Poppin' the Prophylactics: an Analysis of Antibiotics in Aquaculture

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This paper will focus on the problems associated with the use of prophylactic and therapeutic antibiotics used in aquaculture internationally. Aquaculture can, in theory, be a beneficial way of sustainably harvesting fish—but only if done correctly. This paper will provide a background of scientific analysis as to how and why antibiotics are used and detail the problems associated with excessive use, including antibiotic resistance, residues found in human food and accumulation of antibiotics in the environment. Current use and regulation of antibiotics in differing nations will be analyzed, with an emphasis on the countries of Norway and Chile. Norway has proven to be a successful model by decreasing antibiotic usage drastically while still maintaining plentiful yields, as opposed to Chile, a nation that uses an abundance of antibiotics. Alternative approaches will be explored, such as vaccination to prevent disease outbreaks and the use of probiotics and bacteriophages. Finally, proposed policy recommendations and solutions will be examined.

INTRODUCTION AND BACKGROUND ON AQUACULTURE PRACTICES

Aquaculture is defined as the farming of fish that intensify production for human consumption under controlled conditions, including breeding, containment, feed and medications.[1] The negative impacts of aquaculture are not limited strictly to the environment but also involve public health. Aquaculture can produce fish that have higher levels of natural and synthetic toxins, such as pesticides and persistent organic pollutants.[2] This result is due to contaminants in fish feed as well as improper location of aquaculture facilities where there exist high levels of natural containments such as arsenic.[2] Antifungals, disinfectants, antiparasitic pesticides and anesthetics are often used illegally in aquaculture and many are banned in places like the European Union (E.U.) because of concerns of carcinogenic and mutagenic properties.[3] This paper will focus specifically on the use of prophylactic and therapeutic antibiotics in aquaculture internationally and on how abuse can have adverse health effects in human populations. Antibiotic abuse is a known problem and there are ways to prevent and solve this issue.

Aquaculture is growing in prominence as an alternative way of obtaining seafood. Production is currently increasing 9.25% per year and it is estimated that aquaculture will account for half of all seafood consumed in the world by 2020.[4] Because aquaculture is heavily increasing, it is imperative that current practices are safe and sustainable and do not have negative human health implications. The increase in efficient aquaculture starting in the 1960s was driven by the newfound ability to control for disease with improved pen water quality, more nutritious feeds and genetic manipulation to aid selective breeding.[2] Because of depletion of wild fish stocks, aquaculture is viewed as an alternative and efficient way to replenish and produce fish.[2,5] Aquaculture's other benefits include, but are not limited to, wetland preservation, agricultural and human waste control and desalinization of lands.[6] Drawbacks include, but are not limited to, demolition of natural habitats, the release of effluent, introduction of fish diseases and escape of farmed fish into wild populations, causing disease transmission and impacting genetic diversity.[6]

A background of scientific analysis as to how and why antibiotics are used will be discussed, as well as the problems associated with excessive use, including antibiotic resistance, residues found in human food and accumulation of antibiotics in the environment. Current use and regulation of antibiotics in differing nations will be analyzed, with an emphasis on the countries of Norway and Chile. In countries such as Chile, China and several Asian-Pacific nations, there is a lack of regulations as well as weak enforcement on how many and which specific antibiotics can be used.[4,7] Norway has proven a model of success by decreasing antibiotic usage drastically while still maintaining plentiful yields. Alternative approaches will be explored, such as vaccination to prevent disease outbreaks and the use of probiotics and bacteriophages. Finally, proposed policy recommendations will be examined.

PART A: ANALYSIS OF THE SCIENTIFIC DATA

How and Why Antibiotics are used in Aquaculture

Antibiotics are defined as "drugs of natural or synthetic origin that have the capacity to kill or to inhibit the growth of micro-organisms" and are non-toxic to the host, used in order to serve as treatment for disease.[8] Prophylactic antibiotics refer to antibiotics given in order to prevent disease, as opposed to therapeutic antibiotics, which are given in order to treat disease.[5] In the U.S., infectious disease among aquaculture is a top limiting factor that accounts for 45.4% of losses in aquaculture.[9] A wide range of bacteria creates major setbacks in production and antibiotics aid in effectively eliminating these diseases from spreading.[4]

Antibiotics are necessary in aquaculture due to a lack of sanitation in dense, overcrowded pens where there are no barriers to properly isolate healthy fish from infected ones. This issue is most prominent in developing countries in the Asian-Pacific region and other counties like Chile, where 90% of world aquaculture production occurs. In these countries, regulations are lax and antibiotic usage is abundant compared to countries such as the U.S. and Norway.[4,7] When an outbreak occurs, the farmer is pressed for time and because of limited resources, he or she often uses antibiotics inappropriately due to "ill-informed decision-making based on a rushed diagnosis."[10] The farmer, not wanting to waste valuable time, will then often quickly administer antibiotics regardless of the correct dose or even the correct antibiotic, in order to save as many fish as possible.[10] In addition to a lack of cleanliness as a factor, the fish are often stressed and therefore more susceptible to disease. For these reasons, their immune system response is slower and prophylactics aid in the ability to keep the fish from attracting a variety of diseases.[7] Prophylactics also increase digestion efficacy and conserve energy in the fish.[8] The antibiotics kill harmless endemic pathogenic bacteria in the fishes' intestines, which causes an increase in the absorption of nutrients.[8] Because of this, the nutrients fed to the fish are more efficiently absorbed with less energy expended, thus achieving growth promotion.[8]

On average, countries use roughly seven to thirteen different kinds of antibiotics.[5] Prophylactic antibiotics are often given through medicated feed and, less commonly, by injection and baths.[7] Although the medicines given to fish aid in combating the spread of infectious diseases, they are merely a palliative to the problem of limited resources. High densities of fish, a lack of barriers to isolate infected fish from healthy ones and general unclean pens result in high rates of infections.[7,11] Due to the negative consequences of antibiotic use, the use of prophylactics is not warranted since they pose potentially grave threats to human health, including increased antibiotic resistance and residues found on consumer seafood. Therapeutic antibiotics in all countries should only be issued sparingly, when appropriate, and should be monitored heavily by governmental oversight agencies. For example, in the U.S., 11 agencies are responsible for directly and indirectly regulating aquaculture.[2] The National Fish Hatchery System and U.S. Geological Survey are examples of two of these agencies that aid in disease reduction.[2]

Negative Impacts of using Antibiotics in Aquaculture

I. Antibiotic Resistance

Antibiotic resistance is the primary detrimental effect of administering prophylactic and therapeutic antibiotics to fish in aquaculture. Owing to the presence of antibiotics in aquaculture, antibiotic resistance has risen and therefore may be a possible contributing factor of antibiotic resistance in human populations.[5] Although in most developed nations the antibiotics that humans use are not used in aquaculture, antibacterials common in aquaculture sometimes overlap with human medicine, thus creating resistant bacteria that will not respond to antibiotics used in human treatment.[10] Fish pathogens' resistance can be indirectly transferred through horizontal gene transfer to human pathogens because of the possibility that the pathogens have resistant genes and a constant presence of residues of antibiotics in the fish's bodies.[3] Antibiotics in aquaculture are most likely creating bacterial strains that are resistant to several different kinds of antibiotics. According to the Center for Disease Control and Prevention (CDC), resistant strains of *Escherichia coli* and *Salmonella spp* have been traced back to antibiotic usage in animals.[8] Resistance can occur in non-pathogenic bacteria, which can then transfer their resistant genes to pathogenic human intestinal bacteria, leading to illnesses in humans that are not treatable by antibiotics.[1] It has been observed that after only two years of an antibiotic reaching the market, even if it is a new class, resistance begins to occur.[12] Since the discovery of antibiotics in 1962, many new classes of antibiotics have been found, but in recent years this number has slowed dramatically.[12] Although efforts such as using a combination of different antibiotics are effective at combating disease, they only slow the trend of resistance and do not stop it.[12] Currently, animals account for half of all antibiotic consumption worldwide.[12] Scientists believe ,although there is some controversy, that antibiotic usage among animals is the cause for resistance in humans.[12] A team of Korean scientists from the Research Division for Industry and Environment, Korea Atomic Energy Research Institute, performed a study analyzing four freshwater aquaculture farms in Jeollabuk-do, Korea and found bacteria resistant to multiple antimicrobials in 58.3% of the tested strains and bacteria resistant to individual antimicrobials in 41.7% of tested strains.[13] In addition, 100% of bacteria tested showed resistance for ampicillin.[13] Similarly, a study in Australia from the School of Pharmaceutical and Medical Sciences at the University of South Australia, uncovered single and multi-resistant bacteria collected from different areas in Australia. Results showed that bacteria showed some level of resistance to 18 of the 19 antibiotics. Because no antibiotics are officially listed in Australia, it would be incorrect to state that the resistance is due directly to antibiotic use. Yet numerous studies conducted in countries where antibiotics are known to be used have data very similar to the data found in this study; thus, it can be concluded that in aquaculture species and environments, antibiotic resistance is fairly common.[4]

These studies are only a small sample of the several publications suggesting that the abuse of antibiotics in aquaculture is creating strains of bacteria resistant to antibiotics used by humans. In many developed countries, prophylactic use has been banned and only limited therapeutic use is allowed.[7] However, this is not the case for much of the developing world.[7] For example, quinolones, which are heavily used in human medicine as an effective antibiotic, are used without restriction in Chile and China.[7] It has been found that 100-110 metric tons (MT) of quinolones are used for animals (the vast majority being aquaculture) while 10-12 MT are used in human medicine. [7] In addition, several studies have cited populations of antibiotic-resistant bacteria either directly underneath or around aquaculture habitats. One such study showed populations of bacteria resistant to tetracycline, quinolone and penicillin in the sediments around its fish farms.[3] Additionally, comparisons of bacteria before and after antibiotic treatment showed dramatically higher levels of antibiotic-resistant bacteria and antibiotic resistance genes within a fish after treatment.[5] Although we cannot assume a causal relationship between antibiotics and antibiotic-resistant bacteria, the overwhelming evidence has made this theory widely accepted among scientists.[5]

II. Antibiotic Residues

Antibiotic residues from the excessive use of antibiotics in aquaculture can accumulate in the tissues of farmed fish and shellfish, thus causing possible adverse health effects in humans. For instance, individuals who are very sensitive to certain antibiotics can have allergic reactions from trace residues and efficient diagnosis of what the patient was allergic to may be hindered by a lack of knowledge of what antibiotic was ingested or even which food triggered the allergic reaction.[7] Allergies are most common with those who administer the antibiotics and work with large concentrations of it. Workers in aquaculture facilities in Thailand and the Philippines reported sometimes administering prophylactic antibiotics daily.[5] Many do not have proper gear for handling antibiotics, nor do they know of the potential toxicity and health risks of the chemicals to which they are being exposed.[5] Aquaculture workers are at risk when they inhale, ingest and come into contact with dust aerosols that contain antibiotics used to medicate and feed fish.[11] This contact can result in altering their intestinal flora by increasing selection for antibiotic resistant bacteria.[11] Allergy and toxicity are also critical problems that workers face when administering large quantities of antibiotics in food mills.[7,5] This situation is especially of concern since certain antibiotics have direct poisonous properties.[5] In addition, workers can be exposed to microbes that can cause harmful diseases and infections, including fish pathogens that have been demonstrated to be contagious in humans.[2] In fact, there was a reported case of four different workers in a tilapia farm becoming infected with a pathogen previously never found to have infected humans.[2]

An additional health problem for humans is that intestinal microflora, which sustain a healthy gastrointestinal tract by preventing pathogenic bacteria from growing, can be disrupted from long exposures to these residues.[10] Resistant pathogenic bacteria can proliferate in the gut, endemic bacteria already in the gut can increase uncontrollably and increased susceptibility to entering pathogens such as *Salmonella spp*. can occur.[10] On the other hand, use of some antibiotics has been shown to leave no long-term residues. For example, a study demonstrated that no residues were found on shrimp tissues after 25 days of withdrawal of using oxytetracycline.[14] Yet one popular antibiotic, chloramphenicol, creates immediate danger of residues because of its toxic and probable carcinogenic properties. Although the chance of direct toxicity from consuming antibiotic fed fish is very low, chloramphenicol is an exception to this rule; studies have illustrated that this particular chemical leaves direct residual traces in human food and is highly toxic.[8] In human medicine, this antibiotic is used as a "last-resort" drug for conditions such as meningitis and conjunctivitis and therefore is still important in therapeutic cases.[10] Yet this drug making its way into human food poses significant public health risks. Since even trace residues can be associated with bone marrow depression and can induce a fatal form of human aplastic anemia, a ban on use in animals used for food consumption was instituted in the E.U. as well as in other countries.[1] However, as stated above, chloramphenicol is still one of the most widely used antibiotics worldwide in aquaculture and its use is posing a threat to human health.

Similarly to chloramphenicol, nitrofurans are another popular broad-spectrum group of antimicrobials. Although now outlawed by the E.U., illegal use is still rampant.[1] Nitrofurans are an antibiotic class that when used inevitably result in residues absorbed into the body that do not break down, even when the food is fully cooked.[15] Other antibacterials such as malachite green, fluoroquinolones and gentian violet also leave behind residues and have been seen to have carcinogenic properties.[16] Some of these drugs, such as fluoroquinoles, are very important, effective and powerful antibacterials used in human medicine. However, they must be administered with caution and care in incidences where they are warranted, and should not appear in food meant for human consumption.[16]

Although certain toxic and probably carcinogenic antibiotics have been banned in the U.S. and several countries in Europe, their use in developing countries (such as Chile, China and several Asian-Pacific nations) is widespread because of lack of regulations and enforcement and therefore residues continue to be a problem.[4,7] There is often a delay in response to detecting chemicals like chloramphenicol and nitrofurans in imported seafood, leading to contaminated seafood products being sold and consumed.[10]

III. Persistence and Accumulation of Antibiotics in the Surrounding Marine Environment

Many farms, such as salmon aquaculture in open water pens, are environmental hazards: not only do they accumulate waste, diseases and chemicals, but the wild fish populations nearby also ingest the antibiotic loaded food pellets. This occurrence leads to remains of antibiotics like tetracycline and quinoles in wild fish populations.[1] Both wild fish and harvested scavengers (such as crab) near Mediterranean fish farms have been found to have levels of antimicrobials that exceeded the safe limit for consumption.[3] It has been estimated that 70-80% of fish antibiotics have been released into the environment.[13] In addition, antimicrobials are often non-biodegradable and can be released through urine and feces into the aquatic surroundings in an unmetabolized form, paving the way for significant contamination.[7,13]

Currently the risk of direct toxic effects, to low levels of pharmaceuticals in aquatic habitats, is unlikely; more research should be conducted to evaluate the risks and probable chronic effects of having low levels of antibiotics in marine environments spanning long periods of time.[17] In addition, considerable underestimation of risk is highly plausible since studies do not typically analyze the interactions that pharmaceuticals have with each other.[17] Although the antibiotics used in aquaculture are indeed present in the aquatic environment, their concentrations are at very low levels. However, precautions should still be taken so that even low levels do not pose a deleterious threat to human health in the future.

Conclusion of Scientific Evidence

While aquaculture is a modern tool that has the potential to succeed and thrive as a sustainable, profitable business, the misuse and unrestricted use of antibiotics creates public health problems such as strains of antibiotic-resistant bacteria, residues in food and accumulation of pharmaceuticals in the environment. These consequences counteract the progressiveness of aquaculture as a practice. With the implementation of a stricter set of regulations, mandatory guidelines and effective enforcement, the development of a more sustainable way of farming fish is very plausible. Regulations, alternatives, recommendations and proposed policy solutions will be discussed in Part B. Currently, some countries such as Scotland, Canada, Norway and the U.S. have moved away from antibiotic usage and doing so was in no means an inhibiting factor toward successfully farming salmon.[7,11,18] Unfortunately, the vast majority of aquaculture farms administer antibiotics liberally and for the reasons laid out above, it is crucial that governments work to execute policies about antibiotics that protect human health.

PART B: REGULATIONS, ALTERNATIVES AND RECOMMENDATIONS

The Problem to be Addressed

With heightened sanitary and hygiene tactics and the implantation of vaccines in aquaculture industries by governmental agencies, tighter controls on antibiotics have ensued and have lead to a dramatic decrease in antibiotic usage in countries such as the U.S., the E.U. and Norway.[7] This reduction was accomplished without hindering productivity, thus demonstrating that it is indeed financially possible for these countries to create an aquaculture industry that does not heavily rely on antibiotics.[4,19] The problem to be addressed is that although there are preventative and alternative approaches to antibiotic use, there is a lack of policy enforcing antibiotic use restriction in aquaculture industries worldwide.[4,19] Furthermore, a lack of resources in developing nations makes it difficult to transition to sustainable and healthy forms of aquaculture production. Although feasible in Norway and other countries, this approach can be more difficult for other less affluent countries.

Current Use and Regulation of Antibiotics in the U.S. and Abroad

Regulation of antibiotics through the use of policy and legislation vary from country to country and are overseen by governments and various regulatory agencies.[3] These regulations are complex and oversee several practices ranging from food supply, feed safety, choice of farm location, water quality and pollution control.[2] The International Office of Epizootics (OIE), the Food and Agriculture Organization (FAO), the World Health Organization (WHO) and the Committee for Veterinary Medicinal Products (CVMP) (a European regulatory committee), are a few of the many organizations that are involved with aquaculture and have voiced concern regarding the public health threats associated with the misuse of antibiotics globally.[3] Since regulatory practices differ substantially both between and within countries, efforts have been made to homogenize these practices.[2] For example, the Hazard Analysis and Critical Control Points (HACCP) program is an active and required program in the E.U. and U.S. that works to assure appropriate safety for both domestic and imported aquaculture goods.[2] The WHO and FAO both support this program and have made detailed reports recommending how other international markets can institute a similar HAACP program.[2] Movements have been created for national governments to support this program, which would thus greatly facilitate standardized international policy on aquaculture production.[2]

In the U.S., the use of antibiotics in aquaculture is heavily restrictive; it must be FDA approved and may only be used for treatment.[9] With this restriction, the use of antibiotics has decreased due to a number of reasons including antibiotic resistant bacteria concerns, the usage of prevention and health management instead of treatment, vaccines as an emerging practice and FDA limitations.[9] Restrictions internationally among countries who sought to reduce antibiotic treatments include almost complete eradication of prophylactics and prohibition of therapeutic antibiotics that are currently used for human medicine.[7] Maximum residue levels (MRL) and acceptable daily intake (ADI) are already mandatory by several regulatory agencies and the E.U. in order to protect consumers.[3] MRLs were established in the belief that ingestion of "low-level doses" of these residues for long time periods can possibly increase antibiotic-resistant bacteria.[3] However, not all countries have such laws or enforcements and there is no standardization of MRLs internationally.[3] Efforts must be made to create uniformity since different agencies choose to set their own MRLs.[3]

Quinoles are one such class of antibiotics that have been banned in the U.S. and Norway due to their popular use in human medicine, accumulation in sediments and ability to create cross-resistance; yet in Chile and China, quinole use has increased dramatically.[7] In Chile, the National Fisheries Service recently proposed a monitoring program to address this problem, since fluoroquinoles are used in human medicine and are on their last generation.[11] Since each subsequent generation has a broader spectrum of activity against bacteria compared to the previous generation, when an antibiotic is on its last generation its ability to combat bacteria is limited, posing serious issues to people trying to fight bacterial infections and diseases. The abundant use of antibiotics is primarily concentrated in developing countries such as in the Asian-Pacific region and Chile where regulation is weak with regard to which and how many antibiotics can be administered.[4] In addition, many countries have sparse data on the quantity and amount of antibiotics used in their fish farms, so accurate estimates of how much each country contributes to total use of global antibiotic usage cannot be estimated with accuracy.[20] Regulations and enforcement vary substantially between countries and are dependent on local governments.[20]

Antibiotics are Unnecessary to Production: A Focus on Norway and Chile

Comparing Norway's and Chile's Antibiotic Input and Fish Yields

A comparison of countries that differ with antibiotic treatment demonstrates that antibiotic usage does not correlate with better yields of fish, nor does using fewer antibiotics reduce profit.[11] This fact is important to note since several countries, such as the U.S. and Norway, are able to produce thriving aquaculture farms with minimal antibiotic use, especially prophylactics. Although China is the leading producer in aquaculture worldwide and most aquaculture is produced in Asia, Chile will be discussed and compared to Norway since both countries farm salmon, which is a very distinct fish from fish farmed in other countries.[5] In addition, Chile is ranked as the 10th top producing aquaculture country in the world and Norway is 11th— thus they are similar in total production.[5] Although the conclusions drawn from salmon farming can aid in providing general recommendations to other fish species, the diversity of fishes can require different approaches because what works for one species may or may not work for another. Regardless, it is still useful to examine what Norway has been able to successfully accomplish.

In 2007, Chile used up to approximately 385 metric tons of antibiotics to produce a yield of 300,000 metric tons (MT) of Atlantic salmon as opposed to Norway, which produced 820,000 MT of salmon with less than one metric ton of antibiotics.[5,6] In fact, the amount of antibiotics used in Chile is in geographical area about one fourth of that in Norway.[5] In 1987, Norway used 48 tons of antibiotics; today, it only uses about one ton per year.[18] Chile is using antibiotics at a rate 1400 times that of Norway with less yield.[11] (The potential for confounders such as an increased use of vaccinations or hygienic measures were not discussed in the article.) The importance of this comparison illustrates how abstaining from antibiotics did not inhibit the successful farming of salmon in Norway. High yields were obtained with minimal usage through less harmful, alternative approaches that did not have detrimental effects on the environment and human health. In Chile, the bacteria *P. salmonis* has caused devastating economic losses to the salmon aquaculture industry and there is no vaccine that prevents the spread of this disease.[11] *P. salmonis* is also endemic to other regions of the world including Norway, Scotland and the U.S., where antibiotic usage is limited and measures to control this pathogen through hygienic procedures have proven successful without antibiotic usage.[11] This particular pathogen is an opportunist and does not infect healthy fish. It is only problematic among stressed fish raised in improperly managed environments, thus a feedback loop is created. When fish are kept in unsanitary conditions they become more susceptible to disease, thus disease becomes common, thus causing more unsanitary conditions and more disease. Therefore, the use of prophylactic antibiotics to control for *P. salmonis* is unnecessary and easily avoidable with careful and sanitary husbandry techniques.[11]

Norway as a Successful Model

Norway has successfully created an aquaculture industry through implementation of a management program that controls and limits antibiotic usage. Norway simultaneously increased yields and decreased antibiotic inputs, which is attributable to the implementation of hygiene standards, a tight monitoring system of antibiotics and fish vaccinations.[11] Mass vaccination was one of the biggest contributions to combating disease in the Norwegian farmed salmon industry. Furunculosis, a devastating salmon disease, is the primary reason for abundant antibiotic usage.[18] A vaccine was created in response and within only two years went from a research trial stage to being used by 99% of salmon farms.[18] In addition to vaccination, zoo-sanitary measures for disease control, zoning controls and selective breeding of salmon for disease resistant traits were established.[18]

A centralized regulatory agency closely monitors the amount of antibiotics and prescriptions at the site of aquaculture facilities.[11] Because of this extremely close monitoring, 1) the use of antibiotics is strictly limited, 2) abuse of antibiotics, such as prophylactic use, is identified early and 3) infections and epidemics are discovered early and containment measures such as isolation are quickly performed to prevent disease spread.[11] In order for therapeutic antibiotics to be used in Norwegian aquaculture farms, they must be prescribed by a veterinarian or an authorized feed mill and the veterinarian must fill out a lengthy prescription form with details regarding location, reason for illness, species of fish, etc.[21] However, as successful as Norway was, it was difficult for the country to change its entire system around. Norway was able to do this through combined efforts from the governmental organization, the National Veterinary Institute and the Norwegian fish farming industry.[18] A 3% levy on national vaccine sales for animals was used to fund research on vaccines as well as various benefits to the veterinary pharmaceutical companies.[18] Since resources and efforts to produce a vaccine are risky for companies, risks were lowered by the government, which incentivized companies to make development of new vaccines possible.[18] Paul Midtlyng and his colleagues write "there is a lesson that extraordinary problems and challenges require extraordinary measures" and we cannot rely on simple methods to accomplish this, for they "will not be sufficient to resolve epidemic health problems."[18] Lastly, although Norway teaches us that it is possible to create a preventative system against disease, when disease does spread, alternatives must be used to combat disease from spreading. Moreover, although Norway has proven its ability to effectively minimize antibiotic usage without decreasing yields, this tactic may not necessarily work in other nations due to factors such as differing water temperature, dissimilar diseases, etc. Since salmon is the only type of fish cultured in Norway, as opposed to in other countries that have a diversity of fishes, effort, research and resources was focused only towards salmon.[19] Furthermore, tropical waters host a variety of different pathogens, which make vaccinations in different countries more difficult.[19]

Alternative Approaches: Preventative and Therapeutic Solutions

Prevention of disease by creating farms that are hygienic, clean and not overcrowded is the first step towards halting the spread of infectious diseases among fish. Many other tactics can be used as well to help decrease the risk and spread of diseases in aquaculture. Vaccines are one such measure that is a very useful tool for combating diseases. Although not "impenetrable shields," mass vaccination against diseases such as furunculosis and vibriosis are effective and can decrease mortality substantially.[8] Vaccines are currently used in the U.S. and the E.U., but are not common in Asian nations (with the exception of Japan) although aquaculture is heavy in that region of the world.[19] The majority of fish farms are small and do not have much technical support, so farmers use antibiotics instead of preventive measures since antibiotics are widely available.[19] In addition, lack of resources to understand fish diseases as well as the economic investment and commercialization to produce vaccines are barriers to the development and use of vaccines.[19] Vaccinations can be administered orally, injected, or given through immersion (fish are sprayed or dipped in concentrated vaccine solutions).[8,22] The method used depends on a variety of factors such as stress of the fish, dosage and how long the vaccine will last.[8,22] Injections are typically the better form of administration. However, they are often more expensive, there is a greater chance of adhesions to the fish and considerable time is required to inject each fish.[8,22] Oral forms are easier to administer and do not cause the fish stress.[22] Vaccines are an excellent preventative measure since they do not leave residues on the fish tissues or in the environment and they provide long lasting protection.[19]

Probiotics are another tool that has proven to be of great aid. Probiotics are "mono- or mixed cultures of live microbes that when applied to animal or human, generate a beneficial effect on health of the host."[23] They help combat pathogenic microbes by obstructing the pathogen's cellular functions and outcompeting it for nutrients and space, therefore supporting healthy digestion and contributing to effective disease prevention.[23]

Even with excellent conditions, diseases are inevitable and techniques to control diseases while limiting the use of antibiotics are essential for controlling bacterial infections and promoting sustainable fish farms.[20] The use of bacteriophages is a promising alternative approach to combating disease in aquaculture facilities and can hopefully be implemented in the near future. Bacteriophages are viruses that kill only specific strains of bacteria, as opposed to antibiotics that are broad-spectrum and kill off beneficial bacteria as well.[20] Phage usage is advantageous since it directly targets the problem causing pathogen.[20] Phage can be applied to a variety of organisms at any point in their development, from larvae to mature stages, and can be administered through various means. Moreover, it can most likely be used in open systems such as open water salmon aquaculture farms.[20] However, a disadvantage to using phages compared to broad spectrum antibiotics is that the phages are strain-specific, so a fish farmer cannot just quickly administer the phages without testing to see which bacteria is causing harm, like one could do with antibiotics.[20] This loss of time could be detrimental to the health of the fishes. Also, there are also concerns that the phages may transfer virulence factors, turning non-pathogenic bacteria pathogenic; therefore, testing is necessary prior to implementation.[20,24] Nevertheless, bacteriophages can be one of many alternative tools to antibiotics for creating healthier farms for both fish and people.

Future Priorities, Recommendations, and Research

Antibiotic resistant bacteria are not confined within national borders and therefore the issue regarding antibiotic resistance, antibiotic residuals found on human food and antibiotic persistence in the environment is a global problem that can only be combated through international effort. The WHO, FAO and OIE are three such global organizations that are current key players in assessing and combating human health threats from antibiotic usage. Based on the available scientific evidence examined in the earlier portion of this paper, it is clear that action must be taken in order to address this dire issue. Creating policy is not enough to combat all the problems associated with aquaculture. Enforcement, education of small-scale farmers, investments into vaccines and world trade agreements are but a few broad topics that must be addressed.

Focus should be directed towards nations such as China and Chile, where regulations and enforcement regarding antibiotic usage in aquaculture is poor.[5] Although, as examined earlier, Norway has been shown to be a successful model in pioneering for sustainable and healthy aquaculture practices, it is not practical to assume that other countries will be able to replicate Norway's practices. For instance, Thailand is very different from Norway: it is a lower-income country and farms different species of fish. The dissimilar chemical and physical environment between countries makes it hard to propose standard international regulations.[11] However, policy makers and governmental agencies can look at what successful countries have done and then apply within reason the same practice. Specific policy proposals are beyond the scope of this review and therefore only points of interest and general recommendations will be explored. Key issues (not in any particular order) to be addressed are the following:

1. Research. The most up-to-date research must be conducted regarding aquaculture practices. A review made available of antibacterials used at international, national and local levels would help scientists create targeted and specific studies to further research in this field and screen for residues and resistance factors.[5,14] A short term goal could be having international agencies and the industries come together to create a comprehensive inventory of all materials like antibiotics, metals and other chemicals used in aquaculture at all levels and make the list available for viewing.[5,14] This list would be vital since record-keeping of the amount and kinds of antibiotics used in aquaculture are not mandatory in many countries.[20] Creating a surveillance program is the first step towards gathering all information together so that longer-term and more important sustainable goals can be achieved. In Australia, for example, there are no registered antibiotics, although there is much speculation, stories and evidence that antibiotics are in fact being used.[4] In addition, surveillance of bacterial resistance is crucial to ensuring that levels of residues on fish remain at safe levels.[3]

2. Vaccines. In Norway, the government heavily supported research for vaccines in order to decrease the need for antibiotics.[18] Research needs to be conducted on the epidemiology and etiology of fish diseases endemic to Asian-Pacific countries so vaccines can be developed for the variety of fish species farmed in these countries.[19] In fact, 11 out of the 15 top aquaculture-producing countries are in Asia, which accounts for 94% of global production.[5] China is the top producing country and accounts for 71% of global production.[19] Research on vaccines in the Asian-Pacific region is vital and partnerships between the private sector, governments and universities will need to play a role in making this happen.[19]

3. Hygiene and Sanitary Measures. In order to prevent the need for antibiotics, a focus on improving conditions on the fish farms to avoid preventable disease epidemics among fish populations is necessary. Pens should be kept clean and overcrowding should be eliminated or at the very least minimized. Infected fish should be isolated immediately and zoning controls should be instituted.

4. Enforced Ban on Certain Antibiotics. An international agreement must be created that restricts prophylactic antibiotic use, use of antibiotics that are used in human medicine (i.e. quinoles) and use of antibiotics that have been shown to be harmful to humans (i.e. nitrofurans and chloramphenicol).[5] Restricting these antibiotics will help combat the three major problems with antibiotic usage: resistance, residues found on seafood products and accumulation in the marine environment.

CONCLUSION

These broad policy aims attempt to form a platform towards addressing issues in aquaculture, and are a bold stepping stone towards a global solution in respect to sustainable aquaculture practices. These points aim to change aquaculture practices abroad and aim to protect the environment, human health and most importantly prevent the spread of antibiotic resistance worldwide.

CONCLUDING REMARKS

Through actual practice, it has been demonstrated that aquaculture with limited use of antibiotics is possible logistically and finically through dealing with both local and global approaches.[7] The list of future recommendations aims at addressing this issue. The scientific evidence speaks for itself and now it is the job of regulatory agencies, governments and citizens to combat the excess and overuse of antibiotics in the aquaculture industry. Human health and aquaculture practices are closely intertwined, and by improving aquaculture practices, the health of the public can be improved as well.

References

1. Cañada-Cañada, F., Peña, A. M. de la, & Espinosa-Mansilla, A. (2009). Analysis of antibiotics in fish samples.Analytical and Bioanalytical Chemistry, 395(4), 987–1008. doi:10.1007/s00216-009-2872-z
2. Cole, D. W., Cole, R., Gaydos, S. J., Gray, J., Hyland, G., Jacques, M. L., … Au, W. W. (2009). Aquaculture: Environmental, toxicological, and health issues. International Journal of Hygiene and Environmental Health,212(4), 369–377. doi:10.1016/j.ijheh.2008.08.003
3. Grigorakis, K., & Rigos, G. (2011). Aquaculture effects on environmental and public welfare – The case of Mediterranean mariculture.Chemosphere, 85(6), 899–919. doi:10.1016/j.chemosphere.2011.07.015
4. Akinbowale, O. l., Peng, H., & Barton, M. d. (2006). Antimicrobial resistance in bacteria isolated from aquaculture sources in Australia. Journal of Applied Microbiology, 100(5), 1103–1113. doi:10.1111/j.1365-2672.2006.02812.x
5. Sapkota, A., Sapkota, A. R., Kucharski, M., Burke, J., McKenzie, S., Walker, P., & Lawrence, R. (2008). Aquaculture practices and potential human health risks: Current knowledge and future priorities.Environment International,34(8), 1215–1226.
6. Food and Agriculture Organization of the United Nations, & Food and Agriculture Organization of the United Nations. (2011). World aquaculture 2010. Rome: Food and Agriculture Organization of the United Nations.
7. Cabello, F. C. (2006). Heavy use of prophylactic antibiotics in aquaculture: a growing problem for human and animal health and for the environment. Environmental Microbiology, 8(7), 1137–1144. doi:10.1111/j.1462-2920.2006.01054.x
8. Serrano, P.H., 2005. Responsible use of antibiotics in aquaculture. FAO Fisheries Technical Paper. No. 469. FAO, Rome.
9. "Animal Husbandry and Disease Control: Aquaculture." U.S. Food and Drug Administration. U.S. Department of Health and Human Services, 9 May 2012. Web. 17 Mar. 2013. http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/ucm082099.htm.
10. Rigos, G., Bitchava, K., & Nengas, I. (2010). Antibacterial drugs in products originating from aquaculture: assessing the risks to public welfare. Mediterranean marine science, 11(1), 33–41. Retrieved from search.proquest.com/asfa/docview/1024658473/13CEFD2927E2479E5B8/1?accountid=14496
11. Burridge, L., Weis, J. S., Cabello, F., Pizarro, J., & Bostick, K. (2010). Chemical use in salmon aquaculture: A review of current practices and possible environmental effects. Aquaculture, 306(1–4), 7–23. doi:10.1016/j.aquaculture.2010.05.020
12. Coates, A. R., Halls, G., & Hu, Y. (2011). Novel classes of antibiotics or more of the same? British Journal of Pharmacology, 163(1), 184–194. doi:10.1111/j.1476-5381.2011.01250.x
13. Lim, S. J., Jang, E., Lee, S.-H., Yoo, B.-H., Kim, S.-K., & Kim, T.-H. (2013). Antibiotic resistance in bacteria isolated from freshwater aquacultures and prediction of the persistence and toxicity of antimicrobials in the aquatic environment. Journal of Environmental Science & Health, Part B -- Pesticides, Food Contaminants, & Agricultural Wastes, 48(6), 495–504.
14. Nogueira-Lima, A. C., Gesteira, T. C. V., & Mafezoli, J. (2006). Oxytetracycline residues in cultivated marine shrimp (Litopenaeus vannamei Boone, 1931) (Crustacea, Decapoda) submitted to antibiotic treatment. Aquaculture, 254(1–4), 748–757. doi:10.1016/j.aquaculture.2005.11.021
15. "Import Alert 16-129: Detention Without Physical Examination of Seafood Products Due to Nitrofurans." U.S. Food and Drug Administration. U.S. Department of Health and Human Services, 27 Nov. 2012. Retrieved from: http://www.accessdata.fda.gov/cms_ia/importalert_31.html.
16. "Import Alert 16-131: "Detention Without Physical Examination of Aquacultured Catfish, Basa, Shrimp, Dace, and Eel from China- Presence of New Animal Drugs and/or Unsafe Food Additives." U.S. Food and Drug Administration. U.S. Department of Health and Human Services, 12 July. 2012. Retrieved from: http://www.accessdata.fda.gov/cms_ia/importalert_33.html.
17. O. A. H. Jones, N. Voulvoulis , & J. N. Lester. (2004). Potential Ecological and Human Health Risks Associated With the Presence of Pharmaceutically Active Compounds in the Aquatic Environment . Critical Reviews in Toxicology,34(4), 335–350.
18. Midtlyng, P. J., Grave, K., & Horsberg, T. E. (2011). What has been done to minimize the use of antibacterial and antiparasitic drugs in Norwegian aquaculture? Aquaculture Research, 42, 28–34.
19. Grisez, L., & Tan, Z. (2005).Vaccine development for Asian aquaculture. (P. (ed) Walker, Ed.). Fish Health Section, Asian Fisheries Society, Quezon City (Philippines).
20. Defoirdt, T., Sorgeloos, P., & Bossier, P. (2011). Alternatives to antibiotics for the control of bacterial disease in aquaculture.Current Opinion in Microbiology, 14(3), 251–258. doi:http://dx.doi.org/10.1016/j.mib.2011.03.004
21. Lillehaug, A., B. T. Lunestad, and K. Grave. (2003). "Epidemiology of bacterial diseases in Norwegian aquaculture-a description based on antibiotic prescription data for the ten-year period 1991 to 2000." Diseases of aquatic organisms 53.2, 115-125.
22. Heppell, J., & Davis, H. L. (2000). Application of DNA vaccine technology to aquaculture. Advanced Drug Delivery Reviews, 43(1), 29–43. doi:10.1016/S0169409X(00)00075-2
23. Sihag, R. C., & Sharma, P. (2012). Probiotics: The New Ecofriendly Alternative Measures of Disease Control for Sustainable Aquaculture. Journal of Fisheries & Aquatic Science, 7(2), 72–103.
24. Oliveira, J., Castilho, F., Cunha, A., & Pereira, M. J. (2012). Bacteriophage therapy as a bacterial control strategy in aquaculture. Aquaculture International, 20(5), 879–910. doi:10.1007/s10499-012-9515-7