

Herpesviruses in Fish

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Herpesviruses cause diseases in many animals including humans, monkeys, birds, cattle, horses, seals, dogs, rodents, snakes, turtles, frogs, oysters and fish. The herpesviruses that infect fish produce several important diseases, and some fish herpesviruses are regulated by both state and international law. To avoid serious losses, damage to the producer's reputation, and loss of access to markets, fish growers need to know about these diseases.

The biology of herpesviruses is unusual. Herpesviruses can exist for many years in a resting stage in apparently healthy carrier animals. During this stage (called "latency"), the genetic code of the virus hides within the animal's cells but no actual virus is produced. Later, the genetic code of the virus is reactivated and new virus is made. The newly made virus may cause disease in the infected animal, or the animal may continue to appear healthy but shed virus that can infect and produce disease in other animals. An excellent example of this process is chicken pox, a very common human herpesvirus disease.

The chicken pox virus is so widespread that almost all humans are infected by the time they are teenagers. When children are infected, they develop chicken pox disease and usually recover in a week or so. While they are sick they shed virus that can infect other children. Once they have recovered the infective virus is gone, but the genetic code for the virus continues to lurk in nerve cells. The virus may remain in this stage for the rest of the person's life, but in some individuals the combination of old age and stress makes conditions right for the virus to come out of hiding and cause a disease called shingles. Adults suffering from shingles can spread the virus and cause chicken pox in children.

Fish herpesviruses appear to behave very much like the human chicken pox herpesvirus. Fish that survive

herpesvirus infections appear healthy and normal but are likely to carry the genetic code of the herpesvirus. Those carrier fish may, when stressed, release new virus into the water and infect fish not previously exposed. Those newly infected fish may develop a disease and spread the virus to other fish; they also become carriers and may infect other fish at a later time. It is these healthy looking carrier fish that make it very difficult to control herpesviruses in fish.

In this publication we will look more closely at the fish herpesviruses that most often affect cultured cyprinids and catfish in the southeastern U.S.

Carp, koi and goldfish herpesviruses

There are three herpesviruses that infect goldfish or koi.

Common name	Scientific name
Carp pox, Fish pox	<i>Cyprinid herpesvirus-1</i> (CyHV-1)
Herpesviral hematopoietic necrosis virus (HVHN), also known as Goldfish herpesvirus (GHV)	<i>Cyprinid herpesvirus-2</i> (CyHV-2)
Koi herpesvirus (KHV)	<i>Cyprinid herpesvirus-3</i> (CyHV-3)

Carp pox

Of the koi and goldfish herpesviruses, carp pox is most like chicken pox in humans. The virus is globally distributed in koi and common carp. When the immune systems of infected fish are slowed by cold temperatures, the virus sometimes produces a skin disease, but it is rare for fish to die. In almost all cases, warmer water temperatures help the fish to recover and the skin to heal. It is likely that these survivors are the source of the virus that infects the next generation.

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Typical carp pox growths on the skin of a koi.

The skin disease caused by the carp pox virus is quite easy to recognize. Diseased fish have soft, pink, translucent, wart-like growths on their skin. The growths are so fragile that they can usually be removed by gently rubbing a finger over the growth. This is not a good treatment for carp pox because the growth is likely to come back and because the rubbing damages the skin and makes it susceptible to secondary bacterial infection. However, verifying that the growths are soft and fragile does help to distinguish carp pox from some similar looking tumors and parasite infections. The best way to manage carp pox disease is to just wait for spring, or to slowly warm the fish to temperatures in the mid 70s to the mid 80s (°F). It is very rare for fish to die from carp pox, but large growths do sometimes leave scars on valuable show fish. Therefore, it may be important to warm show fish that have carp pox disease when the growths are still in their early stages.

Goldfish herpesvirus

The goldfish herpesvirus (GHV, also known as herpesviral hematopoietic necrosis virus or HVHN) was first reported in 1995, but its importance was not understood until a new test was developed in 2006. We now know that the virus is global in distribution and that it can kill goldfish on farms, at small breeders, and even in backyard pools and aquaria. Most goldfish populations carry the virus but, like carp pox, disease outbreaks are sporadic and are triggered by stress and water temperature. The disease is most common when water temperatures are in the 70s (°F). It usually occurs in the spring and fall, either when water temperatures first enter the 70s (°F) or when fish from ponds with warmer water are harvested and moved to holding facilities with cooler water.

The disease caused by GHV can take on several different appearances. The most common sign of the disease is anemia. The virus attacks the tissues (head, kidney) that form new blood cells. Diseased fish have low numbers of red blood cells, so their gills are pale. The head also may look pale because the fish's brain (somewhat visible through the goldfish's thin skull) is white instead of the usual pink. In other cases of GHV disease, there are small patches of dead gill tissue and the skin may lose the mucus and surface layers, making it feel rough instead of smooth and slick.

The disease can be prevented if the combinations of stress and temperatures in the 70s (°F) can be avoided. It can be treated by elevating temperatures into the low to mid 80s (°F). At these higher temperatures, the fish's immune system is able to successfully defeat the disease. Of course, surviving fish are GHV carriers.



A goldfish with normal red gills (above) and a goldfish with anemia and the pale gills typical of GHV disease (below).

Koi herpesvirus

The other important cyprinid fish herpesvirus is koi herpesvirus (KHV), which first appeared in the 1980s. After initial outbreaks in the U.S. and Europe, it rapidly spread throughout the world to wherever koi and common carp are produced (with the possible exception of Australia). When first introduced into new fish populations, it may kill 70 to 95 percent of the fish. Its spread has had a devastating effect on koi producers and hobbyists, and it has seriously reduced global production of farmed common carp, one of the world's most important protein resources. Today, the virus continues to cause sporadic disease outbreaks in farmed and wild common carp and koi populations.

KHV disease is dealt with very differently than carp pox and GHV. With carp pox and GHV, producers assume that the virus is present and make management changes to reduce disease losses. With KHV, producers, dealers and hobbyists all work hard to prevent its introduction, and infected populations are often destroyed to prevent the further transmission of the disease by surviving carriers.



This fish does NOT have KHV. The white patches of gill tissue are the result of a columnaris bacterial infection. Also noticeable on this fish is a "notched nose." Some koi owners consider a "notched nose" to be a sign of KHV disease, but it is also clearly noticeable on this fish with only a bacterial infection.

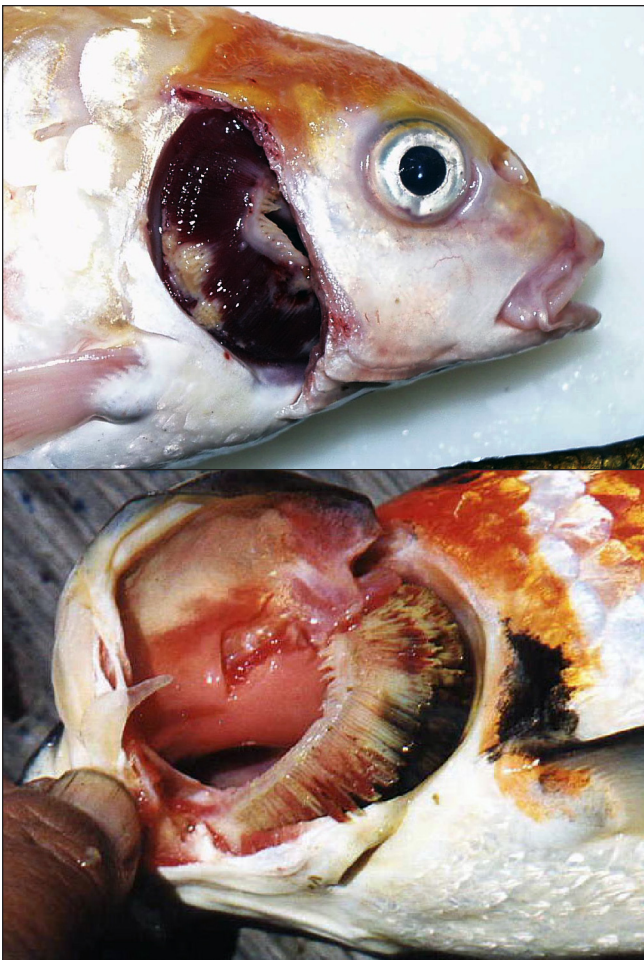
Because the KHV is avoided instead of managed, biosecurity and sensitive tests for carrier fish are tremendously important. These issues will be discussed in later sections of this publication.

The disease produced by KHV almost always causes patches of dead gill tissue. These patches are often white, but they may be yellow or brown if debris or bacteria stick to the damaged gill. In the early stages, the dead patches of gill may be surrounded by more normal looking gill tissue. It is also fairly common for the skin to lose the mucus and surface layers so that it feels rough instead of smooth and slick. Diagnosis must be made carefully because several common bacterial infections, including columnaris, can mimic KHV disease. Fish with KHV disease swim lethargically and congregate around aerators where it is easier for them to take up oxygen through their damaged gills. The disease usually occurs when infected fish are first held at water temperatures in the 70s (°F). If temperatures are elevated into the 80s (°F), many fish will recover and be immune to further KHV disease; however, these survivors are carriers and are a threat to other koi at koi shows or when sold or moved to new collections where KHV disease has not previously occurred. Survivors of KHV outbreaks should never be sold or taken to koi shows. Most producers and breeders elect to destroy infected koi and carp populations to prevent the spread of the disease.

Catfish herpesviruses

There are two known herpesviruses of catfish. These are the channel catfish virus (CCV) and a herpesvirus of black bullheads. The scientific names for these viruses are Ictalurid herpesvirus-1 (IcHV-1) and Ictalurid herpesvirus-2 (IcHV-2).

The CCV is widespread in North America and is present in almost all commercial populations of channel



Koi with KHV infection. The fish on the top is in the early stages and has sharp-edged white patches of gill tissue. The fish on the bottom has a more advanced case of KHV with widespread destruction of gill tissue.



These very famous pictures of CCV disease are from the collection of Dr. John Plumb. The fish on the top has a swollen abdomen and pop-eye typical of CCV. The fish on the bottom have CCV, but also a co-infection by columnaris bacteria. The swollen abdomen is from CCV, while the eroded fins and tails are caused by columnaris disease.

catfish. Given that channel catfish are commonly reared in state hatchery and stocking programs, it is also very likely that CCV is widespread in wild catfish populations. As with carp pox and the GHV, catfish producers assume that the virus is present and manage their facilities to reduce the probability that the disease will develop.

The CCV produces disease in young catfish during their first summer in production ponds. It typically occurs in the southeastern U.S. during the summer months when water temperatures are above 90 °F. Outbreaks in fish older than 6 months, or at cooler temperatures, are extremely rare, but there have been reports of CCV disease occurring in fry still held in hatchery tanks at temperatures in the 80s (°F). CCV disease is not a major problem in the catfish industry, but it does cause serious losses if it occurs in fingerling ponds. The CCV disease has never been reported in wild fish populations or in the northern half of the U.S. where water temperatures rarely reach the 90 °F threshold associated with CCV disease in the Southeast. The primary method of

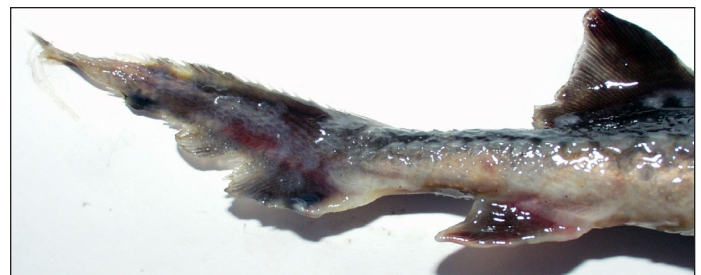
managing CCV is to avoid stressing young fish during the summer months when temperatures are above 90 °F. CCV disease could probably be treated by cooling fish to temperatures well below the 90 °F threshold, but this is rarely practical in large commercial production ponds during the summer months. Farmers sometimes turn on supplies of cool well water in the hope that the fish will take refuge in the cooler waters near the inlet pipe.

The primary sign of CCV disease in channel catfish fingerlings is a bloated, fluid-filled abdomen. CCV disease often occurs with infections of columnaris bacteria, and it can easily be confused with ESC disease that may produce similar bloating under some conditions.

The other important herpesvirus of catfish is IchHV-2, which was first reported in farmed black bullheads in Italy in the early 1990s. The virus spread rapidly and decreased the production of farmed black bullhead in Italy by more than 90 percent. The IchHV-2 disease has never been reported in North America, but if introduced here it could cause serious harm to wild and farmed populations of bullhead catfish. More troubling is the fact that experiments have shown channel catfish to be very susceptible to IchHV-2. In parallel exposure experiments, the IchHV-2 virus kills more fish than does CCV. The IchHV-2 disease also occurs at cooler temperatures than CCV disease (the 70s rather than the 90s °F), so it would be likely to produce disease over a broader geographic area. It is extremely important to prevent IchHV-2 from being introduced into North America.

Sturgeon herpesviruses

Several herpesviruses are found in sturgeon. Two of the most important were called white sturgeon herpesvirus-1 (WSHV-1) and white sturgeon herpesvirus-2 (WSHV-2), but they are now formally recognized as Acipenserid herpesvirus-1 and Acipenserid herpesvirus-2 (AciHV-1 and AciHV-2). In young sturgeon (less than 6 months of age) both herpesviruses have caused mortality of up to 50 percent. The viruses tend to target fish that are feeding well and growing rapidly. Lesions usually are not visible to the naked eye, but microscopy reveals severe damage to skin cells. The AciHV-2 also produces a



The tail of a white sturgeon experimentally infected with AciHV-2. Note the soft, translucent skin growths that resemble those of carp pox.

disease in older fish that causes white blisters and ulcers on the skin. Mortality from this form of the disease rarely exceeds 10 percent. The AciHV-2 has been shown experimentally to kill juvenile shovelnose and pallid sturgeon. Both herpesviruses are present in wild sturgeon populations in the western U.S. and are very important in sturgeon aquaculture, especially when wild broodstock are used.

Trout and salmon herpesviruses

There are two well-known herpesviruses of salmonids. They are Salmonid herpesvirus-1 (SalHV-1) and Salmonid herpesvirus-2 (SalHV-2; common name *Oncorhynchus masou* virus or OMV). The SalHV-1 was initially isolated from rainbow trout in the state of Washington, but it is not an important cause of disease. OMV, however, does cause an important disease in Pacific salmon and in rainbow trout. The disease is usually characterized by skin ulcers and red or white spots in internal organs. Survivors often



On the top is a rainbow trout with OMV disease. The pale gills and white spots on the liver are typical symptoms. On the bottom is a wild Masu salmon with a jaw tumor (arrow) caused by OMV. Pictures courtesy of Dr. Mamoru Yoshimizu of Hokkaido University, Japan.

develop tumors in their jaws. The disease most commonly occurs in 1-month-old alevins and at temperatures below 57 °F. The OMV is found only in Japan and has never been reported in North America. It is very important to prevent the introduction of this virus.

Avoiding herpesviruses

Some fish herpesviruses are so widespread that avoidance is essentially impossible. These include carp pox (CyHV-1), the herpesvirus of goldfish (CyHV-2), and channel catfish virus (IcHV-1). For these viruses, managing to prevent disease outbreaks is the correct approach (see “Managing herpesviruses”). The other fish herpesviruses still have limited distribution. For these, the best approach is to ensure that they are not brought onto the farm.

Herpesviruses can enter a farm with infected fish, contaminated water supplies, contaminated equipment, and human and animal visitors. All of these routes should be addressed in a farm biosecurity plan as described in SRAC Publication Nos. 4707 and 4708. One of the most important parts of a biosecurity plan is ensuring that infected fish are not brought onto the farm. Unfortunately, the ability of the herpesviruses to persist in healthy looking survivors can make the detection of infected fish very difficult.

Fish that survive herpesviruses carry the genetic code for the virus, but most of the time little, if any, infectious virus is present. This means that tests to detect herpesviruses by cell culture (the standard practice with fish viruses) will almost always be negative even when the fish actually carry the virus. Cell cultures are useful for diagnosing herpesvirus infections when fish are sick with the disease, but are essentially useless for detecting carriers. A better approach is to test fish for the genetic code (DNA) of the virus. These tests go by the abbreviation PCR (polymerase chain reaction). PCR tests are very sensitive and specific but may still fail to detect very low-level carriers. The PCR tests are not currently recognized for regulatory purposes, but they are used to identify viruses grown in cell cultures.

The other way to test for herpesviruses is to look for evidence that the fish has been exposed to a herpesvirus. When fish are exposed and then begin to develop disease, their immune systems produce virus-fighting molecules called antibodies. These antibodies persist in the fish’s blood for months or years following the disease. With some herpesviruses, most notably KHV, blood samples can be submitted to a few specialized labs that can detect the antibodies. If the antibodies are present, the fish has been exposed to the herpesvirus and is likely a carrier. These tests are able to detect survivors for months or years after the disease outbreak.

The other big testing challenge is with fish that have been exposed to the virus but have not yet developed the disease. These fish have too little virus to be detected by any method and have not yet produced antibodies. Thus, exposed fish that have not yet developed the disease are a very great risk for disease transmission, but are undetectable by laboratory testing.

Keeping herpesvirus infected fish off of a farm takes more than testing. To the greatest extent possible, use farm-raised broodfish and do not bring new fish onto the farm unless absolutely necessary. If new broodfish must be brought onto the farm, they should be obtained from a source that has a program to prevent herpesvirus infection. Wild broodfish are the most risky. If new fish are brought onto the farm, quarantine them with careful biosecurity (SRAC Publication Nos. 4707 and 4708) until they have experienced several weeks (at least 3) at the water temperature where the herpesvirus of concern is likely to cause disease. Test any sick fish by cell culture. After the quarantine, test the survivors by PCR or an antibody test (if available).

A common aquaculture biosecurity practice is to isolate new broodfish, disinfect their eggs with iodine, and then move only the disinfected eggs onto the main farm. While this is always an excellent idea, it is important to be aware that this strategy may not offer full protection from herpesviruses. There is convincing evidence that egg disinfection often fails with herpesviruses. It is possible that fish herpesviruses may be transmitted within eggs instead of on egg surfaces. Virus inside the egg is protected from the iodine by the egg shell.

In summary, avoiding herpesviruses is achieved by the following measures.

- Use on-farm broodstock and avoid new fish introductions if possible.
- If new fish are introduced, get them from reliable sources with good histories and not from the wild.
- Quarantine new fish and then test for the virus.
- Don't rely on egg disinfection to prevent herpesvirus introductions.

Treating herpesvirus infections

If fish are infected by herpesviruses, there are very few treatment options. **There are no treatments that can be used to clear the virus from carrier fish.** If fish are dying during an outbreak of disease, losses can be greatly reduced by manipulating water temperatures. Most herpesviruses produce disease only at certain temperatures. Moving sick fish out of those temperatures greatly reduces mortality, and these survivors are generally resistant to future disease caused by the same virus. However, you

must keep in mind that **all herpesvirus survivors are carriers with the potential to spread the virus to new places.** Temperature treatments are not appropriate unless there will be no opportunities for the survivors to spread virus to new fish populations. Outbreaks of KHV and the goldfish herpesvirus disease can be treated by elevating water temperatures into the mid 80s (°F), but any fish treated in this manner must be considered virus carriers with the potential to infect other fish. Signs of carp pox disease disappear at water temperatures above about 72 °F. Channel catfish virus losses are greatly diminished by reducing water temperatures into the 70s (°F).

Currently, there are no vaccines in the U.S. for fish herpesviruses. There is a KHV vaccine available in some other countries. Vaccines are an attractive way to help prevent the introduction of KHV or to prevent disease outbreaks from widely distributed viruses such as the goldfish herpesvirus and CCV. If effective, practical, and economically feasible vaccines do become available for fish herpesviruses in the U.S., they will be of great benefit, but there are two important things to keep in mind. The first is that vaccinated fish are likely to test positive by PCR and antibody tests. There may be no way to distinguish safe, vaccinated fish from dangerous carriers. The other concern is that vaccinated fish, while protected from the disease, may still be able to serve as virus carriers.

Managing herpesviruses

Avoidance is always best, but some herpesviruses such as carp pox (CyHV-1), the herpesvirus of goldfish (CyHV-2), and channel catfish virus (IcHV-1) are so widespread that avoidance is nearly impossible. The best approach for these viruses is to manage your farm in a way that decreases the likelihood of a disease outbreak and that minimizes losses should an outbreak happen. In general, disease outbreaks are prevented by avoiding stress during the temperatures and seasons when the disease is likely to occur.

Carp pox

The best management for carp pox is to make sure that koi and common carp have adequate nutrition, good water quality, and low parasite loads during the winter when temperatures are low. If possible, try to avoid very low temperatures in the winter and rapid temperature changes.

Goldfish herpesvirus (CyHV-2)

Goldfish fry often carry the virus when they leave the hatchery. Disease occurs the first time water temperatures drop into the lower 70s (°F) at the same time fish experience stress. The disease is often seen in young fish during periods of fluctuating fall temperatures. If fall tempera-

tures drop rapidly through the 70s to colder temps, losses are minor, but if temperatures drop into the 70s (°F) and remain there for some time, losses may be significant. The best scenario is for temperatures to drop briefly into the 70s (°F) and then move back into the 80s (°F) for some time. When this temperature pattern occurs, fish begin to develop the disease but the rising temperature slows the virus and gives the fish time to make a strong immune response. These fish may then be immune to the disease when the temperatures drop again later.

A very common trigger for goldfish herpes virus (CyHV-2) disease in the Southeast is mid-summer harvest and handling. If fish are stocked out and grown at high temperatures, the carriers do not develop disease. However, when the farm harvests and moves fish to cooler holding facilities (especially if that move involves long-distance shipment at cool temperatures) outbreaks of the disease are likely to occur. These outbreaks can be prevented by gentle handling at the highest temperatures consistent with good survival. It is also very helpful to hold fish at warm temperatures (in the 80s °F) following summer shipments at cool temperatures.

Channel catfish virus (CCV)

Disease most often occurs when young of the year are stressed (by harvest or poor water quality) at water temperatures in the 90s (°F). Thus, the dangerous time of year in the Southeast is July through August. When disease outbreaks occur, losses can be reduced by lowering temperatures, but this is very difficult in large earthen ponds. Running cool well water may help, but even large

flows of well water have small effects on pond temperatures. Harvesting sick fish and moving them to cool water in a holding facility is generally not done because the harvesting stress is likely to make things worse. In managing CCV outbreaks, it is also important to remember that columnaris disease often occurs with CCV.

Summary

- There are many important herpesviruses of fish.
- Survivors of herpesvirus infections carry the virus and may infect other fish later.
- Carriers are extremely hard to detect using laboratory tests.
- Some herpesviruses have limited distribution so the best protection is a good biosecurity program to prevent introduction. These herpesviruses include *Oncorhynchus masou* virus (SalHV-2), koi herpesvirus (CyHV-3), Ictalurid herpesvirus-2 (IcHV-2), and sturgeon herpesviruses (AciHV-1 and AciHV-2).
- Other herpesviruses are widespread, but losses can be prevented by carefully managing stress during disease temperature windows. These herpesviruses include carp pox (CyHV-1), goldfish herpesvirus (CyHV-2), and channel catfish herpesvirus (IcHV-1).
- When outbreaks of herpesvirus diseases occur, losses can be minimized by manipulating water temperature, but **survivors will be carriers** of the virus.
- There are no drug or chemical treatments for herpesvirus infections in fish.

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