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Food safety hazards that occur during the production stage: challenges for fish farming and the fishing industry

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Summary

Seafood derived from wild fish as well as farmed fish has always been an important source of protein in the human diet. On a global scale, fish and fish products are the most important source of protein and it is estimated that more than 30% of fish for human consumption comes from aquaculture.

The first part of this paper outlines the hazards and challenges associated with handling fish during farming and capture. The authors describe infectious agents that cause disease in fish as well as humans, zoonotic agents, intoxications due to bacteria and allergies caused by the consumption of fish.

Although only a few infectious agents in fish are able to infect humans, some exceptions exist that may result in fatalities. However, the greatest risk to human health is due to the consumption of raw or insufficiently processed fish and fish products.

The second part of the paper considers environmental contaminants in seafood that may pose a risk to human health, such as medicinal products and residues associated with aquaculture, persistent lipophilic organic compounds and metals (methyl-mercury, organotin).

The authors include an updated overview of the various factors associated with farmed and captured fish that may cause risks to human health after consumption. Moreover, they discuss the challenges (in the widest sense) associated with handling fish during capture and farming, as well as those encountered during processing.

Keywords

Allergy – Aquaculture – Capture fishery – Contaminant – Fish – Fish farming – Fish handling – Fish processing – Food safety – Metal – Persistent lipophilic organic compounds – Residue – Seafood – Wild fish – Zoonotic agent.

Introduction

Over the past three decades, aquaculture has developed to become the fastest growing food-producing sector in the world. A large proportion of fish products come from small-scale producers in developing countries or low-income-deficit countries. More than 80% of global aquaculture products are produced in fresh water. From its early development in Asia, aquaculture has undergone huge development and is today highly diversified. Aquaculture consists of a broad spectrum of systems, from small ponds to large-scale, highly intensified commercial systems. The production of Atlantic salmon (*Salmo salar*) in marine net pens is one example of an intensified commercial system that has developed during the last 20 to 30 years.

The main aquaculture products are finfish, crustaceans, molluscs and aquatic plants. The Food and Agriculture Organization (FAO) of the United Nations has estimated that more than 30% of all fish used for human consumption originates from aquaculture. These fish comprise primarily herbivorous species, such as tilapia and carp. In export value, finfish (Atlantic salmon) and crustaceans (shrimps) are the most important products. In 2004, the total global production in aquaculture was 17.3 million tonnes of carp (*Cyprinius carpio*), 1.2 million tonnes of tilapia (*Tilapia* spp.), 1.1 million tonnes of salmon, 0.5 million tonnes of rainbow trout (*Oncorhynchus mykiss*), 0.5 million tonnes of shrimp and more than 10 million tonnes of molluscs (55). The production of algae is estimated to be more than 12 million tonnes. The People's Republic of China is, by far, still the largest producer of aquaculture products in the world.

Current conditions and practices in aquatic animal production

Food safety hazards in aquaculture include fish disease agents and hygienic aspects (microbiological agents), and contaminants such as environmental pollutants. However, in a broader sense, these risks also include those related to the handling of fish during catching, farming, slaughter and processing for human consumption.

Zoonotic agents in fish

In general, true zoonotic agents associated with fish, crustaceans and molluscs are few. Many commensal and pathogenic bacteria, viruses, fungi and parasites associated with fish have temperature growth limits that will not support their development in humans.

However, there are some exceptions. In the following section, bacterial and parasitic agents which can cause disease in both fish and humans are discussed.

Fish pathogenic bacteria as potential causal agents for disease in humans

Viruses, bacteria, fungi and parasites in fish may cause disease or food-borne infections in humans. Under normal conditions, practically no infectious agents which cause disease in fish also infect humans. Nevertheless, under certain conditions, bacteria which cause fish diseases may also infect humans, without necessarily being regarded as a major human health problem.

Bacteria

Bacteria represent a major and important group of micro-organisms because of their frequent occurrence and activities that may have a negative impact on fish quality. Generally, seafood from cold waters harbours lower numbers of potentially pathogenic micro-organisms than seafood from warmer waters. The presence of human pathogenic bacteria in fish and fish products may also be attributed to contamination during processing.

Several bacteria are, however, reported to cause infection and mortality in both fish and humans (6) and these represent a particular hazard, caused either by handling infected fish on fish farms or in grocery stores (12, 28) or by the ingestion of raw or inadequately processed infected fish and/or contaminated fish products.

Vibrio **species**

To date, some 12 species of the *Vibrio* family, which have marine and estuary environments as their main habitat, have been shown to cause disease in humans (6). Human pathogenic *Vibrio* species can be detected in temperate waters, especially during the summer months, but at lower frequencies than in tropical waters.

The most important *Vibrio* species associated with disease problems in humans, due to ingestion or other routes of exposure, are *V. cholerae*, *V. parahaemolyticus* and *V. vulnificus* (25, 54, 92, 106). The last has been associated with wound infection and septicaemia, while the first two mainly cause gastro-intestinal symptoms.

In the United States of America (USA), *V. vulnificus* has been reported to have caused deaths, not by food poisoning after the consumption of seafood, but because of its ability to cause wound infection, especially in soft tissues, either with penetrating injuries or through contamination of existing wounds (18, 90, 91).

Amaro and Biosca (3) reported that Biotype 2 of *V. vulnificus*, which is considered an obligate pathogen causing skin lesions, septicaemia and mortality in eels (*Anguilla* spp.), may also be an opportunistic pathogen in humans (3, 66). Skin-penetrating scratches received while handling fish have been reported to cause necrotising dermo-hypodermatitis in fish workers (26), as well as local cellulitis and even life-threatening disease due to fish-spine injuries (18). As a consequence, appropriate care must be taken by consumers at risk, as well as by fishfarmers handling diseased eels (3). Both the infected fish and the water may be sources of infection (3).

In Israel, *Vibrio* infections caused by *V. alginolyticus, V. parahaemolyticus, V. vulnificus* and non-typable

Vibrio spp. were reported in humans, due to changes in the way that pond-raised fish were being packed (12). In most cases, these infections were initiated by exposure to the fins of the fish. An epidemiological study showed that the reason for this was a change in trade patterns. The producers had changed their delivery practice from packing fish in ice to packing live fish in containers. When producers changed back to selling the fish on ice, no further infections were recorded.

In Japan, V. parahaemolyticus has been reported as the most common cause of food poisoning (86).

Photobacterium damselae (previously *Listonella damsela*, *V. damsela*), which causes skin ulcers in several fish species, in particular, damselfish (*Chromis punctipinnis*), has also been considered an important pathogen in humans, as several cases of progressive necrotising wounds have been reported (1, 83). Infection in humans has usually been caused either by injuries from fins or by contamination of wounds exposed to water (23, 86, 97). Before 1993, all cases in humans had originated from wound infections but Perez-Tirse *et al.* (97) described a septicaemic condition in a patient caused by a knife injury when filleting blue fish (*Pomatus saltatrix*).

Hafnia alvei

Hafnia alvei, a Gram-negative, facultative anaerobic bacterium of the family Enterobacteriaceae, is found in natural environments, such as sewage, soil and water, but is also a gastro-intestinal commensal. This bacterium is not usually considered pathogenic but has occasionally been reported to cause disease in fish as well as terrestrial animals and humans (93).

Hafnia alvei has been associated with epizootic haemorrhagic septicaemia in rainbow trout (56); kidney pathology in cherry salmon (*O. masou*) (107); and mortalities in brown trout (*S. trutta* L.) in freshwater aquaculture (101), but not in marine aquaculture (93). In humans, *H. alvei* has been associated with several disease conditions, such as:

- septicaemia
- gastroenteritis
- meningitis
- pneumonia
- wound infections (51, 117).

However, so far, there have been no reports of the bacterium transferring from fish to humans. Nevertheless, in some regions there may be a combination of marine fish farming and human activities, such as disposal of sewage in areas where people swim, which may lead to the transfer of *H. alvei* between humans and fish and vice versa. Based on challenge experiments with *H. alvei* in gilthead seabream (*Sparus aurata* L.), Padilla *et al.* (93) concluded that, although the gilthead seabream seemed to have a considerable resistance to experimental infections, the bacterium could remain viable in the fish without clinical signs for some three months. This means that aquaculture and human activities should take place in separate areas as farmed fish may represent a risk for the transfer of *H. alvei* to humans.

Streptococcus iniae

The genus *Streptococcus* includes many species that can cause disease in different hosts, including fish in sea, brackish and fresh water as well as in mammals and humans (79). *Streptococcus iniae* has been described as a cause of disease in both fish ('mad fish disease') and people (49, 58). It is a Gram-positive, beta-haemolytic bacterium that was first isolated from diseased Amazon freshwater dolphins (*Inia geoffrensis*) (99), but was later described in cultured fish species, such as rainbow trout (*O. mykiss*), tilapia, channel catfish (*Ictalurus nebulosus*), Japanese flounder (*Paralichthys olivaceus*) and yellowtail (*Seriola quinqueradiata*) (32, 79).

In fish, infection with *S. iniae*, previously described as *S. shiloi* and *S. difficile* (32, 33), is characterised as a septicaemic disease which may become chronic. In humans, disease caused by *S. iniae* was not described until 1995 to 1996, when the bacterium was isolated from a group of patients in Canada who had handled fresh whole tilapia from infected farms (116, 125). This was despite the fact that the bacterium had been identified as early as 1991 (21, 49). The disease condition in humans, characterised principally by septicaemia, cellulitis, endocarditis, meningitis and pneumonia, has been particularly associated with people of Asian ethnicity, caused by their handling live and freshly killed fish (mainly tilapia) contaminated with *S. iniae* during food preparation (49, 80, 89, 116, 125). The bacterium is most often introduced through wounds and abrasions in the skin. In the reported cases from Canada, the affected patients were elderly and many had poor health and compromised immune systems. The risk of healthy humans acquiring disease is minimal (125).

Mycobacterium species

Several *Mycobacterium* spp., such as *M. marinum*, M. *chelonei* and *M. fortuitum*, have been reported in both fish and humans. Fish with mycobacteriosis pose a particularly significant threat of transmitting the infection to humans and thus may well become hazardous to human health (89). Mycobacteriosis is a chronic disease reported in seawater, brackish water and freshwater fish species, in aquaculture and aquariums as well as from the wild (89). Human infection with *M. marinum* has been reported in many countries since 1951, yet it is still considered rare. It is mainly associated with granulomatous skin lesions, especially lesions acquired by aquarists when cleaning fish tanks. The infection usually enters through open wounds or abrasions exposed to contaminated water in which infected fish have been kept or while processing fish (20, 22, 78, 110). In the USA, rockfish infected with *M. marinum* are believed to cause skin problems in humans (95).

Table I
An overview of outbreaks of listeriosis from marine sources
(103)

Country	Year	Number of outbreaks	Source
United States of America	1989	2	Shrimps
New Zealand	1991	4	Smoked shellfish
Australia	1991	2	Smoked shellfish
Sweden	1994	6	Smoked/brine-cured fish
Canada	1996	2	Crabsticks
Finland	1999	5	Smoked trout

Contaminating bacteria as potential agents for disease in humans

Erysipelothrix rhusiopathiae

Infection with *Erysipelothrix rhusiopathiae* (erysipeloid) is also known as 'fish handler's disease', 'fish hand', 'blubber finger', etc., in humans, since it is most commonly characterised by swollen fingers (65). The bacterium is reported to occur on fish, and the infection is most often introduced to humans through skin wounds. Thus, the disease must be considered as occupational in humans, due to handling fish and fish products contaminated with *E. rhusiopathiae*. The disease is usually benign, but may be fatal in some cases. Fatal endocarditis has been described following the gutting of eels (65).

Listeria

Listeria monocytogenes has been isolated on a regular basis from a wide variety of seafood products, including fresh, frozen, fermented, cold smoked and salted fish derived from aquaculture as well as captive fisheries. It is a problem often associated with fish and fish products from temperate climates (17, 24, 53). The organism is ubiquitous in nature and regarded as a zoonotic agent, causing meningitis and abortions in sheep and septicaemia in lambs, as well as food-borne illness in humans (17). The occurrence of *L. monocytogenes* in seafood is reported to range from 0% to 75% (8).

'Ready-to-eat' products, such as refrigerated, vacuum-packed products with a long shelf life, are of particular concern for *L. monocytogenes*, especially when they are inadequately heated before consumption (17, 53). Table I gives an overview of outbreaks of listeriosis caused by marine sources (103).

It has been shown that bacterial growth occurs during the fermentation process at 8°C and storage at 4°C. The ability to grow at low temperatures, together with halotolerance, enables bacteria to reproduce in salted products (24, 103). *Listeria monocytogenes* has also occasionally been found in smoked salmon and it is thought that the bacterium is introduced through water during the production process (102). Cold smoking does not eliminate *L. monocytogenes* (31) and, although bacterial counts are reduced by hot smoking, the bacterium is not completely eliminated from smoked products (62). The isolation of different strains of *L. monocytogenes* from raw fish and final products indicates that contamination may take place at several stages in the production chain between harvesting and production for consumption (53).

Outbreaks of listeriosis in humans due to contaminated seafood have been reported from many parts of the world, particularly from industrialised countries (53, 103). Outbreaks have been related to different types of food items, including products such as shrimps, vacuum-packed smoked salmon and fermented fish. Most cases of listeriosis in humans occur in immunocompromised people, the elderly and pregnant women, and the disease is characterised by septicaemia, intra-uterine infection and meningitis. It may also cause abortions (stillbirths). However, more recently, *Listeria* has been associated with mild gastro-intestinal symptoms (53). Disease caused by *L. monocytogenes* is rare and a high infectious dose is required. The zero tolerance policy established in many countries for *Listeria* in fish products may be over-protective from a public health point of view (53).

Other bacteria

Aeromonad bacteria are ubiquitous in the environment and several *Aeromonas* species have been reported to cause disease in fish, as well as being potential food-borne pathogens that may cause disease in humans (89).

Although *Salmonella* spp. may be harboured and survive in fish, seafoods seldom harbour *Salmonella*. Fish may be exposed to *Salmonella* through consumption of contaminated feed or living in contaminated water. The occurrence of *Salmonella* in feed has, for a long time, been a well-recognised problem worldwide. However, research has shown that the level of *Salmonella* contamination in the feed must be extremely high if the bacteria are to persist in the fish for more than a few days (87). If *Salmonella* is present in freshwater or marine fish species, this is mainly due to faecal contamination (124).

Food-borne pathogenic bacteria such as *Campylobacter, Shigella* and *Yersinia* are seldom associated with fish. Nevertheless, the fish pathogenic bacteria *Y. ruckeri* has been reported to occur in humans (50).

Edwardsiella tarda, which causes 'red disease' in eels as well as enteritis in penguins, is also sporadically reported as causing gastroenteritis and septicaemia in humans (72).

Parasites in fish as potential agents for disease in humans

A great majority of freshwater and seawater fish species harbour parasites. These are more common in wild fish than in farmed fish. Most of these parasites are harmless to humans but some may make the fish products unsuitable for human consumption, either due to quality deterioration ('milky flesh') or because humans may be an aberrant or final host of the parasites.

The use of raw, inadequately cooked, salted or smoked fish, common in many countries, has zoonotic potential and has been reported to have caused serious disease conditions in humans. To avoid disease problems caused by parasites, fish that is going to be used for sashimi, sushi or other raw fish dishes should be frozen before use.

Trematodes

The number of food-borne infections caused by trematodes has increased dramatically in Eastern Europe in recent years, where millions of people are affected by *Opisthorcis* spp. (119).

In Asia, cyprinids are the most important group of fish species used in aquaculture and species belonging to this group are the principal hosts of trematodes, such as *Clonorchis sinensis*, *Opisthorcis felinus* and *O. viverrini*. If infected fish and their products are inadequately prepared before consumption, the risk of human infection is obvious. The consumption of 'hot rice congee' in the People's Republic of China and raw fish in the Republic of Korea is reported to cause infection with *Clonorchis* spp. in humans, while the dish 'koi-pla' in Thailand has been reported to cause infection with *Opisthorcis* spp.

The trematode *Heterophyes heterophyes* is another parasite that is reported to cause problems in the Middle East and Asia, but other heterophyides are also of importance (61, 94).

Pain and discomfort are the most common effects of acute trematode infection. More chronic infections, i.e. with *Clonorchis* spp. and *Opisthorcis* spp., can result in cholangio-carcinoma, chronic diarrhoea and hepatic cancer (119).

If, however, the contamination of aquaculture premises with untreated human and reservoir-animal excreta can be avoided, such problems may be diminished considerably (119).

Cestodes

The pseudophyllean cestode *Diphyllobothrium latum* is reported from many regions throughout the world. Several fish species act as intermediate hosts in which plerocercoids occur in the muscular tissues or on the viscera (85). Consuming raw or lightly cooked fish may result in infection in humans as the parasite establishes itself in the gut.

Nematodes

Anisakis

Anisakiasis is usually associated with the consumption of raw, wild, caught fish as *Anisakis* spp. are seldom a problem in farmed fish. The parasite has a complex life cycle involving passage through a number of hosts, including fish and mammals. The stage that infects fish is found as a distinct 'watch-spring coiled shape'. When uncoiled, the parasite is approximately 2 cm long. Usually, *Anisakis* is localised on the outside of internal organs but may occasionally be found in the flesh or beneath the skin. If infected fish are eaten by a marine mammal, the life cycle is completed.

However, *Anisakis* is also able to infect humans if raw, fermented or inadequately cooked fish is eaten. In such cases, humans will act as aberrant hosts.

This parasite is one of the most significant factors in reducing the quality of seafood and may thus harm human health, either through infection with *Anisakis* or allergic reaction (81). Several cases of gastro-intestinal problems caused by anisakiasis have been reported from the Netherlands and Japan (115, 127). Most of these cases have been associated with the intake of raw fish, in particular, herring. In the Netherlands especially, the dish 'groene herring' has played a role.

Gnathostoma

Spirurid nematodes, such as *Gnathostoma* spp., normally found in the stomachs of carnivorous animals, such as dogs, have also been reported to occur in humans if the larvae of the parasites are ingested. Humans are an aberrant host to the parasite. When larvae are ingested, they migrate from the intestine to the skin and musculature, causing the so-called 'larvae migrans' syndrome. However, they may also invade other organs, causing serious problems (100).

Intoxications caused by fish consumption

Clostridium botulinum

Clostridium botulinum type E is a strict anaerobic bacterium that may occasionally be present in fish. This bacterium is a recognised commensal in fish in fresh water, as well as in sea water. Under optimal growth conditions, the bacterium may produce a potent neurotoxin in processed fish (63, 67, 69). To avoid problems, it is important to control the factors that can prevent the growth of this organism in fish and fish products, such as temperature and salt concentration.

The anaerobic bacterium *C. botulinum* has been reported to cause intoxication in farmed fish, as well as terrestrial animals and humans (19, 30, 68, 109). Thus, *C. botulinum* may become an important hazard to the food safety of aquaculture products. The condition in pond-cultured fish is usually called botulism or 'bankruptcy disease' and, as in humans, it is due to the potent neurotoxin produced by the bacterium. In countries where fermented fish (both farmed and wild salmonids) is a speciality, unhygienic production conditions may result in intoxication and death in humans.

Histamine fish poisoning

Scombrotoxic fish poisoning, also known as scombroid or histamine fish poisoning, is caused by bacterial spoilage of a limited number of fish species. These comprise mainly:

- mackerel (*Scomber scombrus*)
- bonito (*Sarda* spp.)
- various tuna species (*Thunnus* spp.)
- swordfish (*Xiphias gladius*)
- common dolphinfish (mahi-mahi) (*Coryphaena* spp.).

As bacteria break down fish proteins, by-products, such as histamine and substances blocking histamine breakdown, may build up in fish. The human tolerance limit for histamine is 10 mg per 100 g. In general, there is no risk of histamine poisoning in well-iced fish.

Allergies to fish and seafood

Eating fish may produce severe allergic reactions. Allergies to fish, shellfish and mussels are among the most common food allergies triggered by immunoglobulin-E antibodies, and allergic reactions to seafood antigens may produce severe symptoms, including angio-oedema and anaphylaxis. These symptoms do not differ from allergic reactions to any other type of food (82).

Even though allergens are more or less species-specific, there is a high degree of cross-reactivity among different fish species. This means that a patient who is allergic to one fish species is at a high risk of being allergic to other species.

There are no specific symptoms for allergic reactions to food. Consequently, after ingesting seafood, the clinical manifestations of an allergic reaction do not differ from allergic reactions to any other type of food (82).

An allergy to fish and shellfish often becomes evident during the first year of life but, in general, presents later than an allergy to eggs and milk (96). While many children outgrow their allergies to eggs, cows' milk, wheat and soy, they may continue to be hypersensitive to fish and shellfish in later life (14, 29, 64, 104).

There is no evidence supporting the contention that the prevalence of fish allergy has anything to do with the level of fish intake, despite comments made in the literature. Studies on fish allergy in Reykjavik (high consumption) and Uppsala (low consumption) showed that, although the population in Reykjavik ate two to three times as much fish as that of Uppsala, there were no significant differences in prevalence between these two populations (57).

Fish consumption in Norway is among the highest in Europe; the median value being about 65 g per day. Of this, approximately two-thirds is lean white fish and about one-third is fatty fish (H. Meltzer, personal communication). However, the prevalence of seafood allergy in the Norwegian population is low (< 1%). The importance of seafood allergy to the health of the Norwegian population is marginal.

The first isolated allergen from fish is the calcium-binding protein, parvalbumin. Since patients usually react to both raw and cooked fish, it is assumed that the allergen is heat resistant. However, recent data indicate that some individuals react only to raw fish, while others react only to cooked, suggesting the existence of additional allergens. The lowest dose of fish reported to produce an allergic reaction is 5 mg.

Established thresholds for food allergens are important tools for food production and labelling. However, at present there are insufficient data available to establish such thresholds. Consequently, no values have been established for food allergens in European Union (EU) legislation.

Residues in fish

Residues of antibiotics and chemotherapeutics in fish

In aquaculture, particularly in fish-farming, various types of antimicrobials have always been needed to combat or prevent disease (126). In some countries, antibiotics were even used as growth promoters. Before the 1990s, the use of medicinal products was high in countries with a large aquaculture industry. The use of drugs for 'fire-fighting' (i.e. solving an immediate problem) was markedly reduced in many countries (60) during the 1990s, reflecting the introduction of widely available and effective vaccines against some of the most serious fish diseases in aquaculture.

However, some medicinal products are still in use, giving rise to several public health aspects, such as toxicity, drug hypersensitivity and the development of antibiotic resistance in fish pathogenic bacteria, as well as in environmental bacteria and human pathogens. The risk of transfer of antibiotic resistance to human microflora is probably low in countries where the use of antimicrobials is limited. However, in countries with less restrictive legislation, the risk of contaminating fish and fish products with resistant bacteria is greater (2).

So-called 'integrated farming', which combines intensive animal husbandry (in particular, of pigs and poultry) and aquaculture, may represent a route of transmission of bacterial resistance genes from fish to humans (98). Wastes from the animals are a source of feed for the fish in such production systems.

Malachite green

Malachite green is an industrial dye that has effectively been used to treat fungal infections in fish. However, it has not been authorised as a veterinary drug, and its application in aquaculture is not permitted. Although malachite green has been abandoned for use in food-producing animals for many years, the active substance and its metabolite, leuco-malachite green, are still being detected in fish and fish products. In eels, the related crystal violet (also known as gentian violet) dye has been found. The EU has set the minimum required performance limit for malachite green to be two parts per billion of the analytical method used to detect the substance (48).

The EU (52) has reported that residues of leuco-malachite green and malachite green have been detected in fillets of pangassius (*Pangassius hypothalamus*), eel and Pacific salmon (*Oncorhynchus* spp.), respectively. Despite the fact that malachite green has been banned on the Chinese mainland since 2002, this chemical was found in freshwater fish in local markets in Hong Kong, leading the Hong Kong Government to take measures to safeguard food safety in fish (5).

Environmental contaminants in fish

A wide variety of chemical contaminants may be present in the environment, including persistent lipophilic organic compounds, as well as metals (e.g. methyl-mercury and organotin). In particular, there are numerous lipophilic organochlorine contaminants, including: – poly chlorinated dibenzo-p-dioxins (PCDDs) and furans (PCDFs) (collectively, PCDD/Fs)

- polychlorinated biphenyls (PCBs)
- camphechlor
- hexachlorcyclohexane
- dichlorodiphenyltrichloroethane and its metabolites
- aldrin
- chlordane
- dieldrin
- endrin
- heptachlor
- hexachlorbenzene.

Most of these compounds are, however, no longer produced and levels in the environment are generally decreasing.

In contrast, the environmental levels of another group of chemicals, brominated flame retardants (BFRs), some of which are still in use, seem to be increasing (27, 107). This group includes, for example:

- polybrominated diphenyl ethers (PBDEs)
- tetrabromobisphenyl A (TBBPA)
- hexabromododecane.

Lipophilic, persistent organic compounds have a strong tendency to bio-accumulate in fatty tissues and will also biomagnify in food chains. The highest levels are found in the fatty tissues of species at the end of the food chain.

Organometals, such as methyl-mercury, also have the potential to bio-accumulate in the food chain, and the concentrations increase with the age and size of the individual. Persistent organic pollutants (POPs) in fish are predominantly derived from their diet. Owing to their lipophilic nature, POPs are particularly likely to be present in fatty, predatory fish, such as:

- wild herring
- mackerel
- tuna
- salmon.

In contrast, methyl-mercury does not accumulate in fatty tissue, but becomes concentrated with age and as it progresses along the food chain. The highest concentration of methyl-mercury is found in older, predatory fish at the top of the food chain (e.g. tuna, trout).

The diet of wild fish cannot be controlled and the only way to reduce the exposure of these fish to contaminants is to reduce the spread of contaminants into the environment.

Potential risks associated with contaminants throughout the food chain

Contaminants in fish farming

Feed is the main source of POPs and metals in farmed fish (34). Since the safe production of farmed fish starts with fish feed, the development of feed products with low levels of undesirable substances has become pivotal (34). The concentration of several POPs (e.g. dioxins and BFRs) and metals (e.g. methyl-mercury) in fillets of farmed fish has been reported to correlate with their concentration in feed (10, 70, 77, 84).

These POPs are highly persistent, fat-soluble environmental pollutants that are ubiquitous in the marine ecosystem and are readily biomagnified in the food chain. Fish oils, extracted from marine pelagic fish species, such as capelin (*Mallotus villosus*), sand eel (*Amodytes* spp.) and blue whiting (*Micromesistius* spp.), used in high-energy fish feeds, are considered to be the main source of POPs in farmed salmon (34, 120).

The potential threat of POPs to human health is not related to a single chemical component, but to a mixture of several related congeners of different basic chemical structures. For dioxins and dioxin-like PCBs, there are 29 different chemical forms that share a similar toxic mechanism (114). The profile of these 29 congeners, and hence the total World Health Organization (WHO) toxic equivalency (TEQ) in feed (the WHO-TEQ), is often not reflected in the fish. Some congeners (such as dioxin-like PCBs) are more predominant in feed than in fish, when compared to other congeners (such as dioxins) (11, 70). The different 'carry-over' or transfer of the chemical forms shows the complexity of aiming for a 'feed-to-fork' approach to controlling undesirable substances along the food chain. When selecting new feed resources to 'tailor' a fish product that is low in certain contaminants, differences in feed-fish transfer dynamics for each contaminant congener must be taken into consideration.

Several strategies are being developed on how to produce fish low in undesirables by designing specific diets and optimising feeding strategies, taking into account both cost efficiency and fish welfare.

There are three main approaches that, alone or in combination, may reduce the levels of PCDD/Fs and dioxin-like PCBs in fish feed and farmed fish. There is a large variation in the levels of PCDD/Fs and dioxin-like PCBs found in fish oil, depending on such factors as seasonal variation, fish species, age or geographical origin (34, 88). Thus, it is possible to select marine ingredients with relatively low background levels of POPs for use in fish feeds (71, 84).

Another strategy is to replace fish oil with alternative terrestrial feed ingredients that contain lower levels of dioxins. Plant oils have lower PCDD/F and dioxin-like PCB levels than most commonly used fish oils, and thus have great potential to reduce the level of dioxins in farmed salmon (7, 11). Moreover, several techniques are available that remove POPs from fish oils without affecting the nutritional status of the oil (16, 26). As a result, the POP levels in fish fillets can be reduced considerably.

The toxicity of mercury depends on the chemical form. The organic, methylated form of mercury is considerably more toxic than inorganic forms (9). Inorganic mercury is methylated to organic mercury through microbial, predominantly anoxic processes in aquatic ecosystems (73, 118). Methyl-mercury is the dominant form of mercury in fish, and fish meal is the main source for methyl-mercury in fish feeds. Methyl-mercury is efficiently accumulated in fish muscle, which is one of the main organs for methyl-mercury deposition (13, 15, 59, 75). Methyl-mercury has a higher assimilation level (41% to 23%) than dietary inorganic mercury (6% to 4%) (10). In the terrestrial system, inorganic mercury is the dominant form. Mercury uptake by plants from the soil is low; therefore the concentration of mercury in plant feedstuffs is limited.

The use of novel feedstuffs in fish feeds may remove current problems caused by POPs and metals, but may also introduce new challenges to food safety. Higher levels of pesticides, such as endosulfan, have been found in some plant oils, compared to fish oils. The use of alternative marine feed ingredients, such as krill, will introduce high levels of fluorine to the feed. That may limit the use of this resource, due to current legislation on maximum permitted levels of fluorine in feed.

Hazard identification and hazard characterisation of contaminants

The ability of a chemical to cause adverse health effects and thus its tolerable daily intakes (TDI) and/or tolerable weekly intakes (TWI) are established by risk assessments performed by international bodies (123). The TDI of a chemical represents the amount of the chemical that can be safely consumed throughout life with no risk of any significant adverse health effect.

Some chemicals are carcinogenic. For genotoxic carcinogens, it is not possible to establish a dose threshold below which there is no effect. Several methods are used for quantitative risk assessment of such chemicals. Recently, the European Food Safety Authority (EFSA) has recommended using the ‘margin of exposure’ (MOE) as a harmonised approach for assessing the risks posed by substances which are both genotoxic and carcinogenic (46).

Toxicity of important contaminants in fish

The most important contaminants in fish for consumer health are methyl-mercury and POPs, since fish may contribute significantly to dietary exposure to these compounds. It is, however, important to differentiate the generic term ‘fish’, since there are great variations in both nutritional values and levels of contaminants. These variations may depend on such factors as:

– the origin of the fish and the species in question

– the season of harvest

– the type of fish tissue consumed

– the content of contaminants in the feed of farmed fish.

Mercury

Methyl-mercury, which is the most toxic mercury compound, is the predominant form of mercury in fish. The percentage of methyl-mercury to total mercury ranges between 65% and 100%, depending on the fish species (74, 75, 105). The primary target of methyl-mercury toxicity is the nervous system. Based on a number of intoxication incidents (Minamata and Niigata in Japan, rural Iraq), the Joint FAO/WHO Expert Committee on Food Additives (JECFA) derived a provisional TWI (PTWI) for methyl-mercury of 3.3 µg per kg of body weight (bw) per week.

This PTWI was maintained over several re-evaluations, but JECFA noted that pregnant women and nursing mothers may be at greater risk than the general population (121). In 2003, JECFA (122) revised the PTWI to 1.6 µg per kg of bw per week, to protect the developing foetus. *In utero* exposure is the most sensitive period, and an effect on neurodevelopment was considered to be the most sensitive health outcome. This evaluation took into account new data from large epidemiological studies performed in the Seychelles and the Faroe Islands, as well as additional epidemiological data. Moreover, EFSA supported the decision by JECFA to reduce the PTWI for methyl-mercury, since it was based on the most susceptible stage of life (i.e. the developing foetus and intake of the mother during pregnancy), rather than on the risk to the general adult population (44).

Dioxins and dioxin-like compounds

There are, in total, 210 different congeners of PCDD/Fs which are not intentionally produced, but formed as by-products or impurities from most combustion and several industrial processes. Moreover, PCDD/Fs are also found in soil and sediment, and these may act as secondary sources of dioxins in the environment.

Among the 210 congeners, the 17 PCDD/Fs with chlorine substitution in positions 2, 3, 7 and 8 are the most toxic. All 17 congeners, as well as 12 dioxin-like PCBs (sometimes collectively called ‘dioxins’), have the same mode of action binding to the Ah receptor and show comparable qualitative effects, but with different potencies. These differences in potency are expressed in toxic equivalency factors (TEFs) (126). Consensus on the TEFs for PCDD/Fs and dioxin-like PCBs for human risk assessment (WHO-TEFs) was obtained at a WHO meeting in 1997 (114). Long-term exposure leads to increased dioxin levels in fatty tissues and may result in developmental effects in children, as well as cancer and several other diseases.

The EU Scientific Committee for Food (SCF) and JECFA established tolerable intake levels for ‘dioxins’ in 2001 (37, 45, 122). Both committees concluded that the risk assessment should be based on the effects of 2,3,7,8-tetrachlordibenzo-p-dioxins (TCDDs), the most toxic congener, on the developing male reproductive system, resulting from the maternal body burden. A threshold approach was used to derive a TDI of 2 picograms (pg) TCDDs per kg of bw. This was extended to include other PCDDs, PCDFs and dioxin-like PCBs and, because of their long half-lives in the human body, this TDI was expressed over a longer time period (a week or month). The SCF established a group PTWI intake of 14 pg WHO-TEQ per kg of bw (37). In addition, JECFA established a group provisional tolerable monthly intake of 70 pg WHO-TEQ per kg of bw (122). There are some differences in the approaches used by other authorities to assess the risks of dioxins and dioxin-like compounds to human health.

Polychlorinated biphenyls

Theoretically, there are 209 different congeners of PCBs, in total. They are all lipophilic, and the lipophilicity increases with the increasing degree of chlorination. Polychlorinated biphenyls are highly persistent and accumulate within food chains. The type and potency of the toxicity of the congeners vary with the number of chlorines substituted and the placement of the chlorine on the phenyl rings.

Owing to their unique physical and chemical properties, PCBs have been widely used commercially since the 1920s, as dielectric and heat exchange fluids and in a variety of other industrial applications. Since the 1970s, there have been restrictions on the use of PCBs in several EU countries, and today PCBs are banned in most countries. However, entry into the environment, due to improper disposal practices of PCB-containing materials or leakage from transformers and hydraulic systems still in use, cannot be excluded. The PCBs are listed in Annex A of the Stockholm Convention (4) on POPs. This Convention seeks the global elimination of the production and use of all intentionally produced POPs listed in annexes A, B and C of the Convention (http://www.pops.int).

For technical purposes, PCBs have never been used as single compounds, but always as complex technical mixtures. Dioxin-like PCBs exhibit toxicological effects on the liver, thyroid, immune function, reproduction and behaviour, similar to those caused by TCDD/Fs. The dioxin-like PCBs are included in the tolerable intake levels established for PCDDs and PCDFs.

The other group of PCBs, non-dioxin-like PCBs, constitutes a major part of the PCB congeners found in human tissues and food. These PCBs do not bind to the Ah receptor and do not show dioxin-like toxicity, but exhibit a different toxicological profile, affecting, in particular, the developing nervous system and neurotransmitter function. Mixtures used to study the toxicity of PCBs contain both non-dioxin-like and dioxin-like PCBs. It is therefore difficult, if not impossible, to differentiate between the toxic effects of dioxins and non-dioxin-like and dioxin-like PCBs.

Currently, there is no reliable, health-based guidance value for non-dioxin-like PCBs to use in human risk assessment. Dietary intake is considered the main pathway of exposure to non-dioxin as well as dioxin-like PCBs. Fish, particularly fatty fish, is considered an important source for these chemicals.

Brominated flame retardants

The brominated bisphenols, diphenyl ethers, cyclododecanes, phenols and phthalic acid derivatives are the five major classes of BFRs; the first three classes representing the highest production volumes. At present, five major BFRs (TBBPA, hexabromocyclododecane [HBCD] and three commercial mixtures of PBDEs) constitute the overwhelming majority, but the situation changes as new substances are introduced and older ones discontinued.

Some of these substances are persistent organic contaminants in the environment, with the potential to contaminate the food chain long after production has ceased. Risk assessment is difficult, since databases on toxicology and exposure to humans from different sources are very limited. Risk assessment reports and scientific opinions of the European Commission Scientific Committee on Toxicity, Ecotoxicity and the Environment and the Scientific Committee on Health and Environmental Risks are available for pentabromodiphenyl ether, octabromodiphenyl ether, decabromodiphenyl ether, HBCD and tetrabromobisphenol (35, 36, 38, 39, 40, 41, 42, 43).

Polybrominated diphenyl ethers

Theoretically, there are, in total, 209 different congeners of PBDEs. These congeners are lipophilic and the lipophilicity increases with the increasing degree of bromination. Tri- to hexa-BDEs are easily absorbed, slowly eliminated (persistent) and bio-accumulated, and are more bioactive than deca-BDE. Deca-BDE may be transformed to lower brominated BDEs.

There are three principal commercial PBDE flame retardants produced:

– PentaBDE

– OctaBDE

– DecaBDE.

These mixtures have different compositions of congeners and purity. DecaBDE is, however, mainly composed of deca-BDE. PentaBDE and OctaBDE were banned in the EU in August 2004. Several toxic endpoints have been identified. However, in general, the toxicological databases are poor. The liver is the target organ for PBDEs. Penta-BDE is the most toxic congener and deca-BDE the least. As a result of the limited toxicological data, any basic characterisation of the health risk from human exposure to PBDEs is extremely uncertain.

Hexabromocyclododecane and tetrabromobisphenol A

Toxicological knowledge on these BFRs is very limited. The BFR HBCD is commercially available in the EU as a mixture of three stereo-isomers: α, β and γ. The α-isomer predominates in food. All toxicological studies on HBCD were conducted with the commercial mixture. The extent of metabolism of the commercial HBCD is unknown. Hexabromocyclododecane is also hepatotoxic, with a lowest-observed-adverse-effect level (LOAEL) of 100 mg/kg bw/day. It has not been shown to cause developmental toxicity, but neuro-developmental effects have been observed after administration to neonatal mice, using a protocol similar to that with PBDEs (with a LOAEL for HBCD of 0.9 mg/kg bw/day) (111).

In the United Kingdom (UK), following a similar approach to that taken for PBDEs, the Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) considered that a target MOE of 3,000 to 10,000 was required for HBCD. Comparison with the LOAEL of 100 mg/kg bw/day indicates that exposures below 10 mg/kg bw/day would not be a concern (111).

Since TBBPA is a single compound, the database is relatively more complete than it is for PBDEs and HBCD. Furthermore, COT evaluated TBBPA in 2004 (112).

Repeat-dose studies revealed that there were no toxicologically significant effects at doses up to 10,000 mg/kg bw/day, after administration for 90 days. No long-term carcinogenicity study is available. However, TBBPA is not mutagenic and there is no indication of relevant carcinogenicity in humans. That is, TBBPA has weak oestrogenic effects in *in vitro* studies, but no effects were revealed in a recent two-generation study in rats, with doses of up to 1,000 mg/kg bw/day. There are conflicting results from two neurotoxicity studies in rats. No adverse effects were found in the two-generation study, but a study where rats were administered TBBPA during pregnancy showed some behavioural effects. The Committee on Toxicity of Chemicals judged these effects to be random and derived a TDI of 1 mg/kg bw/day from a no-observed-adverse-effect level (NOAEL) of 1,000 mg/kg bw by use of an uncertainty factor of 1,000.

Polybrominated biphenyls

The toxicological profiles of polybrominated biphenyls are expected to resemble those of the PCBs. However, TEFs have not been allocated for the co-planar congeners, and relevant toxicological evaluations have not been conducted.

Risk characterisation

Assessments of fish consumption that have recently been performed in the UK and the EU (113) indicate that methyl-mercury, the PCDD/Fs and the dioxin-like PCBs are the principal contaminants of concern. That is, consumption of specific fish species could result in the consumers exceeding their respective PTWIs for these contaminants. High-level consumers of predator fish species that accumulate methyl-mercury with age (e.g. tuna and old freshwater trout) may exceed the PTWI of 1.6 µg/kg bw/week. The PCDD/F levels in certain oily fish species may lead some high-level consumers to exceed the TWI of 14 pg toxic equivalents/kg bw/week, even without taking into account other sources of dietary exposure.

It is, however, important to note that the PTWIs for methyl-mercury and dioxin-like contaminants were set to protect the most susceptible life stage, i.e. the developing foetus exposed as a result of the body burden (i.e. concentration of the contaminant in the body) of the mother. Thus, the subgroup of special consideration for methyl-mercury is women who are pregnant or may become pregnant, while, for dioxins, girls and women of reproductive age are the subgroup of concern, due to the very long half-life of dioxins in the human body. The body burden during pregnancy is determined by the total previous intake over many years. Life stages other than the foetal stage are likely to be less susceptible.

Intakes of fish containing other chemical contaminants mentioned above are not a health concern, because they result in intakes below the available toxicological comparator (e.g. TDI) or contribute only minimally to overall human dietary exposure.

Risks and benefits of consuming wild and farmed fish

It is well known that fish, particularly oily fish, are an important source of long chain fatty acids (LC n-3 polyunsaturated fatty acid or PUFA), reducing the risk of cardiovascular diseases, as well as having beneficial effects on foetal development. Seafood is also a valuable source of certain minerals, vitamins and protein. However, balanced against this are the possible detrimental effects of contaminants found in certain fish species.

Scientific publications, as well as the national and international press, have questioned if the presence of certain contaminants and residues represents a health risk to fish consumers. In these discussions, the main emphasis has been on the chemical assessment and possible health risk of consuming wild or farmed fish, while little or no consideration has been given to the nutritional value. In an effort to bring together the nutritional and toxicological considerations, food safety authorities in several countries have requested their relevant scientific committees to weigh the nutritional benefits against the possible risks of fish consumption, and such benefit-risk assessments have recently been performed in the UK and EU (113). In Norway, a similar assessment is being completed by the Norwegian Committee on Food Safety.

It is important to understand the mechanisms and interactions between nutrients and contaminants in seafood if researchers are to give sound scientific advice on the amount and type of seafood that should be recommended to promote health and maximise safety in different groups of the population. At present, there is no agreed methodology for taking both the risks and benefits of seafood into account in a quantitative way. The organisation EFSA advised that a framework should be developed which allows such a quantitative comparison, based on a common scale of measurement (47).

To protect animal and human health, internationally agreed maximum permitted levels have been set for several chemical contaminants in both feed and food. National and international monitoring programmes exist to ensure that the levels present are acceptable. In addition, aquaculture industries are using hazard analysis critical control point principles to ensure the acceptable quality of their products.

If fish and fish products contain values of environmental contaminants above the accepted international levels, this will almost certainly have a significant impact on international trade. Importing countries will introduce bans on fish and fish products. They have already done so due to contaminants such as cadmium, dioxins and malachite green.

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Dangers pour la sécurité sanitaire des aliments en phase de production : les enjeux pour l'aquaculture et le secteur de la pêche

T. Håstein, B. Hjeltnes, A. Lillehaug, J. Utne Skåre, M. Berntssen & A.K. Lundebye

Résumé

Les aliments provenant de poissons sauvages et élevés constituent depuis toujours une source importante de protéines pour l'alimentation humaine. À l'échelle mondiale, les poissons et leurs dérivés représentent la première source de protéines et l'on estime que plus de 30 % du poisson consommé provient de l'aquaculture.

La première partie de cet article décrit les dangers et les défis associés à la manipulation du poisson dans les élevages et lors des prises en mer. Les auteurs décrivent les agents pathogènes affectant les poissons et l'homme, les agents de zoonoses, les bactéries responsables de toxi-infections alimentaires et les allergies associées à la consommation de poisson.

Bien que peu d'agents infectieux des poissons soient capables d'infecter l'homme, il existe quelques exceptions, qui s'avèrent parfois fatales pour l'homme. Les plus grands dangers pour la santé publique résident néanmoins dans la consommation de poisson cru ou insufisamment cuit.

La deuxième partie de l'article traite des polluants environnementaux affectant les poissons et les fruits de mer et dangereux pour la santé publique, tels que les médicaments vétérinaires et les résidus de produits utilisés dans les élevages, les polluants persistants tels que les composés organiques lipophiles et les métaux (méthyl-mercure, organotine).

Les auteurs font l'inventaire actualisé des divers facteurs de risque associés aux produits de la pêche et de l'aquaculture pouvant menacer la santé des consommateurs. En outre, ils abordent les divers enjeux, au sens large, associés à la manipulation du poisson pendant la prise et en phase de production, ainsi que ceux résultant de la transformation du poisson.

Mots-clés

Agent de zoonose – Allergie – Aquaculture – Composé organique lipophile persistant – Contaminant – Manipulation du poisson – Métal – Pêche en mer – Poisson – Poisson d'élevage – Poisson et fruit de mer – Poisson sauvage – Résidu – Sécurité sanitaire des aliments – Transformation du poisson.

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Peligros para la inocuidad de los alimentos que surgen durante la fase de producción: problemas de la piscicultura y la industria piscícola

T. Håstein, B. Hjeltnes, A. Lillehaug, J. Utne Skåre, M. Berntssen & A.K. Lundebye

Resumen

Los alimentos derivados de los peces, tanto salvajes como de vivero, siempre han sido una fuente importante de proteínas para el ser humano. A escala mundial, el pescado y sus derivados constituyen la principal fuente de proteínas, y se calcula que más del 30% del pescado para consumo humano proviene de la acuicultura.

En la primera parte del artículo los autores destacan los peligros y problemas asociados a la manipulación de peces en las actividades de cría o captura. Asimismo, describen a los agentes infecciosos que provocan enfermedades en los peces y el ser humano, agentes zoonóticos, intoxicaciones de origen bacteriano y alergias causadas por el consumo de pescado.

Aunque son muy pocos los agentes infecciosos de los peces capaces de infectar al hombre, hay ciertas excepciones a esta regla que pueden dar lugar a casos mortales. Con todo, el mayor riesgo para la salud humana radica en el consumo de pescado o productos a base de pescado crudos o insuficientemente cocinados.

En la segunda parte los autores examinan los contaminantes ambientales presentes en los alimentos de origen marino que pueden resultar peligrosos para la salud humana, tales como productos medicinales y residuos asociados a la acuicultura, compuestos orgánicos lipofílicos persistentes o metales (metilmercurio, organotina).

Los autores ofrecen información actualizada sobre los diversos factores relacionados con los peces de vivero o capturados que pueden entrañar riesgo para la salud humana una vez consumidos. Además, examinan los problemas (en su sentido más amplio) vinculados a la manipulación de peces durante su captura o cría y en el curso de su procesamiento.

Palabras clave
Acuicultura – Agente zoonótico – Alergia – Alimento de origen marino – Compuesto orgánico lipofílico persistente – Contaminante – Inocuidad de los alimentos – Manipulación del pescado – Metal – Pez – Pez de vivero – Pez salvaje – Piscicultura – Procesamiento del pescado – Residuo.

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DISCUSSION Fishery products are important not only from a nutritional point of view, but also as an item of international trade and foreign exchange earner for a number of countries in. the world. Fish and shellfish are highly perishable, and prone to vast variations in quality due to differences in species, environmental habitats, feeding habits. In addition, they can also function as carriers of several microbial and other health hazards. Therefore mainte-nance of quality is of utmost importance in production and trade of fishery products. Most of current quality control techniques are time ...Â Food safety hazards that occur during the production stage: challenges for fish farming and the fishing industry. Rev. Sci. Fish and fish products are the most important source of protein and it is estimated that more than 30% of fish for human consumption comes from aquaculture. More than 80% of global aquaculture products are produced in freshwater (HÃ¥stein et al., 2006; FAO, 2009). Aquaculture production includes the selection of breeding stock, the rearing of fry and fingerlings and the growth of adult fish. There are wide variations in methods and practices for the production of different species (FAO/NACA/WHO, 1997).Â Food safety hazards that occur during the production stage: challenges for fish farming and the fishing industry. Rev. Sci. Food safety hazards occur when food is exposed to hazardous agents which result in contamination of that food. Food hazards may be biological, chemical, physical, allergenic, nutritional and/or biotechnology-related. Hazards may be introduced into the food supply any time during harvesting, formulation and processing, packaging and labelling, transportation, storage, preparation, and serving.Â The proliferation of Aspergillus and the corresponding production of aflatoxin are affected by drought during the growing season and high humidity during storage. Aflatoxin is a potential carcinogen associated with the development of liver cancer. 4.2.1.2 Deoxynivalenol (Vomitoxin).