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Disease control in aquaculture and the responsible use of veterinary drugs and vaccines: The issues, prospects and challenges

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Abstract. Aquatic animal diseases are the most significant constraint to the development and management of aquaculture worldwide. As aquaculture is growing rapidly and poised to help in bridging the gap in the global supply and demand of aquatic animal food products, management of health and reducing losses due to disease in aquaculture is gaining high priority. One of the key areas of success in managing aquatic animal health in aquaculture has been the development of vaccines. There has been significant progress in vaccination against certain diseases and pathogens; however, vaccines are not yet available for many important diseases. Science and research into vaccination is progressing well and there is hope that more vaccines will be available in the coming years.

Keywords. Vaccination – Aquaculture – Health management – Disease.

Lutte contre les maladies en aquaculture et utilisation responsable de médicaments vétérinaires et vaccins : Problématique, perspectives et défis

Résumé. *Les maladies des animaux aquatiques sont la contrainte majeure pour le développement et la gestion de l'aquaculture dans le monde. Vu que l'aquaculture est en expansion rapide et vise à contribuer pour réduire l'écart entre l'approvisionnement global et la demande de denrées alimentaires provenant d'animaux aquatiques, une priorité grandissante est accordée à la gestion de la santé et la réduction des pertes dues aux maladies en aquaculture. L'un des domaines-clés de succès dans la gestion de la santé des animaux aquatiques en aquaculture a été le développement de vaccins. Des progrès significatifs ont été réalisés en matière de vaccination contre certaines maladies et pathogènes, toutefois il n'y a pas encore de vaccins disponibles pour un grand nombre de maladies importantes. La science et la recherche concernant la vaccination avancent nettement, et on a bon espoir que davantage de vaccins seront disponibles lors des prochaines années.*

Mots-clés. *Vaccination – Aquaculture – Gestion de la santé – Maladie.*

I – Introduction

Aquaculture is still the fastest growing food-production sector in the world. It provides a significant supplement to, and substitutes for, wild aquatic organisms and creates employment, generates income and provides opportunities for human development. However, disease is a primary constraint to the growth of many aquaculture species, and is now responsible for severely impeding both economic and socio-economic development in many countries of the world. Addressing health questions with both pro-active and reactive programmes has, thus, become a primary requirement for sustaining aquaculture production and product trade. There is now convincing evidence of the serious socio-economic, environmental and international trade consequences arising from trans-boundary aquatic animal diseases.

1. What causes diseases?

The OIE International Aquatic Animal Health Code lists several infectious diseases of importance and significance to global aquaculture and aquatic production. They are all caused by pathogens (virus, bacteria and parasites) and are capable of spreading through the movement of infected host species. In addition to the OIE listed diseases, there are many diseases of regional or national interest, which have significant impacts on aquaculture productivity. Some of these are well-studied and understood, while others are of unknown aetiology or newly emergent. Such diseases can pose equal, if not greater, challenges for aquaculture development in some regions.

Non-infectious diseases are also common in aquaculture and, although they generally receive less attention than exotic diseases, can have equally devastating effects on production over a very short period. Such diseases are usually caused by ubiquitous opportunistic agents or other biotic and abiotic conditions. For example, inadequate management, poor water quality, inappropriate nutrition, aquatic environmental degradation, and exposure to chronic or acute contamination have all been linked to mass mortalities of a wide range of cultured and wild species.

2. Why do disease outbreaks occur?

The rapid and ongoing development of all aquaculture sectors continues to call for better health management and improved capacity to face new health challenges. This is particularly apparent with increased interest in species diversification, as well as new grow-out techniques. The rapid expansion of these sectors continually surpasses the rate of education, research and adaptation of expertise in health management. The actual risks have to be assessed – frequently through controlled and repeated experimental challenges – in addition to extensive field surveys and epidemiological data collection (e.g. husbandry and environmental factors associated with the disease outbreak). Although our capability to manage most of these health issues has grown immensely over the last 20-30 years, the new challenges continue to call for further improvements.

A multitude of factors has contributed to the health problems currently faced by aquaculture. As noted above, over the past three decades, aquaculture has expanded, intensified, and diversified, based heavily on movements of live aquatic animals and animal products (broodstock, seed and feed). This trend has been triggered by changing circumstances and perspectives, especially world trade liberalisation. New outlooks and directions have accelerated the accidental spread and incursion of diseases into new populations and geographic regions, for example, through movements of hatchery produced stocks, new species for culture, enhancement and development of the ornamental fish trade.

3. What do we do to combat diseases?

Measures to combat diseases of fish and shellfish have only recently assumed a high priority in many aquaculture producing countries/regions of the world. Development of such measures was stimulated by the serious socio-economic losses and environmental impacts caused by aquatic animal diseases, as well as threats to food availability/security and the livelihoods of vulnerable sectors of society. Many countries have improved their policies and legislature, laboratory facilities, diagnostic expertise, control protocols, and therapeutic strategies, in order to handle disease outbreaks better. In addition, many farmers, especially in developed countries, have improved their capacity to respond quickly and effectively to emergent disease situations. They have also greatly enhanced their disease prevention awareness. Similar efforts towards strengthening aquatic animal health capacities in many developing countries are also being actively pursued, though many are still marginal.

A number of international and regional codes of practice, agreements, and technical guidelines exist and are aimed, at least in part, at providing a degree of standardisation for the protocols used to minimise the risks of disease associated with movements of aquatic animals. National programmes and legislation are also being implemented in many countries, particularly in developed regions, and these include some good examples of successful fish health control policies and programmes with effective diagnostic accreditation programmes, as well as quality assessment and quality control (QAQC) procedures. These aquatic animal health programmes emphasise good management, adherence to strict hygiene practices and sanitation standards, general layout of farm premises and site selection, as well as strict quarantine protocols with biosecure facilities. Other successful examples exist under well-defined legislation, including mandatory reporting of disease outbreaks or detection of specific pathogens, as well as recommended mitigation measures, and intensive educational and training support.

II – Disease diagnosis and tools

Diagnostics is the determination of the cause of a disease (clinical pathology). The techniques used range from gross observation to highly technical biomolecular-based tools. Pathogen-screening is another health management technique, which focuses on detection of pathogens in sub-clinical, or apparently healthy, hosts.

These tools include both immunoassay and DNA-based diagnostic methods, e.g., fluorescent antibody tests (FAT), enzyme-linked immunosorbent assays (ELISA), radioimmunoassay (RIA), *in situ* hybridization (ISH), dot blot hybridization (DBH) and polymerase chain reaction (PCR) amplification techniques. They are currently used to screen and/or confirm the diagnosis of many significant pathogens of cultured finfish [e.g. channel catfish virus (CCV), infectious haematopoietic necrosis virus (IHNV), infectious pancreatic necrosis virus (IPNV), viral haemorrhagic septicaemia virus (VHSV), viral nervous necrosis virus (VNN) and bacterial kidney disease (BKD)], as well as shrimp diseases [e.g. white spot syndrome virus (WSSV), yellowhead virus (YHV), infectious hypodermic and haematopoietic necrosis virus (IHHNV) and Taura syndrome virus (TSV)]. Similar tools are under development for molluscan pathogens (*Haplosporidium* spp., *Bonamia ostreae*, *Marteilia refringens* and *Herpes* virus). These molecular-based techniques (immunoassays and nucleic-acid assays) provide quick results, with high sensitivity and specificity, at relatively low cost, and are particularly valuable for infections which are difficult to detect (e.g., sub-clinical infections) using standard histology and tissue-culture procedures. Molecular tools are also useful for research into the pathology and immunology of specific infections. They can be used for non-lethal sampling, and are valuable for monitoring challenge experiments under controlled laboratory conditions. Further development of this technology is likely to enhance more rapid detection (field monitoring and laboratory examination) and diagnosis of disease, which is crucial for early and effective control of emergent disease situations.

III – Disease treatment

With respect to the treatment of disease or pathogen eradication, most countries still rely on chemotherapeutants, especially for the control of infectious microbial diseases of finfish. In some production facilities, the prophylactic use of drugs, chemicals and biologicals are necessary to meet the sanitation standards used to maintain high health status/certification. Prophylactic drugs are also used to minimise diseases caused by opportunistic infectious agents, and prevent spread via personnel and equipment. Chemotherapy has value in preventing and controlling aquatic animal diseases, but must be used in a judicious manner.

In addition to the direct threat of aquatic pathogens to sympatric wild populations, the confluent nature of the aquatic environment means that use of chemical treatments (disinfectants, therapeutants, etc.) in some culture systems may also have untargeted effects. Although considered essential for intensive culture of some species, inappropriate chemical use is coming under increased scrutiny and revised disease management practices.

Active treatment of disease can be problematic, especially for easily stressed aquatic animals or those grown at extremes in their geographic and physiological tolerance range. Other approaches to disease prevention include:

(i) control of movement of animals onto the farm/site;
(ii) destruction of clinically sick animals;
(iii) emergency harvest of clinically healthy animals;
(iv) sanitary measures, such as disinfection; or
(v) fallowing prior to re-stocking.

While chemotherapy will perhaps remain one of the main strategies for controlling transmissible diseases in the foreseeable future, especially in finfish, there is increasing recognition of its limitations in terms of aquaculture situations, host species and pathogen groups against which they are effective. In some cases, rather than providing a solution, they may complicate health management by triggering toxicity, resistance, residues and, occasionally, public health and environmental consequences.

In addition to side-effects, the efficacy of chemotherapeutants in certain aquatic environments (e.g. open water systems and shellfish beds) is questionable, both with respect to treatment goals, as well as the cost of untargeted effects. Occasional misleading claims and advertising regarding the use of antibiotics and other therapeutic drugs has further complicated the use of chemicals for treating health problems. Other problems with effective chemotherapeutant use include:

(i) the lack of pharmokinetic data on many drugs used;
(ii) the lack of standardised protocols for use;
(iii) safety issues, such as handling, storage and application;
(iv) low numbers of licensed products;
(v) cost and time involved in registration/licensing requirements; and
(vi) existing legislation, which can range from very restrictive to no regulations at all.

IV – Major issues of antibiotic use and opportunities for the future

Antibacterial substances are utilized in aquaculture production to combat bacterial diseases. There is evidence that some antibacterials are used as prophylactics and growth promoters, although it is not considered to be a good management practice. The resulting hazards could be:

(i) presence of high residue levels of approved antibiotics and/or residues of unapproved or banned antibiotics,

(ii) development of resistance to antibiotics in microbial pathogens in the environment.

The presence of residues of antimicrobials over approved maximum residue levels (MRLs) could be reduced through applying good management practices, HACCP procedures, education, awareness building and working with farmers, pharmaceutical manufacturers, veterinary control authorities and other service providers. Hazards due to the use of unapproved or banned antibiotics differ depending on the type of antibiotic, dose level, national regulations, etc., and there are no harmonised regulations yet to deal properly with this situation at an international level. Unapproved antibiotics (extra-label use of antibiotics) are used in two main situations:

(i) Extra label use of an approved antibiotic in aquaculture (e.g. for a species, for a period or for doses for which it has not been specifically approved). There are countries that admit this type of extra-label use, provided that it is done under the responsibility of a certified professional (e.g. a veterinarian).

(ii) Extra-label use of an antibiotic not specifically approved for use in aquaculture (e.g. an antibiotic approved for use in humans) is accepted by some countries only if a certified professional takes this responsibility.

Since there are no international regulations, the use of an approved (or non-regulated) antibiotic in one country may be a violation in another country. Residues of specifically banned antibiotics are a compliance violation, and it is not related to level detection of the banned substance.

The release of large quantities of antibiotics into the environment, due to animal production (including aquaculture) and human use has led to the development of antibiotic resistance by pathogenic bacteria and potential serious risks to human health. A recent study "indicates that antimicrobial-resistant *Salmonella* are present in imported foods, primarily of seafood origin". Thirty fish species of capture and aquaculture origin were found to contain multi resistant strains of *Salmonella*. Other authors have reported increased bacterial resistance levels on and around fish farms related to the antimicrobials agents used at the farms. A full strategy to achieve a responsible use of antibiotics in aquaculture seems to be urgently needed.

1. How to regulate the use of antibacterials?

- Both Europe and the USA have strictly regulated controls on the use of veterinary medicines, particularly for use in food animal species.
- Before any such medicine can be approved for sale, a range of safety and efficacy requirements must be satisfied.
- Included in these is a requirement that residues of the veterinary medicine must be below a predetermined safe level when the animals are slaughtered. This level is the maximum residue level (MRL) (Europe) or tolerance (USA).
- Certain compounds, including chloramphenicol and the nitrofurans are specifically prohibited for use in food animals in Europe and in the USA.
- Programmes of sampling and analysis of the edible tissues of food animals produced in Europe and in the USA are carried out to ensure that producers do not slaughter animals until residues of any medicines used have fallen below the predefined safe levels (MRLs).
- These programmes also check for the presence of any residues (no matter how small) of drugs that are prohibited for use in food animals. Action is taken if either the MRL is exceeded or prohibited residues are found.
- Both Europe and the USA require that countries exporting food animal products into their markets operate a programme of checks for residues that will ensure that imported food is safe for their consumers.
- If imported food is found to contain residues in excess of the MRL or to contain any residues of prohibited drugs, again action will be taken. This will normally result in a prohibition of imports from the country concerned until the cause of the unsafe residue has been traced and action to guarantee that no further breach will occur has been taken.
- Producers wishing to export to Europe or the USA must take care that sufficient time has elapsed between medication and slaughter to ensure that no residues in excess of the MRL are present in the edible tissues and they must never, in any circumstances, use prohibited medicines. In the case of aquaculture, these are chloramphenicol and nitrofurans. Malachite green residues are also now unacceptable. Use of prohibited substances in any part of a production unit or at any stage of processing/handling risks transfer of residues to export animal tissues.
- Regulatory authorities in exporting countries can assist producers by developing tighter regulation of the supply of veterinary medicines and enforcing that regulation, as well as operating compliance and residue monitoring programmes.

V – Vaccination and future opportunities

Vaccination is an alternative prophylactic method to control disease impacts. While some commercial vaccines have proven effective in providing protection against certain diseases (mainly of finfish), vaccination is still not possible against shrimp and molluscan pathogens. Their development requires considerable research on the target pathogen, as well as any resultant disease, and involves careful planning, field trials and cost evaluation.

Fish vaccines, developed during the last two to three decades, have also become an established, proven and cost-effective method for controlling certain infectious diseases in cultured animals worldwide. There are now many commercially available vaccines for finfish diseases, e.g. enteric red mouth (*Yersinia ruckeri*), furunculosis (*Aeromonas salmonicida*), cold water vibriosis or Hitra disease (*Vibrio salmoninarum*), *Vibrio anguillarum* serotypes 01 and 02, *V. ordalli*, *Photobacterium (Pasteurella) damsela* subsp. *piscicida, Streptococcus* sp., and infectious pancreatic necrosis (IPN), as well as many more that are under development e.g. *Flavobacterium psychrophilum*, *Renibacterium salmoninarum*, infectious haematopoietic necrosis (IHN), viral haemorrhagic septicaemia (VHS), infectious salmon anaemia (ISA), viral nervous necrosis (VNN) and *Ichthyophthirius multifilis* ("Ich"). In addition to reducing the severity of disease losses, vaccines also reduce the need for antibiotics; leave no residues in the product or environment, and do not induce pathogen resistance. A good example of the results of enhanced vaccine use is the reduction of antibiotic use in Norwegian salmon production (see Fig. 1). Advances are also being made in both fish and shellfish immunological research towards stimulation of specific and non-specific defence mechanisms.

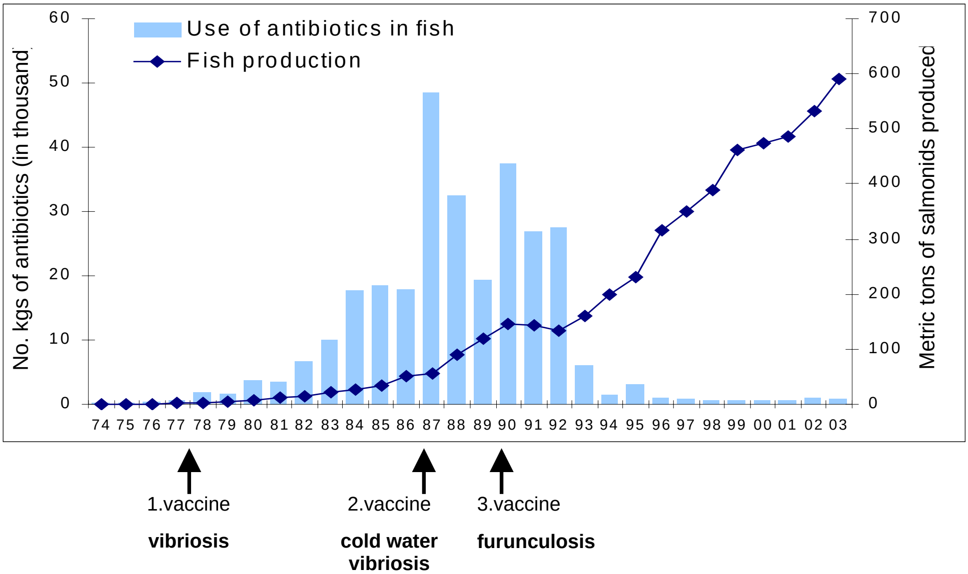

Fig. 1. Effect of vaccination on the use of antibacterials in Norway 1974 – 2003 (Norwegian Veterinary Authority)

Infectious disease is currently the single most devastating problem in shrimp culture and presents on-going threats to other aquaculture sectors. In addition, there is increasing concern over the consequences of newly emerging diseases in aquaculture. Conventional methods of controlling these diseases, such as chemotherapeutants, are ineffective for many new pathogens (notably viruses), thus, molecular techniques are receiving increasing attention for pathogen screening and identification. In addition, these techniques are providing significant insights into pathogenesis (disease development), showing strong potential for disease control and prevention programmes, as well as for treatments of diseases (e.g. DNA vaccines). The increased sensitivity and specificity conferred by nucleic acid (DNA or RNA) based probes has provided significant inroads for early detection of diseases and identification of sub-clinical carriers of infections. This has had a direct effect on enhancing preventative management and control of disease in cultured species. Concomitant with this has been a decrease in the need for reactive treatments using traditional methodologies such as antibiotics, or culling and disinfection. This has been particularly successful for shrimp broodstock selection and breaking the infection cycle perpetuated for years by accidental broodstock transmission of viral pathogens to developing offspring.

Further reading

Bondad-Reantaso, M.G., Subasinghe, R.P., Arthur, J.R., Ogawa, K., Chinabut, S., Adlard, R., Tan, Zilong and Shariff, M., 2005. Disease and health management in Asian aquaculture. *Veterinary Parasitology,* 132. p. 249-272.

Bondad-Reantaso, M.G. and Subasinghe, R.P., 2008. Meeting the future demand for aquatic food through aquaculture: The role of aquatic animal health. In: K. Tsukamoto, T. Kawamura, T.D. Beard, Jr., and M.J. Kaiser (eds). *Fisheries for Global Welfare and Environment*, 5th World Fisheries Congress 2008. Terrapub 2008. Tokyo, Japan, 470 pp.

Subasinghe, R.P., Bondad-Reantaso, M.G. and McGladdery, S.E., 2001. Aquaculture development, health and wealth. In: R.P. Subasinghe, P. Bueno, M.J. Phillips, C. Hough, S.E. McGladdery and J.R. Arthur (eds). *Aquaculture in the Third Millennium*. Technical Proceedings of the Conference on Aquaculture in the Third Millennium, Bangkok, Thailand, 20-25 February 2000. p. 167-191. NACA, Bangkok and FAO, Rome.

Subasinghe, R.P. and Bondad-Reantaso, M.G., 2006. Biosecurity in Aquaculture: International Agreements and Instruments, their Compliance, Prospects and Challenges for Developing Countries, pp. 9-16. In: A.D. Scarfe, C.-S. Lee and P. O'Bryen (eds). *Aquaculture Biosecurity: Prevention, Control and Eradication of Aquatic Animal Disease*. Blackwell Publishing. 182 pp.