once-a-year) check for signs of liver cancer. The AFP (alpha-fetoprotein) test looks for a type of protein in the blood that can be found at higher than normal levels (＞100 ng/ml) in people who have liver cancer. Some people with liver cancer may still have normal AFP levels, so AFP testing alone is not totally reliable. Ultrasound testing is also used for early detection of liver cancer. More sensitive cancer screening tests are still being developed.

AFP tests should be done every six months for people with chronic HBV who:
1. Are men over age 40 and women over age 50;
2. Have cirrhosis;
3. Have a family history of liver disease.

Advocacy Exercise:

Discussion Questions:
1. Do you know what tests are available in your community? What do they cost?
2. Are these tests difficult to get? What can be done to make it easier?

Action Step:
1. What steps can we take to find out what tests are available in my community?
2. How can we collect this information and use it to help others?
Section 4.4: HBV Treatment
Not everyone with chronic HBV will need treatment

Many people with chronic HBV live long and healthy lives without treatment, since HBV can sometimes be controlled by the body’s immune system. However, HBV causes liver damage that leads to cirrhosis and/or liver cancer in about 25% of people. Often people don’t know they have HBV because there are usually no symptoms until they have developed very advanced liver disease, years to decades after becoming infected.

Goals of HBV treatment

The goals of HBV treatment are to bring viral load down and to keep it suppressed, which can prevent, delay, stop, and in some cases reverse liver damage. Blood tests can tell if the treatment is working:

**Undetectable HBV viral load:** When HBV viral load drops to a level that cannot be detected by the blood test, this means the virus is under control, even though a small amount of HBV may still be present. This is a major goal of HBV treatment.

**Normalization of ALT:** After the viral load becomes undetectable, the immune system will stop attacking liver cells, and ALT level will fall back to the normal range. The means the disease is stabilized. Sometimes when people begin HBV treatment, their ALT level may rise while their viral load drops. This can be an indication that the treatment is working and HBV is being cleared. The ALT level should fall back to the normal level eventually.

**HBeAg Seroconversion:** In people who are HBeAg positive, HBV treatment can cause the immune system to produce HBeAg antibodies (anti-HBe) and eliminate HBeAg in the blood, this is call HBeAg seroconversion. When combined with an undetectable viral load and normal ALT, most people who have HBeAg seroconverted may be able to stop treatment and still keep the virus under control. It is still important to keep regularly monitor the disease every 6-12 months.

**HBsAg seroconversion:** Even with treatment, only a very small percentage of people (< 5%) will develop antibodies to HBV surface antigen (Anti-HBs) and become HBsAg negative. HBsAg seroconversion provides the strongest control of the virus, and is the closest to a cure, but people will still need to be regularly monitored (once yearly) to watch for HBV reactivation.

Chronic HBV cannot be cured with treatment

Current HBV treatment cannot get rid of the virus completely. This is because HBV hides small pieces of its DNA inside liver cells, where drugs cannot reach. People with chronic HBV will have to be monitored with blood tests for life.
HBV treatment works better when the viral load is lower and when the liver is healthier. Doctors recommend starting HBV treatment before the development of serious liver damage. (See section 4.3 on HBV diagnostics for more info on when to start treatment.)

There are two types of HBV treatment:

1. **Antivirals:** drugs that help control the virus by interfering with HBV so it cannot make more copies. They are taken once a day by mouth, treatment usually will need to last indefinitely.

2. **Pegylated Interferon:** a man-made form of a natural protein that alerts the immune system of HBV in order to attack the infection. It is a once-a-week injection, the treatment period lasts for one year.

1. **Antiviral Drugs**

There are currently five different drugs registered for chronic HBV treatment. These are pills called “antivirals” that people take once a day by mouth. These drugs work by interfering with the HBV virus so that it cannot make more viruses. They are usually well tolerated, and have few side effects. Because these drugs cannot get rid of the virus completely, most people who are HBeAg negative will have to stay on treatment for life. People who are HBeAg positive and achieved HBeAg seroconversion after treatment may be able to stop treatment after two years, but they will still need to be monitored for reactivation for the rest of their lives. The drugs are:

1. **Lamivudine** (brand name Epivir or Zeffix) or 3TC
   
   – Generic version is available.

2. **Adefovir** (brand name Hepsera)

3. **Entecavir** (brand name Baraclude)

4. **Telbivudine** (brand name Tyzeka or Sebivo)

5. **Tenofovir** (brand name Viread) or FTC

   – Generic version is available.

When these drugs are effective in controlling HBV, they bring the viral load down to such a low level that the viral load test cannot find it in the blood (called undetectable), and keep it there. Some of the drugs are more effective in controlling the virus than others.
Comparison of Effectiveness of HBV Drugs
Percentage of people who have undetectable HBV viral load after one year on treatment

Response Rates for HBeAg-Positive People

<table>
<thead>
<tr>
<th>Drug</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg-IFN</td>
<td>25%</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>44%</td>
</tr>
<tr>
<td>Adefovir</td>
<td>21%</td>
</tr>
<tr>
<td>Entecavir</td>
<td>67%</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>60%</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>76%</td>
</tr>
</tbody>
</table>

Response Rates for HBeAg-Negative People

<table>
<thead>
<tr>
<th>Drug</th>
<th>Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peg-IFN</td>
<td>63%</td>
</tr>
<tr>
<td>Lamivudine</td>
<td>70%</td>
</tr>
<tr>
<td>Adefovir</td>
<td>51%</td>
</tr>
<tr>
<td>Entecavir</td>
<td>90%</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>88%</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>93%</td>
</tr>
</tbody>
</table>
HBV Drug Resistance

One major drawback of these drugs is the development of drug resistance. HBV makes billions of copies of new virus each day when the disease is active, and can make many mistakes in the process. These mistakes are called mutations. When people start on HBV treatment, the drugs will be able to stop most of the normal HBV (called wild type virus) from reproducing. Over time, most of these normal HBV will be under control by treatment. HBV drugs cannot control some mutated HBV, and these viruses will eventually take over, causing the viral load to increase. This is called drug resistance. Most people taking these drugs will develop drug resistant HBV eventually, but some drugs are stronger than others in controlling these mutations.

Drug resistance can also develop when there’s not enough HBV drug in the body to control the virus. This can happen when people don’t take the pills everyday or skip doses. It is very important to take HBV drugs according to the doctor’s direction in order to avoid drug resistance.

Comparison of Development of Drug Resistance

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>24%</td>
<td>38%</td>
<td>49%</td>
<td>67%</td>
<td>NA</td>
</tr>
<tr>
<td>Adefovir</td>
<td>0%</td>
<td>3%</td>
<td>11%</td>
<td>18%</td>
<td>29%</td>
</tr>
<tr>
<td>Entecavir</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Telbivudine</td>
<td>5%</td>
<td>22%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

It’s a good idea to choose a drug that is strong enough to bring down the viral load, and keep it down, so a person won’t develop drug resistance.

- Tenofovir and entecavir are the most effective drugs for controlling HBV viral load and the strongest—they are best for preventing drug resistance. However, entecavir is not as effective in people who has lamivudine resistant HBV.
- Adefovir is the least effective in controlling the viral load.
- Lamivudine and telbivudine are the weakest for drug resistance.

Choosing the right drug is very important when people start treatment for the first time

These HBV anti-viral drugs work in a very similar way to control HBV. If people start treatment using a weak drug and develop drug resistance, a second drug will also become less effective and won’t work as well. This is called “cross resistance”. Many people who were
first treated with weaker drugs like lamivudine or adefovir have fewer treatment options after they developed resistance to these drugs, because the stronger and newer drugs are not as effective against the mutated HBV. This is why it is very important to start treatment with the strongest drugs first (entecavir or tenofovir), so they will control HBV and prevent drug resistance from developing for as long as possible.

Managing Drug Resistance by Switching Drugs or with Combination Therapy

When people develop drug resistance, they will need to either switch to a newer, more potent drug or add on a second newer, more potent drug to what they are already using to treat HBV. Studies have shown that using two drugs instead of one can control mutated HBV more effectively. The decision to switch or add depends on which drug the person has developed resistance to:

### Cross Resistance and Drug Sequencing

<table>
<thead>
<tr>
<th>Drug Resistance</th>
<th>Switch to a Different Drug or a Different Combination</th>
<th>Add a Second Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine resistance</td>
<td>Switch to emtricitabine+tenofovir</td>
<td>Add adefovir or tenofovir</td>
</tr>
<tr>
<td>Adefovir resistance</td>
<td>Switch to entecavir</td>
<td>Add entecavir</td>
</tr>
<tr>
<td>Lamivudine+adefovir resistance</td>
<td>Switch to emtricitabine+tenofovir</td>
<td>Add lamivudine or telbivudine</td>
</tr>
<tr>
<td>Entecavir resistance</td>
<td>Switch to adefovir or tenofovir;</td>
<td>Add adefovir or tenofovir</td>
</tr>
<tr>
<td></td>
<td>Switch to emtricitabine+tenofovir</td>
<td></td>
</tr>
<tr>
<td>Telbivudine resistance</td>
<td>Switch to emtricitabine+tenofovir</td>
<td>Add adefovir or tenofovir</td>
</tr>
</tbody>
</table>

In some cases, an HIV/HBV coinfected person may need to keep taking lamivudine for their HIV after it stops working for their HBV. If so, it is important to add another drug that will work against HBV.

**Antiviral Treatment Side Effects**

In general, most people will have very mild or no side effects from these HBV drugs. In rare cases, there may be some serious side effects, especially if the person’s liver is seriously damaged by HBV, or they have existing kidney problems. Some of these drugs are still very new, so there might also be potential long-term side effects when people take these drugs for many years or decades.

Common side effects may include: dizziness, nausea, vomiting, headache, tiredness, stomach pain, itchiness, weakness, diarrhea, and indigestion.
More serious side effects may include:

- Peripheral neuropathy: damage to the nerves in the hands and feet. Symptoms are burning or numbing sensations in the hands and feet; these can be very painful.

- Lactic acidosis (high acid level in the blood), and severe hepatomegaly with steatosis (an enlarged fatty liver). People who are overweight are particularly at risk. Symptoms include feeling very weak or tired, unusual muscle pain, trouble breathing, stomach pain with nausea and vomiting, feeling cold (especially in your arms and legs), feeling dizzy or lightheaded, or a fast or irregular heartbeat. If you are experiencing these symptoms, go to the doctor immediately. A blood test can confirm this condition and you may need to stop the drug right away.

- Tenofovir and adefovir may cause severe kidney damage (nephrotoxicity), especially in people who already have kidney problems. Kidney function should be checked before starting treatment with tenofovir or adefovir, and monitored regularly during treatment with these drugs, by assessing creatinine clearance rate. Creatinine is a natural waste product produced by the body and processed by the kidney. A low creatinine clearance rate can mean the kidney is not functioning properly.

**Pegylated interferon**

Pegylated interferon (PEG-IFN) only works for about 1 in 3 people with chronic HBV. It has not been well studied in people coinfected with HIV, but an older form of interferon was found to work for about 1 in 10 people who are HBV/HIV coinfected. The major advantage of this treatment is the duration: treatment period lasts only one year. Studies have shown that some people who’ve been successfully treated (who have developed antibodies to HBeAg, or HBeAg seroconversion) are able to keep the virus under control without further treatment (long-term follow up of these people are still ongoing), but it is still important to keep regular monitoring HBV (every six months) to make sure it doesn’t come back (reactivate).

**PEG-IFN treatment is more likely to work in some people than others**

Before choosing this treatment, people should talk to their doctor and decide if this treatment is right for them. PEG-IFN works better for people who:

- Are under 40 years old;
- Are HBeAg positive;
- Are infected with HBV genotypes A and B;
- Have a lower viral load (less than 2 million IU/ML); and
- Have higher ALT (> 3 times ULN) at the start of treatment.
Early Predictors of PEG-IFN Treatment Response

Studies have shown that after the first 3 months of PEG-IFN treatment, if the viral load did not drop by 1 log from the start of treatment (a ten-fold decrease, for example, from 20,000 down to 2,000), PEG-IFN is not likely to be effective in that person, and treatment should switch to oral drugs. If the viral load dropped to under 2,000 IU/ML after 3 months of treatment with Peg-IFN, HBeAg positive people have a 50% chance of reaching HBeAg seroconversion, and HBeAg negative people have a 50% chance of keeping the virus under control one year after treatment.

PEG-IFN Side Effects

The major disadvantages of PEG-IFN treatment are the serious side effects and the cost. Most people will experience symptoms that can make it difficult for them to stay on treatment in the beginning, but symptoms usually get better after the first few months. People have found it helpful to know the potential side effects before they start treatment, and to take steps that can help lessen the symptoms.

PEG-IFN side effects include:

- Flu-like symptoms (feeling weak, feverish, aching muscles and joints);
- headache, nausea, and appetite loss
- fatigue, low energy
- anxiety, irritability, insomnia, mania and mood swings;
- mild to serious depression, including suicidal thoughts in rare cases;
- low white blood cell counts (neutropenia);
- low red blood cell counts (anemia),
- low platelets (thrombocytopenia)

PEG-IFN is also used to treat hepatitis C. Please see section 5.4 Hepatitis C Treatment, for more information about how to better manage these side effects.

Pegylated interferon is very expensive in Thailand (about 56,000 THB per month). It can be very hard to get depending on your health coverage, and may be only available to the few people who can afford it.

Treatment for HBV/HIV coinfection

Treating both HBV and HIV can be complicated because people might not need to be on treatment for both infections at the same time. The good news is that three HIV drugs are also effective against HBV (tenofovir, lamivudine, and emtricitabine). People coinfected with HIV and HBV should choose an HIV combination with tenofovir plus either emtricitabine or lamivudine, with a third protease inhibitor or non-nucleoside.
Consideration of HIV drug resistance should also be taken into account when choosing ARVs. Using two drugs that are active against HBV may help prevent or delay the development of HBV drug resistance. Some ARVs are also liver toxic, please see section 5.5 for more information about this issue.

Coinfected people should not use entecavir for HBV treatment, because it also has a very weak effect on HIV. This weak effect can lead to the development of HIV drug resistance to 3TC.

If you have to stop taking your HIV drugs or change them for any reason, be very careful and talk to your doctor beforehand. Because the drugs are controlling both HIV and HBV, if they are stopped or changed, HBV can become active again and cause serious liver damage very quickly. This can potentially be fatal.

Different treatments are used for people who have only HBV vs. people who are coinfected with HIV and HBV in Thailand:

**People with HBV only:**
Current regimen: 3TC or tenofovir  
Preferred regimen: tenofovir or entecavir or pegylated interferon

**People with both HIV & HBV:**
Preferred regimen: tenofovir + 3TC + efavirenz

**People with HIV only:**
Current regimen: GPO-vir (d4T + 3TC + NVP) or GPO-vir-Z (AZT + 3TC + NVP)  
Preferred regimen: tenofovir + 3TC + efavirenz

---

**Advocacy Exercise**

**Discussion Questions:**

1. Does the government pay for HBV drugs for people who need treatment?  
2. What drugs are available? Are they easy to get?  
3. Do doctors know about HBV treatment guidelines from Thailand (or other countries)?

**Action Step:**

1. How can we share this information with others in the community?  
2. What would be useful for people who need better access to HBV care and treatment?
Section 5.1: Hepatitis C Transmission
(how you get it)
Hepatitis C (HCV) is spread by direct blood-to-blood contact

HCV is a blood-borne virus, spread when infected blood directly enters a person’s bloodstream. HCV is a very small virus, much smaller than HIV, so there is a lot of it even in a tiny amount of blood, but—unlike HIV—the hepatitis C virus stays alive on surfaces outside of the body for days. HCV is ten times more infectious than HIV. Bleaching syringes can prevent HIV, but it does not work as well to stop HCV; only sterilization with heat kills HCV. Since IDU don’t have easy access to clean injection equipment, and HCV is not easy to kill, HCV is common among injection drug users.

The most common ways to catch HCV are:

- Sharing anything that another person has used to inject drugs with, including needles, cookers, ties, cotton, straws, water and even measuring syringes;
- Getting a tattoo with any shared, unsterilized equipment: needles, ink, and inkwells;
- Getting a contaminated blood transfusion or blood product (more common in some countries than others);
- Undergoing surgery or other invasive medical procedures (vaccination, blood draws, endoscopy) with unsterilized, shared equipment, or kidney dialysis, in a facility that does not practice infection control;
- From mother to infant; the risk is about 4%, but if the mother is also HIV-positive, the risk is higher—up to 20%;
- Having unprotected sex with a person who has HCV;
- Needle-stick injury or other occupational hazard (health care providers)

When possible, avoid sharing toothbrushes, razors, manicuring equipment and any other personal care items that may have come in contact with another person’s blood.

HCV cannot be passed by sharing eating utensils or by eating food made by a person with HCV; or drinking from the same glass. HCV is not spread by casual contact (hugging, holding hands, etc)

Sharing straws to snort methamphetamines and pipes to smoke other drugs may be risky. It also may be possible to get HCV from sharing straws to smoke methamphetamines or pipes to smoke drugs, since people may get burns on their lips from a hot pipe. HCV can be passed by sharing personal care items that may have blood—even tiny amounts—such as razors, toothbrushes, and manicuring equipment. Health care workers have gotten infected with HCV from needle stick accidents.
Although it is not always possible, it is important to use clean injection equipment (needle, measuring syringes, cookers, cotton, water and ties) every time you get high. A person who already has HCV can get infected again—this is called re-infection. Not sharing your injecting equipment or using clean/new equipment protects you and the people that you are getting high with.

HCV can be spread during unprotected anal and vaginal sex with a person who has HCV. Although the hepatitis C virus has been found in semen and vaginal fluid, it is mainly found in blood. No one is sure there is enough HCV in semen and vaginal fluid to pass the virus to other people, but we do know that people have become infected from unprotected sex. HCV is more common among sex workers, men who have sex with men, and people who have had more than one sex partner.

The risk for sexually transmitted HCV is greater when blood is involved, even when the amount is too small to see. So, rough, unprotected anal and vaginal sex, fisting (also called fist-fucking; when a person puts his/her hand and forearm into another person’s anus or vagina), group sex, and sex with a woman during her period can put a person at risk for HCV. Using condoms for anal and vaginal sex, and latex gloves with plenty of water-based lubrication for fisting can reduce the risk of sexually-transmitted HCV.

There have been outbreaks of sexually transmitted HCV among HIV-positive gay men.

Outbreaks have been reported so far in some European countries, Australia and the United States. Several factors seem to be involved, including:

- Unprotected anal sex,
- Longer, rougher intercourse,
- Fisting,
- Sex with many partners and group sex,
- Being infected with another sexually transmitted infection, such as syphilis,
- Meeting sex partners through the internet,
- Use of “party drugs”, such as ecstasy, crystal meth, and cocaine, which can lower inhibitions.

HCV can be passed from mother to infant, in the womb, or during labor and delivery. If the mother has HCV—but not HIV—there is about a 4% risk that her baby will have HCV. The risk of mother-to-infant transmission (MTIT) of HCV is higher—up to 20%—if the mother is also HIV-positive.

Coinfected mothers can do reduce the risk of passing HIV and HCV to their infants by taking antiretroviral therapy. HIV treatment takes care of the mother’s health, and greatly lowers the risk of passing HIV and HCV to the infant. A planned caesarian section (c-section) also reduces the risk of passing HIV and HCV to the baby. Planned c-section is recommended only for pregnant women who are HIV/HCV coinfected.
Unfortunately, it is not possible to use HCV treatment during pregnancy because one of the drugs—ribavirin—causes birth defects, and the other—interferon—is dangerous for infants and children under two years old.

Unlike HIV, the hepatitis C virus has not been found in breast milk. HIV-negative mothers who have HCV can safely breast-feed their infants as long as their nipples do not have any cuts or cracks.

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**Advocacy Exercise:**

**Discussion Questions:**

1. Do people in my community know how to protect themselves against HCV?
2. Are clean syringes, injection equipment, and condoms easy to get in my community?

**Action Step:**

1. How can we help make clean syringes and condoms more available?
Section 5.2: Natural History of HCV and HCV in HIV+ people:

What happens to people who have HCV, and people who have both HIV and HCV?
HCV has two stages, acute and chronic (lifelong)

Acute infection is a term for the first six months after a person gets HCV. Most people—80%—don’t feel sick at all during acute HCV, and don’t know that they have HCV.

The symptoms of acute HCV include:

- Jaundice (yellow skin and eyes);
- Fever;
- Feeling tired and weak;
- Nausea, vomiting, stomach pain, and appetite loss;
- Dark urine.

HCV is not always chronic

Since most people don’t have any symptoms, they don’t seek health care, and their HCV goes undiagnosed. HCV is not always a lifelong infection. Some people (15% to 45%) will get rid of the virus without treating it, usually during acute infection. The medical term for this is spontaneous viral clearance. HIV-negative people, women, children and young adults, and people who have symptoms during acute HCV are more likely to spontaneously clear HCV. HIV-positive people are less likely to clear HCV without treatment; experts think that up to 20% of HIV-positive people will get rid of their HCV without treatment versus 15 – 45% in HIV-negative people.

HCV treatment is most effective during acute infection

Finding out that you have HCV during acute infection can make a big difference, because HCV treatment is much more likely to work—meaning it will get rid of the virus—during acute HCV. Usually, experts suggest that people who have acute HCV should wait for about 12 weeks before they start HCV treatment, since they may spontaneously clear HCV and won’t actually need treatment.

Most IDUs have been living with HCV for many years. Some people may have only recently started to inject drugs, and don’t have HCV. Sharing injection equipment would put them at high risk for HCV.

At least 55% of HIV-negative people and at least 75% of HIV-positive people will develop Chronic HCV

Most people who get HCV develop a chronic (lifelong) infection. Many do not have any symptoms at all, but the most common symptoms are being forgetful, feeling tired, and/or depressed. Sometimes people with very mild liver damage have symptoms, and there is no clear link between having symptoms and liver damage. Many people don’t have any symptoms until they have very serious liver damage.
Chronic HCV does not always cause serious liver damage

Having chronic HCV does not always mean that you will have serious liver damage, or that you need treatment. Some people live with HCV for many years, and will never have liver damage; they will die from other, unrelated causes.

Liver damage from HCV happens slowly, usually over decades. It can take from 15 to 50 years for an HIV-negative person who has chronic HCV to develop cirrhosis. The amount of time someone have had chronic HCV—the longer a person has been infected, the more likely he or she is to develop liver damage. People with serious liver damage (cirrhosis) are at risk for very serious complications, such as liver cancer and liver failure. (For more information about liver damage, see Section 2: The Liver).

HIV/HCV Coinfection: Impact of HIV on HCV

HCV is a serious problem for HIV-positive people. HIV increases the risk for liver damage from HCV. In fact, coinfected people are twice as likely to get cirrhosis than people with HCV alone. HIV speeds up the rate of liver damage from HCV; some coinfected people have gotten cirrhosis in less than 10 years.

HCV is treatable, no matter what a persons HIV status is, but HCV treatment does not work as well for HIV-positive people.

HIV treatment can help to slow down liver damage from HCV

HIV treatment, also called antiretroviral therapy, or ART, may help keep the liver in good condition by keeping the immune system strong. Coinfected people with less than 200 CD4 cells are at the highest risk for serious liver damage from HCV.

HIV/HCV Coinfection: Impact of HCV on HIV

So far, no one is sure about the impact of HCV on HIV, though we know HIV can accelerate progression of HCV. Experts do agree that being coinfected with HCV makes treating HIV more complicated. A liver that is damaged from HCV may be less able to break down medications, since most HIV meds are processed and broken down by the liver.

HCV coinfection triples the risk for liver toxicity (also called hepatotoxicity) from HIV meds. It is important to know which drugs are easier on the liver than others. However, many studies in HIV/HCV coinfected people have shown that the benefits of HIV treatment outweigh the risks. (For more information, see Section 5.5: Treatment Issues for HIV/HCV Coinfected People).
Advocacy Exercise:

Discussion Questions:

1. Do we know people in the community who’ve died from HCV?
2. What can we do to prevent more deaths from HCV?
3. When and how did they find out they had HCV? Was it already “too late?”
   What options were they given?

Action Step:

1. How can we get more people tested for HCV?
Section 5.3: HCV Diagnostic Tests
The first step to start dealing with HCV is to find out as much as you can. One way to do this is by getting some blood tests from the medical provider. These tests can tell:

- If the person has been infected with HCV;
- which strain (genotype) of HCV the person has;
- the amount of virus (viral load) in the bloodstream;
- if the liver has been very damaged; and
- how well HCV treatment is working.

Two different blood tests are needed to diagnose chronic HCV:

1. HCV antibody test; and
2. HCV viral load (HCV RNA) test

A positive HCV antibody test result can mean two things

Most people with chronic HCV will get a positive result from a HCV antibody test. But some people without chronic HCV can also test positive, because HCV antibodies remain in the body years after the person has cleared the infection. In order to find out if someone who is HCV antibody-positive has chronic hepatitis C, the person will need to take a HCV viral load test.

A negative HCV antibody test result usually means a person doesn’t have HCV—but not always

Sometimes an HCV antibody test result is negative, even when someone does have chronic HCV. This happens for two reasons. If a person just got infected with HCV, he or she may not have antibodies yet. It takes six to twenty-four weeks for a person to make antibodies to HCV (often called the “window period”). HCV antibody test results may also be negative in HIV-positive people who have HCV. This can happen when a person has less than 200 CD4 cells, because their immune system is not able to make antibodies. So anyone with a CD4 count of less than 200 cells, who has signs or symptoms of hepatitis, such as elevated liver enzymes, or who has been at risk for HCV, should have an HCV viral load test, even when their HCV antibody test is negative.

A HCV viral load test will confirm, or rule out chronic HCV for people with positive antibody test results

The HCV viral load test looks for the hepatitis C virus in the blood. If the virus is detected, the person is currently infected with HCV. If no hepatitis C virus is found in a person’s blood, usually they will need to have a second HCV viral load test, six months later, to rule out chronic hepatitis C.
There are two different types of HCV viral load tests, qualitative (measures whether or not there is HCV virus in a person’s blood; results are either detectable or undetectable), and quantitative (measures how much hepatitis C virus there is in a person’s blood).

- Qualitative testing can pick up very small amounts of HCV in a person’s bloodstream. It is usually used to diagnose HCV, and sometimes used to measure response during HCV treatment.
- Quantitative testing is usually used to see how much virus a person has in his/her bloodstream before they start HCV treatment, and sometimes used to measure response during HCV treatment.

**HCV Screening Tests and What the Results Mean**

**Step 1: HCV ANTIBODY TEST**

**POSITIVE RESULT**
There are three potential meanings:
1. The person may have acute HCV; or
2. may have chronic HCV; or
3. was infected in the past, but has cleared HCV and is no longer infected.

Need a viral load test to confirm.

**NEGATIVE RESULT**
There are three potential meanings:
1. The person has never been infected; or
2. may be recently infected (within the last two weeks); or
3. may have chronic HCV if the person is HIV positive, especially those with CD4 < 200.

Need a viral load test to confirm.

**Step 2: HCV RNA TEST (VIRAL LOAD)**

**DETECTABLE RESULT**
There are two potential meanings:
1. The person may be recently infected, and has acute HCV; or
2. may have chronic HCV.

Need a second confirmatory viral load test.

**UNDETECTABLE RESULT**
There are three potential meanings:
1. The person has never been infected; or
2. was once infected in the past, but has now cleared HCV; or
3. was recently infected but still in the process of clearing the infection.

Need a second confirmatory viral load test.

**Step 3: Second Confirmatory HCV RNA TEST (VIRAL LOAD) In Six Months**

**DETECTABLE RESULT**
The person has chronic HCV.

**UNDETECTABLE RESULT**
1. The person has never been infected; or
2. was infected in the past but has now cleared HCV.

The person does not have HCV.
The HCV viral load cannot tell whether someone needs HCV treatment

In HIV, a person’s viral load can be used to help make a decision about when to start antiretroviral therapy, but HCV is different. The amount of hepatitis C virus in a person’s blood is not a sign of how serious their hepatitis C is. HCV viral loads are much higher than HIV viral loads—sometimes in the tens of millions. Coinfected people usually have higher HCV viral loads than people with HCV alone. For people who are used to the scale of HIV viral loads, the HCV viral load can be very upsetting. HCV viral loads can be in the tens of millions. But having a high HCV viral load (over 400,000 IU/mL) does not mean that a person needs to start HCV treatment, or that he or she has more liver damage, or that liver damage will develop more quickly.

HCV treatment is more likely to work for people with a low HCV viral load

The HCV viral load is one of the things that predict whether or not HCV treatment is likely to work. The lower the HCV viral load is, the more likely that HCV treatment will work. Viral load testing is also used during and after HCV treatment, to see if treatment is working (for more information, see Section 5.4, HCV Treatment).

HCV Genotype Testing

There are different viral strains of HCV, called genotypes. There at least six different HCV genotypes, each given a number (1,2,3, etc.) in the order of discovery. Within each HCV genotype there are slight differences, called subtypes; these are given a letter of the alphabet (a, b, c, d, etc), so for example someone may be diagnosed with HCV genotype “3a”. A person can be infected with more than one HCV genotype, and people who already have HCV can get infected again (called reinfected) with a different genotype than the one they already have.

It is very important to have an HCV genotype test before starting HCV treatment, because some genotypes are easier to treat than others, and don’t need to be treated for as long as others.

Health care providers can order a blood test to see which HCV genotype a person has. If you are thinking about treating your HCV, it is VERY important to know which HCV genotype (sometimes more than one type) you have. The HCV genotype is the strongest predictor of response to treatment, and can have an impact on the length of HCV treatment.

Genotypes 1, 3 and 6 are the most common in Thailand. HCV treatment is more likely to work for people with genotype 3 or genotype 6 than people with genotype 1. Since some HCV genotypes are harder to treat than others, it is important to avoid getting reinfected with HCV when possible.
Getting More Information Your Liver Health

Liver Enzyme Tests (ALT and AST)

Liver enzymes are proteins that do different jobs in the body. When a person’s liver is injured, these enzymes leave the liver cells and enter the bloodstream. Health care providers check liver enzyme levels using a group of blood tests, sometimes called liver function tests, or LFTs. These tests do not actually measure liver function, and the results cannot predict, or tell someone how much liver disease they have. They are one of the tests used to see if a person needs hepatitis C treatment.

Alanine aminotransferase (ALT, also called SGPT) and aspartate aminotransferase (AST, also called SGOT) are two liver enzymes. ALT is made in the liver. If a person’s ALT keeps increasing over time, it may be a sign of hepatitis B or C progression. AST is made in the heart, intestines, and muscles. Alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), bilirubin, albumin and prothrombin time (PT) are other important liver enzymes.

Many things can cause abnormally high liver enzyme levels, such as: liver toxicity from prescription and over the counter medications, herbs, vitamins and supplements; exposure to toxic fumes; heavy alcohol consumption; acute or chronic viral hepatitis and certain other infections; and while a person is detoxifying from drugs and/or alcohol.

Some HIV medications are broken down by the liver, and can cause abnormally high liver enzyme levels. All HIV-positive people who are taking ARVs or TB drugs—whether or not they are coinfected with hepatitis B or C—should have their liver enzyme levels checked regularly as some ARVs, TB treatment and other drugs can be hard for the liver to break down.

When liver enzyme levels are higher than normal for several months, it can be a signal that the liver is inflamed or damaged. Normal liver enzyme levels do not mean that a person’s liver is healthy—on the other hand, some people may have normal liver enzyme levels for years although they have serious liver damage. It is a good idea to keep a record of your liver enzyme levels over time. If the level goes up and stays up over several tests, it may be a good time to discuss HCV treatment with your doctor, as other causes for abnormal enzyme elevations are ruled out.

Liver Biopsy

A liver biopsy is the best way to find out what condition a person’s liver is in, because health care providers can see how much inflammation (called grade) and scarring (called stage) there is in a sample of liver tissue. During a liver biopsy, a very small piece of liver tissue is removed with a needle. The tissue is then examined to see how much damage there is, and what is causing the damage. Usually, a person will stay in the hospital for a few hours afterwards to make sure that there are no complications.
There are drawbacks to liver biopsy. If the tissue sample is not large enough, or is taken from a less damaged part of the liver, the results will not be accurate. Biopsy is expensive, and many people are not able to have a biopsy done for this reason. Liver biopsy can be painful. There is a small risk of complications—such as internal bleeding, or missing the liver and piercing a nearby organ—and a much, much smaller risk of death.

It is always important to ask how much experience a doctor has had in performing biopsies, what kind of pain medication will be offered, and how long the hospital stay is. It may be helpful for you to ask someone who has had a liver biopsy how it was, and if they recommend the doctor who did it.

**Cirrhosis can be diagnosed without a liver biopsy**

Health care providers can use a combination of blood tests instead. But it is difficult to diagnose mild or moderate liver disease without doing a biopsy, although researchers are looking at different groups of blood tests and less invasive scans as substitutes for liver biopsy.

**Liver biopsy is not always necessary**

Sometimes, people do not get a biopsy before starting HCV treatment. Often, this is because of the cost, or because there is no experienced doctor available to perform one. Liver damage from HCV can develop faster in HIV-positive people, so some healthcare providers think it is a good idea to go ahead and treat coinfected people whether or not they have had a biopsy.

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**Advocacy Exercise:**

**Discussion Questions:**

1. Are HCV tests easy to get in the community?
2. Are all the different HCV tests available? Is cost a problem? Are they covered under your insurance plan?
3. Do doctors take the time to explain test results?

**Action Steps:**

1. What kind of tools can help people understand test results?
2. What can we do to increase access to expensive tests?
3. With whom can we make alliances to increase our understanding of and access to these important tests?
Section 5.4: HCV Treatment and Side Effects
Treating HCV is never an emergency.

HCV treatment is recommended for people who already have some liver scarring and inflammation, because they are at risk for cirrhosis. Treating HCV may be more important for coinfected people because they may get liver damage more quickly than people with HCV alone. Successfully treated HCV can also improve liver and health and make HIV drugs easier to tolerate.

HCV treatment is not recommended for people with very advanced liver damage, because it can cause liver failure. People in this situation need a liver transplant.

HCV treatment is a combination of two drugs

The current standard of care for HCV is 12-72 weeks of treatment with two drugs, pegylated interferon (PEG-IFN) and ribavirin. The length of treatment depends on how a person responds to it after 12 weeks, which HCV genotype they have, how high their HCV viral load is, and HIV status.

Both drugs can cause side effects that can be very serious. It is important for anyone who is thinking about treating their HCV to learn about the risks and benefits of HCV treatment. One of the best ways to do this is to talk with people who have been on HCV treatment.

Pegylated Interferon (PEG-IFN)

Interferon is a protein made by the human body. It sends virus-fighting messages to the immune system. With HCV, a much larger dose of man-made interferon is used for treatment. Pegylation means that a molecule has been attached to the interferon, keeping it in the body longer and making it more effective. Before interferon was pegylated, people had to inject it three times per week (for up to 48 weeks). PEG-IFN is one injection per week (given for 12-72 weeks). PEG-IFN is more effective as well as more convenient than standard interferon. There are two different brands of PEG-IFN; one comes as a powder, is dosed by weight, and needs to be mixed with water before each injection (PEG Intron by Schering Plough); the other brand comes pre-mixed and is not dosed by weight (Pegasys by Roche). Both need to be refrigerated. Standard, non-pegylated interferon is no longer the standard of care, and should not be used.

Ribavirin

Ribavirin is from the same family as some of the drugs used to treat HIV, called nucleoside analogs, but it does not work as an HIV treatment. Ribavirin works against HCV when used with PEG-IFN. It is not very effective by itself and should not be used alone.

Ribavirin is given as pills or capsules, twice a day. The dose depends on a person’s weight.
Access to HCV treatment is an important advocacy issue

Since combination PEG-IFN and ribavirin are so expensive in Thailand, over 85,000 THB per month, very few people in Thailand can afford it. Unfortunately, there is currently no cheaper generic version of PEG-IFN, but hopefully it will be available in the future.

New HCV Drugs

There are many new HCV treatments being developed. Many are antiviral pills that will need to be used with PEG-IFN and ribavirin for several years, until there are drugs that target different steps in the HCV lifecycle. Hopefully, it will be possible to combine these, and treat HCV without interferon and ribavirin.

As with ARVs, the new HCV drugs will need to be taken regularly—missing doses can lead to drug resistance.

Currently, makers of HCV drugs are not required to study them in coinfected people before they are approved, but activists have been working to push companies to study these drugs in coinfected people as soon as it is safe to do so.

HCV treatment can get rid of the virus, but it does not always work

The first goal of HCV treatment is to get rid of the virus. People have cured their HCV when there is no virus in their bloodstream six months after they have finished treatment (called sustained virological response, or SVR).

The second goal of treatment is to improve the condition of the liver, by giving it a break from the virus (called histological response). Sometimes this happens even when someone does not have an SVR, but it is more likely but not universally achieved for people who get rid of the virus.

Even when HCV treatment does not get rid of the virus, it can improve the condition of the liver

Over the long-term, treating HCV can reduce the risk of cirrhosis, liver cancer, liver failure and liver-related death, especially when treatment gets rid of the virus. This is an important advocacy point.
Here are some terms that people use to describe how likely, and how well HCV treatment is working:

**RVR (rapid virological response):** means that a person has no detectable hepatitis C virus in his/her blood after four weeks of HCV treatment. An RVR is a good predictor of SVR, but people who do not have an RVR may still have an SVR. Usually this test is used during clinical trials, not as part of regular care during HCV treatment.

**EVR (early virological response):** means that a person has either a 99% (also called 2-log) drop in the amount of hepatitis C virus in his/her bloodstream, or that there is not detectable HCV in his/her bloodstream.

**pEVR (partial EVR):** means that a person has had at least a 2-log drop in the amount of hepatitis C virus in his/her bloodstream after 12 weeks of treatment.

**cEVR (complete EVR):** means that HCV viral load is undetectable after 12 weeks of treatment. People who have a cEVR are more likely to have an SVR than people who have a pEVR.

**SVR (sustained virological response):** means that a person has no detectable virus in his/her bloodstream six months after finishing HCV treatment. Many experts consider this a cure.

If a person does NOT have an EVR, they are extremely unlikely to have an SVR. People who do not have an EVR usually stop HCV treatment at this point. Access to HCV viral load testing after 12 weeks of treatment is very important: if treatment isn’t working, there is no need for someone to stay on it and suffer the side effects, and no need to pay for an entire year of treatment.

**Non-response:** when a person’s HCV viral load does not drop by much, or at all, after 12 weeks of HCV treatment. HCV treatment should be discontinued, because it isn’t working.

**Null response:** when there is no change in a person’s HCV viral load after 12 weeks of treatment. HCV treatment should be discontinued, because it is not working.

**Breakthrough:** means that HCV was undetectable at one time while a person is on HCV treatment, but HCV viral load becomes detectable during treatment. Usually it is a good idea to have a second viral load test to confirm that HCV RNA is detectable, and if so, to discontinue treatment.

**ETR (end-of-treatment response):** means that a person has no detectable virus in his/her bloodstream when they have finished HCV treatment.

**Relapse:** means that a person had an end-of-treatment response, but their hepatitis C virus came back after they stopped treatment. This has happened to about 18% of people who have been on HCV treatment. Usually, the virus reappears in the bloodstream within the first 12 weeks after finishing treatment.
HCV treatment can last from 12 to 72 weeks. Usually, HIV-negative people with genotype 2 or 3 are treated for 16 to 24 weeks, and people with genotype 1 are treated for 48 weeks. HIV/HCV coinfected people are usually treated for 48 weeks, no matter what their genotype is. People with HCV genotype 1 and a high viral load may be treated for up to 72 weeks, whether or not they are coinfected.

How Well Does HCV Treatment Work?

HCV treatment is more likely to work for:

- People with genotypes 2 and 3;
- People with a low HCV viral load;
- HIV-negative people.

HCV treatment is less likely to work for:

- People who have cirrhosis;
- People who have insulin resistance (when a person’s body is less able to properly use the insulin he or she is making; insulin resistance can cause diabetes);
- People who have a buildup of fat in their liver (called steatosis);
- People who are overweight.

Even though experts know a lot about the factors that predict whether or not HCV treatment will work in general, no one can predict how an individual will respond to HCV treatment.

Results from clinical trials can give people an idea about how well HCV treatment works, but results do not always apply in the real world. People in clinical trials are picked carefully; often they don’t have other medical conditions that are common among people with HCV, may have less liver damage and be in better health overall. This happens for a few reasons: one, it is safer to try new treatments in the healthiest possible people, and two, sometimes people who are unlikely to respond to a treatment are excluded from trials, to make the results look better.

### Response To HCV Treatment*, By HIV Status and HCV Genotype

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<thead>
<tr>
<th>SVR</th>
<th>HCV Only</th>
<th>HIV/HCV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>[56%–61%]</td>
<td>[27%–49.6%]</td>
</tr>
<tr>
<td>HCV Genotype 1</td>
<td>[42%–44%]</td>
<td>[14%–38%]</td>
</tr>
<tr>
<td>HCV Genotype 2&amp;3</td>
<td>[70%–82%]</td>
<td>~ [82%]</td>
</tr>
</tbody>
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*PEG-IFN plus ribavirin; HCV treatment was most likely to work for coinfected people when the ribavirin dose was based on body weight.*
Side Effects of HCV Treatments

The side effects of PEG-IFN and ribavirin can make it difficult for people to stay on treatment, although they are different for each person. In general, side effects are worse for people who have more serious liver damage, and/or are HIV/HCV coinfected. Some people have trouble working during HCV treatment.

It is very important to talk with other people who are, or have been on HCV treatment. Their experience and support can be very helpful. Ask your health care providers about how they manage side effects before you start HCV treatment.

Common Side Effects

Flu-like symptoms, such as feeling weak, feverish, having aching muscles and joints, headache, nausea and appetite loss are very common. These are usually worse for the first day or two after injecting PEG-IFN, so people often take their weekly PEG-IFN when they can rest for a day or two afterwards. These side effects can be managed with low-dose paracetamol, drinking plenty of water and anti-nausea drugs, such as dronabinol (also called Marinol, a pharmaceutical form of marijuana).

Weight loss is common during their HCV treatment. Dronabinol can help increase appetite, and eating smaller, light meals throughout the day may boost energy.

Many people feel very tired during HCV treatment. Regular naps, doing light exercise whenever possible, and methylphenidate or bupropion (these drugs are also called Ritalin and Wellbutrin) may help with fatigue.

Mental Health and Depression

It is important to have access to peer support and mental health care before starting HCV treatment, since interferon can cause anxiety, irritability, insomnia, mania and mood swings. In addition, interferon (and maybe ribavirin) can cause mild to very serious depression. In rare cases, people have become suicidal. People who have been seriously depressed in the past are more likely to become depressed during HCV treatment, but it can happen to anyone.

Sometimes people take anti-depressant medication before starting HCV treatment, because it may take time to find the right medication. Other people prefer to wait and see if they become depressed during HCV treatment. Anti-depressants have their own side effects, so some people prefer to avoid using them unless they need to.

Interferon can cause low white blood cell counts (called neutropenia; these white blood cells fight infections), low red blood cell counts (called anemia; these red blood cells carry oxygen through the body), or low platelets (called thrombocytopenia; these help blood to clot. Coinfected people are more likely to develop neutropenia, anemia and thrombocytopenia during HCV treatment.
Anemia

Usually, people who have anemia feel very, very tired. When anemia develops during HCV treatment, doctors either reduce the ribavirin dose (which may make HCV treatment less likely to work) or use injections of a red blood cell growth factor (called epogen). Unfortunately, epogen is very expensive, so it is not always available. AZT, an HIV drug, can also cause anemia, so it is important for HIV-positive people to avoid AZT while they are on HCV treatment.

Neutropenia can increase the risk of getting a bacterial infection. Usually, doctors will reduce the PEG-IFN dose, or use injections of a white blood cell growth factor (called neupogen), which, like epogen, is very expensive and not always available.

Thrombocytopenia

HIV can cause thrombocytopenia, and sometimes people with serious liver damage have thrombocytopenia, because the liver cannot help to make platelets. When people get thrombocytopenia during HCV treatment, they usually take a lower dose of PEG-IFN. If thrombocytopenia becomes very serious, HCV treatment should be stopped.

HCV Treatment Access in Thailand

In Thailand, HCV treatment is only available to the few people who can afford it, as it is very costly. As a result, HCV treatment has not been widely used here, and doctors might not be familiar with how to manage treatment side effects. White and red blood cell growth factors to manage side effects of HCV treatment are so expensive that access is very limited. But these may help people get through HCV treatment, so access is important.

Hopefully, less-expensive generic interferon, and white and red cell growth factors will be available in the future.

Although many doctors think that it is not possible to treat HCV in people who are using drugs, several studies have shown otherwise. These studies found that people who use drugs could be successfully treated for HCV, when their side effects were treated and when counseling from peers and mental health staff, methadone, clean injection equipment and addiction treatment were available.

There are many new treatments for HCV being studied; hopefully some people will be able to get access to HCV treatment through clinical trials, but it is important to learn about the risks and benefits of the trial first. Some trials are better than others.
Advocacy Exercise

Discussion Questions:

1. How can we increase access to HCV care and treatment?
2. What are the other services that we need, such as peer support programs, better access to methadone, and better ARV regimens?
3. Are there HCV treatment guidelines from Thailand (or other countries)?
4. Do Thailand’s HIV treatment guidelines include recommendations on screening/diagnosing/treating HCV?

Action Step:

1. What are our most important arguments for increasing access to HCV treatment to policy makers?
2. What can we do to get a clinical trial in my community?
Section 5.5: Treatment Issues for HIV/HCV Coinfected People
ARVs and Liver Toxicity

Many ARVs are broken down by the liver. Some ARVs are less liver-friendly than others, especially when someone is coinfected with HCV. Liver toxicity is more likely for coinfected people with serious liver scarring. Having liver enzyme levels checked regularly is very important for coinfected people who are taking ARVs, because these can pick up liver problems caused by HIV drugs and/or other causes.

Getting better HIV treatment options is an important advocacy issue

In Thailand, first-line HIV therapy consists of GPO-vir, which has both nevirapine (NVP) and stavudine (also called d4T or Stavir* from Thai GPO). Although some coinfected people have used nevirapine without having any problem, it is known to cause liver toxicity. Stavudine can cause damage to the part of liver cells that produce energy; these are called mitochondria. Because of these toxicities, GPO-vir may not be the best regimen for people who are HIV/HCV coinfected. Second-line drugs (3TC/TDF/EFV) currently recommended in the Thai treatment guidelines can also be liver toxic. This is why advocating for more treatment options is important.

Tipranavir, an HIV drug for people with a lot of ARV drug resistance that is rarely used, also causes liver toxicity. Darunavir, an HIV protease inhibitor, can be liver toxic. Careful monitoring of liver enzyme levels is recommended for people using this drug.

Treating HCV can lower the risk of liver toxicity from ARVs.

Drug Interactions

Some ARVs drugs should not be used during HCV treatment because they interact with ribavirin.

DDI (also called didanosine, or Videx) should NOT be used with ribavirin because the combination can cause lactic acidosis (when lactic acid builds up in the blood), and pancreatitis—both conditions can be life-threatening. Using DDI during HCV treatment has caused liver failure in people with cirrhosis.

AZT (also called ZDV, zidovudine, or Retrovir) can cause anemia, as does ribavirin. The combination increases the risk of anemia, so AZT should be avoided during HCV treatment.

d4T (also called stavudine or Stavir, one of the drugs in GPO-vir S30) may cause fat loss (called lipoatrophy) and severe weight loss when used during HCV treatment. When possible, d4T should not be used during HCV treatment.

Abacavir (also called Ziagen) may interact with ribavirin, making HCV treatment less effective. It is a good idea for people to avoid this drug during HCV treatment.
HIV and HCV Treatment

Ideally, all HIV-positive people should be tested for HCV, and offered treatment if needed. HCV progresses more quickly in people who are also HIV-positive, so access to HCV treatment is especially important for coinfected people. Treating HCV can improve the condition of the liver, even when a person does not get rid of HCV.

Coinfected people with less than 200 CD4 cells should start HIV treatment before treating HCV. HIV treatment can keep the immune system healthy, which slows HCV progression. Even though coinfected people are at greater risk for liver toxicity from ARVs, the benefits of HIV treatment outweigh the risks. Plus, both treatments have side effects, so it not a good idea to start treating HIV and HCV at the same time.

There is not very much information on how safe, and how well HCV treatment works for people with less than 200 CD4 cells, who are taking ARVs. This is an important question, because people with low CD4 cell counts are at higher risk for liver damage from HCV and in Thailand, many people don’t find out that they are HIV-positive until their CD4 count is under 200.

Interferon and CD4 Cell Count

Interferon can lower the CD4 cell count, even when someone is on ARVs. This can be frightening, but it is temporary. The CD4 cell count goes back up after stopping interferon.

Advocacy Exercise

Discussion Questions:

1. Are HIV positive people tested for HCV? Are the tests free?
2. Is it difficult to change ARVs for coinfected people that are not GPO-vir?

Action Step:

1. How can we increase access to HCV treatment for coinfected people?
2. How can we get more HIV treatment options for coinfected people?
You have the right to be involved in decisions about your own health.

Finding a good doctor/health care provider

Many people who use drugs find it difficult to feel safe talking about one’s drug use with their doctor. Also, some doctors (and other health care providers) are more comfortable working with people who use drugs than others. Ask your friends if they have a good doctor that you can talk to. If you can’t find a good doctor right away, at least you will learn about which health care providers to avoid, or what to be ready for in the case that you meet an intolerant doctor. Consult your local harm reduction center or PLWHA network office for lists of health care providers they suggest.

Ask Questions

Don’t be afraid to ask questions about any tests and/or treatments that your health care provider suggests. Your health care provider should let you know about the risks and benefits of medications. He/she should tell you about the possible side effects, how common these are, and what he/she will do to help you get through hepatitis B and C treatment. You can be prepared by writing down some of your questions before your doctor’s appointment.

Be clear about needs and responsibilities

Direct communication between you and your health care provider is important. Your health care provider can give you better care when you can be honest about what you need. It may take time to develop a relationship with your health care provider, and it is not always possible. Since changing health care providers is not always an option, it is important to ask your health care provider what his/her needs and expectations are, as well as sharing your own needs and expectations.

If you need any drugs with abuse potential, such as pain and anti-anxiety medications, talk with your doctor or health care provider in advance. Ideally, you can make an agreement about how often he/she will be prescribing, what to do if you need a higher dose, and how long you will be using them; make a plan to taper off of pain medication in advance, if needed. While the legal and policy environment make it difficult for people who use drugs to feel safe sharing personal information such as this with her/his provider, it is important to remember that your provider must respect your confidentiality and must treat you, and treat your concerns with respect. If you feel your rights have not been respected, you may contact your local harm reduction center or PLWHA network center to ask for help in negotiating this issue with your provider/health care institution.

Keep appointments

Try not to miss appointments with your health care provider, even if you are using drugs. Some health care providers will use your reliability in attending appointments as a factor in their decision about treating your HIV and/or hepatitis B or C. If you need to miss an appointment, try to call ahead of time to cancel and reschedule.
When you are on treatment it is even more important to keep appointments, because your health care provider needs to monitor your health, response to treatment, and address any side effects.

Be prepared

Make a list of questions in advance. Bring a friend, or family member with you, who can help you remember what your health care provider told you. Your doctor may not have much time to speak with you, so make sure to ask him/her to direct you to someone who can answer your questions, or schedule another appointment.

Share information with your health care provider

If you are using any other medications, vitamins and/or herbs, tell your health care provider or bring them with you to show your provider. Keep an updated list, and tell your health care provider if you are starting a new medication. Some may be liver toxic, or have interactions with other drugs that you are taking, which can make them less effective, and/or increase side effects.

Tell your health care provider about any side effects you are having, even if they seem insignificant to you. They may be the sign of a more serious problem. For example, feeling tired may be a symptom of anemia (low red blood cell count, can be caused by interferon, ribavirin and AZT).

Monitor your health

Ask for copies of your lab work, and keep track of any changes so that you can ask your health care provider about them. Use the lab work sheet provided at the end of this section to keep track of your lab results over time.

Clinical Trials

Your health care provider may suggest that you participate in a clinical trial. Sometimes trials offer access to experimental or approved treatments that are not available otherwise, but it is important to get as much information about the possible risks and benefits before you decide to enter a trial.

Healthcare providers are not always the best source of information about the trial (sometimes people get paid for enrolling people in a study, or their job depends on whether or not they people sign up for the trial). Besides asking about risks and benefits, the most important questions you can ask your health care provider are:

• What kind of treatment do you suggest if I decide not to enter the trial?
• Are there other options?
• If so, can you describe them?

Joining a trial is not an emergency; you have some time to learn more about whether or not it is the best option for you. Ask to take a copy of the informed consent, and read it over. Some NGOs may have more information about the trial; it’s always a good idea to get a few different opinions, especially from community members and advocates.

Thai AIDS Treatment Action Group (TTAG)
18/89 Vipawadee soi 40, Lad yao, Chatuchak, Bangkok 10900
Tel. 02-939-6434 | Fax 02-939-6437
You might want to bring this worksheet with you to your doctor’s appointments and record your lab results. Tracking these results over time will give you a better picture of your disease progression and can tell you if your treatment is working.

<table>
<thead>
<tr>
<th>Date</th>
<th>Ranges</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD4 cell count</strong></td>
<td>From 0 to 1,600 cells/mm³. HIV treatment is recommended when CD4 falls below 350 cells/mm³.</td>
</tr>
<tr>
<td><strong>HIV RNA (viral load)</strong></td>
<td>From undetectable to over 1 million copies/mL.</td>
</tr>
<tr>
<td><strong>HBV DNA (viral load)</strong></td>
<td>From undetectable to over 1 trillion IU/mL</td>
</tr>
<tr>
<td><strong>HCV DNA (viral load)</strong></td>
<td>From undetectable to over 40 million IU/mL</td>
</tr>
<tr>
<td><strong>ALT (SGPT)</strong></td>
<td>ULN (upper limit of normal): Women: 19 units/L Men: 30 units/L</td>
</tr>
<tr>
<td><strong>AST (SGOT)</strong></td>
<td>Women: 9–25 units/L Men: 10–40 units/L</td>
</tr>
<tr>
<td><strong>ALP</strong></td>
<td>Women: 30–100 units/L Men: 45–115 units/L</td>
</tr>
<tr>
<td><strong>GGT</strong></td>
<td>Women: &lt;45 U/L Men: &lt;65 U/L</td>
</tr>
<tr>
<td><strong>Bilirubin (direct)</strong></td>
<td>0.0–0.4 mg/dl (U.S.) 0–7 umol/L (SI units)</td>
</tr>
<tr>
<td><strong>Bilirubin (total)</strong></td>
<td>0.0–1.0 mg/dl (U.S.) 0–17 umol/L (SI units)</td>
</tr>
<tr>
<td><strong>Albumin</strong></td>
<td>3.1–4.3 g/dl (U.S.) 31–43 g/L (SI units)</td>
</tr>
<tr>
<td><strong>PT</strong></td>
<td>11–13.5 seconds (INR &lt; 1.3)</td>
</tr>
<tr>
<td><strong>AFP</strong></td>
<td>&lt;10 µg/L</td>
</tr>
</tbody>
</table>
PRE- and POST-TEST QUESTIONAIRES
This test can be given before and after the training to measure participants’ improvement in knowledge about viral hepatitis. Answers key is at the end.

Please circle only one answer for each question

1) The liver:
   A. Is the body’s filter—everything a person eats, drinks, inhaled, & all drugs, vitamins & medications a person takes goes through their liver
   B. Stops working as soon as a person gets HBV or HCV
   C. Can still keep working even when it is damaged
   D. A and C

2) HBV and HCV:
   A. Are viruses that go into the liver and can cause liver scarring
   B. Worse for you if you get both of them instead of just one
   C. Can be prevented, and treated
   D. All of the above

3) HBV can be prevented by a vaccine
   A. True
   B. False

4) HCV can be prevented by a vaccine
   A. True
   B. False

5) Bleach always kills HBV and HCV
   A. True
   B. False

6) A person can get HBV from:
   A. Eating food cooked by someone who has HBV
   B. Injecting drugs with shared equipment, having unprotected sex with a person who has HBV, at birth, if your mother has HBV
   C. Kissing, hugging and shaking hands with a person who has HBV

7) A person can get HCV from:
   A. Sharing plates, silverware, glasses, food and drinks with a person who has HCV
   B. Injecting drugs with shared equipment
   C. From mother to child, especially if the mother is also HIV-positive
   D. B and C

8) HBV can turn into HCV
   A. True
   B. False

9) HBV and HCV are always chronic (lifelong)—they never go away by themselves
   A. True
   B. False
10) You can only get HBV once
   A. True
   B. False

11) You can only get HCV once
   A. True
   B. False

12) HBV transmission from mother to child can be prevented
   A. True
   B. False

13) HCV transmission from mother to child:
   A. Is not preventable
   B. Happens about 30% of the time
   C. Is less likely when the mother is HIV-negative
   D. A and C

14) HBV and C can cause liver damage because:
   A. A person’s immune system tries to fight these viruses by walling off infected liver cells, causing liver scarring
   B. Both viruses slowly kill all the liver cells
   C. The liver gets tired out from fighting off HBV and HCV

15) Liver damage from HBV and HCV:
   A. Happens to everyone with hepatitis
   B. Always happens in a year or less
   C. Is more likely for people who are also HIV-positive
   D. A and B

16) If a person has HBV or HCV, drinking alcohol every day:
   A. Won’t hurt them unless they have more than 5 drinks per day
   B. Is fine as long as a person drinks beer only
   C. Makes liver disease worse

17) All HIV-positive people should be tested for HBV & HCV
   A. True
   B. False

18) HBV and HCV are diagnosed by:
   A. A single blood test
   B. A liver x-ray
   C. Yellow eyes
   D. A combination of blood tests
19) Liver enzymes:
   A. Are proteins that go from the liver into the bloodstream when the liver is inflamed and liver cells are damaged or dying
   B. Can be higher than normal for many reasons (during drug detox, from ARVs or other medications, street drugs, or heavy drinking)
   C. Are always higher than normal in people who have serious liver damage
   D. A and B

20) Regular liver enzyme testing is important:
   A. For all people on ARVs
   B. For all people with HBV
   C. To tell you how much liver damage you have
   D. A and B

21) If you have HBV, getting a viral load test is important because:
   A. It will tell you how much liver scarring you have
   B. The HBV viral load helps to decide if a person needs to start treatment
   C. A and B

22) If you have HCV, a genotype test is important because:
   A. It can help to predict how likely it is that HCV treatment will work for you
   B. How long you need to be on HCV treatment
   C. How much liver scarring you have
   D. A and B

23) A liver biopsy is:
   A. The best way to see how much liver damage a person has
   B. A test, where a small piece of liver tissue is drawn out with a needle
   C. Not always needed before starting HBV or HCV treatment
   D. A, B and C

24) Liver scarring is also called:
   A. Fibrosis, if it is mild to moderately serious
   B. Cirrhosis, if it is very serious
   C. A and B

25) People with cirrhosis are at risk for:
   A. Liver failure
   B. Liver cancer
   C. A and B

26) HBV and C can be treated:
   A. Only in people with a low viral load
   B. Whether or not a person has HIV
   C. A and B
27) HBV treatment:
   A. Can prevent or delay liver damage
   B. Works only for HIV negative people
   C. Is used for a few weeks

28) HCV treatment:
   A. Works for everyone
   B. Can cure HCV
   C. Does not have any side effects

29) HCV treatment is:
   A. Lifelong, like HIV treatment
   B. A combination of pills (ribavirin) and injections (pegylated interferon)
   for 12-48 weeks

30) Some HIV drugs are hard for the liver to break down
   A. True
   B. False

31) Some HIV drugs also work against HBV
   A. True
   B. False

32) ARV can help to delay liver disease by keeping the immune system healthy
   A. True
   B. False

33) Some ARVs cannot be used during HCV treatment
   A. True
   B. False

34) If you have HIV and HBV, it’s important to talk with your doctor before you
    stop or change your ARVs, because you need to treat both viruses
   A. True
   B. False

35) Even if you can’t get treatment for your HBV or HCV, you can lower your risk
    for liver damage by:
   A. Starting ARV if you also have HIV
   B. Drinking less alcohol, or none at all
   C. Eating more vegetables
   D. A and B
Answers Key:

Q1=D; Q2=D; Q3=A; Q4=B; Q5=B; Q6=B; Q7=D; Q8=B; Q9=B; Q10=A;
Q11=B; Q12=A; Q13=D; Q14=A; Q15=C; Q16=C; Q17=A; Q18=D; Q19=D;
Q20=D; Q21=B; Q22=D; Q23=D; Q24=C; Q25=C; Q26=B; Q27=A; Q28=B;
Q29=B; Q30=A; Q31=A; Q32=A; Q33=A; Q34=A; Q35=D

Post-Training Qualitative Evaluation Questions:

1) The most important things I learned were:

2) I will use the information from this training to:

3) The top 3 advocacy priorities for me and my community are:
   a.
   b.
   c.

4) The actions I plan to take in the next months are:
   a.
   b.
   c.

5) The things I liked best about this training were:

6) This training could be better if:

7) Overall, this training was (circle one):

   Excellent      Very Good      Good      Fair      Poor