Use of veterinary medicines in aquatic animal health

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World food fish production

- almost 60 million tonnes in 2010
  - 12 times expansion over the last three decades
  - 8.8% annual growth rate.
- Aquaculture-produced food products now make up almost 50% of world total food-fish consumption.
- Africa - a small contributor to world aquaculture production. Increasing, with levels reaching to 2.2% of global production in2010
- in Africa aquaculture is dominated by finfish production and until recently

The State of World Fisheries and Aquaculture, FAO, 2012

Intensive farming creates environments conducive to emergence of bacterial pathogens

Fish disease
multifactorial causes

Trout /
Tilapia

Streptococcus

host

pathogen

disease

Climate, water quality, feed, husbandry, trauma, farm design

environment

Antimicrobials

Differing challenges
Differing needs

- Small scale village aquaculture

and

- High technology industrialized aquaculture

Veterinary drugs in aquaculture

- Prevention and treatment of disease

  disinfectants

  antimicrobials

  vaccines

- Parasite control

- Reproduction and growth manipulation

- Anaesthesia and tranquilization

Commonly used drugs approved for use in food fish by FDA

- formalin
- hydrogen peroxide
- florfenicol
- oxytetracycline
- sulfamerazine and sulfadimethoxine/ormetoprim
- chorionic gonadotropin
- tricaine methanesulfonate (MS222)

High enforcement priority aquaculture drugs (FDA)

- chloramphenicol
- nitrofurans
- steroid hormones
- fluoroquinolones and quinolines
- malachite green

Routes of medicine application

- injection – feasible for small numbers of high value animals, particularly brood-stock
- bath or immersion treatment – suitable for application of paraciticides and surface disinfectants to large numbers of small fish. Occasionally used for application of antimicrobials to fry. Usual route of application for anaesthetics
- in-feed medication – main route of application of antimicrobials to large numbers of fish

Limitations of in-feed medication

- reduced palatability
- limited feed intake by sick fish
- many sick fish stop feeding. Medication only reaches healthy fish in the population that are still feeding
- larger stronger fish consume more than weaker fish affecting the correct dosage
- success achieved only with early decision to treat

Paraciticides

- potential to harm non-target organisms, resistance development, regulatory framework covering food producing aquatic animals need to include MRLs for paraciticdes
- avermectin insecticdes - emamectin benzoate – in-feed - resistance development

- pyrethroid – cypermethrin - bath
- organophosphate - azamethiphos – bath – resistance development
- chitin synthesis inhibitor - triflubenzaron
- hydrogen peroxide bath - most environmentally friendly
- numerous others with heavy use in the ornamental fish industry

Other medicinal products

- Disinfectants – important component of biosecurity measures.
  Poorly regulated or unregulated in many countries.
  Malachite green banned from use in food producing organisms. Zero tolerance level for food fish in place in most countries

- Anaesthetics - used for sorting, handling, vaccination and transport. Sporadic low-volume use with low environmental impact.

- Hormones - methylestosterone – androgenisation of fry
  - gonadotropins and gonadotropin-releasing hormones - needed to induce spawning in some fish species

Burridge et al. 2008

Vaccines

- immersion and oral routes – fry —– immunocompetence - limited duration of immunity
- injection – determined by minimum size of the fish and practical husbandry procedures
- complimentary to good farm management and biosecurity
- types of vaccines

  inactivated bacterial
  inactivated viral
  subunit
  (DNA)

- commercial vaccines - licensed
- autogenous vaccines – unlicensed - restricted to use by, or under direction of, a veterinarian

(Summerset et al. 2005)

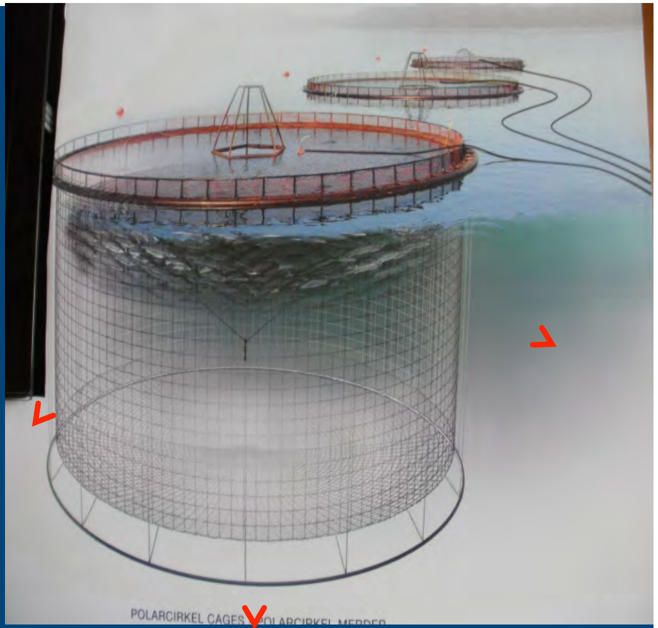
Do antimicrobials have a place in modern aquaculture?

Antimicrobial agents (and classes) used in aquaculture and their importance in human medicine.

Antimicrobial agent (drug class)	Route of administration in aquaculture	Importance of antimicrobial class in human medicine
Amoxicillin (aminopenicillins)	Oral	Critically important
Ampicillin (aminopenicillins)	Oral	Critically important
Chloramphenicol (amphenicols)	Oral/bath/injection	Important
Florfenicol (amphenicols)[a]	Oral	Important
Erythromycin (macrolides)	Oral/bath/injection	Critically important
Streptomycin, neomycin (aminoglycosides)	Bath	Critically important
Furazolidone (nitrofurans)	Oral/bath	Important
Nitrofurantoin (nitrofurans)	Oral	Important
Oxolinic acid (quinolones)[a]	Oral	Critically important
Enrofloxacin (fluoroquinolones)[a]	Oral, bath	Critically important
Flumequine (fluoroquinolone)[a]	Oral	Critically important
Oxytetracycline, chlortetracycline, tetracycline (tetracyclines)	Oral/bath/injection	Highly important
Sulphonamides (sulphonamides)	Oral	Important

Heuer O. E. et al. Clin Infect Dis. 2009;49:1248-1253

Fate of antimicrobials in the environment



Antimicrobials - mainly in-feed medication
Oxytetracycline, oxolinic acid, amoxycillin, co-trimazine (trimethoprim sulphadiazine)

% loss into water before pellet is eaten, leaching, unconsumed feed and excretion from the treated fish

Sediments – consumption by wild fish and invertebrates that might end in the human food chain.

The nature of sediments in ponds and beneath a fish cages exerts a major role on persistence of antimicrobials in the environment

Half life - variable in sediments depending on degree of anoxia.
For oxytetracycline the half life may be as short as 9 days in well oxygenated sediments and in excess of 1 year in anoxic sediments (Bjorklund et al. 1990)

Alderman & Hastings 1998

Intensive use of antimicrobials in aquaculture

- selective pressure creates reservoirs of drug resistant bacteria and transferable resistance genes
- Horizontal transfer of resistance genes may occur in:

  aquaculture environment,
  in the food chain or
  human intestinal tract

- A number of antimicrobials are regarded as critically important for use in humans by the WHO but are still commonly used in aquaculture in many parts of the world

Heavy prophylactic antibiotic use by industrial aquaculture practices

- Emergence of aquatic antimicrobial-resistant bacterial pathogens
- Increased antimicrobial resistance in environmental bacteria associated with aquaculture
- Increased possibility of transfer of resistant bacteria and their resistance determinants to bacteria of terrestrial animals and humans
- Residue risk to human consumers of aquaculture products

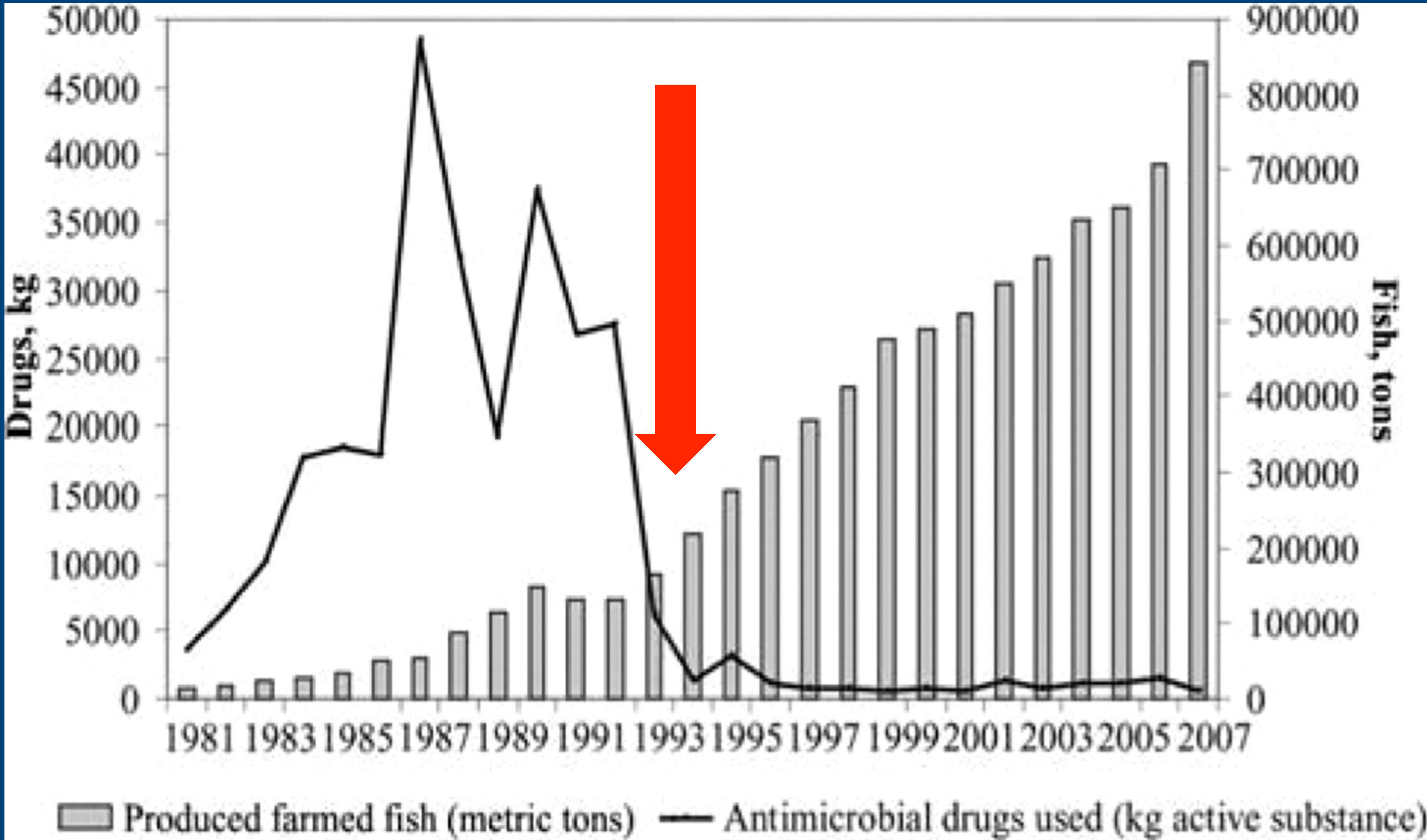
Cabello 2006

Antimicrobial use in well developed aquaculture industries

- established aquaculture species
- justified licensing of antimicrobials needed for the industry together with the necessary regulatory framework.
- antimicrobial usage has declined dramatically since the development of vaccines for these cultured species

Alderman & Hastings 1998

Antimicrobial drug use vs farmed Atlantic salmon (Salmo salar) and rainbow trout (Oncorhynchus mykiss) production in Norway.



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Antimicrobial use in new aquaculture species, particularly in underdeveloped countries

- Some 600 aquatic species farmed world wide (FAO 2012)
- May be dependant on antimicrobial use in the absence of suitable vaccine development.

- Antimicrobial use without regulatory supervision
  - a diagnosis must be made
  - veterinary prescription cascade,
  - high risk of illegitimate use of poor-quality unregulated antimicrobials.

- The end-product may be unsuitable for export to markets in developed countries

Alderman & Hastings 1998

Principles for responsible and prudent use of antimicrobials in aquatic animals

- maintain the efficacy of antimicrobial agents both for veterinary and human medicine and to ensure the rational use of antimicrobials in aquatic animals with the purpose of optimising both their efficacy and safety

- comply with the ethical obligation and economic need to keep aquatic animals in good health
- prevent or reduce the transfer of both resistant microorganisms and resistance determinants from aquatic animals to humans and terrestrial animals
- prevent antimicrobial residues that exceed the established maximum residue limit (MRL) occurring in the food

OIE Aquatic Code Article 6.3.1.

Fish disease
multifactorial causes

Trout /
Tilapia

Streptococcus

host

pathogen

disease

Climate, water
quality, feed,
husbandry,
trauma, farm
design

environment

Antimicrobials

Streptococcus infection in Nile tilapia in Southern Africa

- *Streptococcus iniae*
- *Lactococcus garviae*
- *Streptococcus parauberis*

Inbalanced feeds – ascorbic acid and omega 3 fatty acids

As a result of high stocking density and incorrect feeding practice the dissolved oxygen levels were chronically too low stressing the immune system of the fish

Lax enforcement of legislative controls will promote the injudicous use of antimicrobials to the detriment of

- the consumer
- the environment
- sustainable aquaculture

Future of antibiotic use

- If used judiciously, antibiotics will continue to play a crucial role in seeing fish through times of unanticipated environmental conditions
- Antibiotics should not be used to bridge nutritional and husbandry shortcomings that can be solved in more appropriate ways
- Where possible vaccination should be used to control bacterial disease

Farmers can curtail emergence of bacterial pathogens by:

1. Identifying and understanding underlying causes
2. Following good bio-security practices

but NOT by