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*Review*

# Disease Resistant Fish and Shellfish Are within Reach: A Review

**Trygve Gjedrem**

Nofima AS, Osloveien 1, P.O. Box 210, NO-1431 Ås, Norway; E-Mail: trygve.gjedrem@nofima.no; Tel.: +47-9058-5566

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**Abstract:** Disease in fish and shellfish is one of the main problems facing aquaculture production. Therefore, all attempts should be made to increase the rate of survival and, thus, reduce economic losses. Much has been done to develop vaccines and medical treatments to reduce mortality; and however, farming of aquatic species has a long way to go to optimize the environmental conditions for the animals and, thus, reduce stress and improve animal welfare. However, the good news is that there is the potential to increase disease resistance by selective breeding. By challenge-testing fingerlings from a number of families per generation, and including the rate of survival in the breeding goal, the results so far are very promising. By focusing on one disease at a time it is possible to increase the rate of survival by at least 12.5% per generation for most diseases studied. Unfortunately, selective breeding is only used to a small degree in aquatic species. In 2010, it was estimated that only 8.2% of aquaculture production was based on genetically improved stocks.

**Keywords:** aquaculture; resistance; selection

## 1. Introduction

Aquaculture is the fastest growing primary industry for production of animal protein, with a growth rate of 6%–7% per year [1]. By 2017/2018, aquaculture production is expected to exceed fisheries in terms of volume, and if the present rate of increase continues, in a few more years it will also surpass production of poultry and pigs [1], and, thus, become the highest source of animal protein. One of the reasons for this development is that fish and shellfish are recommended as healthy food and, in addition, they are more efficient converters of energy and protein than terrestrial farm animals. Studies have shown that Atlantic salmon has 2.3 and 1.6 times higher rates of energy retention than poultry and pigs, respectively [2,3]. Further, retention of protein was also higher in salmon compared with poultry (1.5 times) and pigs (1.75 times) [2,3]. In addition, it has been shown that feed conversion rate (FER) has improved by 23% during five generations of selection in Atlantic salmon [4]. Under farming conditions, Atlantic salmon use 1.1 to 1.2 kg feed per kg of growth. Today, Asian countries account for 88% of global aquaculture production, with China as the leading producer [5]. The prospects for further expansion are promising and it has been shown that the potential for future increase of aquaculture production is very high both in fresh water and particularly in marine water [6]. However, the availability of feed resources may reduce the rapid expansion in coming years. Therefore, there needs to be more focus on production of shellfish and seaweeds, which feed on naturally occurring plants and algae in marine waters.

One of the major problems facing aquaculture production are the diseases caused by bacteria, viruses, fungi and parasites. Efficient medicines and vaccines have been developed in recent years to meet the challenges of some diseases. Today, technology allows vaccination of individual fish, which makes it possible to vaccinate a large number of fingerlings. As an example, Norwegian farmers vaccinate every year around 400 million smolts (fingerlings ready for seawater) against several diseases.

Nevertheless, the mortality due to diseases is still relatively high. A major challenge surrounds the medical treatment of disease outbreaks, since it is not possible to sort the infected animals from the non-infected. The medicine must therefore be given to all fish/shellfish in the pond or cage so both infected and non-infected animals are treated. The medicine is usually supplied in pelleted feed.

Mortality is also caused by different stressors such as: handling, high-density, low dissolved oxygen concentration, rapid variation in water temperature and quality, few and irregular feeding per day, among others. These problems occur particularly for non-domesticated strains newly brought in from the wild. To reduce mortality, the industry is continuously searching for methods to increase the welfare of the animals. The feed is of course an important factor and its content should cover all the nutritional needs for the animals. However, although efforts are made to optimize the environmental conditions for animals, still there will be mortality and it is not possible to fully control the spread of pathogens and parasites between and within farms.

The purpose of this paper is to discuss the possibility of increasing the defense mechanisms or resistance of the animals against diseases and parasites through selective breeding.

## 2. Measurement of Disease Resistance

A central question for including a trait in a breeding program is how accurately it can be recorded. A common method of measurement is to count the number of mortalities that occur in different families of fish and shellfish during a certain period of life. However, the heritability of percent survival of fingerlings is rather low, $h^2 = 0.10$ [7] and less than 0.1 for fry [8], which means that it is difficult in practice to standardize the numerous environmental conditions which affect the mortality of fish.

An alternative method is to use challenge test in which fingerlings that are individually tagged from a number of families are kept under standardized environmental conditions (in a tank) and infected with a pathogen at a time. Mortality is recorded until it ceases. The results from challenge testing are very promising and the heritability for rate of survival is usually high ($h^2$ = 0.43–0.69) [9–11]. It has also been shown that the results from challenge tests have been highly correlated with mortality in the field [12,13].

## 3. Some Results from Selection Experiments

The objective of some of the first selection experiments in aquatic species was to reduce mortality. The first selection experiment in brook trout increased the survival rate from 2% to 69% after three generations of selection [14], although family selection was not practiced. Selection response was also obtained for reduced mortality due to furunculosis in brook trout and brown trout [15]. Further, a response of 30%–40% was achieved by selecting four to five generations against dropsy disease in common carp [16,17].

## 4. Breeding Programs to Increase Disease Resistance

Early selection programs to increase growth rate used mass selection or random mating, without collecting information about the relationship between animals. Since growth rate has a relatively high heritability, 0.2–0.4 several of the selected breeders would be closely related. As time went on the animals become inbred and the result would automatically be low selection response or no response. This was most likely the result in common carp [18] and in Nile tilapia [19–21]. These results show how important it is to avoid inbreeding, which can be obtained by producing families and apply tagging or use microsatellites for identification of relationship.

Efficient and sustainable breeding programs are, therefore, family based and selection is usually for the traits of highest economic importance. Today breeding companies will usually include some major diseases in the breeding goal together with traits like growth rate and meat quality traits [22]. The breeding company usually discusses with the farmers which traits should be included in the breeding goal and which traits should be given highest weight in the selection index. One should, however, be aware that as the number of traits is increased in the breeding goal, the genetic gains for each trait will be reduced.

It is encouraging that positive genetic correlations have been reported between growth rate and most diseases [23]. In this study, the average of eight positive estimates of genetic correlation was $r_G$ = 0.25. However, there are also some negative genetic correlation between growth rate and diseases, that between growth rate and Taura Syndrome virus in shrimp, was $r_G$ = −0.12 [23]; between growth rate and VHS disease in rainbow trout $r_G$ = −0.22 [23,24] and between growth rate and WSSV in shrimp $r_G$ = −0.55 to −0.64 [25]. This means that selection for increased growth rate will give a positive correlated response in disease resistance for most species while negative in other.

## 5. Data Collection

Challenge tests for particular diseases have been shown to give very reliable estimates of disease resistance. To get results with high repeatability, a sample of 30 to 50 tagged fry/fingerlings from each family should be sent to a specialized laboratory equipped for such tests. The families of fish/shellfish should be kept in one tank and infected by the pathogen/parasite in question. As mortality starts, each dead fingerling should be removed from the tank and the time of death and tag number recorded. The recording continues until the mortality has ceased [26]. Frequencies of survival will later be included in the selection index as one of the traits in the breeding goal.

The recording of other traits takes place during the grow-out period, as well as at the time for harvesting. At harvesting, some results from test stations will be available. The final selection of animal for breeding should take place when all data are available and selection indices have been calculated [6]. The selection index for each trait should be weighted by its economic importance and its heritability. In addition, genetic correlations between the traits should be taken into account.

## 6. Genetic Gains Obtained

A number of selection experiments and breeding programs have successfully reduced mortality. Some results from selection for disease resistance are given in Table 1. Genetic gain in survival is rather low (5.0%–8.4%) per generation [27–29]. The reason seems to be that it is difficult to standardize the environmental rearing conditions for fish and shellfish over a lifetime, and there will be a number of factors causing mortality. In addition, multitrait selection has been practiced, which has lowered the weight of survival in the selection index. However, by applying challenge tests under standardized environmental conditions, more reliable information can be collected about resistance to disease.

The genetic gain obtained by applying challenge tests for Infectious Pancreatic Necrosis (IPN) [30] and *Vibrio salmonicida* [31] is very high applying single trait selection reaching 19% per generation. The reason for the low genetic gain in White Spot Syndrome Virus (WSSV) resistance, varying from 1.7% [27] to 6.3% [32] is not obvious, it could partly be due to difficulty and inaccuracy of mortality recording. Multi trait selection for Taura syndrome in *P. vannamei* is also high [33,34] while it is of medium magnitude for M. Sydney parasite in oyster [35]. The amoebic gill disease in Atlantic salmon has been shown to have genetic variation ($h^2$ = 0.09–0.56) [36]. The selection strategy is to reduce number of treatments and it is predicted to increase the interval between treatments by 3% per year [36]. Genetic variation is also shown for salmon louse with a heritability of $h^2$ = 0.26 [37].

These genetic gains, obtained through breeding programs, show that it is possible to develop lines which are resistant to diseases and parasites. How long this will take depends on several factors: Magnitude of genetic variation or heritability of the trait, what weight the disease or diseases get in the selection index, and the magnitude of genetic correlation between the diseases and the other traits in the breeding goal. If, for example, the aim was to improve resistance against Taura syndrome only and with a mortality at the beginning of 50% and a genetic gain of 15.4% per generation, it would take five generations to develop a full resistant strain. This rapid gain is because the improvement is cumulative; the newly selected generation builds on those made in previous generations.

New biotechnological developments show promising results to improve disease resistance. A single QTL was found to explain more than 80% of the genetic variation for IPN (Infectious Pancreatic Necrosis) resistance in Atlantic salmon [38,39]. In addition, a QTL for PD (Pancreatic Disease) was found explaining a considerable part of the variation in this disease [40]. The possibility for genetic gain by applying marker-assisted selection has been discussed [41]. These findings when included as a tool in breeding programs will increase the genetic gain in future generations and the methods are already in use by breeding companies.

**Table 1.** Average genetic gains of selection for increased disease resistance. Multi trait selection is marked with *.

| Traits | Genetic Gain per Generation, % | Number of Generations Selected | References |
|---|---|---|---|
| **Survival:** | | | |
| Whiteleg shrimp, *P. vannamei* | 5.7 * | 4 | Gitterle, *et al.* 2007 [27] |
| Blue tilapia, *Oreochromis aureus* | 8.4 * | 4 | Thodesen, *et al* 2012 [28] |
| Red tilapia, *Oreochromis* spp. | 5.0 * | 4 | Thodesen, *et al.* 2013 [29] |
| **IPN resistance:** | | | |
| Atlantic salmon, *Salmo salar* | 18.7 | 1 | Storseth, *et al.* 2007 [30] |
| ***Vibrio salmonicida*:** | | | |
| Rainbow trout, *Oncorhyncus mykis* | 19.0 | 1 | Leeds, *et al.* 2010 [31] |
| **White spot, WSSV:** | | | |
| Whiteleg shrimp, *P. vannamei* | 1.7 * | 4 | Gitterle, *et al.* 2007 [27] |
| Whiteleg shrimp, *P. vannamei* | 6.3 | 4 | Huang, *et al.* 2012 [32] |
| **Taurasyndrom, TVS:** | | | |
| Whiteleg shrimp, *P. vannamei* | 12.4 * | 1 | Fjalestad, *et al.* 1997 [33] |
| Whiteleg shrimp, *P. vannamei* | 18.4 * | 1 | Argue, *et al.* 2002 [34] |
| ***M.sydneyi*, parasite:** | | | |
| Oyster, *S. glomerata* | 11.0 | 2 | Nell and Hand, 2003 [35] |

## 7. Discussion

In farming aquatic species mortality can cause serious economic losses and reduce profits. In addition, it is discouraging for the farmer to harvest and dispose of the dead animals. Therefore every effort should be made to improve the welfare of the animals and increase their survival rate by applying challenge tests. As documented above, selective breeding offers good potential to increase the rate of survival. A genetic gain of 12.5% per generation will have a marked increase in survival rate, since the effect is cumulative. In addition, a breeding program will always select for improved growth rate and because of the positive genetic correlation between growth rate and resistance to most pathogens, selection for improved growth rate will increase the genetic gain for survival.

Biotechnological research can be beneficial by providing additional knowledge about the genetics of diseases. The information about the QTL for resistance to IPN and PD is very promising for increasing the rate of resistance to these diseases through selective breeding. Hopefully the future will bring more knowledge in this field, which will increase our possibility to reduce mortality for aquatic species farmed in aquaculture.

The fact that only a small part of aquaculture production is based on genetically improved stocks is discouraging. Recent estimates [42,43] show that only 8.2% of aquaculture production in 2010 was based on family breeding programs. This is a disadvantageous situation, particularly since it is well documented that it is possible to get a rapid improvement of growth rate, disease resistance and product quality through family based breeding programs.

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## Conflicts of Interest

The authors declare no conflict of interest.

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