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Review article

Aquaculture practices and potential human health risks: Current knowledge and future priorities

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ABSTRACT

Annual global aquaculture production has more than tripled within the past 15 years, and by 2015, aquaculture is predicted to account for 39% of total global seafood production by weight. Given that lack of adequate nutrition is a leading contributor to the global burden of disease, increased food production through aquaculture is a seemingly welcome sign. However, as production surges, aquaculture facilities increasingly rely on the heavy input of formulated feeds, antibiotics, antifungals, and agrochemicals. This review summarizes our current knowledge concerning major chemical, biological and emerging agents that are employed in modern aquaculture facilities and their potential impacts on public health. Findings from this review indicate that current aquaculture practices can lead to elevated levels of antibiotic residues, antibiotic-resistant bacteria, persistent organic pollutants, metals, parasites, and viruses in aquacultured finfish and shellfish. Specific populations at risk of exposure to these contaminants include individuals working in aquaculture facilities, populations living around these facilities, and consumers of aquacultured food products. Additional research is necessary not only to fully understand the human health risks associated with aquacultured fish versus wild-caught fish but also to develop appropriate interventions that could reduce or prevent these risks. In order to adequately understand, address and prevent these impacts at local, national and global scales, researchers, policy makers, governments, and aquaculture industries must collaborate and cooperate in exchanging critical information and developing targeted policies that are practical, effective and enforceable.

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1. Introduction

Aquaculture is the farming of aquatic organisms, including finfish and shellfish, by individuals, groups or corporations using interventions (e.g., feed, medications, controlled breeding, containment) that enhance production. Although the details of the early history and nature of aquaculture are unclear, people have been farming fish for millennia and there is evidence of aquaculture in Egypt and China as early as 2500 B.C. and 1100 B.C., respectively (Landau, 1992). Practiced for centuries, traditional aquaculture was characterized by minimal added inputs, small farm size and low stock density. However, coinciding with the rapid population growth of the 20th century, there has been a sharp increase in demand for seafood products, including finfish and shellfish (particularly in the past 50 years). Initially, much of this demand was met by wild-caught fish, but as world fisheries continue to be over-exploited and depleted, aquaculture systems have undergone unprecedented growth, evolving as a significant contributor to meet demands for seafood.

The increase in seafood production through aquaculture provides a good source of high-quality protein and is an important cash crop in many parts of the world. An estimated 56% of the world's population obtains at least 20% of their animal protein intake from finfish and shellfish (FAO, 2004b). Therefore, the trend of increased aquaculture production is a seemingly welcome sign considering that lack of adequate nutrition is a leading contributor to the global burden of diseases (Ezzati et al., 2002). Yet, as demand for aquaculture products rises, the overwhelming majority of the world's aquaculture systems continue to intensify cultivation methods. These methods are characterized by high stock density and volume; the heavy use of formulated feeds containing antibiotics, antifungals and other pharmaceuticals; and the heavy application of pesticides, and disinfectants. In some instances, particularly in developing countries where the majority of aquaculture production takes place, additional materials such as human and animal excreta are also utilized in the aquaculture environment. These production methods raise a number of potential food safety and human health concerns associated with aquacultured seafood products.

Many researchers and study groups have begun to evaluate the food safety issues associated with intensive aquaculture, but numerous data gaps remain. For example, the precise types and amounts of chemical and biological contaminants present in aquaculture systems are unclear and the subsequent residues in food products are not fully known (on local, national and global scales). As a result, the magnitude of subsequent impacts on food safety and human health is difficult to assess. This is further complicated by the fact that substantial differences exist in aquaculture practices between the developing and the developed world, which makes it difficult to generalize the findings across the board. Moreover, while the majority of global aquaculture production takes place in developing countries, the limited data that exist today regarding the impacts of aquaculture on food safety and human health are generated in developed countries (Howgate, 1998). Therefore, there is a clear need to 1) synthesize the current state of knowledge concerning the impacts of aquaculture on food safety and human health at local, national and global levels; and 2) identify priority areas for future research that would address existing data gaps, particularly in developing countries.

This review outlines the recent dramatic growth in the global aquaculture industry and summarizes our current knowledge regarding the food safety and human health impacts associated with major biological, chemical and other emerging contaminants present in aquaculture systems. Future research priorities aimed at clarifying food safety issues associated with aquaculture practices are also emphasized. Other environmental and ecological issues linked to aquaculture facilities including reductions in water quality, fish escapes, impacts of aquaculture on world fisheries, and destruction of natural habitats are beyond the scope of this review. Readers interested in these topics are encouraged to refer to other published works (Naylor et al., 2000; Paez-Osuna, 2001; Belias et al., 2003; Shahidul and Tanaka, 2004; Islam et al., 2004a; Islam et al., 2004b; Gyllenhammar and Hakanson, 2005; Gozlan et al., 2006).

2. Recent growth and trends in the aquaculture industry

The magnitude of recent increases in aquaculture production is enormous: annual aquaculture production has more than tripled within the span of 15 years, from 16.8 million tons in 1990 to 52.9 million tons in 2005 (Fig. 1) (FAO and Fishery Information Data and Statistics Unit, 2005). According to the latest predictions by the United Nations Food and Agriculture Organization (FAO), total annual global fish production (wild and farmed) is expected to increase steadily, from 129 million tons in 2000 to 172 million tons by 2015, with aquaculture accounting for as much as 73% of the total increase. By 2015, aquaculture is predicted to account for 39% of total global seafood production by weight, up from 28% in 2000 and 4% in 1970.

The global aquaculture industry is dominated primarily by production facilities located in a few Asian countries: eleven of the top 15 aquaculture-producing countries, accounting for 94% of total global production, are in Asia (Table 1). China alone accounts for approximately 71% of total global aquaculture production.

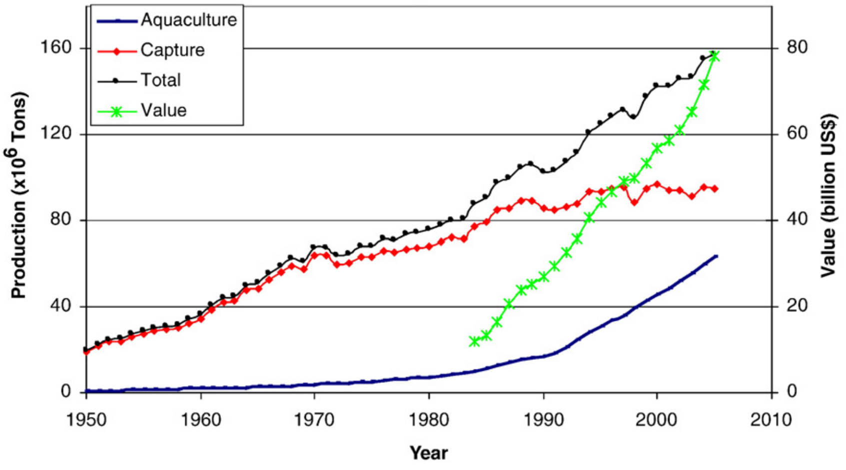

Fig. 1. Global trends in annual seafood production, 1950–2003 (FAO, 2005).

3. Chemical and biological contaminants present in aquaculture environments and their potential impacts on food safety and human health

The intensive aquaculture methods that are practiced in Asia and throughout the world can vary significantly from place to place. However, the majority of aquaculture facilities worldwide rely heavily on the input of formulated feeds and the application of agrochemicals, antibiotics and other inputs, resulting in the presence of many chemical and biological contaminants in aquaculture facilities. This is particularly true in many Asian countries which together produce over 90% of the aquaculture products that are distributed worldwide (to both developing and developed countries). In addition, emerging technologies, including the development of transgenic fish (genetically modified organisms or GMOs), could result in the presence and persistence of transgenes and transgene-associated proteins in aquaculture environments and aquacultured fish if transgenic fish are approved for commercial food production in the future (Kapuscinski, 2005; van Eenennaam and Olin, 2006). The latest research findings regarding the food safety and human health impacts associated with major biological, chemical and other contaminants present in aquaculture environments are distilled below.

3.1. Antibiotics

Antibiotics are a group of natural or synthetic compounds that kill bacteria or inhibit their growth. As a result of the non-hygienic and stressful conditions (Barton and Iwama, 1991) present in aquaculture facilities–including high fish densities, high farm densities in coastal waters and lack of appropriate barriers between farms (Naylor and Burke, 2005)–the risk of bacterial infections among aquacultured fish is high. Therefore, heavy amounts of antibiotics are administered in fish feed for prophylactic (disease prevention) and therapeutic (disease treatment) purposes in aquaculture facilities worldwide (GESAMP (IMO/FAO/USESCO-IOC/WMO/WHO/IAEA/UN/UNEP), 1997; Alderman and Hastings, 1998; Graslund and Bengtsson, 2001; Holmstrom et al., 2003; FAO, 2004a; Cabello, 2006).

Despite the widespread use of antibiotics in aquaculture facilities, limited data are available on the specific types and amounts of antibiotics used. The limited usage data that do exist generally originate from developed countries, while the majority of aquaculture production takes place in developing countries where there are limited or no regulatory guidelines in place (Howgate, 1998). Even when antibiotic usage data are available in different countries, the same antibiotic products are often marketed under different names and the active ingredients frequently are not listed. This makes uniform record keeping and transnational comparisons daunting tasks. Moreover, aquaculture farmers or workers who administer the antibiotics often lack information and/or education regarding the safe and efficient use of these drugs (Graslund et al., 2003; Holmstrom et al., 2003), potentially resulting in excessive usage that invariably goes unreported. Table 2 lists antibiotics compiled by the FAO that are potentially used in aquaculture facilities throughout the world; however, the FAO does not have specific data on actual antibiotic usage patterns.

To investigate worldwide antibiotic usage practices in aquaculture, we conducted a literature review of the 26 antibiotics listed in Table 2. Country-specific reported usage information was compiled for the top 15 aquaculture-producing countries, which together account for 94% of global aquaculture production. Since some countries have recently changed their antibiotic usage practices in aquaculture due to public health concerns, we focused our search only as far back as 1990.

As anticipated, the literature review showed that the amount of information available on reported usage of antibiotics in aquaculture varies by country. Except for North Korea and Egypt, country-specific qualitative usage information, such as whether or not a specific antibiotic is used, was available in one form or another for all of the top 15 aquaculture-producing countries (Table 2). However, there was a substantial lack of quantitative information including the type and total amount of a particular antibiotic used per year on a country-by-country basis. The data presented in Table 2 are heavily biased towards those countries that have good tracking systems and research institutes investigating this issue; therefore care must be taken in the interpretation of these data. For instance, the absence of any data for North Korea and Egypt is not necessarily indicative of a lack in antibiotic usage, but rather a lack of information available in these two countries.

Of the 26 antibiotics examined from the FAO list, oxytetracycline followed by chloramphenicol and oxolinic acid were the most commonly used antibiotics, while sarafloxacin and sulfadimidine were the least used antibiotics between 1990 and 2007 (Table 2). Of the top 13 aquaculture-producing countries (excluding Egypt and North Korea), 92% used oxytetracycline and 69% used chloramphenicol and oxolinic acid during this time period. Of the 26 antibiotics considered from the FAO list, on average, countries used 7 antibiotics in the aquaculture industry, with Thailand and Japan using the highest number of antibiotics (13 each). These figures must be interpreted prudently, however, as recent practices may have changed in some countries. This is particularly notable in Norway, where antibiotic usage has declined significantly over the past 10 years.

Table 1
The top fifteen aquaculture-producing countries (FAO, 2005)[a,b]

Rank	Country	Production quantity (tons)				% of total global production	Cumulative %
		Culture environment			Total		
		Brackishwater culture	Freshwater culture	Mariculture			
1	China	666,944	17,495,858	20,522,700	38,685,502	70.1	70.1
2	India	115,884	2,197,087		2,312,971	4.2	74.3
3	Philippines	254,744	154,677	1,039,083	1,448,504	2.6	76.9
4	Japan		50,276	1,251,302	1,301,578	2.4	79.2
5	Indonesia	501,991	477,343	249,225	1,228,559	2.2	81.5
6	Thailand	345,335	361,126	357,948	1,064,409	1.9	83.4
7	Vietnam	289,571	547,931	130,000	967,502	1.8	85.1
8	Bangladesh	90,604	766,352		856,956	1.6	86.7
9	Korea, Republic of		13,600	826,245	839,845	1.5	88.2
10	Chile	367	3592	599,526	603,485	1.1	89.3
11	Norway			584,423	584,423	1.1	90.4
12	United States of America	260	377,198	166,871	544,329	1.0	91.4
13	Korea, Dem. People's Rep		3700	504,295	507,995	0.9	92.3
14	Egypt	394,540	50,641		445,181	0.8	93.1
15	Taiwan Province of China	122,533	207,788	33,507	363,828	0.7	93.7

[a] Only aquacultured animals, and not plants, are included in these figures.
[b] The actual sizes of the farms may vary significantly from country to country.

Table 2
Reported antibiotic usage by the top 15 aquaculture-producing countries

Antibiotic categories	Generic names	China	India	Japan	Philippines	Indonesia	South Korea	Bangladesh	Thailand	Chile	Norway	Vietnam	North Korea	USA	Egypt	Taiwan	# of countries using antibiotic	% countries using antibiotic
Sulfonamides	Sulfamerazine				√4									√20			2	15.4
	Sulfadimidine								√16,17								1	7.7
	Sulfadimethoxine			√3,26	√4									√25		√14	4	30.8
Potentiated Sulfonamide	Combination of trimethoprim and sulfadiazine		√2		√4				√7,18		√9,15,26	√12					5	38.5
Tetracyclines	Chlortetracycline	√1	√2						√16,17								3	23.1
	Oxytetracycline	√1	√2	√3,15,26	√4,18,24,27,28,30	√5,28	√11	√6	√7,16,17,18,28		√10,15,26,29,31	√6		√20,25		√14	12	92.3
Penicillins	Ampicillin			√3,15,26			√11			√8		√12					4	30.8
	Amoxycillin			√3,15,19,26						√8				√25			3	23.1
	Benzyl penicillin	√1		√15,19							√15,26,31						3	23.1
Quinolones	Ciprofloxacin								√16,20								1	7.7
	Enrofloxacin					√5			√16,17			√12					3	23.1
	Norfloxacin								√16,17,18			√12					2	15.4
	Oxolinic Acid	√1		√3,15	√4,24,27,28,30			√6	√7,17,18,28	√8	√9,10,15,22,26,31	√12				√14	9	69.2
	Perfloxacin								√16,17								1	7.7
	Flumequine			√3,15							√9,10,15,26,31	√12				√14	4	30.8
	Sarafloxacin																0	0
Nitrofurans	Furazolidone	√1			√4,24,27					√8	√23					√14	5	38.5
Macrolides	Erythromycin	√1		√3,15,19,26	√4,24,27,30	√5,28	√11		√7	√8						√14	8	61.5
	Spiramycin			√3													1	7.7
Aminoglycosides	Gentamicin				√4				√16,17	√8							3	23.1
Other Antibiotics	Chloramphenicol	√1	√2		√4,18,24,27,30	√5,28		√6	√7,16,17,28	√8		√21				√14	9	69.2
	Florfenicol			√3,15,26						√8	√9,10,15,26,31					√14	4	30.8
	Thiamphenicol			√3,15,26													1	7.7
	Tiamulin								√16,17								1	7.7
	Nalidixic acid			√26	√4					√8							3	23.1
	Miloxacin			√3, 26													1	7.7
Reported # of antibiotics used by country		7	4	13	10	4	3	3	13	9	7	8	NA	4	NA	8		

References for Table 2: 1. (Yulin, 2000), 2. (Pathak et al., 2000) 3. (Wilder, 2000), 4. (Cruz-Lacierda et al., 2000). 5. (Supriyadi and Rukyani, 2000) 6. (Phillips, 2000), 7. (Tonguthai, 2000), 8. (Cabello, 2004), 9. (Maroni, 2000), 10. (National Institute of Nutrition and Seafood Research (NIFES), 2005), 11. (Korea-US Aquaculture, 2007), 12. (Le and Munekage, 2004), 13. (Benbrook, 2002), 14. (Liao, 2000). 15. (FAO, 2004a), 16. (Holmstrom et al., 2003), 17. (Graslund et al., 2003), 18. (Graslund and Bengtsson, 2001), 19. (GESAMP, 1997), 20. (Park et al., 1994), 21. (EJF, 2003), 22. (Samuelsen et al., 1992a) 23. (Samuelsen et al., 1991), 24. (Tendencia and Pena, 2001), 25. (Capone et al., 1996), 26. (Alderman and Hastings, 1998), 27. (Primavera, 1993), 28. (Inglis et al., 1997) 29. (Samuelsen et al., 1992b), 30. (Primavera et al., 1993), 31. (World Health Organization, 1999).

3.2. Antibiotic-resistant bacteria

An increasing number of studies also have documented elevated levels of bacterial antibiotic resistance in and around aquaculture production environments (Samuelsen et al., 1992b; Alderman and Hastings, 1998; Wegener et al., 1999; Schmidt et al., 2000; Aarestrup, 2000; Tendencia and Pena, 2001; Petersen et al., 2002; Miranda and Zemelman, 2002; Miranda et al., 2003; Petersen and Dalsgaard, 2003; Furushita et al., 2005). Bacterial antibiotic resistance arises and is maintained through mutations in bacterial DNA or through horizontal gene transfer mechanisms including conjugation with other bacteria, transduction with bacteriophage, and the uptake of free DNA via transformation (Fuhrman, 1999; Bushman, 2002; Casas et al., 2005). Table 3 provides an overview of bacterial antibiotic resistance–to antibiotics that are reportedly used by the world's top 15 aquaculture-producing countries–that has been identified in aquaculture environments and reported in the peer-reviewed literature. The data provided in Tables 2 and 3 do not establish nor attempt to establish a causal relationship between the reported usage of specific antibiotics in a given country and increases in antibiotic-resistant bacteria in that country. However, these relationships have been established by several peer-reviewed studies in specific aquaculture environments (McPhearson et al., 1991; Inglis et al., 1991; Inglis et al., 1993; Kerry et al., 1996; Tendencia and Pena, 2001).

Kerry et al. (1996) isolated gram-negative bacteria (predominantly *Plesiomonas shigelloides* and *Aeromonas hydrophila*) from aquaculture ponds in the Southeastern United States and found that the proportion of bacteria resistant to tetracycline, oxytetracycline, chloramphenicol, ampicillin and nitrofurantoin was higher in antibiotic-treated ponds versus untreated rivers (Kerry et al., 1996). In a study conducted in shrimp ponds located in the Philippines, researchers found that the prevalence of multiple antibiotic resistance (to at least two antibiotics) among *Vibrio* spp. was highest in shrimp ponds where oxolinic acid was administered versus ponds where no antibiotics were used (Tendencia and Pena, 2001). Other studies have documented the prevalence of resistant bacteria before and after the introduction of antibiotics. For example, amoxicillin was not used in aquaculture in the United Kingdom until 1990 and isolates of *A. salmonicida* collected from aquaculture environments before 1990 were sensitive to amoxicillin; however, amoxicillin-resistant strains were isolated during a furunculosis outbreak that occurred a few years after the introduction of amoxicillin to aquaculture environments (Inglis et al., 1991; Inglis et al., 1993).

Other researchers have evaluated the presence of antibiotic-resistant bacteria and resistance genes on the fish themselves, including fish collected directly from aquaculture facilities and fish collected from retail markets. In a study of retail fish conducted in Malaysia, researchers isolated *Aeromonas* spp. from fish samples and determined that all isolates were resistant to three or more antibiotics tested in the study (Radu et al., 2003). In addition, Furushita et al. (2003) detected tetracycline-resistant bacteria in fish collected from three different fish farms in Japan and demonstrated that tetracycline resistance genes carried in the fish isolates exhibited high sequence similarities with tetracycline resistance genes present in human clinical isolates (Furushita et al., 2003). In another study, Furushita et al. (2005) demonstrated that the presence of beta-lactamase resistance genes in *Stenotrophomonas maltophilia* isolated from aquacultured yellowtail fish (Japanese amberjack) in Japan was likely the result of horizontal gene transfer events (Furushita et al., 2005). These data suggest that similar gene transfer events could play a role in the transfer of antibiotic resistance determinants between fish-associated bacteria and human bacterial pathogens. A study by Rhodes et al. (2000) that investigated the transfer of oxytetracycline resistance plasmids between aquaculture and hospital isolates provided direct evidence that resistance plasmids have been transferred between *Aeromonas* spp. (fish isolates) and *E. coli* (human isolates) in specific geographic locations (Rhodes et al., 2000). These data support the theory that the development of bacterial antibiotic resistance in aquaculture environments could contribute to or influence bacterial antibiotic resistance occurring among human populations.

3.3. Antibiotic residues

In addition to selecting for bacterial antibiotic resistance, the heavy prophylactic and therapeutic use of antibiotics in aquaculture environments can lead to elevated antibiotic residues in ponds, marine sediments, aquaculture products, wild fish, and other natural aquatic environments that are impacted by aquaculture facilities (Samuelsen et al., 1991; Samuelsen et al., 1992b; Hektoen et al., 1995; Kerry et al., 1996; Alderman and Hastings, 1998; Guardabassi et al., 2000; Le and Munekage, 2004; Koeypudsa et al., 2005; Cabello, 2006). For example, Le and Munekage (2004) evaluated residues of trimethoprim, sulfamethoxazole, norfloxacin, and oxolinic acid in shrimp ponds in Vietnam and found high levels of each drug in water samples and sediments samples; however, the concentrations varied widely depending on the sample (Le and Munekage, 2004). For instance, oxolinic acid found in sediment samples ranged from 1.81 to 426.31 ppm (Le and Munekage, 2004). In another study conducted in Norway, Samuelsen et al. (1992a,b) determined levels of oxolinic acid residues in wild fauna that were affected by medicated fish ponds (Samuelsen et al., 1992b). Results from this study indicated that wild coalfish, mackerel, haddock and crabs from areas impacted by a medicated fish pond had elevated concentrations of oxolinic acid in plasma, liver and muscle tissue (Samuelsen et al., 1992b).

The presence of antibiotic residues in aquaculture environments, as well as subsequent fish products, could result in adverse ecological and public health effects. For example, many antibiotics used in aquaculture are toxic to aquatic organisms, including *Daphnia* and *Artemia* (Jones et al., 2004). In terms of human health, low-level exposures to antibiotic residues present in environmental media and food are not likely to cause acute toxic effects among the general public; however, chronic effects (while more probable) are largely unstudied (Jones et al., 2004). In addition, it is unclear how repeated exposures to mixtures of low-level antibiotic residues could affect individuals who work in aquaculture facilities. Surveys conducted in shrimp farming regions of Thailand and the Philippines reported extensive prophylactic use of antibiotics by aquaculture farmers and workers, sometimes on a daily basis (Primavera et al., 1993; Graslund et al., 2003; Holmstrom et al., 2003). Farmers and workers routinely come into contact with antibiotics in the process of mixing and distributing feed and most are unaware of potential health risks associated with these exposures (Graslund et al., 2003). This often-repeated scenario, combined with the lack of appropriate gear for handling antibiotic applications, contributes to significant risks of inhalation exposures as well as dermal exposures through exposed or injured skin. This is of significant concern especially when environmental exposures to some of these antibiotics, such as chloramphenicol (a potential human carcinogen), have been linked with increased risk of aplastic anemia and leukemia in humans (Yunis, 1989; Malkin et al., 1990; Issaragrisil et al., 2005). Additional research is needed to determine whether chronic exposures to low-level antibiotic residues in aquacultured products can lead to similar and/or other adverse health outcomes in consumers.

3.4. Wastewater and excreta

In China and other Asian countries (e.g., Bangladesh, India, Indonesia, and Vietnam), where the majority of global aquaculture production takes place, there is a long history of administering wastewater, animal waste and human excreta to fish ponds (World Health Organization, 2006a). The waste is consumed directly by the fish and provides nutrients for the growth of photosynthetic organisms (Little and Edwards, 1999; Petersen et al., 2002). Currently, this intentional

Table 3

Reported evidence of antibiotic-resistant bacteria in aquaculture facilities of the top 15 aquaculture-producing countries

Antibiotic resistance to	Generic names	Countries														
		China	India	Japan	Philippines	Indonesia	South Korea	Bangladesh	Thailand	Chile	Norway	Vietnam	North Korea	USA	Egypt	Taiwan
Sulfonamides	Sulfamerazine															
	Sulfadimidine															
	Sulfadimethoxine															
Potentiated Sulfonamide	Combination of trimethoprim and sulfadiazine							√7				√28				
Tetracyclines	Chlortetracycline	√24	√21													
	Oxytetracycline		√1,21	√17,19,25,26	√10	√15	√11,19	√13,14	√5,14,16	√18	√20			√11,22,23		√29
Penicillins	Ampicillin		√3,21	√1,17,25				√7	√9	√6,18	√20			√11,22		
	Amoxycillin			√1						√18				√23		√29
	Benzyl penicillin															
Quinolones	Ciprofloxacin		√21						√5							
	Enrofloxacin									√18						
	Norfloxacin											√28				
	Oxolinic Acid			√25	√10	√15		√14		√18	√20	√28				√29
	Perfloxacin															
	Flumequine			√25						√18	√20					
	Sarafloxacin															
Nitrofurans	Furazolidone		√21		√10				√9	√18	√20					
Macrolides	Erythromycin		√2,8	√26		√15		√7,13,14	√5,14	√18						
	Spiramycin															
Aminoglycosides	Gentamicin		√3,21													
Other Antibiotics	Chloramphenicol		√1,3,21	√12,17,25		√15		√14	√5,9	√6,18	√20	√27		√22		√29
	Florfenicol									√18						√29
	Thiamphenicol															√29
	Tiamulin															
	Nalidixic acid		√1,2,3,21						√4	√18	√20					√4
	Miloxacin															

References for Table 3: 1. (Hatha et al., 2005) 2. (Vivekanandhan et al., 2002) 3. (Ruiz et al., 1999) 4. (Zhao et al., 2003) 5. (Petersen and Dalsgaard, 2003) 6. (Miranda and Zemelman, 2001) 7. (Rahim and Aziz, 1994) 8. (Thayumanavan et al., 2003) 9. (Aoki et al., 1990b) 10. (Tendencia and Pena, 2001) 11. (McPhearson et al., 1991) 12. (Aoki et al., 1990a) 13. (Chowdhury and Baqui, 1997) 14. (Inglis et al., 1997) 15. (Angka, 1997) 16. (Ruangpan et al., 1997) 17. (Furushita et al., 2003) 18. (Mirand and Zemelman, 2002) 19. (Kim et al., 2004) 20. (Sandaa et al., 2005) 21. (Vaseeharan et al., 2005) 22. (Kerry et al., 1996), 23. (Herwig et al., 1997), 24. (Dang et al., 2006), 25. (Kawanishi et al., 2006), 26. (Kawanishi et al., 2005), 27. (Huys et al., 2007), 28. (Le et al., 2005), 29. (Ho et al., 2000).

application of fecal wastes to fish ponds is in decline in many Asian countries as a result of shifts in land use and shifts towards the production of “high-value” species such as shrimp, which cannot be grown in wastewater (World Health Organization, 2006a,b). However, unintentional use of wastewater and excreta in aquaculture systems may be increasing as surface water pollution continues to intensify in areas where aquaculture facilities are situated (World Health Organization, 2006a,b). In addition, in some Asian countries such as Vietnam, the use of wastewater and excreta in aquaculture is still widespread, and, in some northern Vietnam cities, the use of sewage in aquaculture ponds remains the only available method of wastewater treatment and disposal (World Health Organization, 2006a,b).

While wastewater-fed aquaculture systems provide high fish yields at a low cost since little to no additional inputs, such as formulated feeds, are administered to the fish (Petersen et al., 2002), the use of excreta in aquaculture systems could also have negative impacts on human health. Finfish raised in wastewater-fed ponds may harbor pathogens from excreta in their scales, gills, intraperitoneal fluid, digestive tracts and muscle tissue (Edwards, 1992; Khalil and Hussein, 1997; Howgate, 1998). Shellfish exposed to animal and human feces can bioaccumulate pathogenic viruses and bacteria in digestive and muscle tissues (Schwab et al., 1998). Specific human bacterial pathogens could include *Campylobacter jejuni*, *Vibrio cholerae*, *Salmonella* spp., *Shigella* spp., *E. coli* and *Enterococcus* spp. (Howgate, 1998; Petersen et al., 2002; World Health Organization, 2006a,b). In addition, Petersen et al.(2002) found elevated levels of antibiotic-resistant *Enterococcus* spp. and *Acinetobacter* spp. in samples isolated from wastewater-fed fish ponds compared to those isolated from control farms. The authors suggested that these findings could be due to the use of antibiotics in the wastewater-fed ponds or the addition of antibiotic-resistant bacteria through the administration of animal waste (Petersen et al., 2002). Helminthic, parasitic and viral pathogens also have been documented in wastewater-fed aquaculture environments and include *Schistosoma marisoni*, *Cryptosporidium parvum*, *Giardia intestinalis*, noroviruses, rotaviruses, and hepatitis A virus (Schwab et al., 1998; Berg et al., 2000; Butt et al., 2004a; Butt et al., 2004b; World Health Organization, 2006b). Numerous studies have shown that pathogens present in wastewater-fed aquaculture facilities can survive and persist in aquacultured fish and ponds (Feachem et al., 1983; Buras et al., 1987). These pathogens have the potential to colonize and/or infect humans through direct dermal contact with contaminated water or the ingestion of aquacultured fish or pond water (Blumenthal et al., 2000). Yet, few epidemiologic studies have investigated specific infectious disease outcomes associated with wastewater-fed fish and ponds.

In addition to pathogens, wastewater and excreta fed to aquacultured fish can contain numerous heavy metals (Mantis et al., 2005; Drogui et al., 2005; de Souza and Kuch, 2005; Alonso et al., 2005) and organic chemicals including polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs), polychlorinated biphenyls (PCBs), and polybrominated diphenyl ethers (PBDEs) (de Souza and Kuch, 2005; Villar et al., 2006). Fish raised using wastewater can have elevated levels of these contaminants in their edible tissues (Khalil and Hussein, 1997), and individuals consuming these products are at a higher risk of exposure. For more detailed information on the human health impacts associated with wastewater-fed fish, readers are encouraged to refer to the new WHO Guidelines for the Safe Use of Wastewater, Excreta and Greywater Volume 3: Wastewater and Excreta Use in Aquaculture (World Health Organization, 2006a,b).

3.5. Metals

Metals and metalloids (metal like elements) are naturally present in the environment and enter aquatic environments via various geochemical processes. Anthropogenic sources of metals including mining, metalworking and industrial processes also contribute to environmental/aquatic concentrations of metals. In aquaculture environments, additional sources of metals may be copper-based antifoulants that are used to slow the build-up of fouling organisms, and fish feeds that have been amended with (or composed of) various metals to fulfill perceived mineral requirements. Much attention has been focused on potential human exposures to metals, particularly mercury and arsenic, via the consumption of both farm-raised fish and wild-caught species (Clarkson et al., 2003; Schober et al., 2003; Hightower and Moore, 2003; Mahaffey et al., 2004). The adverse human health effects associated with exposures to heavy metals are diverse and include, but are not limited to, neurotoxic and carcinogenic effects. However, only a limited number of studies have investigated differences in edible tissue metal concentrations between farmed and wild-caught fish and the results of these studies are not very clear.

Of the studies that have compared concentrations of metals in the same fish species originating from farm versus wild environments, Foran et al. (2004) reported higher levels of organic arsenic in farm-raised salmon compared to their wild-caught counterparts, while concentrations of cobalt, copper and cadmium were found to be higher in wild-caught salmon. Similar findings also were reported by Calvi et al.(2006) who observed higher levels of arsenic, lead and zinc in farm-raised eel versus wild-caught eel, while calcium levels were higher in wild-caught samples. It is worthwhile noting here that the levels of inorganic arsenic, which are the more toxic forms of arsenic affecting human health, were below the limit of detection in both the wild-caught and the farm-raised salmon in the Foran et al. (2004) study. In a separate study Yamashita et al. (2005) evaluated mercury concentrations in commercially available fish in Japan and found that farm-raised blue fin tuna had higher concentrations of mercury and methyl mercury compared to wild blue fin tuna caught from the same region. The authors suggested that the use of large predatory fish such as mackerel as feed for the farmed tuna might have contributed to the higher levels of mercury observed in these fish.

In another study, Alam et al. (2002) reported no significant differences in metal concentrations between farm-raised carp versus wild carp that originated from the same polluted lake in Japan, indicating the importance of the aquatic environment in terms of subsequent metal concentrations in edible fish tissue. Similarly, Urena et al. (2006) reported no significant differences in tissue concentrations of various metals between wild-caught and farm-raised eel, even though significant differences were observed for the organ concentrations. Overall, the studies that do provide relative comparisons between farm-raised versus wild-caught animals provide limited evidence that the consumption of farm-raised fish (versus wild-caught fish) may lead to higher exposures to select metals. In addition to comparisons between wild-caught and farm-raised fish, it also may be of interest to include fish caught by recreational fishermen (close to densely populated areas) in future comparisons. These fish could have higher levels of contaminants than wild-caught fish–that are likely to have been caught in less polluted areas–and thus, including recreational catches in fish comparisons may provide additional information on potential exposures experienced by largely overlooked groups including recreational and subsistence fishermen.

3.6. Organohalogens

Recently, an increasing number of studies have focused on potential exposures to various halogenated organic compounds (organohalogens) resulting from the consumption of aquacultured food products. These compounds include PCDDs and PCDFs (commonly referred to as dioxins), PCBs, and PBDEs. Whereas the adverse health effects associated with dioxins and PCBs have long been recognized and extensively reviewed (International Agency for Research on Cancer, 1997; Faroon et al., 2001; Steenland et al., 2004), limited data are available regarding the adverse health effects associated with PBDEs (Darnerud et al., 2001; de Wit, 2002; Birnbaum and Staskal, 2004).

While numerous studies have documented the occurrence of various organohalogens in different seafood products, very few studies have provided relative comparisons between the levels of these compounds in wild-caught versus farm-raised animals. Studies often report data on different organohalogens, as well as different fish species, making it difficult to use these data to estimate potential human exposures to organohalogens resulting from the consumption of farmed versus wild fish. Hites and colleagues have performed extensive work to address this data gap by providing quantitative comparisons of several contaminants (dioxins, PCBs, PBDEs) and organophosphates (OPs), obtained by analyzing substantial quantities of tissues of farm-raised and wild-caught salmon (Hites et al., 2004a; Hites et al., 2004b; Hamilton et al., 2005). Their results show that the farm-raised salmon had higher levels of these contaminants in muscle tissue compared to their wild counterparts (Hites et al., 2004a; Hites et al., 2004b; Hamilton et al., 2005). Similarly Antunes and Gil (2004) reported significantly higher levels of total PCBs in dry muscle tissue of farm-raised sea bass from Portugal (31 ng/g) compared to wild-caught counterparts (13 ng/g). Total dichlorodiphenyltrichloroethane (DDT) concentrations also were higher in the farm-raised fish compared to the wild-caught fish (30.5 versus 5.4 ng/g) (Antunes and Gil, 2004). In a separate study, Easton et al. (2002) reported higher levels of PCBs, PBDEs and OPs (except toxaphene) in farmed salmon compared to wild-caught salmon (total PCBs: 51,216 versus 5302 pg/g; total PBDEs: 2668 versus 178 pg/g; and total OPs: 41,796 versus 12,164 pg/g). Similar results also were reported by Hayward et al. (2007) for PCBs (9.0 versus 4.0 ng/g) and PBDEs (1.1 versus 0.3 ng/g) on a wet weight basis. Comparison of these data across the board is somewhat challenging as some studies have presented lipid-adjusted concentrations while others use concentrations based on dry weight or wet weight.

In some studies, contamination with these compounds has been traced back to fish feed (Easton et al., 2002; Antunes and Gil, 2004; Carlson and Hites, 2005). For instance, Easton et al. (2002) reported mean DDT and PCB concentrations of 36 and 66 ppb in salmon feed, while concentrations in the salmon tissue were 30 and 51 ppb, respectively (Easton et al., 2002). By contrast, DDT and PCB levels in the wild-caught salmon were 6 and 5 ppb, respectively (Easton et al., 2002). Similar results were also reported by Antunes and Gil (2004) who compared DDE, DDD and DDT concentrations in feed pellets used in two different fish farms and further compared the concentrations of these contaminants in tissue samples of sea bass raised in those farms (Antunes and Gil, 2004). The authors reported that DDE concentrations (dry weight) in feed pellets were 18 ppb for Farm-1 and 24 ppb for Farm-2. Accordingly, the DDE concentrations in the muscle samples were 77 ppb for Farm-1 and 170 ppb for Farm-2 (Antunes and Gil, 2004).

3.7. Other agrochemicals

Other agrochemicals also are used in aquaculture including pesticides, antifungals, disinfectants, fertilizers and other water treatment compounds. Runoff from agricultural sites adjacent to aquaculture facilities can serve as additional, but inadvertent, sources of pesticides in aquaculture environments. Graslund and Bengtsson (2001) have compiled an extensive list of chemicals used in South-East Asian shrimp farming. Such extensive lists, if established on a country-by-country basis, could be useful for tracking various contaminants that are of significant public health concern. Currently, some countries do require testing of chemical residues in imported fish. For example, the United States Food and Drug Administration (FDA) began testing imported catfish, trout, tilapia, basa, salmon, and shrimp for antifungals, such as malachite green and leucomalachite green in 2001 (Andersen et al., 2006). These chemical-based dyes are suspected carcinogens and mutagens and are therefore banned from use in aquaculture and aquacultured products in countries including the U.S., Canada and the European Union (Andersen et al., 2006). However, this type of testing on imported aquaculture products is limited to a few chemicals and the frequency of testing is rather low compared to the enormous amount of potentially contaminated aquacultured products.

Potential human exposures to the aforementioned agrochemicals used in aquaculture can occur via three different exposure scenarios: 1) direct consumption of animal tissues that contain the chemicals; 2) consumption of crops grown with sediment and/or water from fish ponds that were used to raise farmed fish; and 3) direct consumption of ground or surface water that has been contaminated with chemicals from aquaculture facilities. The third scenario is more common in areas of the developing world that lack drinking water systems, where the majority of individuals obtain their drinking water from local wells and/or streams.

3.8. Transgenes

Beyond known human health issues associated with current aquaculture practices, emerging biotechnologies such as the development of commercial transgenic fish may pose additional human health concerns if these fish are ultimately approved for commercial production and human consumption. The first transgenic goldfish was produced in 1984 (Zhu et al., 1985) and throughout the past 20 years over 35 additional fish species have been genetically engineered including Atlantic salmon, tilapia, Coho salmon, catfish, carp, zebrafish and rainbow trout, to name a few (Zbikowska, 2003; Kapuscinski, 2005; van Eenennaam and Olin, 2006). Transgenic fish are defined as those that are genetically engineered to carry recombinant DNA sequences or constructs (transgenes) in their genomes, resulting in the expression of proteins such as growth hormones, antifreeze proteins, lactoferrin, cecropin and antisense GnRH that were not originally present in the non-transgenic animal (van Eenennaam and Olin, 2006). The expression of these proteins can result in faster growth, increased resistance to fish pathogens, increased resistance to colder temperatures and enhanced nutritional qualities of edible fish tissue, to name a few.

To date, no transgenic fish species have been approved for human consumption in the United States, China or other major aquaculture-producing countries (Niiler, 2000; Fu et al., 2005). However, a biotechnology company, Aqua Bounty (Waltham, MA), is currently awaiting an approval decision by the FDA for a transgenic Atlantic salmon that has been engineered to carry a growth hormone gene from Chinook salmon that is linked to an antifreeze promoter gene from ocean pout (Du et al., 1992). If their product is approved by FDA and marketed worldwide, salmon aquaculture productivity could increase significantly. Yet, numerous unanswered questions remain regarding the potential environmental and human health effects associated with the mass commercialization and consumption of transgenic fish (Zbikowska, 2003; FAO, 2003; Zhang and Yang, 2004; Kapuscinski, 2005; van Eenennaam and Olin, 2006). Few studies have evaluated the nutritional qualities of transgenic fish (Zhang et al., 2000) and to our knowledge, no studies have comprehensively evaluated the potential allergenic or toxic effects associated with the consumption of these fish. Significant data gaps remain concerning the expression of traits in transgenic fish, and risk assessment methods have not been adequately developed to assess the variety of potential adverse impacts that may be associated with these genetically modified organisms (Kapuscinski, 2005).

4. Conclusions and future priorities

Global aquaculture production continues to increase at exponential rates, as facilities worldwide, particularly in Asia, intensify production practices. Given that lack of adequate nutrition is one of the leading contributors to the global burden of diseases (Ezzati et al., 2002), increases in seafood production through aquaculture are seemingly beneficial to human health, especially since aquacultured fish can serve as an important source of protein in low income areas.

However, recent research has provided evidence that current aquaculture production practices could lead to exposures to various biological and chemical agents that are of significant concern to human health.

Currently, the majority of the world's aquacultured fish are produced in Asian countries where aquaculture facilities are characterized by the heavy use of many chemical and biological agents, including antibiotics, metal-based compounds, pesticides, other agrochemicals, and animal and human excreta. As a result of these inputs, research findings have provided evidence that aquaculture environments, as well as fish and shellfish harvested from these environments, can have elevated levels of antibiotic residues, antibiotic-resistant bacteria, persistent organic pollutants, metals (i.e., arsenic, methyl mercury, lead), parasites, and viruses compared to their wild counterparts. However, there is a real need for improved calculations of human exposures to contaminants originating in aquaculture environments in order to verify potential human health risks. Specific populations at risk could include individuals working in aquaculture facilities who come in direct contact with chemical and biological agents, populations living around these facilities who may contact or ingest contaminated water and/or fish, and consumers who regularly prepare and eat aquacultured products. Resulting potential health effects could range from chronic health outcomes associated with chemical and metal exposures, to infectious disease outcomes associated with exposures to bacteria, antibiotic-resistant bacteria, viruses, helminths and parasites. In addition, emerging technologies in aquaculture such as the development and potential commercialization of transgenic fish could pose additional health concerns that have yet to be adequately explored.

Additional research is necessary not only to fully understand the human health risks associated with aquacultured fish versus wild-caught fish but also to develop appropriate interventions that could reduce or prevent these risks. However, currently there is a lack of available information regarding certain aquaculture practices that would help researchers to design improved, more targeted studies. For example, there is no comprehensive inventory of antibiotics and other antimicrobials that are currently used in aquaculture at local, national and international levels. Therefore, it is unclear which antibiotic residues and what types of antibiotic-resistant bacteria would be the most important to screen for in aquaculture environments and aquacultured products. Similarly, there is a lack of detailed data concerning the levels and types of agrochemicals used on a country-by-country basis, making it difficult for researchers to determine which agrochemicals (i.e. pesticides, antifungals etc.) may be the most important compounds to investigate. Moreover, the globalization of world economies and all types of agriculture make it increasingly difficult to track how aquacultured products are moving throughout the world, and therefore, understand which populations are being the most exposed to potentially contaminated products. As the recent massive U.S. recalls of Chinese seafood indicate, ensuring the safety of aquacultured products will be increasingly difficult in our globalized world where varying degrees of regulation exist in different countries.

In light of these issues, short term goals need to be developed that are focused on preventing the current situation from deteriorating any further, and long term goals need to be developed that focus on gradually changing current aquaculture practices to alleviate potential public health problems at their roots. One important short term goal could be to establish, in conjunction with aquaculture industries, countries and international agencies such as the FAO, a comprehensive inventory of antibiotics, metals, agrochemicals and wastewater that are currently used in aquaculture at local, national and international levels, for both the developed and the developing countries. Long-term goals should be to identify alternative methods of aquaculture, focusing on improved hygienic conditions that negate the need for the heavy use of antibiotics and agrochemicals. These efforts should be accompanied by the development of an international agreement, under the umbrella of the World Health Organization that places restrictions on the use of the following inputs in aquaculture: 1) important human antibiotics; 2) antibiotics that could be harmful to human health, such as chloramphenicol; 3) agrochemicals, including certain pesticides and antifungals, that are associated with adverse human health effects; and 4) untreated animal and human excreta that may contain high levels of pathogenic bacteria, viruses and parasites.

In the meantime, outreach/communication efforts to consumers of aquacultured products should be enhanced in order to educate people about the potential health risks associated with the consumption of certain aquacultured species. However, as of yet, there is not a clear, satisfactory guide to assist consumers in balancing these issues and determining what types of fish and shellfish, they should purchase and consume. Although the organic aquaculture movement is still at its infancy, primarily due to the absence of internationally recognized standards for the production, as well as the handling, of aquaculture products, its sheer existence in Asia and across various geographical areas of the world is encouraging (Tacon and Brister, 2002). As with the organic produce and meat products that are currently marketed in the US, a certification system which guarantees customers that the aquacultured products that they are about to buy were grown under hygienic, “clean” conditions (i.e. without animal/human excreta or antibiotics) would go a long way in this regard.

In conclusion, the potential impacts of current aquaculture practices on human health are varied and broad-reaching and may differ among geographical regions. But the active flow of aquaculture products in the global market means that potential human exposures to contaminants found in aquaculture products are not confined to the areas where aquaculture production is taking place. In order to adequately understand, address and prevent these impacts at local, national and global scales, researchers, policy makers, governments, and aquaculture industries must collaborate and cooperate in exchanging critical information and developing targeted policies that are practical, effective and enforceable.

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