Fish Health News You Can Use

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This Issue

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In the Next Issue

- Being a fish health detective
- “Normal flora”
- Aeromonas bacteria

Introduction

Question: *So why did those fish get sick and die?*

Answer: *They were “stressed.”*

We’ve all heard it, but **what does it mean?**

“Stress” is defined in many different ways. “Stress” is sometimes used to describe a situation, sudden or prolonged, that exceeds a fish’s ability to adapt. For example, if water temperatures are above 70F, Chinook salmon are not able to adequately adjust their biochemistry. When this happens, biochemical reactions in the fish go wrong, normal energy pathways fail, cells quit working, and the fish dies. Other examples of these kinds of events would be critically-low oxygen, injuries, and diseases so severe that widespread damage to cells and organs kills the fish. These kinds of experiences are a common cause of death in fish, but they are not what physiologists are talking about when they say that fish “died from stress.”

Figure 1: An example of a fish in a stressful situation. Perception that there is a dangerous predator nearby produces a physiological response in the goldfish.

In this issue of Fish Health News, we are going to define stress as a physiological response that helps animals to survive what is, or seems to be, a dangerous situation. In other words, the stress response is something that the fish does to increase its chance of survival when things go wrong. It is not something that is done to the fish, it is instead a finely tuned mechanism that the fish uses to adapt to, and survive, a life-threatening situation.

Triggering a Stress Response

The stress response can be triggered by a genuinely dangerous situation like:

- Escaping a predator
- Dealing with an injury or disease
- Being at the bottom of the pecking order (no food, no mates, no fins!)

In these examples (above), the stress response helps the fish to adapt and survive. However, the stress response can also be triggered by a situation that the animal *perceives* as dangerous, *but really isn't.* For example:

- Being picked up in a net
- Being raised at high density
- Traveling in a fish truck
- A bath treatment for disease

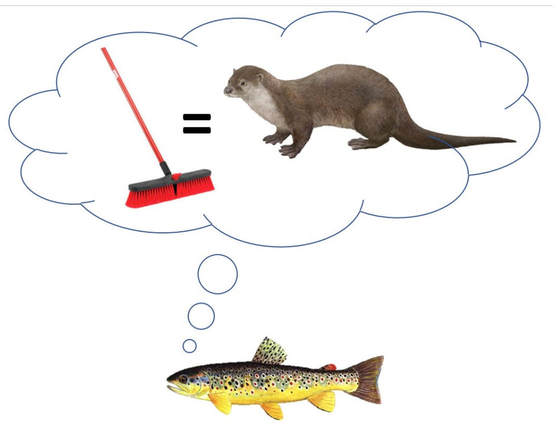

Figure 2: To a fish living in a raceway a broom and an otter may both trigger a predator avoidance stress response. Only one danger is real (the otter) but both may trigger the same response.

When the fish is responding to a true emergency, the stress response is beneficial. It increases the fish's ability to adapt and survive by mobilizing the immune system for peak response and altering energy use to ensure the fish can make a quick getaway. Unfortunately, the stress response also always has negative side effects (just like the drugs that your Dr. prescribes). This means that when a fish launches a stress response to a perceived danger, not a real one, the fish experiences the downside of the stress response without any real benefit at all. That's bad because those side effects include excess energy use, slower growth, decreased immune function, and problems with water and salt balance.

The Stress Teacup Analogy

An important consideration for fish managers (and humans in our daily lives) is that stress (real or imagined) is additive. One big event can trigger a stress response on its own but so can the sum of many smaller stressors. Imagine a teacup. Every small stress puts another slosh of tea into the cup. When it runs over, a stress response (with its benefits and side effects) occurs. If the cup is empty, an operation like marking and tagging might not cause it to overflow. However, if the cup already contains a slosh of disease, a splash of bad water quality, and a glug of "chased by otters", the same marking and tagging operation would overflow the cup and trigger a stress response.

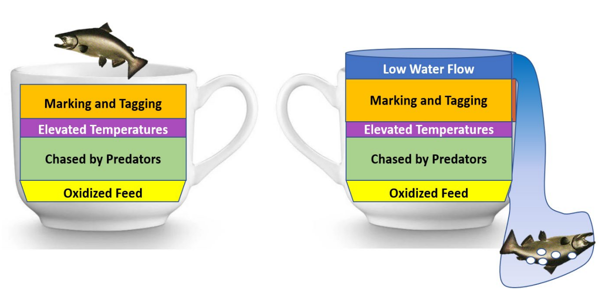

Figure 3: The cup analogy for stress. Common events have filled the stress cup to the brim so the additional stress of low water flow triggers a stress response that leads to infection and death.

It is also important to note that sloshes of stress don't stay in the cup forever. If the severity of the stressor is reduced, there might be enough room in the cup to accommodate the Low Water Flow stress.

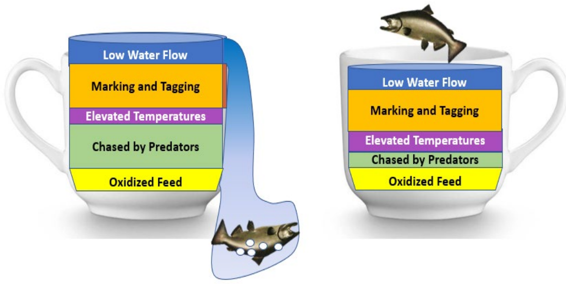

Figure 4: By reducing the stress associated with predators (anything from bird nets to more careful sweeping) the amount of "Chased by Predators" stress is reduced and there is room in the cup for some low water flow stress.

It is also true that stressors don't stay in the cup forever, as time passes, their contribution fades away and leaves more room.

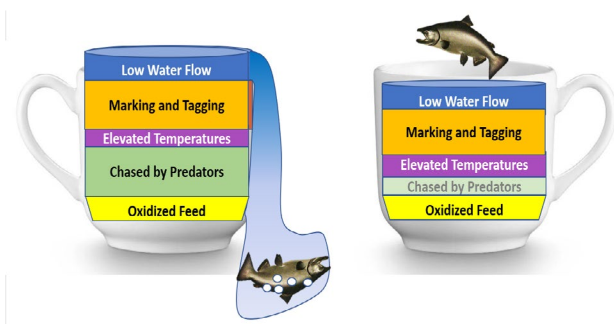

Figure 5: In the cup on the right, time elapsed since the predator incident has allowed the stress contribution to fade leaving room for some low water flow stress. In other words, the fish had time to recover some before new stress was encountered.

The flip side of course is that repeated real or perceived encounters with predators may put additional sloshes of stress in the cup and that stress may accumulate faster than the sloshes fade away. The cup fills just as quickly with repeats of the same stress event as it does with different stress events. The cup still runs over.

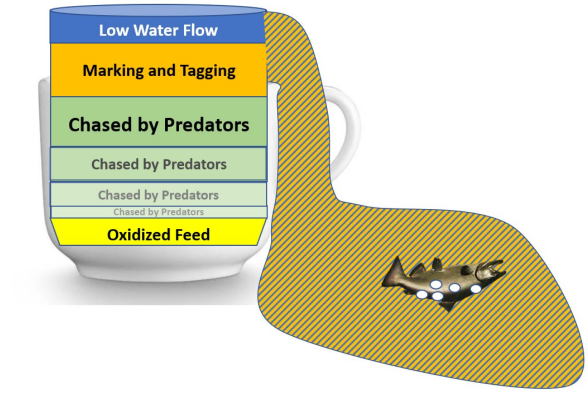

Figure 6: Multiple incidents of the same kind of stress all add a contribution to the teacup. In this example, repeated predator stresses have filled the cup even though some of the earliest contributions are starting to fade away.

Keep in mind that when that teacup overflows it is not an accident of fish physiology. It is a carefully orchestrated and purposeful response by the fish to a dangerous situation. There are downsides (even the best drugs have adverse side effects) but, in life-threatening situations, the benefits outweigh the downside effects. Unfortunately, in aquaculture we must often deal with a more frustrating situation where the fish incorrectly perceives a situation as life threatening even though it isn't. For example, an otter and a raceway broom might both trigger a predator avoidance stress response, but only the otter is really dangerous. The broom triggers the side effects of the stress response without providing any benefits.

Stress, the good effects

Dangerous situations (real and perceived) can be sudden and short lived or they can be long drawn-out disasters. Examples of sudden emergencies ("acute" stress) for fish include:

- Being chased by a predator
- Becoming trapped on a rock ledge next to a waterfall
- Being picked up in a dip net
- Experiencing a sudden drop in oxygen
- Neurotoxins (algal or fungal)

Acute stresses like these trigger a "flight or fight" response that helps the fish to make a quick escape or to launch a counterattack.

Figure 7: To a fish, common non-life-threatening hatchery practices like this may be perceived by a fish as being the same as being picked up by a raven and dropped on a stream bank. Along with minor net-derived skin damage, this can predispose the fish to diseases.

Fish respond differently to long lived emergencies ("chronic" stress). Examples of chronic stress include:

- Poor water quality
- Liver toxins (algal and fungal)
- Disease
- Bad feed
- Injury
- Chronic predation
- Overcrowding
- Loss of social status (not just true for teenagers!)
- Excessive water speeds in a pRAS
- Competition for mates and spawning sites

Most of these chronic situations compromise the fish's ability to obtain and metabolize feed so the stress response to chronic emergencies is designed to make more energy available for critical needs. Of course, this re-allocation of energy comes at the expense of other "luxury" functions like growth, weight gain, and reproductive success.

Figure 8: New circular tank systems will come with new stressors including water quality and water speed. If these stressors are not carefully managed, they will contribute to disease risk.

Acute Stress Hormones +/-

The acute stress response is mediated by a hormone called epinephrine, which is more commonly known as adrenaline. When a fish is chased by a predator (or a dip net), input from the fish's senses go to its brain. If the situation is perceived as life threatening, nerves from the brain carry the message to special cells in the wall of large veins in the front part of the fish's kidney. When those cells get that message, they dump adrenalin into the fish's blood. The blood vessels carry the adrenalin straight to the fish's heart where it increases the heart rate and the strength of the heartbeats. The next stop is the gills where the adrenaline opens more blood passages through the gill filaments and increases the breathing rate. The net effect is that there is a huge increase in oxygen carried by the blood. This whole process takes only a few seconds. Another function of adrenaline is to release sugar from starches stored by the liver and muscles and dump it into the blood. Increased oxygen and food delivery to the muscles allows the fish to fight or flee. The adrenalin response happens so quickly that it can help a fish escape from a predator.

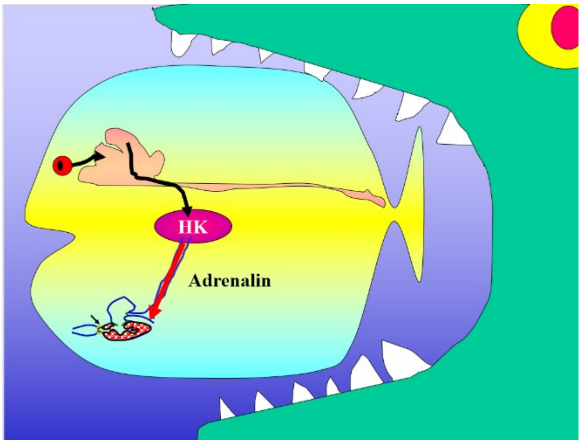

Figure 9: The predator is detected by the eyes and lateral line of the prey fish. Sensory information is processed by the brain. The situation is perceived as dire so the brain signals for adrenaline release by cells in the walls of veins in the kidney.

Adrenaline has some addition effects that can also help a fish survive a fight or flight situation. The hormone cascade triggered by acute stress events "activates" immune cells, like white blood cells, to make them more effective and quicker to respond to any foreign invaders like bacteria or viruses. Adrenaline can also enhance a fish's blood clotting mechanisms to optimize clotting time in case the fish is injured.

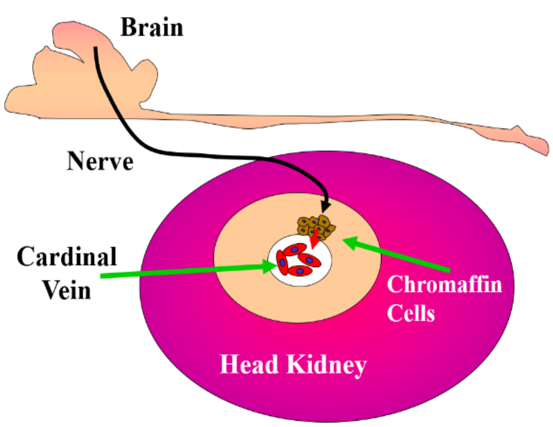

Figure 10: Nerves from the brain trigger adrenaline release by chromaffin cells in the wall of large veins in the kidney.

So, a fish jazzed on adrenaline is much faster and stronger, but the fish chooses to release adrenaline only when there is an emergency. The reason is that there are serious negative side effects to adrenaline.

Figure 11: If adrenaline makes anormal fish into a super fish, why not make it all the time? The answer: Negative side effects.

Remember that fish in freshwater are always losing salt through their gills and skin and soaking up water from the environment. It takes a lot of energy for the gills and intestines to pump replacement salts into the blood, and it takes a lot of energy for the kidney to pump out all of that extra water. Fish in saltwater have equally difficult problems because they lose water and soak up salts. When adrenaline is released, more water and blood move through the gills. This provides extra oxygen to the fish but it also allows much more water and salt to move through the gill membranes so salt and water balance in the blood is much more difficult to maintain and even more energy is required.

The good side of the acute stress response (adrenaline) is that it provides a big energy boost for fight or flight, and it provides a short-term increase in other defenses like immunity and blood clotting. The downside is that it makes it very difficult for the fish to maintain the right salt and water balance and it uses up a lot of energy. When survival is on the line, adrenaline is released and the fish deals with the biological consequences later, ideally when the emergency is over.

Chronic Stress Hormones +/-

When a fish's brain perceives a chronic stress situation (a long-term problem that interferes with feeding and metabolism), it sends a message to the pituitary gland. The pituitary releases a hormone into the blood that eventually makes it to special cells on the kidney. When these kidney cells get the message, they release cortisol into the blood.

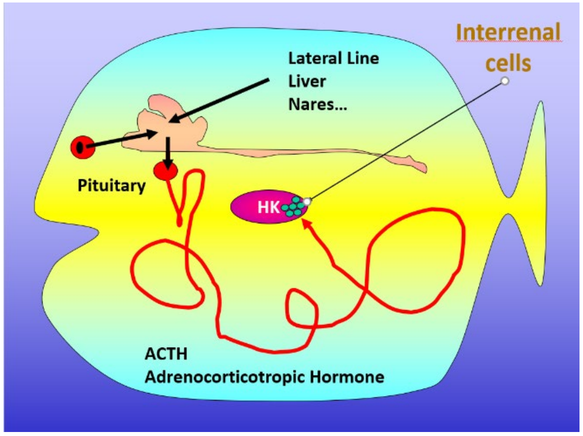

Figure 12: When the brain perceives stress, it sends a hormone message to the pituitary. The pituitary releases a hormone that causes cells in the kidney to release cortisol.

Cortisol is a steroid hormone that, like adrenaline, helps the fish by promoting the release of stored energy. Cortisol switches a starving fish over from using stored fats and carbohydrates as energy to breaking down its own proteins for energy. This extra energy helps the fish to survive a chronic stress event.

So, a fish with elevated cortisol levels has a lot of extra energy, but the fish chooses to elevate cortisol levels only when it perceives an emergency. The reason is that, as with adrenaline, there are negative side effects to cortisol that get more severe the longer the stress continues.

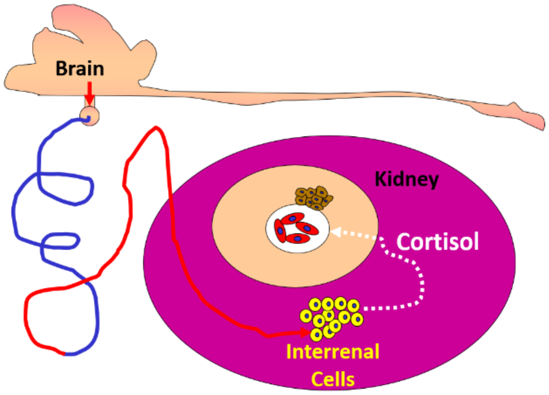

Figure 13: The hormone message from the pituitary causes interrenal cells to release cortisol. The cortisol works its way into blood vessels in the kidney and is then dispersed throughout the fish.

One of the major groups of proteins that cortisol targets for energy are the proteins in the blood. Among these are many critical components of the immune system. Cortisol slows the synthesis of new immune proteins, like antibodies, and promotes their destruction for energy. The net effect is that the immune system of the fish is compromised and begins to respond to threats more slowly and less effectively. Cortisol also targets proteins in muscle as energy storage, leading to depleted muscles and overall poor body condition. It also suppresses reproductive hormones, reproductive behavior, and spawning success, all activities that are critical for both fish and hatchery managers.

Why would fish have a hormone that screws up their immune systems? It is important to consider that everything in a fish that is made of protein is important. When the situation is so dire that proteins are used as energy, the fish tries to spread the damage among everything that is made of protein, but the immune system takes a big hit.

The good side of the chronic stress response is that it provides emergency energy when stress makes it difficult to obtain energy from feed. The downside is that it also leads to the destruction of muscles, a major down regulation of the immune system, and reproductive failure. Extended periods with elevated cortisol levels are very detrimental, especially when they are elevated in response to a perceived threat rather than a life or death situation.

Preventing Stress

Obviously keeping fish alive requires that we don't cause obvious, immediate, emergencies like life threatening injuries, rapid temperature changes, and severe diseases that would quickly kill fish. Less obvious though are more subtle or seemingly harmless situations that trigger the good and bad sides of acute or chronic stress responses. It is important to keep in mind that little stresses add together to make big stresses. If we think back to the teacup analogy, the goal should be to keep the teacup as empty as possible to leave room for the big sloshes of stress that we cannot control (increased water temperature, decreased flows, etc.).

Figure 14: Managing water speed in pRAS systems is critical. If speeds are too high the fish are stressed by overexertion and infectious disease outbreaks occur.

To avoid unnecessary stress:

- Handle fish gently to avoid damage to skin or gills
- Maintain good water quality and high oxygen
- Provide the right amount of quality feeds
- Prevent and manage diseases through biosecurity and through early diagnosis and treatment
- Maintain steady temperatures within the optimal range
- Avoid social stress caused by overcrowding or a wide range of fish sizes
- Protect fish from predators
- Maintain correct water speeds in circular tank systems

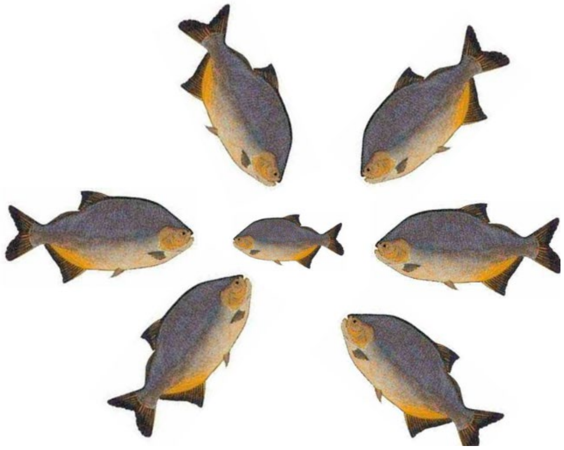

Figure 15: Social interactions are a source of stress. As any high school student knows, being at the bottom of the pecking order is very stressful.

We must work to avoid situations where a stress response is NOT useful to the fish and there are no benefits, just side effects. Examples of these include:

- The use of nets or brooms in a manner that the fish perceives as life threatening predators
- Netting fish and holding them out of the water (perceived by the fish as a life-threatening stranding event)
- Loud noises or disruptions that trigger a flight or fight response
- Chemical treatments that do not directly address a serious fish health problem

- Circular tanks with excessive water speeds

Figure 16: A plane flying overhead looks like a predatory bird and may be a source of stress.

Dealing with Stress

When there is an unavoidable event that is likely to be perceived as an emergency and trigger an acute stress response, for example assessing the ripeness of broodfish, there are three approaches that can be used to prevent or reduce a stress response:

1. Take every possible measure to make the event less stressful. This would include not carrying fish long distances, not removing fish from the water, and managing the event so that fish aren't chased back and forth. Faster and smoother is better. Less stressful events leave more room in the teacup.
2. When stressors do occur, leave time for the fish to recover before the next stressful event occurs. Let stress fade from the teacup before adding more and causing it to overfill.
3. Block the perception of danger by the careful use of tranquilizers. Tranquilizers will keep the fish from perceiving that the situation is dangerous. This is a nifty trick, but you must remember that tranquilizers are themselves a significant stressor (we don't often put fish on respirators when they are under anesthesia!).

Figure 17: When anesthetics are used for fish surgery, veterinarians run oxygenated water through the gills of the fish to counteract some of the negative side effects of anesthetic use.

4. It is also very important to keep in mind that while a tranquilizer might keep a fish from *perceiving* a harmless situation as life threatening, they provide *no protection from a situation that actually is life threatening*. For example, a tranquilizer does not prevent the adverse effects of a rapid temperature change or damage to delicate structures like skin and gills. Work with your fish health expert for advice on fish anesthetics for tranquilization.

Preventing stress and keeping the teacup as empty as possible is always the goal, but when the teacup overflows and stress responses do occur, there are several ways to mitigate the negative side effects. Remember that the response to a sudden life-threatening emergency (like being chased by a predator) is the release of adrenaline. Adrenaline increases oxygen delivery to the fish's muscles, but it also causes the fish to lose salt and gain water faster. The addition of salt to the water can make it much easier for fish to maintain water and salt balance. Work with your fish health expert to make sure that the dose it right and always monitor the salt concentration to make sure that it Is not too high or too low.

Chronic (slow) emergencies cause the continual release of cortisol that helps provide energy when feeding is impaired, but it has the side effect of damaging the fish's immune response. When stress and resultant immunosuppression is expected, reducing disease exposure through biosecurity, management of water flows to flush disease organisms, and maintaining optimal water temperatures is very helpful. It is also important to closely monitor fish for signs of infectious diseases so that diseases can be addressed before they overwhelm immunocompromised fish.

The Summary

Stress is hormone-driven response that helps fish to survive life-threatening situations.

The stress response is triggered by events that are actually life threatening, but also by events that the fish just perceives as life threatening.

The stress response helps the fish to survive, but also has negative side effects.

Stress is additive. Several small stresses can add up to a big problem.

Two stresses separated by a recovery period are much better than two stresses that happen at the same time.

Acute stressors (sudden emergencies) cause the release of adrenaline that helps fish fight or flee but also disturbs water and salt balance in the fish's tissues.

Chronic stressors (slow, long lasting emergencies) trigger the continual release of cortisol that helps provide energy but also damages the fish's ability to mount a strong immune response.

To protect fish from the adverse side effects of stress:

1. Reduce the frequency and severity of both real and perceived life-threatening situations. Gentle handling, a good environment, and good feed!
2. Prevent stress side effects by judiciously using tranquilizers to reduce perceived stress, deal with water and salt balance problems by adding salt to the water, and step up disease prevention measures when a cortisol response is suspected.

Factoids

Fish are not alone in having a stress response. Humans and other animals have a very similar stress response mediated by the same hormones that we see in fish and accompanied by the same negative side effects. Even stressed out insects produce octopamine, which is analogous to adrenaline, and ecdysteroids, which are related to cortisol.

In some cold-blooded animals, the release of adrenaline causes rapid changes in skin color so that they match their background. In these animals, disappearing is their version of "flight."

Figure 18: Green anole lizards darken as part of their stress response. (photo by Robert Michniewicz (edited by Ark) - made by Robert Michniewicz, CC BY 3.0, https://commons.wikimedia.org/w/index.php?curid=2274394)

In mammals, including humans, an autoimmune disease (Addison's disease) sometimes destroys the adrenal cortex in the kidneys. This is where mammals make adrenaline and cortisol. Patients with Addison's must take oral cortisol every day and increase the dose in chronically-stressful situations. In addition, they must carry an adrenaline syringe so that they can successfully respond to an acutely stressful situation. The challenges faced by Addison's Disease patients are ample evidence of the importance of constant and precise regulation of these critical hormones.

Some groups of fish, especially catfish, have "alarm substance cells" in their skin. When the skin of a catfish is damaged, alarm substance is released and it triggers a stress response (fight or flight) in nearby fish of the same species. It is likely that "alarm substance" has some function other than serving as a seemingly-altruistic warning to other fish.

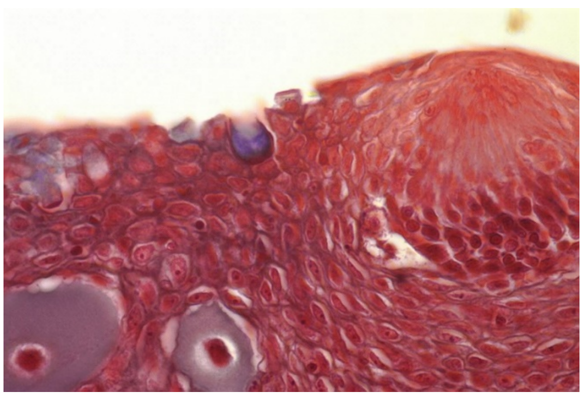

Figure 19: The top layer of catfish skin (epidermis). The gray cells to the bottom left are alarms substance cells. The purple cell in the center is a goblet cell releasing mucus. The red structure to the right is a taste bud (found all over catfish).

The message from the brain to trigger cortisol production by special cells in the kidney travels via hormones secreted by the brain through the blood to the pituitary gland and then by a pituitary hormone through the blood to the kidneys. This hormone (ACTH) is one of as many as 20 hormones made by the pituitary gland. The pituitary is a major pathway used by the brain to regulate metabolism and a host of other functions.

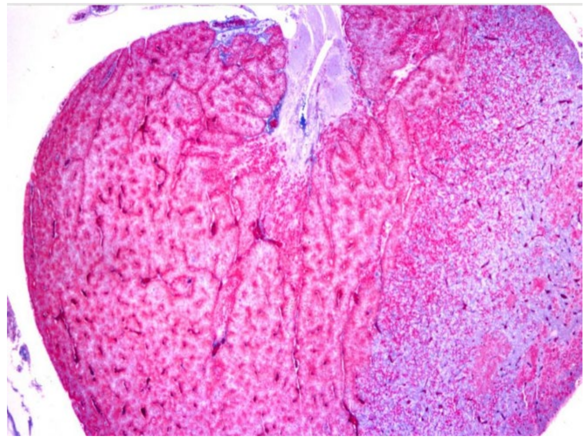

Figure 20: The fish pituitary (circular structure) has many kinds of hormone-secreting cells and is connected to the brain by a stalk of nerves and blood vessels (top center).

Benign tumors in the pituitary gland can secrete too much cortisol and trigger a chronic stress-response. In humans this produces "Cushing's disease" so these tumors are routinely removed by neurosurgeons. Veterinary patients with Cushing's disease are treated with drugs that suppress the cortisol producing system so that cortisol levels are nearer to normal.

When fish are subjected to acute stress, adrenaline is released and more blood and water are pumped through the gills. In freshwater, this causes the fish to lose salt and gain water but, in the ocean, the exact opposite occurs. Acutely stressed fish in seawater gain salt and loose water. So, what is the supportive treatment for acute stress in ocean fish? In many cases, a slight *reduction* in salt concentration is helpful.

In most fish, the cells in the kidney that release cortisol (interrenal cells) occur in small groups that are difficult to identify without special stains. Strangely though, in gray triggerfish the interrenal cells occur in a complex network of stacked cells that are readily identifiable. Nobody knows why.

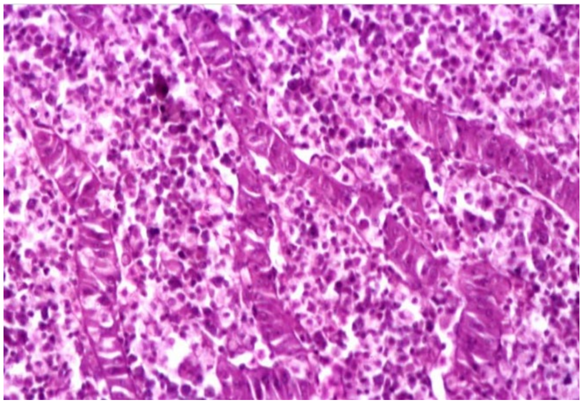

Figure 21: A Gray Triggerfish kidney. The purple cords of cells are cortisol-producing interrenal cells.

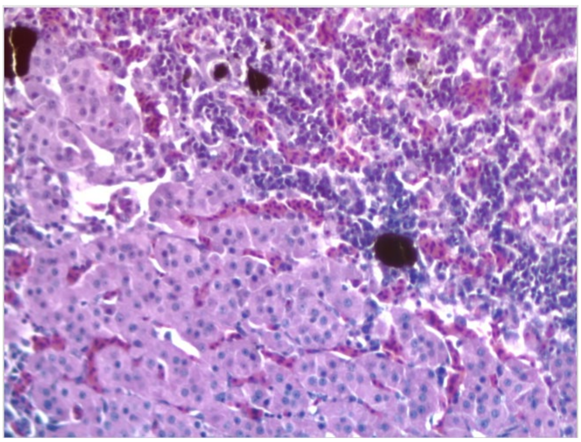

Figure 22: The kidney of a channel catfish. In many cases cortisol-producing cells are very difficult to identify, but the mass of plump pink cells to the bottom left are most likely interrenal cells.

Cortisol hormone levels are used to objectively evaluate stress levels in animals. Cortisol can be measured in a variety of sample types like blood, tissues, eggs, hair, whiskers, urine, feces, and even in water samples.

Open-water freshwater fish, like threadfin shad or hybrid striped bass, develop an especially strong acute stress response when held in fish hauling trucks. In plain water, hauling mortality may be more than 95%. However, in 3-5 parts per thousand of salt (about a tenth of seawater) mortality in carefully-handled fish may be near zero.

Salt levels in fish blood are critical in the control of water balance in cells throughout a fish's body. High salt levels in blood cause cells to shrink like raisins. Low salt causes them to expand like balloons…they may even pop. However, these are not the problems that you see first when salt concentrations in blood are too high or too low. The electrical charges that carry messages through nerves, and that trigger muscle contraction, are dependent on a finely tuned movement of sodium, potassium, and chloride ions across cell membranes. If blood concentrations are wrong, nerves and muscles malfunction and muscles throughout the fish's body may contact and stay contracted.

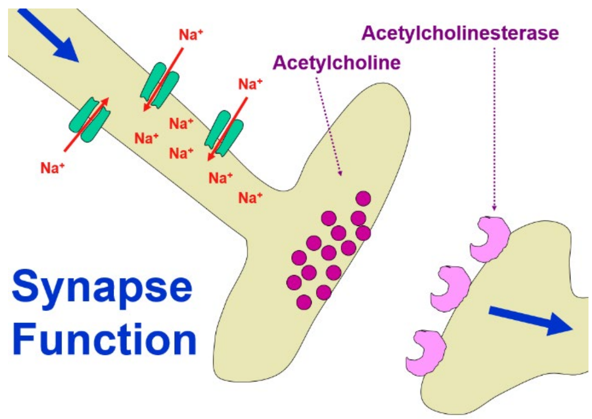

Figure 23: Nerve messages propagate by electrical signals caused by the movement of sodium ions. Neurotransmitter release is also triggered by movements of sodium and potassium salts. Stress disrupts salt balance and compromises nerve function.

Some freshwater fish species have a difficult time living in water with very low concentrations of ions like sodium and potassium and they must rely on their food as a critical ion source. In these species, if you withhold feed for a day or two and then trigger an acute stress response with a dip net, or even loud noises, blood sodium and potassium quickly drop to critical levels. The fish's nerves and muscles quit working and the fish turns rigid, bends into a crescent shape, and then sinks to the tank bottom. In some cases, they can slowly mobilize sodium and potassium from emergency stores and then pop up and swim normally again. In other cases, they die.

Many disease organisms are finely tuned to take advantage of a cortisol stress response. For example, when the immune response gets too strong, the chicken pox virus (a herpesvirus) goes into hiding inside nerves cells near the spine. Decades later when a stressful situation happens, the host's immune system is weakened. The virus responds by sliding down the nerves to the skin and then infecting and killing skin and nerves cells. The disease caused by the return of the virus is the "shingles" and the relationship between chronic stress and the shingles is striking. Herpesviruses in fish do similar things.

Figure 24: Climate change, less water and higher temps, will both add to the stress experienced by fish.

In the hot dry summer of 2015, Chinook salmon juveniles exposed to temperatures persistently above 70 degrees would sometimes roll over when the shadow from a passing biologist moved across the raceway. The most likely explanation is that they were critically low on salts in their blood and that the acute stress response triggered by the shadow (probably perceived as an avian predator) was enough to drop those levels to where nerves and muscles didn't work anymore.

In our conversations about salt loss, we have discussed just plain salt – sodium chloride or NaCl. This is the dominant salt in fish blood so most salt movement across gill membranes is sodium and chloride ions, however, potassium, and small amounts of calcium and magnesium are also lost. The best science is that treatment with NaCl is adequate, but there may be times when the addition of small amounts of these other ions is helpful.

The cells that are in kidney vein walls and produce adrenaline are called "chromaffin cells." Why? Because scientists doing histology decades ago found that these cells stained brown when exposed to certain chrome salts. At that time they didn't know what the cells did, but they knew that they had an "affinity for chrome."

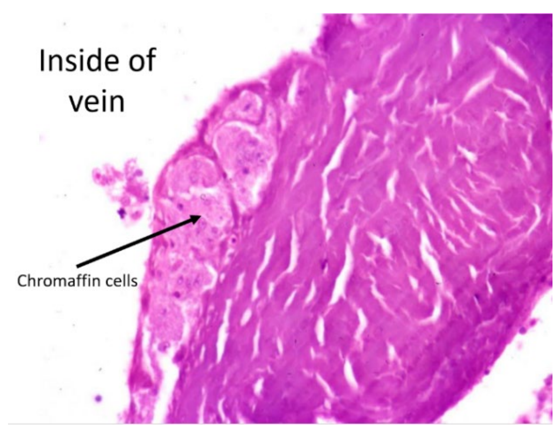

Figure 25: In the kidney of a fish, chromaffin cells in a vein wall are positioned to release adrenaline directly into a major vein.

Some fish disease organisms, like the virus IHNV, seem to be able to infect seemingly healthy fish living in great conditions. Others like ich are still fish disease specialists but produce disease only when the immune system of fish is not in top form. There is a third fascinating group that includes bacteria and fungi (really oomycetes of course!) that live free in the environment, have no need for fish hosts, and that are not highly specialized to infect fish or avoid fish immune systems. This third group causes disease only when immunocompromised fish are exposed to high concentrations of the potential disease organism.

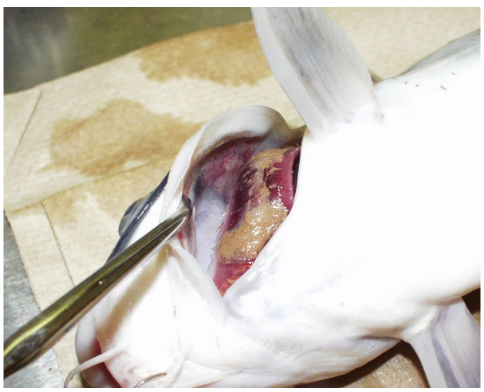

Figure 26: When channel catfish are stressed by a temperature drop of more than 10 degrees in 24 hours, their immune function is compromised and they develop gill infections caused by the fungus-like oomycete saprolegnia.

Great examples on normally benign organisms that can act as pathogens in stressed fish include the oomycete saprolegnia and bacteria in the *Aeromonas hydrophila* group. These *Aeromonas* bacteria are common on the skin and in the intestines of health fish where they are part of the "normal flora". However, when the host immune system is compromised, often by a chronic stress response, these bacteria are perfectly happy to make themselves home in organs throughout the fish where the damage that they cause, especially at warm temperatures, will quickly kill fish stressed by other problems.

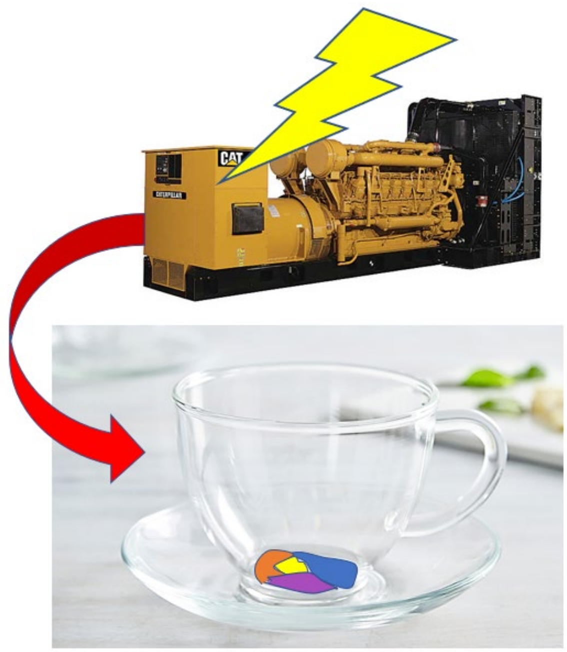

Figure 27: The goal for hatchery managers is to keep the stress teacup as empty as possible to leave plenty of room for unexpected events.