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Practical management of bacterial diseases in finfish aquaculture to minimize AMR

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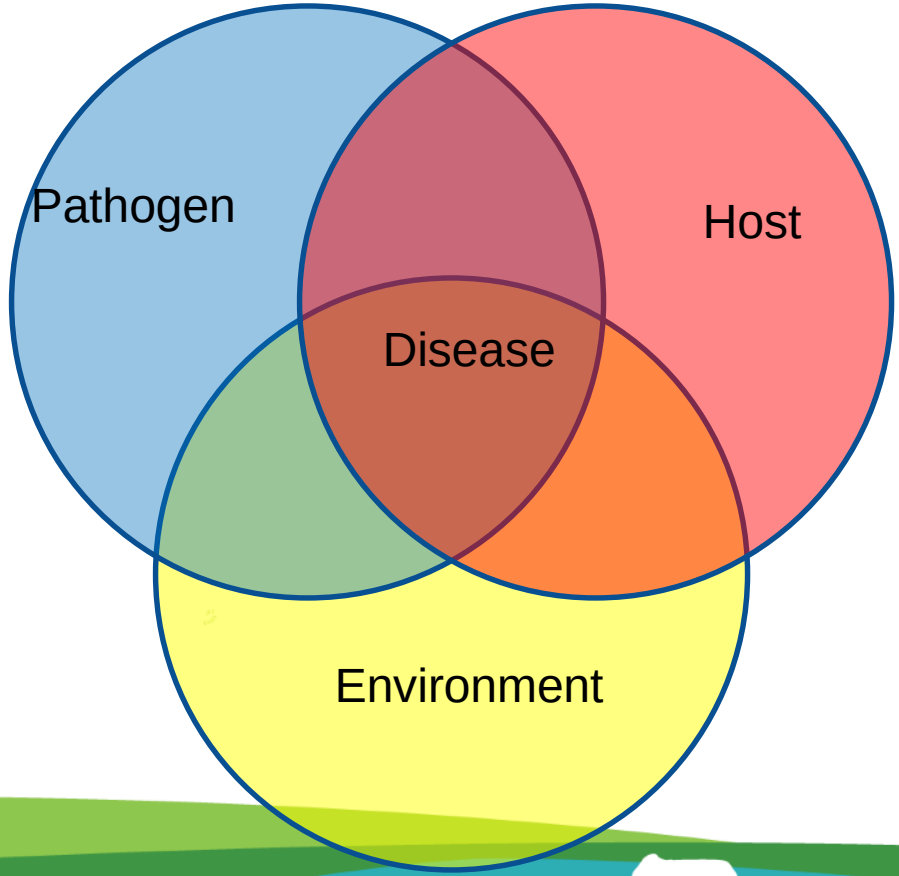
ANTIMICROBIAL RESISTANCE MANAGMENT

- AVOID DEVELOPMENT-
  - Biosecurity
  - Disease prevention
  - Alternative treatments
  - Judicious use
- REDUCE PERSISTANCE of AMR
  - Crop rotation/complete harvest
  - Monitoring and disinfection?
  - Antibiotic use restriction or rotation

Disease prevention- reduces need for antibiotics

If you don’t correct underlying cause disease will reoccur after treatment



Disease prevention starts at the planning stage and is continuous

- Site selection
  - Soil type- Alkalinity, hardness (conditions stabilize algal populations and provide essential minerals)
  - Water source- (biosecurity, temperature, volume, nutrients, contaminants)
  - Location- local stressors, predatory bird roosting sites, flyways, proximity to aquaculture or wild fisheries, Cages-tidal flushing proximity to other aquaculture and prevalence of toxic algae
- Fish
  - Genetics- selection for disease and stress resistance

Disease prevention

- Manage the environment to minimize stress and physical injury
  - Water quality-
    - Oxygen
    - Ammonia
    - Nitrite/chloride
  - Handling

    Avoid rough handling- damage to mucus layer

    Avoid handling at critical temperatures or stages
  - Manage predators
  - Prevent aggression and cannibalism- remove dead fish from pond

Feeding management

- Good quality feed, freshness and amount
  - Nutritionally complete- protein vitamins and fatty acids
  - Stored in dry place and used quickly
- Physical-
  - Proper size for fish- too large can damage mouth, too small wastage & nutrient loss
- Amount and frequency-
  - Want to evenly distribute to all fish for even growth
  - Too much may bypass acid stomach barrier
- Avoid pathogens- live feeds must be disease free and pasteurize any fresh feeds.

Prevent all diseases-

- Actively manage to minimize viral and parasitic diseases (Predispose fish to bacterial disease and suppress feeding- resulting in subtherapeutic treatments)-
- Vaccines-if effective for bacterial pathogens and viruses

Biosecurity- avoid obligate pathogens and introduction of AMR

- Surveillance, quarantine and monitoring
- Used of certified specific pathogen free stocks
- Use pathogen free water, and processed feeds or SPF live/fresh feeds
- Between farm security-
  - On farm equipment, nets
  - Limited access
  - Cleaning/disinfecting trucks, trailers, boats entering facility
- Within farm security
  - Avoid water movement between ponds
  - Disinfect nets and equipment
  - Predator and scavenger control- mammals, birds and reptiles can shed fish pathogens

Biosecurity-Avoiding obligate pathogens and AMR strains

- Fish source- critical factor
  - Improper use of antibiotics during early stages can result in build up in system
    - Fry and eggs sometimes given prophylactic bath treatments during handling- these may be critical during establishment of microbial flora and allow establishment of AMR.
  - Know how fish produced and antibiotic usage- hatchery GAP
    - Due to economics of hatchery systems and susceptibility of young- improper use of antibiotics at this stage is more common (also opportunity to spread pathogens and antibiotic resistance through industry)
    - Disinfection of tanks and ponds between batches.
    - Separation of eggs from brooders and disinfection of egg surface (iodine, formalin, potassium permanganate)

Alternatives to treatment

- Many diseases do not need to be treated with antibiotics-
  - disease and environment- evaluated by a professional who understands the system
  - Many bacterial disease are secondary- correct predisposing factor or allow to run its course
- Management to reduce pathogen load or transmission dose
  - Fecal oral transmission- Allow time for gut to clear before feeding- reduces defecation where feeding- ESC every-other day feeding during peak disease season

    (feed restriction may help with others by reducing close contact)
  - Probiotics or prebiotics?

Non-antibiotic alternatives

- Chemical treatments that interrupt transmission or stimulate resistant state in host
  - Copper sulfate makes catfish less susceptible to columnaris disease
  - Salt 1-5 ppt reduces F. columnare's ability to adhere to fish
  - Potassium permanganate, chloramine T and other oxidizers kill surface bacteria and free bacteria in the water

Judicious Use of Antibiotics-medicated feeds- minimizes selective pressure

- Use when needed and effective
  - Must be diseased- no prophylactic use, no use for growth promotion
  - must be susceptible bacteria pathogen- susceptibility testing
  - Fish must feed well enough to get a therapeutic dose
- Give for full treatment duration- antibiotic must persist long enough to kill pathogen
- Use fresh good quality medicated feed- reliable licensed feed producer
- Careful feeding practices- avoid wastage- AMR can develop in bacteria that grow in wasted feed

Eliminate improper use

- Do not use on non- bacterial diseases
- No prophylactic use- to prevent something that may happen
- Do not use where non-therapeutic levels occur
  - Bath treatment where poor uptake occurs and persistence of antibiotic is not adequate to kill the pathogen
  - Medicated feed if not feeding fast enough or feeding poorly
  - Medicated feed for less than recommended treatment period

REDUCE PERSISTANCE

- Minimize use-AMR is a natural process. There is cost to the bacteria to maintain this state, minimal antibiotic use will minimize selective pressure and result in lower numbers of AMR pathogens.
- Complete harvest and disinfection of production system prevents build up in system.
- Crop rotation if practical- breaks pathogen cycle
- Voluntary antibiotic use restriction or rotation on a facility for 2-3 production cycles.
- Impact of antibiotic use may be broad- many R-plasmids code for more than one resistance gene so use of any of these antibiotics helps maintain it in the population (characterize R-Plasmids?).

Examples in Channel catfish production

- Major pathogens
  - *Flavobacterium columnare*
  - *Edwardsiella ictaluri* (Enteric septicemia of catfish) and *E piscicida*
  - *Aeromonas hydrophila*

- Approved antibiotics- All medicated feeds all by Veterinary prescription

  Terramycin-Oxytetracycline 10 days- 21 day withdrawal (rarely used- has been in past)

  Romet- Sulfadimethoxine-Ormetoprim 5 days- 3 day withdrawal (occasionally used)

  Aquaflor- Florfenicol 10 days- 15 day withdrawal (commonly used)
- Cost $800 per ton vs. $390 for non-medicated- use of medicated feed affected by economics

Routine stress management

- Dissolved oxygen intensely managed over summer months
- Chlorides maintained above 100ppm to reduce nitrite toxicity
- Use fresh, well formulated feeds
- Stock fish in cool months to reduce handling stress

Columnaris disease

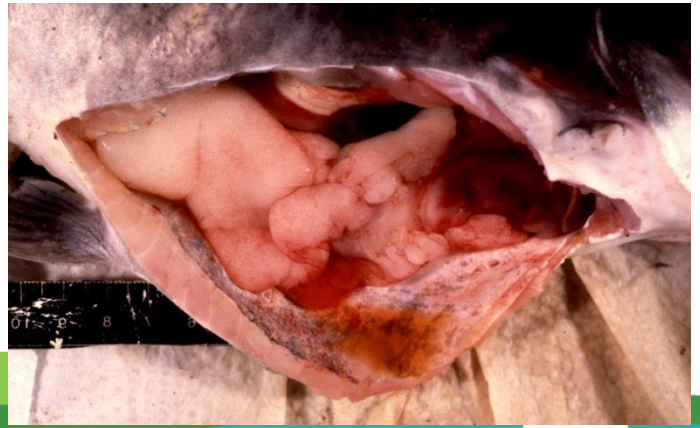
Flavobacterium columnare produces necrotic lesions on skin and gills. Very often secondary to other pathogens or physical damage.

Management

- Avoid damaging mucus layer-
  - Handle during cool weather
  - Use smooth surfaces or water cushion when handling
  - Treat hauling tanks with 1-3 ppt salt
  - Avoid damage to gills- particulates, ammonia, parasites
- Manage ESC, Winter mortality, CCV
- Vaccinate (effectiveness in fry not great, likely better in older fish)
- Treatment with copper sulfate has been shown to help, don’t restrict feed
- Antibiotic medicated feed- Aquaflor (labelled), Terramycin not labelled effective but not used, Romet not labelled and may not be effective
- AMR does not appear to be common (often not evaluated) but bystander effect-other bacteria become AMR

Enteric Septicemia of catfish

- Gram- enteric bacterium *Edwardsiella ictaluri* invades the host through the intestinal mucosa. Facultatively intracellular.
- High losses after stress or in naïve population (especially fingerlings)
- Temp window 22-27 C.
- *E. piscicida* infections similar



management

- Avoid stress (DO and Nitrite)
- While in temperature window- feed on alternate days
  - This reduces transmission- enteric pathogen. Gut clearance before feeding reduces bacterial shedding when fish concentrated for feeding. (Wise & Johnson 1998. J. World Aquac Soc 29, 170-176).
- Vaccination- helps in fingerlings but losses still occur
- Antibiotic treatment- Aquaflor (labelled), Romet (labelled), Terramycin (not labelled)
- AMR- relatively common often MDR- FloR and TetR found on self transmissible plasmid

AMR in catfish pathogens- Observations

- Highest resistance seen in *Aeromonas sobria*
  - This is a secondary pathogen, not usually the target of antibiotic treatment but often present during columnaris disease
  - Also highest resistance to terramycin which is rarely used now
- Second highest level of resistance seen in *E. ictaluri*
  - If resistant, usually resistant to both Aquaflor and Terramycin
  - Industry has seen increasing levels of Aquaflor resistance. May seriously impact treatment options.
- Challenges- much of industry uses continuous production (partial harvest of population and restocking) allowing build up of AMR in system. Some systems now going to batch production

Summary

- Management to minimize diseases is the most important component for AMR management
- AMU only when necessary and effective
  - The cost of treating now includes the loss of options in future
- Antibiotic resistance will develop and may occur in non-target pathogens