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ESC — Enteric Septicemia of Catfish

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Enteric septicemia of catfish (ESC), caused by the gram negative bacterium *Edwardsiella ictaluri*, is one of the most important diseases of farm-raised channel catfish (*Ictalurus punctatus*). ESC accounts for approximately 30 percent of all disease cases submitted to fish diagnostic laboratories in the southeastern United States. In Mississippi, where channel catfish make up the majority of case submissions, it has been reported at frequencies as high as 47 percent of the yearly total. Economic losses to the catfish industry are in the millions of dollars yearly and continue to increase steadily with the growth of the industry.

ESC was first recognized as a new infectious bacterial disease of pond-raised channel catfish in 1976 through the examination of diseased specimens from Alabama and Georgia submitted to the Southeastern Cooperative Fish Disease Laboratory (SECFDL) at Auburn University. The disease was similar to another disease of catfish caused by the gram negative bacterium *Edwardsiella tarda*, but differed in several characteristics. ESC was described in a published account in 1979 and the causative bacterium was described as a new species in 1981.

Although recent evidence indicates that ESC may have been present in Arkansas as early as 1969, records from fish diagnostic laboratories indicate that it was not prevalent in the industry immediately following its discovery. Only 26 cases were recorded by the SECFDL between January 1976 and October 1979, and ESC occurred in only 8 percent of the total cases reported by the Mississippi Cooperative Extension Service in 1980 and 1981. Between 1982 and 1986 the increase in ESC incidence was explosive and the impact on the catfish industry significant. ESC is now known to occur throughout the geographic range of the catfish industry.

Species susceptibility

The channel catfish is the fish most susceptible to infection by *Edwardsiella ictaluri*, but white catfish, brown bullhead, and walking catfish are also susceptible. Blue catfish (*Ictalurus furcatus*) occasionally contract ESC but have been shown to be resistant to experimental infection. *Edwardsiella ictaluri* has been isolated from diseased ornamental fish such as the danio, green knife fish, and rosy barb. Other fish species, such as the rainbow trout, chinook salmon, blue tilapia and European catfish, have been experimentally infected with the bacterium, but natural outbreaks in these species have not been reported.

Range

ESC is primarily a pathogen of channel catfish cultured in the southeastern United States. The disease has been diagnosed from catfish production areas in Mississippi, Arkansas, Alabama, Louisiana, Georgia and Florida. It occurs less frequently in Virginia, Texas, Idaho, Indiana, Kentucky, California, Arizona and Maryland. Natural fish kills in wild populations of catfish due to ESC are rare; only two cases are on record.

Clinical signs and diagnosis

Behavior

Catfish affected with ESC often are seen swimming in tight circles, chasing their tails. This head-chasing-tail, whirling behavior is due to the presence of the *Edwardsiella ictaluri* in the brain. Affected fish also sometimes hang in the water column with the head up and tail down. In addition, catfish with

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ESC tend to stop eating shortly after becoming infected.

External Signs

ESC-affected catfish frequently have red and white ulcers (ranging from pinhead size to about half the size of a dime) covering their skin (Fig. 1); pinpoint red spots (called petechial hemorrhages) especially under their heads and in the ventral or belly region (Fig. 2); and longitudinal, raised red "pimples" at the cranial foramen between the eyes (Fig. 3) that can progress into the "hole-in-head" condition. Internal build-up of fluid can lead to a swollen abdomen and exophthalmia (popeye) (Fig. 4).

Internal Signs

Clear, straw-colored or bloody fluid is often present in the fish's body cavity. The liver typically has characteristic pale areas of tissue destruction (necrosis) or a general mottled red and white appearance (Fig. 5). Petechial hemorrhages can be found in the muscles, intestine and fat of the fish. The intestine is also often filled with a bloody fluid.

Diagnosis

ESC typically is diagnosed by culture and isolation of the causative bacterium from the internal organs or brain tissue on tryptic soy agar (TSA) with 5 percent sheep's blood or brain heart infusion (BHI) agar. Isolates from the internal organs and brain of catfish streaked on these media take about 2 days at 25 to 30° C to become readily apparent. Growth of *Edwardsiella ictaluri* often is not detectable at 24 hours. The 48-hour cultures are typically composed of very high numbers of extremely small, punctate, white colonies. The bacterium should be gram negative, weakly motile, rod shaped (0.75 x 1.25 μm), oxidase negative, fermentative in O/F glucose or glucose motility deeps (GMD), triple sugar iron (TSI) slant reaction K/A with no H_2S, and negative for indole production in tryptone broth.

Figure 1. Red and white ulcers on the skin of a channel catfish with ESC. (Photo courtesy of Joe Newton)

Figure 2. Petechial hemorrhaging caused by ESC on the ventral surface of a channel catfish. (Photo by John Hawke)

Figure 3. This red and white lesion at the cranial foramen of a channel catfish fingerling is a sign of ESC of catfish. (Photo courtesy of Al Camus)

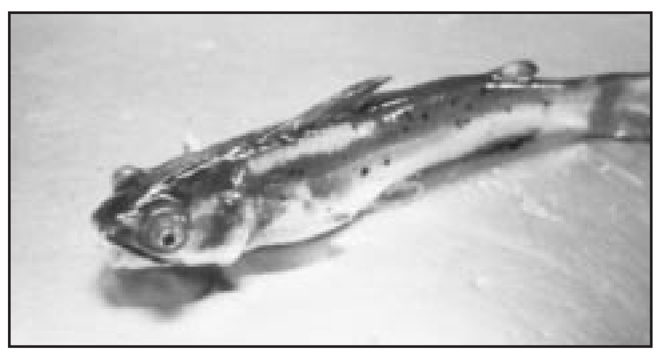

Figure 4. The exophthalmia in this channel catfish fingerling was caused by fluid build-up from an infection with Edwardsiella ictaluri *bacterium. (Photo by Bob Durborow)*

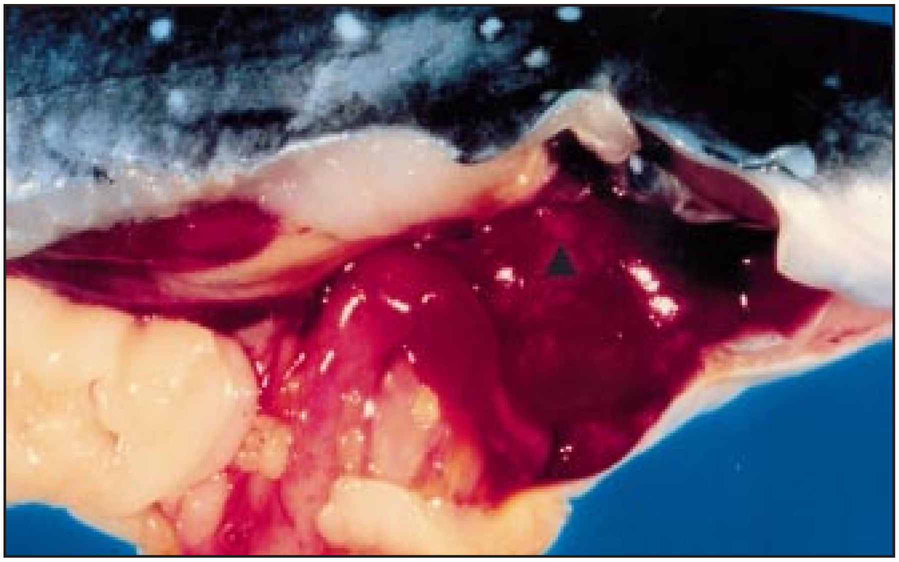

Figure 5. The white mottling (indicated by the arrow) in the liver of this channel catfish with ESC indicates the presence of the bacteriaum Edwardsiella ictaluri. *(Photo courtesy of Joe Newton)*

Confirmation can be made with serological (immunological) tests including the slide agglutination test, indirect fluorescent antibody test (IFAT), enzyme immunoassay (EIA) or enzyme linked immunosorbent assay (ELISA). *Edwardsiella ictaluri* also may be identified using miniaturized biochemical test systems such as the Minitek system (BBL Microbiology Systems) and the API 20E system (bioMérieux Vitek, Inc.).

Edwardsiella ictaluri can be identified with the API 20E system by generation of the code number 4004000.

Cause of ESC

Enteric septicemia of catfish can occur when a susceptible host (channel catfish) encounters a virulent pathogen (*Edwardsiella ictaluri*) under environmental conditions that are conducive to proliferation of the pathogen and stressful for the host. Although ESC may occur in healthy fish in non-stressful environmental conditions, stress factors such as handling, close confinement, improper diet, low water chlorides, poor water quality, and water temperature fluctuations all lead to increased susceptibility to infection. The introduction of ESC-infected fish into a pond containing healthy fish, or stocking healthy fingerlings into a pond containing older catfish that are carrying *E. ictaluri*, can result in the perpetuation and spread of ESC. Fish that survive an outbreak can carry the bacterium in the brain, kidney and liver for extended periods (up to 200 days). These survivors develop specific immunity that protects them from subsequent infection and disease.

Edwardsiella ictaluri was originally thought to be an obligate pathogen because it only survives for a short time in water; however, it was later demonstrated to survive for up to 95 days in sterile pond mud at 25°C. Pathogenesis studies have shown that *E. ictaluri* can enter catfish through the gut, the nares (nasal openings), and possibly the gills. Transmission probably occurs from fish to fish via the water by organisms shed with the feces, by cannibalism of infected fish, or by feeding on dead, infected carcasses. Another way ESC can be transmitted is by birds picking up dead fish from one pond, flying to another pond and dropping the infected carcasses. *Edwardsiella ictaluri* can be transferred from pond to pond on wet nets and equipment, but allowing the equipment to air dry in direct sunlight should be sufficient to kill the bacteria.

ESC occurs within a specific temperature range sometimes referred to as the "ESC window." Outbreaks typically occur in the spring and fall when water temperatures are between 20 and 28°C (68 to 82°F). Mortalities slow and usually stop outside this temperature range.

Prevention and treatment

Prevention

Prevention of ESC is difficult because of its widespread distribution throughout the catfish industry. Various management practices, however, can reduce the incidence of ESC. These include reducing stress, using proper nutrition and feeding practices, and administering drugs and chemicals correctly. In the future, genetic improvement of fish stocks and vaccination may become important factors in preventing ESC.

Stress – The most common advice given for the prevention of bacterial disease in fish is to avoid stress. This is a difficult goal to accomplish because commercial aquaculture is stressful by nature. Stocking density may be the most important factor, with higher stocking densities increasing the efficiency of disease transmission and spread throughout a population. Although reduction of stress is helpful for prevention of disease, it is not always effective because *E. ictaluri* can cause disease even in the absence of apparent stress.

Nutritional supplements – Improved nutrition through vitamin and mineral supplements may increase the resistance of catfish to *E. ictaluri* infection, but few studies have demonstrated that nutritional supplements effectively decrease the risk of ESC. Research indicates that increasing the amounts of various individual vitamins and minerals, such as vitamin E (60 to 2500 iv. mg/kg), iron (60 to 180 mg/kg), vitamin C (50 to 2,071 mg/kg), folic acid (0.4 to 4 mg/kg) and zinc (5 to 30 mg/kg), in the feed did not increase resistance to experimental infection with *E. ictaluri*. In contrast, sources of dietary lipid appeared to have an effect on resistance to infection. Menhaden oil increased susceptibility to ESC infection compared to corn oil or beef tallow as a lipid source.

Winter feeding – Winter feeding programs were found to affect susceptibility to ESC infection the following spring. Year 1 fish that were fed in December, January and February were more resistant to *E. ictaluri* infection the following spring, while year 2 fish that were fed in the winter were less resistant to infection. Further research is needed in this area.

Immunostimulants – Immunostimulants and/or immunomodulators, such as β-glucans, cell wall extract of the yeast *Saccharomyces*, extracts of the blue green algae *Spirulina* or extracts of *Ecteinascidia turbinata*, were found to enhance non-specific immunity in channel catfish but did not improve resistance to infection by *E. ictaluri*.

Genetic improvement – Various crosses of different strains of channel catfish and crosses with other species of catfish have been examined for resistance to infection by *E. ictaluri*. Higher resistance to infection was noted in the Red River strain as compared to Mississippi-select and Mississippi-normal strains. The cross between Norris strain females and Marion x Kansas males showed improved resistance to ESC. Resistance to infection was also seen in the blue catfish. Hybrids of Norris female channel catfish and blue catfish males had intermediate resistance between pure strain blue catfish and pure strain channel catfish.

Specific pathogen free (SPF) fish – The production and stocking of specific pathogen free fingerlings, while a possibility, has not been widely accepted by the industry because stocking fish that have never been exposed to ESC into ponds containing fish that are carriers can lead to extremely high mortality rates. The opposite approach is often practiced where fingerlings that are survivors of an ESC outbreak are actually preferred because of their acquired immunity to subsequent infection.

Vaccination – Vaccination is being examined as a means of preventing outbreaks of ESC. Formalin killed vaccines, in which fish are immersed for a short time, are widely used in the trout and salmon industries to protect fish populations against certain bacterial infections. Vaccinated salmonids typically have much higher survival rates with less demand for medicated feeds and better feed conversion than unvaccinated fish. Unfortunately, favorable results with killed vaccines have not been consistently obtained in channel catfish and their commercial marketing has not been well accepted by the catfish industry. New live, *attenuated* ESC vaccines have recently been developed and will soon be marketed.

Treatment

Treatment of ESC can be approached in a variety of ways. A good pond manager makes daily observations on feeding response, behavior and mortality, thus making an early diagnosis possible. Traditionally catfish infected with ESC are treated with feeds containing antibiotics. First, samples of sick fish should be submitted to a fish diagnostic laboratory for a complete diagnosis. The causative bacterium can then be isolated and tested for antibiotic sensitivity. Fish should be treated as soon as a diagnosis has been made because fish progressively reduce feed intake during an infection, making medicated feed treatments less effective. Currently, only Romet 30®, Romet B® (Hoffmann-LaRoche, Inc.) and Terramycin® (Pfizer, Inc.) are approved by the U. S. Food and Drug Administration (FDA) to treat food fish. *E. ictaluri* is usually sensitive to both Romet® and Terramycin®; however, their effectiveness is limited for several reasons.

Romet 30® – Romet 30® is a potentiated sulfonamide that is a combination of sulfadimethoxine and ormetoprim. The combination of the two drugs is more effective than either of them used separately. The Romet 30® is incorporated into the food and fed at a rate of 23 mg of active ingredient per pound of fish (50 mg/kg of fish) per day for 5 days. Permitted feed mills add the drug to the fish food at concentrations ranging from 66.6 pounds of premix per ton to 5.6 pounds per ton. The amount of food to be given each day depends on the concentration of the drug in the food.

Romet imparts an objectionable taste to the feed and causes catfish to eat poorly after the first day it is offered. This problem has been alleviated to some degree by increasing the amount of fish meal (for more desirable flavor) or by adding the drug to the feed at a lower concentration and increasing the amount that is fed daily. The dosage of 50 mg/kg/day remains the same and more medicated pellets are available per fish. Infected catfish fingerlings are now commonly fed Romet 30® formulated at 11.1 pounds of premix per ton of feed (the tag on the bag will indicate the formulation). This particular formulation is fed to the fish at 3 percent of their body weight each day for 5 days. There is a 3-day withdrawal period after the treatment is completed before any catfish may be released as stocker fish or sold for human consumption. It was discovered in research trials that feeding Romet medicated feed every other day or at 2-day intervals improved survival over daily feedings. This approach seems to keep the fish hungry so they accept the feed better and the drug persists in the tissue long enough to maintain a therapeutic level in the tissues throughout the treatment period. It is important to note, though, that Romet is not labeled by FDA for feeding on an interval schedule.

Romet B® – Romet B® is the form of Romet that can be bought by individuals to mix into their own feed. The recommended dosage is 10.1 grams of the Romet B® premix per 100 pounds of fish per day for 5 days. The amount of feed to be fed (calculated as a percent of body weight) for various concentrations is listed in the following table.

Feed intake of fish (% body weight)	Pounds of Romet B® premix per ton of feed
0.5	88.8
1	44.4
2	22.3
3	14.8
4	11.1
5	8.9
6	7.4

The Romet B® is first mixed with corn oil or 5 percent gelatin (1 gallon of oil per 200 pounds of feed) which is applied to a floating pelleted feed to give a uniform coating (a cement mixer works well for this). The coated feed should be air-dried and used immediately or rebagged and stored for no more than 6 months in a cool, dry environment. The drug has a long shelf life even after addition to feed but the nutritional value of the feed will become degraded with prolonged storage. No feed should ever be used if it has become moldy.

Terramycin® - Terramycin® (oxytetracyline HCl) medicated feed is administered at 25 to 37.5 milligrams of active ingredient per pound of fish for 10 days. There is a 21-day withdrawal period before fish can be sold for human consumption. Terramycin® (TM 100) has 100 grams of oxytetracycline active ingredient per pound of premix. Feed mills use the following amounts of TM 100 when manufacturing Terramycin® medicated feed (feeding rates vary according to the strength of the medicated feed mixture as shown in the following table):

Terramycin® (100) premix per ton of feed	Concentration of Terramycin® in finished feed	Feeding rate of fish (percent body weight)
100 lbs.	5.00 g/lb.	0.5 - 0.75 %
50 lbs.	2.50 g/lb.	1.0 - 1.50 %
25 lbs.	1.25 g/lb.	2.0 - 3.00 %

Terramycin® has several characteristics that reduce its effectiveness in treating fish disease.

Because the drug is heat sensitive, it cannot be incorporated into an extruded, floating pellet. Consequently Terramycin® medicated feed is only available as a sinking pellet. Many fish farmers view this as a problem because they cannot tell if the medicated feed is being consumed. Research is being conducted on an ambient temperature-processed floating pellet that may ultimately solve this problem. The absorption of digested Terramycin® in catfish is also very low (less than 5 percent) and, in a population that is feeding poorly, many fish will not receive a therapeutic dose.

Economic considerations of treating – Economics must be considered when determining the best treatment procedure. Does the cost of the treatment exceed the value of the fish? Do the number of fish dying (or likely to die) have a high enough value to justify the cost of the treatment? The following example demonstrates how economics plays a role in treatment considerations:

A 1-acre pond stocked with 3,000 9-inch catfish fingerlings averaging 190 pounds per 1,000 has 570 pounds of fish. If they are consuming 4 percent of their body weight per day, they will eat about 23 pounds of feed daily. During the course of a 10-day medicated feed treatment, the fingerlings will consume 230 pounds of feed. The cost of medicated feed would be approximately $85 above the cost of regular feed in this particular example. If 30 fish die each day for 14 days, and each fish is worth about 24 cents, the producer would lose more than $100 worth of fish. In this particular case, spending $85 on the medicated feed treatment might be an economically good decision if the treatment is effective in stopping the mortalities.

Antibiotic resistance – Strains of *E. ictaluri* have been isolated that are resistant to Romet® and/or Terramycin®. There is evidence that improper use or over use of antibiotics increases the chance for resistant strains to appear. Medicated feeds should always be used as labeled when a proper diagnosis has been obtained and a disease condition exists, not as a **preventive** measure. Medicated feed should be fed for the total number of days recommended, and not stopped because the fish quit dying. A mixture of medicated and non-medicated feeds should not be fed. The total weight of fish in the pond must be known, and fish must be fed at the recommended percent body weight per day so all fish in the pond receive a therapeutic amount of drug. Medicated feed withdrawal recommendations should be observed before processing.

Chemical treatments – The use of chemical treatments, such as copper sulfate to control algal blooms and parasites, should be avoided during the ESC temperature window. The increased stress due to degraded water quality and the possible immunosuppressive effect of copper sulfate can result in severe outbreaks of acute ESC with high mortality rates. Ponds with a history of yearly outbreaks of ESC probably should be drained and the pond bottoms treated with hydrated lime, disked, and dried before refilling and restocking.

Other methods of control – Recent research has shown that, in some cases, the mortality rates in populations of catfish infected with ESC can be reduced by withholding feed for a period of time. There is merit to this practice and it is widely practiced throughout the industry. However, there are risks involved, as untreated fish can continue to die at a high rate. The success of this method is explained if the pathogenesis of ESC is examined. The bacterium is transmitted very efficiently via the oral route during feeding by ingestion of bacteria-contaminated water along with the feed. Some investigators have noted increased rates of infection by feeding fish during a water-borne experimental challenge. Therefore, by withholding feed from a population that is in the early stages of an ESC outbreak, the transmission efficiency of the disease is reduced and losses may be diminished. A drawback to this method is the lack of growth or even loss of weight by the fish population during this period.

The water temperature should be carefully monitored during ESC outbreaks. If water temperatures are rising rapidly in the spring and approaching 28° C (82° F), it may be wise to withhold an expensive medicated feed treatment because chances of an outbreak will lessen and the fish will stop dying when water temperatures climb above this level. Likewise, if pond temperatures are dropping in the fall and will soon drop to 20° C (68° F) or below, it is best to not treat because losses will probably be minimal. However, if it is the middle of the so-called “ESC window” and the temperatures are to remain stable for several weeks, treatment is advisable.

Management of ESC in the future

ESC will probably continue to be a serious problem for the catfish industry in the near future. Since its discovery 20 years ago, hundreds of scientific articles have been published on various aspects of its pathobiology and major advances have been made in our understanding of the disease, its causative agent, and the immune response of the channel catfish. In the future, a combination of good management techniques, vaccination, and improved antibiotics will enable the catfish producer to better cope with this disease problem. Genetically improved stocks of fish with increased resistance to ESC should be available in the near future. With the application of modern molecular biological techniques to the study of fish diseases, transgenic fish containing genes for disease resistance, genetically engineered live viral vaccine vectors, and live attenuated bacterial vaccines are on the threshold of development.

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