Chapter 15
Waterborne Parasitic Diseases in Ocean

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Glossary

Autoinfection	Reinfection of a host by the progeny of a parasite already present in the same host individual without exposure to the external environment.
Cyst/Encapsulation	A cyst is a structure to aid dissemination or protection of a parasitic stage derived from the parasite and in some cases additionally from the host. A capsule differs by being derived from the host, often as a cellular response.
Erythema	Abnormal redness of the skin due to local congestion as in inflammation, caused by irritation or injury to the tissue.
Hermaphrodite parasite	An individual containing both male and female gametes that can be functional concurrently or with one following the other; some able to form zygotes.
Hypersensitivity reaction	A damaging and sometimes fatal reaction produced by the normal immune system, which requires a pre-sensitized, immune state of the host.
Life cycle of parasite	The orderly sequence of distinct stages through which the agent progresses in the course of development to maturity or sexual stage.

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Life history of parasite	The life cycle of an agent including facultative paratenic hosts, feedback strategies, interaction with the environment, and other ecological influences.
Paratenic host	A specific host, also termed "transport host," which acquires a stage of an agent that does not develop to the subsequent stage and can be either acquired by another paratenic host or by a final host; that host can be critical in completing a life cycle.
Pathogenesis	The production or development of a disease, specifically the cellular reactions and other pathologic mechanisms occurring in the progression of the disease.
Reservoir host	A definitive host that serves as an alternant relative to the host of interest for an agent that disseminates infective stages.
Salinity	An expression of concentration of salts dissolved in water, including primarily chloride, sodium, magnesium, sulfur, calcium, and potassium but with other elements in low concentrations. It is usually expressed as parts per thousand (ppt) or parts per million (ppm) and usually based on the electrical conductivity ratio of the sample to "Copenhagen water," an artificial seawater manufactured to serve as a world "standard" or more recently in practical salinity units (psu) as the conductivity ratio of a seawater sample to a standard KCl solution. Full strength seawater is considered 35 ppt, or 35 g of salt per liter of solution; salinity in estuaries can fluctuate from 0 to over 35 ppt daily, seasonally, or yearly, depending on winds, rain, currents, temperature, and geography.
Urticaria	An allergic reaction comprising pale, pink, focal swellings, or wheals, on the skin that itch, burn, or sting; also referred to as "hives."
Zoonosis	An animal disease transmissible to humans under natural conditions or a human disease transmissible to animals.

Definition of the Subject and Its Importance

Several parasites that infect marine and coastal animals or contaminate the marine and coastal waters can infect humans and present a significant public health risk. Historically, parasites from the marine environment were ignored as representing a risk. More recently, more researchers have investigated actual or potential human

marine infections; easily observable worms and other metazoans have been experimentally studied to determine if they can infect model mammals; some humans are now more likely to come into contact with infective parasites; immunocompromised people are more susceptible to parasitic infections; molecular methods have been used to differentiate known or potential infective parasitic species; improved molecular and serological methods have been developed to detect known protozoan and metazoan parasites; and infectious parasites have been investigated in detail. As discussed in this chapter, some parasites involved with marine waters and seafood products can kill large numbers of people, other fatal ones are rare, many cause human illness, and infections or the possibility of infections keeps people from eating seafood or entering marine waters. Moreover, the economic loss of seafood products from actual or perceived problems involving parasites in seafood caused by media exposure can be significant [1, 2] just as it is when involving perceived contamination of seafood by oil or other toxicants (gulfseagrant.tamu.edu/oilspill/pdfs/latourismPerception_BPOilWave1.pdf).

Introduction

Textbooks once considered parasites of marine origin or those in the marine environment as posing no public health risk. Over the last few decades, more and more parasites in different groups have been determined to be zoonotic agents that either are known to infect humans or can serve as a potential public health risk based on experimental infections in nonhuman mammalian hosts or are closely related to known human-infecting agents. These parasites include metazoans and "protozoans" that occur in water or in seafood products. Protozoa occurs in quotation marks because its historic higher taxonomic groups are not necessarily closely related [3] and some include stages with more than one cell. For example, a single myxosporidian spore may develop from a stage consisting of 13 cells, and molecular data demonstrate no relationship between Myxosporea and any group consisting of members with single cells and recognized as a protozoan. At least one metazoan taxonomic group, ascaridoid nematodes, has members that produce excretions and secretions (ES) that are potentially harmful to susceptible people.

Numerous factors are involved with risk of infection. For example, the likelihood of a visitor or traveler getting infected by eating raw seafood in well-known urban Japanese or other Asian restaurants is relatively low, but dining in rural local restaurants or street shops has a higher risk of infection with a variety of parasites [4]. The highest worldwide risk for a helminth infection is from preparation of raw or inadequately cooked seafood at home. This is usually because restaurants typically use products historically known not to be infected in the region from which they were collected or the products were frozen and then thawed. Public health risk also occurs for personal contact with parasites for people using coastal and marine water for either occupation or recreation.

An apparent increase in human infections has occurred because of increased opportunities to get infected. (1) A global spread and increased popularity of

"exotic cuisines" at least partially relates to increased human infections because of the increase in various media such as television and magazines. This has led to an increase in homemade raw seafood products, which are much more likely to contain infective parasites than products served in restaurants. (2) The increased popularity of raw products also relates to an increase and translocation of people throughout the world. People that move or visit abroad take their cuisines with them. They may eat infected products in their new surroundings that are similar to the uninfected products they ate in their native country. They can also spread their diseases as they travel, allowing new intermediate hosts and reservoirs to become established. (3) Much of the world's population is becoming more affluent, and with that more people are able to try new cuisines. Also, there is more opportunity to partake of established cuisines. For example, in Vietnam the improved economy has increased the traditional social activities that are conducive to eating more raw seafood and, consequently, acquiring more parasites. (4) With the resulting increase in people and demand for healthy fishery products, there has been increased utilization of different fishing grounds, species, and stocks. Even though some stocks are overfished, methods are now available for ships to go farther to sea or deeper to catch replacement products, possibly with improved transportation and storage systems. When a specific fish is assumed to be free from parasites harmful to humans, when the same species is caught in a different location, when it is maintained on a vessel longer, or when it is produced on fish farms, that resulting fish product may have or it may acquire harmful parasites. Also, fishing a previously underutilized species may result in obtaining an infected stock. (5) Regulations such as those protecting specific animals may result in an increased public health risk. For example, protecting seal pups and reducing seal fashions increases the final host population for *Pseudoterranova* spp., which results in a heavily infected cod intermediate host population. Also, the need to discharge fisheries wastes from commercial and subsistence vessels results in increased infections in fishes and marine mammals that feed on the wastes. Alternatively, regulations in some countries are lacking in regard to fishery products or for imported fishery products but not necessarily all meats, leaving consumers with the false impression that the products are safe. (6) Climatic and environmental health conditions are always changing, and, with those changes, infection dynamics of parasites quickly change. For example, during the El Niño of 1997–1998, the junction of the warmwater Kuroshio Current from the south with the cool Oyashio Current from the north moved 3,000 km northward from Kyushu to Hokkaido, Japan. This migration of the current's junction and its temperature elevation of 3.4°C caused an increase in abundance of krill, the intermediate host of *Pseudoterranova azarasi* and members of the *Anisakis simplex* complex. The sea lion final host of *P. azarasi* occurred in Hokkaido but not Kyushu, and, in addition, protected cetaceans that are the final hosts of *A. simplex* sensu lato migrated north so as to feed heavily on krill or on fish that ate the krill, acquiring the juvenile nematodes from them. Consequently, the Japanese used to eating nearly parasite-free seafood from Hokkaido began acquiring infections. In contrast, pollution from Southeast Asia kept some fish intermediate hosts of *A. simplex* sensu lato from migrating to Japan, especially to southern Kyushu, reducing the number of

anisakiasis cases there [5]. Each few years, climate in some regions worldwide changes enough to influence the seafood production and the parasitic infections. (7) Reduced resistance in some people because of disease, organ transplants, or immunosuppressive drug therapy relate to an increased susceptibility to various parasites, especially parasites that can replicate in or on humans with being challenged by an additional dose of parasites.

Increased documentation of human infections results from increased technical abilities. (1) Improved media coverage allows people to know when an epidemic occurs. It also stimulates potentially infected people to get examined, sometimes unnecessarily and to the detriment of the seafood industry. (2) Diagnostic tests are becoming better and more available both because of research plus technical advancements and because various funds are made available to survey regions or satisfy needs. (3) The same can be said for accurate identifications. Molecular means make it easy to detect parasites that cannot be seen grossly or a juvenile that cannot be morphologically associated with an adult, upon which the species has been named and described. (4) With good identifications and detection methods, more critical examinations can be obtained and compiled, allowing for useful epidemiological assessments.

The organization involves five sections. The first treats parasites that people acquire from the marine environment by eating seafood. The second treats those where people get infected with parasites by contact with them, either directly by active penetration by the parasites or indirectly by passive association with the agents. In the third, people get disease from allergens from parasites or parasite products. This is followed by a section on management, control, and treatment of the infectious parasites. The final section briefly examines what is required in the future to reduce, eliminate, or keep infections under control. In the first section on acquisition of parasites by eating inadequately prepared food, examples are divided into those that mature in humans and those that do not. The reason for this is that worms that mature in humans are voided or produce eggs that can be detected in fecal examinations. Those parasites that do not mature in the patient or produce cyst dispersal stages are more difficult to detect without immunological or invasive techniques. Moreover, the consumer not able to provide proof of a parasitic infection is less likely to find medical help, and the medical community is less likely to specifically diagnose, report the condition, or show a follow-up interest in the case. Several of these agents that have not yet been reported are treated as potential public health risks. The first two sections are each divided by taxonomic groups. In some cases the same parasites or members of the same parasitic group fit into more than one section, and the possible confusion is discussed in the different cases.

Parasites Acquired When People Eat Infected Seafood Products

Zoonotic parasitic diseases acquired by eating inadequately prepared infected seafood products include most of those treated by disease researchers and reported in recent literature. Some of the responsible agents are seen grossly, such as 5–10 m of

senile cestode strobilae protruding out of the anus of alarmed seafood consumers or a 4-cm-long ascaridoid nematode being vomited or passing out through the nose of someone recently eating uncooked cod. Most zoonotic diseases are recognized by the signs of a disease or fortuitous findings of diagnostic features. Not all infections are diseases. A few hundred small marine heterophyids probably can line the human intestine without apparent symptoms, but more may cause pathological alterations and result in disease. A lot of factors involving the patient and the history of the infection can influence the alterations. Perhaps easier to envision would be a non-marine example of the hookworm *Necator americanus*. A barefoot boy can pick up a few dozen juveniles penetrating his feet from the warm, moist soil. There may be a slight itching and rash where the juveniles enter, but as they are carried to the lungs, pass up the respiratory tract to the mouth, are swallowed, and ultimately attach to the intestine as 7- to 11-cm-long adults, they produce no symptom. On the other hand, increase the number, say above 50, and pathological changes can occur during all the phases. Most important, once attached, the blood loss becomes enough to produce anemia and protein deficiency, and the resulting loss of iron and protein may retard growth and mental development. This will be associated with abdominal pain, diarrhea, loss of appetite and weight, and "disease." Numbers of worms alone can shift an "infection" without disease to a "disease."

Parasites That Mature in Humans

Helminths (Worms in General)

Most agents that mature in humans are helminths. Helminth diseases consist largely of those acquired by eating inadequately prepared seafood products usually infected with platyhelminths and nematodes, but occasionally with other agents. Some agents are freshwater parasites that, because of their complicated life cycles, have one or more stages that enter the coastal or marine environment. Presently, several of these are treated as freshwater cases because of the epidemiological aspects of the case. As more cases are studied, more human infections that involve strictly marine parasites will be demonstrated.

Many more cases of marine helminth infections probably exist than are reported or recognized by physicians. Surveys involving fecal examinations exhibit adult worms or their eggs, but, for a variety of reasons, the samples are difficult to acquire and the corresponding infections are difficult to correctly diagnose or get reported. Most medical attention is not likely to culminate in confirmed reports of identified agents because physicians or technicians not familiar with proper techniques, means to correctly identify the agents, or people to consult are interested in treatments and not the specifics of a parasitic infection. Even when treated, the patient never knows what was causing the signs of disease because the agents are killed and digested or degenerate. On the other hand, in some countries where considerable raw or insufficiently prepared seafood is

consumed, attention by researchers and the medical community results in an abundance of case reports. The Japanese and Koreans provide good examples of documented cases of infections by marine parasites.

Platyhelminths consist mostly of hermaphroditic soft-bodied worms. Those hermaphrodites of medical marine significance are cestodes (tapeworms) and trematodes (flukes), and most of those that mature in humans were consumed as larval stages. For many, the taxonomic identification is confused and the life cycle is partially or fully unknown. Moreover, infections are often undiagnosed because fecal examinations are not always conducted or are conducted by those without parasitological training. Moreover, the eggs of many species are similar in appearance.

Cestodes

Cestodes infective to humans from marine hosts are members of the family Diphyllobothridiidae in the Diphyllobothriidea, previously classified in the artificial assemblage Pseudophyllidea, now represented as comprising two unrelated clades, "Bothriocephalidea" and "Diphyllobothriidea" [6]. *Diphyllobothrium latum* is the best known member of the group, and it is considered a freshwater member with a cyclopoid-freshwater fish-bear/human/vertebrate cycle. Unpublished studies attempting to infect Mississippi marine fishes with the agent were unsuccessful; most copepod species developed a strong cellular response to the larva, and a mixture of "infected" copepods did not produce an infection in the Atlantic croaker. However, five human infections reported from eating the estuarine mullet *Liza haematocheila* in Korea were identified as *D. latum* on the basis of morphological characteristics [7]. Molecular tools should be able to confirm that identification as those tools have confirmed or corrected identifications of other species mentioned later.

Many human case reports have been identified as *Diphyllobothrium pacificum*, which typically matures in the pinnipeds. A recent taxonomic assessment of *D. pacificum* [8] involved numerous available specimens of variously misidentified species, including *D. latum* and *D. pacificum*. As it turned out, the classic publication [9] reporting human infections by *D. pacificum* in Peru was actually dealing with *Diphyllobothrium arctocephalinum*. Both *D. pacificum* and *D. arctocephalinum* occur along the South American Pacific coast in fur seals and secondarily in humans, with *D. pacificum* ranging north into Alaska and Japan and *D. arctocephalinum* restricted to the Southern Hemisphere, ranging south to South Australia and South Africa [8]. In one review, there are ten reported species of *Diphyllobothrium* from humans [10], including 6 from Japan [11], and in another there are 15 species [12]. Of the latter 15, not including *D. arctocephalinum*, there are eight nominal species in marine final hosts that also have been reported from humans: *Diphyllobothrium cameroni* (Hawaiian monk seal), *Diphyllobothrium cordatum* (Arctic seals, walruses), *Diphyllobothrium hians* (Arctic seals), *Diphyllobothrium orcini* (killer whale), *D. pacificum* (sea lions, eared seals),

Diphyllobothrium scoticum (leopard seal, southern sea lion), and *Diphyllobothrium stemmacephalum* (harbor porpoise, bottlenose dolphin).

The species commonly infecting humans in Japan and previously referred to there as *D. latum* has been confirmed as *Diphyllobothrium nihonkaiense* ([8, 12], and others) (Fig. 15.1). The brown bear (*Ursus arctos*) is its natural definitive host, but it commonly infects humans, with some preserved worms measured as long as 8.8 m. Since infections are acquired from Pacific salmons (mainly cherry, pink, and chum salmons plus the Japanese huchen), either from the sea or just leaving the sea, it is considered a marine infection. Molecular studies have shown that human infections in Far East Russia up to the Kamchatka Peninsula reported as *Diphyllobothrium klebanovskii* are conspecific, identical to *D. nihonkaiense*. Molecular sequences also suggest the existence of two genotypes, biologically homogeneous populations not defined by locality [13]. Infections also involve consumers in Canada [14]. Moreover, salmon are exported to many countries, resulting in genetically confirmed infections in consumers in France and Switzerland [15] as well as New Zealand [16]. Another "freshwater" species, *Diphyllobothrium ursi*, also infects salmons and both brown and black bears as well as humans and dogs that feed on salmon or eat salmon-liver paste [17]. Cestodes and other parasites maturing in terrestrial definitive hosts that infect anadromous fishes such as Pacific salmonids or their freshwater fish or invertebrate hosts can be eaten by marine fishes, which in turn, serve as paratenic hosts. On the other hand, freshwater fishes can become paratenic hosts of helminths of marine origin. They can feed on infected marine fishes entering brackish river mouths or lower reaches of the rivers, or they can feed on anadromous fishes migrating upstream. A confirmed example is the plerocercoid of *Diphyllobothrium alascense* of dogs and rarely humans from the anadromous boreal smelt (*Osmerus mordax*) being transferred to the paratenic freshwater burbot (*Lota lota*) [18].

Members of *Diplogonoporus* have been reported from over 200 people in the twentieth century. Most cases have been identified as *D. balaenopterae*, or the names are probably synonyms of that species, a species that infects consumers in Japan but also Korea [12, 19]. A case from Spain probably represents infection from fish imported from the Far East [20]. Genetic analyses of 18S rDNA, ITS1, and cox1 nucleotide sequences of isolates were obtained from five Japanese cases [21]. The phylogenetic analysis of that material revealed little divergence and a close relationship to *Diphyllobothrium stemmacephalum*, a species maturing in the harbor porpoise and bottlenose dolphin rather than in whales as in *D. balaenopterae*. Data suggest that not only is *Diplogonoporus* paraphyletic, but those genetic data show that so are *Spirometra folium* and *Spirometra decipiens* [22].

Coastal Peruvians of ancient times had infections of *Diphyllobothrium* sp. as determined from coprolites [23], but infections of *D. pacificum* recently seem to be less prevalent in the northern Pacific Ocean, resulting from decreasing numbers of marine mammals and commercially important fishes like the pollack [8].

Not only have diphyllobothriid species been misidentified in the past, but human infections have been and will probably continue to be missed in many cases. They are most easily detected when a human expels lengthy portions of senile strobilae.

Fig. 15.1 Author in Meguro
Parasitological Museum,
Tokyo, Japan, standing next
to an 8.8-m-long specimen
(> 10 m before fixation) of
the tapeworm
*Diphyllobothrium
nihonkaiense* and the
curators, the late Shunya
Kamegai on *right* and Jun
Araki on *left*

Signs are variable but usually not severe [11, 24]. Most cases are probably not reported. The author did not experience any symptoms from an infection of four long specimens of *D. latum* other than mild discomfort several hours prior to periodic release of senile strobilae. The treatment of choice for the adult tapeworm infections in humans is a single dose of praziquantel (10–20 mg/kg) plus 30 g of magnesium sulfate as a purgative, if specimens are to be adequately studied.

Trematoda (Digenea, Flukes)

Trematodes have a molluscan first intermediate host from which free-living cercariae are shed. The cercaria of most groups encysts or becomes encapsulated as a metacercaria in a second intermediate host, and this metacercaria matures as a hermaphroditic individual in a vertebrate final host when the second intermediate host is eaten. Because there are so many trematode taxonomic groups and species, there are numerous exceptions to the basic life cycle, and some of these involve species that can infect humans. For example, the well-known freshwater sheep liver fluke, *Fasciola hepatica*, encysts as small white spherules (metacercariae) on vegetation. Most people that get infected do so by eating raw watercress on which the metacercariae have encysted. Schistosomes do not encyst but develop through the juvenile stage (schistosomula) in the final host where they ultimately mature in a blood vessel as separate male and female worms.

Depending on the taxon, the larval stage in the egg (miracidium) either hatches and penetrates its molluscan host or hatches after being eaten by a specific mollusk. The germ cells develop through a series of two or more asexual phases before shedding a continual production of hundreds to millions of infective cercariae. Some species have broad specificity in the molluscan, second intermediate host, or

final host. Second intermediate hosts differ by family of trematode, but those discussed below include fishes, crustaceans, insects, mollusks, and none. Most of those marine/estuarine species reported from humans have a broad specificity of mammal or avian hosts. Most are rather small intestinal worms that necessitate a microscope to detect them unless hundreds are present, and each of these produces a continuous flow of a large number of small (25–30 μm long) eggs in the human feces for weeks or years. Most species are difficult to obtain in a healthy condition after medicinal treatment, are not transferred from the medical community to taxonomic parasitologists, are difficult to distinguish from one another, and produce minimal symptoms in light infections. Consequently, the number of human-infecting species and the prevalence and intensity of infections with marine trematodes are most certainly underestimated. Most of what is known has come from parasitologists within the medical community of Japan and Korea, where consumers eat an abundance of raw and "inadequately" prepared seafood products.

According to recent literature [25], an estimated 18 million people are infected with fish-borne intestinal trematodes. This was considered an underestimate, and it included some freshwater species. In the Republic of Korea, 17 species represent five families (Heterophyidae, Echinostomatidae, Plagiorchiidae, Neodiplostomatidae, and Gymnophallidae) [26]. Of those, ten are heterophyids and, of those, seven are prevalent among residents who consume raw flesh from estuarine fishes in south and west coastal areas [25–27]. Those are *Heterophyes nocens*, *Heterophyopsis continua*, *Pygidiopsis summa*, *Stellantchasmus falcatus*, *Stictodora fuscata*, *Stictodora lari*, and *Acanthotrema felis*. Documentation of all food-borne trematodes in humans includes 70 species in 14 families [25], but several are not from marine hosts and presently infected people are estimated to surpass 50 million.

Heterophyidae (Opisthorchioidea).   As with zoonotic infections from eating fishes in Japan, Korea, China, and Thailand, such infections from Vietnam are now being recognized as a food safety risk in a country whose people have a strong tradition of eating raw fish [28]. The heterophyids use a snail first intermediate host, a fish second intermediate host, and either a bird or mammal definitive host. A prevalence of heterophyid infections with *Haplorchis pumilio* (100%), *Haplorchis taichui* (70%), *Haplorchis yokogawai* (6%), and *S. falcatus* (3%) was determined from expelled (25 mg/kg praziquantel, followed by a saturated solution of magnesium sulfate) adult worms in a survey of residents from coastal Nam Dinh Province south of Hanoi in 2005. The recent finding of those parasites in Vietnam suggested to the surveyors [28] that some may be introduced rather than endemic, increased in magnitude with intensification of aquaculture, or increased because of increased consumption and importation of raw fish. Difficulty presently exists in determining from which fishes the infections are acquired in people throughout Vietnam as well as the rest of the world where people eat raw fishes. Human-infecting species are beginning to be recognized in food fishes as those fishes are examined for parasites. For example, examination of wild and cultured grouper (*Epinephelus bleekeri*, duskytail grouper, and *Epinephelus coioides*, orange-spotted grouper, both marine species) have revealed *Heterophyopsis continua* and *Procerovum varium* (recognized as

Fig. 15.2 Living encysted metacercariae of the heterophyid *Phagicola nana* in fillet of largemouth bass, *Micropterus salmoides*, from Mississippi estuary. The cysts average 0.30 mm across
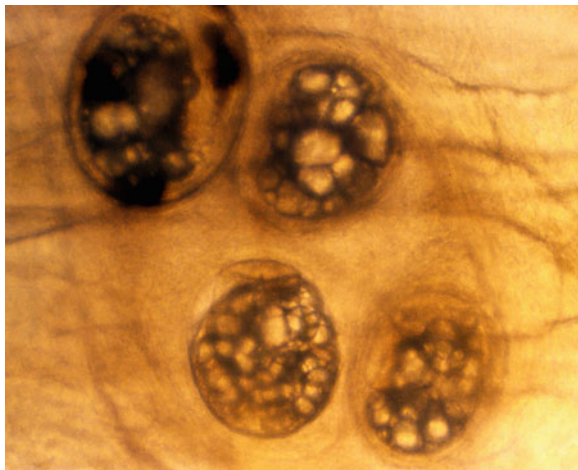
a freshwater parasite), and examination of mullet (*Mugil cephalus*) have revealed *Pygidiopsis summa* and *H. continua* from brackish water in Khanh Hoa Province in central coastal Vietnam [29]. The long tradition of eating raw fish has intensified with increasing affluence; a higher prevalence between men (69%) and women (23%) can be explained because the social gatherings where consumption of raw or pickled fish occurs have historically been male-oriented [28]. Concern exists for the exportation of infected fresh fishes, some freshwater species, because aquaculture in rural Vietnam is increasing in economic importance [30].

Human infections have been known from Japan for decades even though most are freshwater species [25]. All three species of *Metagonimus* are freshwater species in regard to the snail host, but, in Korea, one, *Metagonimus yokogawai*, infects a marine fish, which consumers eat raw. Actually, an amphidromous fish, the sweetfish, *Plecoglossus altivelis*, spawns in rivers near the sea. Then, the fish fry feed on plankton at sea until 5–7 cm TL at which time they enter into the river mouths. Infections can be acquired from the fish in estuarine habitats. Sequence data readily separate the three species [31].

In the Western Hemisphere, there are several heterophyids that present a human health risk. For example, in the USA, species of *Phagicola* represent one of several potential infectious genera (not accepting *Phagicola* as a junior synonym of *Ascocotyle*). Knowledge about human infections from the Southeast US has not progressed much beyond anecdotal mention [1], but *Phagicola nana* (Fig. 15.2) from several fishes [32], *Phagicola longa* [33] from mullets (Fig. 15.3), and several other species (Fig. 15.4) probably occur in many consumers who eat inadequately prepared fish. *Heterophyes heterophyes*, a heterophyid from the Middle East has been reported from fish-eating patients in Florida never having left the USA [34, 35]; these infections were most likely species of *Phagicola*. Actually, even capillarid eggs get misidentified as those of *H. heterophyes* in Egypt, where the trematode is common [36]. Unlike many heterophyids in the USA that exhibit

Fig. 15.3 Mounted and stained adult specimen of the heterophyid *Phagicola longa* from an experimental infection originating from a metacercaria in *Mugil cephalus* from Mississippi

Fig. 15.4 Living encysted metacercariae of the heterophyid *Phagicola diminuta* in gills of Gulf killifish, *Fundulus grandis*, a bite-sized fish from Mississippi estuary

a high "site specificity" in the second intermediate fish hosts, meaning found in one or few specific organs or tissues, *P. nana* occurs in many tissues such as the muscular fillets in addition to the viscera, gills, and other sites [32]. Moreover, *P. nana* infects a few different fishes such as the largemouth bass (*Micropterus salmoides*) and several sunfishes (Centrarchidae), popular recreational fishes in estuaries of the Southern US that are consumed in a variety of cuisines. Most heterophyid species infect specific organs in specific small fishes that are eaten raw in their entirety by specific groups of people, if eaten at all. As with several different parasites, some heterophyids that constitute public health risks constitute species complexes that are difficult to distinguish by morphological features. For example, what is commonly reported as *Centrocestus formosanus* is a mixture of morphologically similar species. Members of this complex are common in the Far and Middle East, but some apparently have been introduced into Hawaii, USA mainland, and Mexico through introduced infected snails (*Melanoides tuberculatus*) in the aquarium trade on vegetation and with fishes [37]. Members

of this basically freshwater heterophyid complex infect a large number of fish hosts, including some estuarine species.

The reason for stressing heterophyids is because, even though most species measure 1 mm long or less, they often occur in large numbers, influence public health, and can result in severe pathological changes in humans. A series of studies in the 1930s based on human infections in the Philippines was summarized in 1940 [38]. Five heterophyids were identified from 33 of 297 autopsy cases, not all randomly chosen: *H. yokogawai* (16 cases, 13 alone), *H. taichui* [5], *Haplorchis calderoni* [2], *Haplorchis vanissima* [1], and *Diorchitrema pseudocirrata* [6]. These occurred either singly or with other species. The other species consisted of the microphallid *Microphallus brevicaecum*, which was originally identified as a heterophyid (*Heterophyes brevicaeca* but later recognized as *Spelotrema brevicaeca*) (in 11 cases), an echinostomid identified as *Euparyphium ilocanum* [2], and an unidentified plagiorchiid (*Plagiorchis* sp.) [1], plus the common heterophyids already listed. All the trematodes occur normally in the intestine, where lesions were not found to be severe. More important, eggs of the heterophyids *H. yokogawai* and *H. taichui* and the microphallid *M. brevicaecum* were also associated with acute and chronic lesions in the heart and other visceral organs such as liver, spleen, kidneys, brain, spinal cord, and lungs. *Diorchitrema pseudocirrata* also occurred in some of those lesions in mixed infections but never by itself. Worm eggs, especially from degenerated adults, enter into the blood and lymphatic streams and are carried to different visceral tissues where they provoke the cellular reactions. Adhesions and hemorrhaging were common complications. Of 34 positive cases (1 did not exhibit an intestinal infection), 15 (44%) had visceral complications (1 in brain with fatal hemorrhaging, 1 in spinal cord, and 13 in heart). Of 89 enlarged hearts in these charity patients in the Philippines, the 13 (15%) with myocardial or valvular lesions associated with worm eggs were assumed to have caused the heart dysfunction, a value attributed to heterophyid-caused fatal heart disease [39]. Adult worms (Fig. 15.5) identified as *Heterophyes heterophyes* also encapsulate in the human brain [40].

An enormous number of infective metacercariae can occur in some habitats. To appreciate the life cycle, each adult out of the thousands that can be present in the intestine of a human or in that of a domestic dog or cat produces thousands of eggs, with several hundred laid daily for several weeks or months. One dog was reported to host 13,000 specimens of *H. heterophyes*. Each egg produces a miracidia that can infect a snail. In the lakes along the Nile Delta and in the Bardawil Lagoon, over 90% of the host snail population can be infected (Figs. 15.6, 15.7). Just short of 500 cercariae can be released from each of the abundant snails daily for a year, but with decreasing cercarial production over time. Each cercaria survives 1–2 days, and mullets are common hosts. Eleven emaciated specimens of *Liza ramada* contained 1,730–6,000 metacercariae per gram for an estimated 582,000 metacercarial cysts in one 255-mm-long fish. A specimen of *Mugil cephalus* from the same location had 1,136 metacercariae per gram [41]. Fishermen, seafood dealers, children of those people, and those who taste fish being prepared commonly become infected because the rules established for protection of the consumers buying the products

Fig. 15.5 Close-up of living 0.8-mm-long adult specimen of the trematode *Heterophyes* sp. from Bardawil Lagoon, Northern Sinai, Egypt, showing diagnostic sclerites in the modified genital sinus, often misstated as a "gonotyl," below the ventral sucker
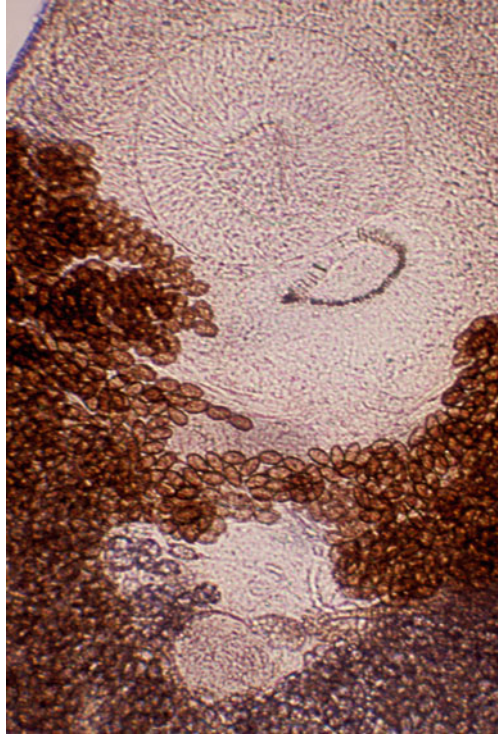

Fig. 15.6 Street vendors selling fresh fish in El Arish, Northern Sinai, Egypt

are not always followed by the handlers. Moreover, fishermen do not always completely cook their fish.

Microphallidae (Microphalloidea). Members of small intestinal trematode complexes other than Heterophyidae also have been misidentified. Microphallidae constitutes one of those families. One or more microphallid members also have

Fig. 15.7 Close-up of activities in Fig. 15.6, showing vendor displaying salted mullet. A regulation at the time was to keep fish salted for 8 days before selling them to the public. Eight days was necessary for the heavy infections of heterophyid metacercariae to lose their infectivity

a relatively broad specificity of the final host and can also cause severe potentially fatal pathologic lesions [38, 42]. As mentioned above, *Microphallus brevicaecum* from shrimp has been determined to be the cause of human mortalities in the Philippines. Microphallids are superficially similar to heterophyids and also infect birds and mammals and occasionally fishes, reptiles, and amphibians, but the microphallids have entirely different cercariae, differ phylogenetically, and use crustaceans such as crabs and palaemonid and peneid shrimps as second intermediate hosts rather than fishes.

Troglotrematidae (Gorgoderoidea). *Nanophyetus salmincola* is another small, about 1-mm-long, trematode that infects the intestine of numerous mammals, including humans. In fact it is probably unknowingly the most common helminth in people of the North American Pacific Northwest. It produces gastrointestinal distress, fatigue, loss of weight, and peripheral eosinophilia when numerous specimens occur in humans, and can be diagnosed easily from its relatively large, 0.090–0.100-mm-long, diagnostic eggs that appear in stools about a week after eating infected fish. No symptom occurs in most light infections. Basically a freshwater parasite, cercariae form metacercariae in several salmons and steelhead trout (*Oncorhynchus mykiss*, also known as sea-run rainbow trout) as well as freshwater fish and amphibians that do not make oceanic migrations. Infections in the Pacific Northwest are attributed to eating raw, incompletely cooked, cold-smoked salmon and steelhead trout and their eggs [43]. A second species, *Nanophyetus schikhobalowi*, needs to be studied molecularly to determine if it is conspecific with *N. salmincola*. It had been demonstrated to infect as many as 98% of the people in some eastern Siberian villages.

The trematode in the Pacific Northwest serves as host for the rickettsial agent, *Neorickettsia helminthoeca*, which in turn causes "salmon poisoning disease" of canines. Dogs that are fed infected salmon may die, but humans and other non-canines are not known to be affected. Nevertheless, the loss of dogs in the Arctic can be a serious problem.

Gymnophallidae (Gymnophalloidea). Gymnophallids mature in shore birds, gulls, and diving ducks. However, members of Gymnophalloides also infect mammals. Human infections with *Gymnophalloides seoi* are known only from Korea, but most are tiny, <1 mm, and it and other species all use a variety of mollusks as first and second intermediate hosts and probably infect people throughout the world where mollusks are consumed raw. *Gymnophalloides seoi* is acquired primarily from eating the raw oyster, *Crassostrea gigas*, known as the Japanese oyster, Miyagi oyster, giant oyster, immigrant oyster, and giant Pacific oyster, and infects the intestine and possibly pancreatic duct of human consumers [25, 27]. Nevertheless, like *G. seoi*, which infects the Palearctic oystercatcher, *Haematopus ostralegus*, most members of this genus can be experimentally administered into a variety of birds and mammals, suggesting the human health risk. Studies with mice demonstrate that *G. seoi* produces focal responses for 2–3 weeks, at which time the mucosal integrity is restored. If provided with immunosuppressive treatment, the mice underwent minimal goblet cell hyperplasia, extended retention of worms, and invasion of the submucosa. Even though genetics of hosts also play a role in this sequence, immunosuppressed humans are at risk for transference of eggs and worms to remote organs as with heterophyid infections. With a relatively low production of eggs relative to heterophyids, a total of 100 specimens would be necessary to produce 8,400 eggs per day, considerably fewer than most heterophyids [25].

Echinostomatidae (Echinostomatoidea). Members of some other trematode families also infect the small or large intestine but grow slowly and reach larger size (roughly 3–7 mm) compared with those mentioned above (0.5–2.0 mm); a few marine members are known to infect humans. A total of 21 members of Echinostomatidae are listed as causing human infections, some resulting in gastroenteritis [25]. Of those, all were from freshwater mollusks except two. One, *Acanthoparyphium tyosenense*, can be acquired in Korea from eating at least the raw bivalves *Mactra veneriformis* and *Solen grandis* and the gastropod *Neverita bicolor* available at a coastal village seafood market [44]. The gastropod first intermediate hosts *Lunatia fortuni* and *Glassaulax didyma* shed cercariae that infect the gills of the popularly eaten bivalves. Ducks serve as the natural definitive host, but experimental infections in chick and seagull have confirmed the adult infection [25]. Related species, and there are several, such as what was identified as *Acanthoparyphium spinulosum* in the oyster *Crassostrea virginica* from Texas, USA, are probably also commonly infective to humans, but such infections are limited only by the infrequency with which the molluscan second intermediate hosts are eaten raw [45].

Plagiorchiidae (Plagiorchioidea). Human infections with *Plagiorchis* spp. are uncommon, but 12 cases have been reported. *Plagiorchis vespertilionis* occurred in a man from coastal Republic of Korea who often ate raw mullet and gobies and was not known to eat caddisfly larvae, mayfly larvae, or dragonfly nymphs. The insects were suggested as possible intermediate hosts and are known hosts for many other species of *Plagiorchis*. The patient also contained *Heterophyes nocens*, acquired

from fish [46]. Nevertheless, fish were suggested intermediate hosts, and perhaps the infection was transmitted by eating raw estuarine fish that had recently fed on infected dragonflies or some infected insect larva, joining the freshwater parasite with the coastal habitat. Members of *Plagiorchis* and related genera mature in birds and mammals plus accidentally in amphibians and reptiles. They are relatively large (3–5 mm) and usually occur in low numbers in the final hosts.

Didymozoidae (Hemiuroidea).   Humans do not get infected by didymozoids! These trematodes of fishes are unusual in that they occur usually in pairs of either hermaphroditic individuals or as separate sexes like mammalian schistosomes and occur encysted in the flesh, encysted in other tissues, or even free in body spaces other than the lumen of the alimentary tract like most trematodes. The group is mentioned because people eat infected fish products and diagnosticians find the small reniform didymozoid eggs (roughly 0.015–0.030 mm long but in some species up to 0.040 mm) of the worms in human stool samples, leading those diagnosticians to assume either an active trematode or protozoan infection. Such misidentifications have been reported from people eating marine fishes in Japan, Taiwan, and the Philippines, but cases could occur throughout the world where infected fish are abundant, especially in pelagic tropical and subtropical fishes [47].

Nematoda (Roundworms)

Nematodes, or roundworms, comprise both free-living and parasitic groups. Parasitic groups that have marine members exhibiting a public health risk also fit into different groups: those that mature in humans, those that have larvae that can infect humans eating inadequately prepared seafood, those that produce excretions or secretions that result in an immunological response in humans, and those that can be acquired by being in the water with free-living stages or handling infected products. When consumers think of parasites in seafood, they typically think of anisakiasis involving grossly apparent nematode juveniles. Of the many nematode groups, each may have a different strategy in completing a life cycle. An example cycle will be mentioned for each major group of worms.

Trichinellidae (Dorylaimia, Trichinellida). Trichinellosis has received considerable attention over the last 150 years of control efforts, but in the past 20–30 years, there has been a dramatic reemergence as an emerging zoonosis [48]. The reasons are severalfold involving changing agricultural, marketing, environmental, and economic practices and conditions, but basically prior attentions involved *Trichinella spiralis* in domestic pork. In the 1940s and 1950s, a large number of marine and terrestrial mammals in Alaska were examined for what was then known as *T. spiralis*, and most had infections [49]. A total of 320 native individuals from three Alaskan areas given intradermal tests showed that 28% from Wainwright, Alaska, tested positive. There are now at least ten recognized species or genotypes, and the involvement of the sylvatic cycle of some of those is responsible for new

human cases. For purposes of this review, *Trichinella nativa* and to a lesser degree *Trichinella britovi* play a role. *Trichinella nativa* infects the carnivores that inhabit the marine environs: polar bear (*Ursus maritimus*), walrus (*Odobenus rosmarus*), Arctic fox (*Alopex lagopus*), and wolf (*Canis lupus*), but it is even known from China in domestic pigs. This species differs from the others in that it can survive the freezing process, the process that keeps domestic pork safe to eat. Uncertainty exists in how long the frozen juveniles remain infective, but, when juveniles from walrus meat were stored at −20°C for up to 20 months, some remained infective to experimental guinea pigs [50]. There was a gradual degradation process that rendered some noninfective. The freezing resistance appears to be related to the parasite-nurse cell-host complex, and the nurse cells yield a cryoprotectant when occurring in carnivore muscle tissue but not when in rodents [51]. Outbreaks are common in the Canadian Arctic where uncooked walrus meat is eaten raw, frozen, and aged by Native Americans as "igunaq" [52], but some that get infected also eat the products cooked [53]. This product is produced by placing meat and fat tissues into skin bags, which are sewn shut and aged about a meter under a cache of rocks or gravel along a beach. When meat from experimentally infected seal was prepared as igunaq and allowed to ferment, as air-dried meat (nikku), and as both raw and partially cooked sausage (core temperature less than 50°C), it remained infective for at least 5 months under laboratory conditions. The food product was fed to cats and the extracted juveniles were orally inoculated into mice [54]. Whale is usually eaten as muktuk, a preparation of fermented skin and blubber containing no muscle [53].

Trichinella britovi also occurs in temperate areas of the Palearctic region where people obtain infections primarily from eating wildlife. Apparently, it cannot resist freezing for a long period; the juveniles of *T. spiralis*, which have been reported from a variety of marine mammals, die after 4 days at −10°C. The status of infections from marine mammals requires additional research. The cycles of all the species are similar to each other but different from other nematodes in this chapter. The definitive host, including human, eats uncooked infected meat from another definitive host, and the juveniles are released when the cyst is digested in the stomach. The juveniles invade the mucosa of the upper intestine and develop into mature adults within 2 days. After 4 days, the mated female starts depositing motile juveniles, a process that continues for 4–16 weeks and produces up to 1,500 juveniles in the nonimmune host. These juveniles pass within the lymphatic system or mesenteric venules to muscles, usually striated ones, where it encysts. Striated muscle tissue stimulates development of nurse cells and capsule formation within 2–3 weeks (Fig. 15.8). The coiled juveniles can survive in human muscle for years, even though calcification may occur within 6–9 months. Infections can be fatal with as few as five juveniles per gram of muscle, but infections can be much higher, especially if the initial dose in an immunologically naïve consumer contains hundreds of cysts in striated muscle. A low initial dose establishes a protective immunity to challenge doses.

Paracapillaria philippinensis (until recently [55], a trichinellid that was and still is referred to by some as *Capillaria philippinensis*) seems to be spreading

Fig. 15.8 Section of coiled specimen of juvenile *Trichinella spiralis* encapsulated in striated muscle tissue
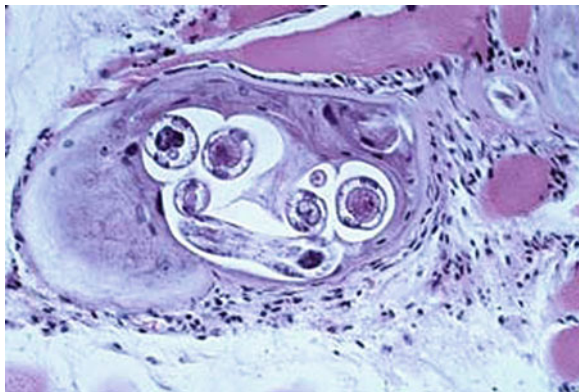

geographically. This small intestinal nematode produces mortality in humans. More than 2,000 human cases have been reported from the Philippines and Thailand, with several of those from more recent cases in Korea, Japan, Taiwan, India, Iran, United Arab Emirates, Egypt, Italy, Spain, and the United Kingdom [56], but with some of those acquired from eating freshwater fishes or imported fishes. The number of human cases is being reduced in Thailand, but infections probably contribute significantly to mortality there [57]. The life cycle probably includes a bird definitive host as shown by experimental infections in a fish-eating rail and heron, even though many mammals can host transient infections, and humans and the Mongolian gerbil can die from infections in less than 2 months [58]. Eggs passed by the definitive host hatch in a variety of freshwater and estuarine fish species. At least when the gerbil or human eat the infected fish, the juveniles develop into males and females that release a first-stage juvenile from a thin-shelled egg, which in turn can autoinfect the host and produce adults, with a female that produces the typical capillarid thick-walled eggs that are released in the feces. Even though most second generation females are oviparous, a few females still produce juveniles that can progress to autoinfection and hyperinfection, a condition in which the produced juveniles penetrate the intestinal mucosa and proceed with migration. At autopsy, 1 l of bowel fluid contained an estimated 200,000 specimens in all stages [58].

Signs of infection in humans are varied: they can include abdominal pain, diarrhea, vomiting, heart irregularities, edema, and weight loss, with the blood exhibiting low protein, calcium, potassium, and sodium, and with high immuno-globulin E (IgE) with diminished levels of IgG, IgM, and IgA for several months after treatment with albendazole. Albendazole seems more effective than thiaben-dazole and mebendazole because there is no relapse, presumably because only albendazole affects the larval stages [58].

Epidemiological studies are lacking in most reports, but where infections are common, elderly aboriginal groups with infections in Taiwan prefer Chou-Bao, which includes soaking raw, small entire fish in fermented millet [56], and infected Filipinos consume Kinilaw, which consists primarily of raw pilchards,

Fig. 15.9 Specimens of the
giant kidney worm,
Dioctophyme renale,
removed from a mink's
abdominal cavity in
Louisiana. This species
usually devours all the
parenchyma in the right
kidney of the mink and other
fish-eating carnivores, but
these specimens ended up in
the cavity and matured
without killing the host
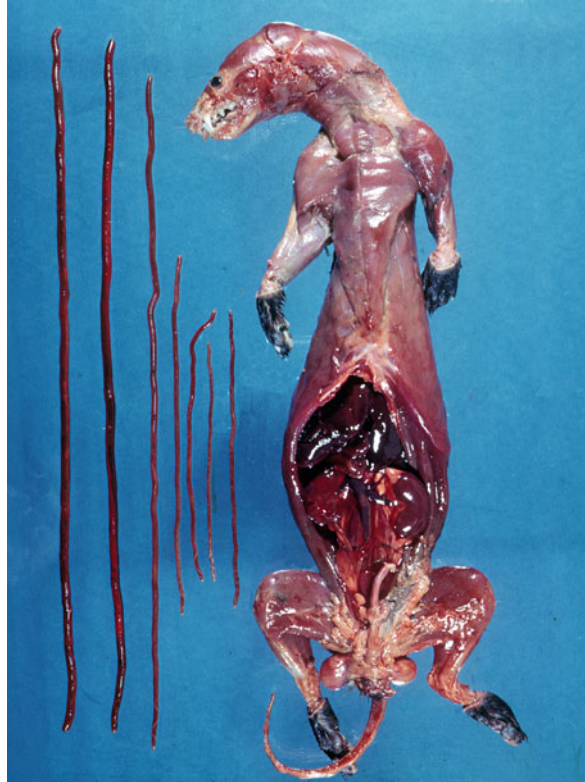
or other small fishes from coastal lagoons, marinated in vinegar, garlic, onions, ginger, tomato, and various peppers. The small fishes throughout SE Asia also are eaten whole as raw products, and some native groups (Ilocanos of Northern Luzon, Philippines) use animal organs and intestinal juices to season rice and other foodstuffs [58]. Most human cases have been traced to consumers that eat small, raw entire fish, but exact causes are not known. When diagnosis is delayed, the disease can be severe, with up to 30% fatality in some localities in the Philippines.

Dioctophymatidae (Dorylaimia, Dioctophymatida).The giant kidney worm, *Dioctophyme renale*, rarely infects humans, but the potential because of aquaculture and new cuisines is increasing. Even though usually considered a freshwater parasite, it also is common in the estuarine environment [1]. Its life cycle involves an oligochaete and a fish, amphibian, or reptilian paratenic host. Its counterpart *Eustrongylides* will be discussed later because it does not mature in humans. *Dioctophyme renale* matures in and completely devours the kidneys of its definitive host. The site is usually restricted to the right kidney, probably because of migratory behavior of the acquired juvenile. If it does not encounter the right kidney, it can mature in the peritoneal cavity, where it also causes harm (Fig. 15.9); it can also

become encapsulated and form a subcutaneous nodule [59]. Human infections are usually diagnosed by the worm eggs in urine, followed up by radiological exams to detect enlarged or calcified kidneys. The worm has a cosmopolitan occurrence, but most human infections are from Iran and from freshwater habitats. In fact, human coprolites dated about 3,375 YBC from an archeological site in Switzerland suggest that human infections were more prevalent in the Neolithic than now [60]. In the USA, sylvatic infections are common in the mink (*Mustela vison*) in brackish marshes of southern Louisiana [1].

Acanthocephalans (Spiny-Headed Worms)

Acanthocephalans from marine products are not known to mature in humans. However, a few from terrestrial arthropods such as cockroaches do produce eggs in humans. In fact, eggs were found in human coprolites from a cave in Utah dated about 1869 BC ± 160 years and 20 AD ± 240 years [61]. On the other hand, juveniles can attach in the lumen of the intestine without maturing, and, because they are in the lumen and can be voided in the feces, they are treated here. This seems to be the case for *Corynosoma strumosum* in a person from Alaska [62] and *Bolbosoma* sp. from a Japanese fisherman [63]. The first case was noticed when the infected male was treated with Atabrine. The worm matures in seals but is known as a juvenile in dogs, otters, birds, and other fish-eating birds. When fresh marine fish were fed to mink, some mink died [64]. Even though not routinely detected in people, *C. strumosum*, common as adults in pinnipeds and as juveniles from birds and other mammals in the Holarctic, was considered probably to be common in humans but for a short duration [18, 62]. The second case was detected because the worm had penetrated the intestine and was surgically removed because the disease was initially diagnosed as appendicitis.

Acanthocephalans are like nematodes because they both have separate males and females. However, all species are parasitic, and molecular data place them with rotifers. The life cycle includes an arthropod or crustacean and a vertebrate. In the case of the two palaeacanthocephalans mentioned above, the crustacean is unknown, but it could be small or large. The life history is typically completed by seal, whale, or sea otter by feeding on a paratenic fish host containing an encysted or encapsulated larva or juvenile. Most acanthocephalans have a rather specific crustacean and final host and a larger but still rather specific range of paratenic hosts. Even though the definitive host is quite specific, the worm may attach in the intestine of non-closely-related hosts. For example, two palaeacanthocephalan species that mature in a few teleost fishes can be acquired by local dasyatid stingrays as juveniles from amphipods and attach to the spiral valve without developing further or without migrating to the viscera or muscles as paratenic parasites [65]. Stingrays are not typical final hosts for any acanthocephalan.

Information on additional juvenile acanthocephalans that penetrate through the alimentary tract and cause a host response, sometimes severe, appears later in the next section of this chapter.

## *Parasites with Larvae That Can Infect Humans Eating Inadequately Prepared Seafood*

The best-studied parasitic infections in humans eating raw marine seafood are caused by members of the ascaridoid genus *Anisakis* and first recognized in the 1960s in the Netherlands, Japan, and the USA, even though Native Americans in Alaska passed specimens of both *Anisakis* sp. and *Pseudoterranova decipiens* sensu lato in feces [66]. There is now confusion in the names given the human disease because ascaridoids other than species of *Anisakis* also induce similar infections. These agents plus infections and potential infections by non-ascaridoid members of a variety of classes, based on the ability of such species to cause disease in nonhuman mammals, are also discussed in this chapter. In 1988, a group interested in standardizing nomenclature of ascaridoid diseases recommended calling disease involving a member of *Anisakis* as "anisakiasis" and disease caused by any member of the family Anisakidae as "anisakidosis," even though some authors use a name referring to the responsible generic agent or the host response, such as "eosinophilic granuloma." DNA-based techniques have allowed accurate diagnosis, species differentiation, and phylogenetic relationships. Diseases caused by members of other higher taxa also create some confusion with terminology of the names.

Anisakidae (Spirurina, Ascaridomorpha). Species of *Anisakis* are the most widespread cause of notable and severe human disease. Until recently, human infections were divided into two types of juveniles, *Anisakis* type I and type II [67] based on the presence of a caudal spine and the length of the ventriculus, a glandular structure separating the muscular esophagus and the intestine. A group of 21 species based on adults were divided into three primary species [68], including *Anisakis simplex* with ten junior synonyms, *Anisakis typica* with one synonym, and *Anisakis physeteris* with three synonyms. With improved molecular tools, some of those junior synonyms have been accepted, and additional species have been recognized. *Anisakis* type I juveniles comprise the *Anisakis simplex* complex: *Anisakis simplex* sensu stricto, *Anisakis pegreffii*, *Anisakis simplex* C [69], *Anisakis ziphidarum*, and *A. typica*. *Anisakis* type II juveniles comprise *A. physeteris, Anisakis brevispiculata*, and *Anisakis paggiae*. All of these can be differentiated and are considered human pathogens. The differences in pathogenesis and location in the human probably reflects the different species, at least in part. Recent polymerase chain reaction amplification (PCR) methods show that *A. pegreffii* comprises the source of most infections in consumers in Italy but that *A. simplex* sensu stricto is the most common species in people in Japan (Figs. 15.10 and 15.11) even though fish in the Sea of Japan are known to be infected with *A. pegreffii* [70]. Also, *A. pegreffii* seems to cause gastric distress in humans and *A. simplex* seems to mostly affect the intestine.

Fig. 15.10 Section of
Anisakis simplex in ileum of
human patient in Japan. Note
the characteristic eosinophilic
response, referred to as
"eosinophilic granuloma,"
surrounding the diagnostic
section of the worm

Fig. 15.11 Section through
degenerating specimen of
Anisakis sp. in stomach of
experimentally infected
miniature pig showing
juvenile with infiltrated
eosinophils and surrounding
infiltrate consisting almost
exclusively of eosinophils
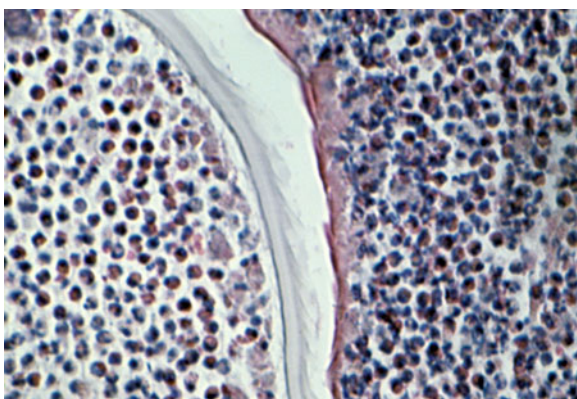
Exceptions involve the abdominal cavity, mesentery, and oral cavity [71]. Juveniles typically measure 1–3 cm in length.

The different species can be differentiated by cetacean host and geographical locality. *Anisakis schupakovi* infects the Caspian seal, *Pusa caspica*, and belongs in the genus as do a couple other species from delphiniids in South America rivers and other isolated habitats. Tabularized reviews list which species of *Anisakis* have

Fig. 15.12 Egg of
Hysterothylacium reliquens
showing infective third-stage
juvenile representative of
ascaridoids infective to
humans. In this species, the
juvenile hatches and the free
juvenile is eaten by an
appropriate copepod, which
in turn is eaten by an
appropriate fish. That fish or
the copepod is eaten by a
paratenic host or by the
definitive fish host

been confirmed molecularly from different cetaceans, cephalopods, and fishes [70]. The life cycle of *Anisakis* spp. includes a cetacean final host, from which worm eggs (Fig. 15.12) are deposited in feces and embryonate in seawater; the active, hatched third-stage juvenile (the same as for *Pseudoterranova decipiens*), also referred to as a larva, is eaten by a crustacean [72]. The juvenile hatching from most nematode groups is a second-stage juvenile. Euphausids are known to host the infective third-stage juvenile. A variety of paratenic hosts, including specific fishes, squids, and crustaceans can acquire and maintain the infective juveniles by feeding on the euphausid or some undetermined crustacean hosts. The appropriate cetacean feeds on any appropriate animal with an infective juvenile. In some cases, there can be a large cluster of these worms, involving third-, fourth-, and fifth-stage juveniles and adults attached within a stomach ulcer. As with several ascaridoids in a variety of genera and host groups, individuals not embedded in the ulcerated tissue will leave the ulcer and forage among the digesting prey in the stomach only to return at a later time.

Cultured fish usually do not exhibit ascaridoid infections present in their wild counterparts because they are fed a diet that does not contain infective juvenile worms. Such is not always the case. Infected prey can enter a sea pen or be fed to the cultured fish in fish farms or cages. When juvenile specimens of the greater amberjack, *Seriola dumerilli*, and three-line grunt, *Parapristipoma trilineatum*, were imported into Japan from China for grow-out in fish farms, they were determined to be heavily infected with *Anisakis pegreffii* [73]. The Japanese Ministry suggested the fish were fed wild infected fish before being exported. In any event, it required that the products, originally grown for sashimi (raw fish), be frozen prior to taking them to market, considerably reducing their value.

Humans become infected with juveniles of *Anisakis* when they eat uncooked or inadequately prepared seafood containing an infective third- or fourth-stage juvenile. Symptoms and signs of infection probably vary by species of *Anisakis*, condition of worm, and condition and genetics of patient. Some patient complaints include sudden epigastric pain, nausea, diarrhea, and urticaria occurring within an

hour but usually at about hour 6. Because infections are difficult to diagnose, the acute infection caused by a migrating or encapsulated juvenile develops into a chronic case with intermittent abdominal pain lasting from weeks to several years. There may be a slight fever and moderate leukocytosis up to 15,000 leukocytes per cubic milliliter. Peripheral eosinophilia can vary from 4% to 41% and will be discussed later in the chapter. The condition presenting other vague symptoms cannot be diagnosed with various immunologic assays because the sera cross-reacts with related nematodes or even with human sera [74], but more specific serological tests are being perfected and various molecular tools are being developed [75, 76]. Most prior cases have been identified morphologically after misdiagnoses of appendicitis, ileitis, cholecystitis, Crohn's disease, and tuberculosis peritonitis, and a variety of neoplasms resulted in resection of the corresponding lesions. In most cases, the worms penetrate or embed in the ileum or duodenum but occasionally penetrate the stomach as for *A. pegreffii*. Anisakiasis occurs in the Netherlands and other European countries, Japan, the USA, and Chile, and cases are remaining high. When the estimated prevalence of *A. simplex* (*A. pegreffii*?)-specific IgE assay in the population of Madrid, Spain, was tested by enzyme-linked immunosorbent assay (ELISA) as well as for cross-reactivity, 12% of the healthy population tested positive compared with 22% in southern Spain determined with a somewhat different technique [76] and without any indication of cross-reactivity. Those testing positive in Madrid were more likely to admit to being habitual consumers of fresh (Fig. 15.13) or undercooked fish as opposed to eating frozen and cooked products like reported for the negative population.

As with "*Anisakis simplex*," "*Pseudoterranova decipiens*" also was recognized as a single species. It infected fishes and humans and could be identified by a morphological diagnostic juvenile and a variable adult, but the adult matured in pinnipeds rather than cetaceans. Recently, however, this agent of human infections that was supposed to occur worldwide has been shown to include several species, most in specific pinnipeds and consequently in specific geographic regions. Molecular and biochemical tools, backed with morphological features, have shown this species to represent a complex of at least six species: *Pseudoterranova decipiens* sensu stricto, *Pseudoterranova krabbei*, *Pseudoterranova bulbosa*, *Pseudoterranova azarasi*, *Pseudoterranova cattani*, and *Pseudoterranova decipiens* E. There are also exceptions to the strict host specificity within this genus: *Pseudoterranova ceticola* and *Pseudoterranova kogiae* both infect the cetaceans *Kogia simus* and *Kogia breviceps* (dwarf and pigmy sperm whales, respectively) [70].

When consumers eat infective juveniles of *Pseudoterranova* spp., the condition is usually not serious. Specimens are typically longer than those of *Anisakis* spp., roughly 4 cm versus 2 cm but dependent on age and development of worm, species, and temperature, and they usually have a more reddish or darker coloration. Whether they occur in the flesh or viscera of the fish depends on the species of worm and species of fish for both *Anisakis* spp. and *Pseudoterranova* spp. Specimens are often noninvasive and void in the feces or vomited; they tickle the throats of those eating inadequately prepared seafood when they migrate from

Fig. 15.13 Italian fisherman
aboard fishing boat with catch
including sardines infected
with *Anisakis pegreffii*. Fresh
fish from boats in the Port of
Civitavécchia, Italy, are
boxed, iced, and sold to
restaurants, seafood dealers,
and others

the stomach back up the esophagus into the oropharynx, or they are coughed up into the mouth. *Pseudoterranova* spp. that cause disease usually involve the mucosal or submucosal tissues of the stomach. The common name of *P. decipiens* from the harbor seal had been "codworm" because the species was so abundant in cod, the second intermediate/paratenic host, especially during strict protection of harbor seal pups, which contained heavy infections. Actually, the "sealworm" consists of *P. decipiens* sensu stricto and *P. krabbei*, which can occur in mixed infections in *Phoca vitulina* and *Halichoerus grypus*, and both infect the cod, *Gadus morhua* [70]. Infections of large, 2–4-mm-long, unidentified fourth-stage juveniles of species of *Pseudoterranova* have become more prevalent and better recognized in Chile during recent years. Of 15 patients, all but one appeared to lose the infection through the mouth after irritation; one was voided through the anus with intense diarrhea. The patients all enjoyed seviche or fried fish [77]. Differing clinical signs between human infections in the USA and Japan may be different because the cause is from separate species. These may be *P. bulbosa* and *P. azarasi* in Japan and *P. decipiens* sensu stricto and *P. bulbosa* in the USA (Fig. 15.14) [70].

The life history of *Pseudoterranova decipiens* sensu lato is more studied than that of known species of *Anisakis* sp. [78]. The life cycle differs slightly from that of known species of *Anisakis* sp. The first intermediate host is a small crustacean such

Fig. 15.14 Commercial fillet with conspicuous specimens of *Pseudoterranova decipiens* sensu lato

as several mycidacean species that spend part of their life in the benthos [79]. The hatched third-stage juveniles are not active. The agent in the crustacean appears to require a fish or large invertebrate paratenic host to complete the history in the pinniped.

Members of *Contracaecum* have been reported from both pinnipeds and fish-eating birds. Even though morphologically they appear similar, those from the pinnipeds and birds are molecularly separated, perhaps with those species from seals representing *Phocascaris*, which is paraphyletic within *Contracaecum* [70]. Like for *Pseudoterranova decipiens, Contracaecum osculatum* from phocid seals consists of a complex of at least five genetically recognized, but not all named, species. There are 11 mammalian species that have been sequenced. Because they are from temperate and polar areas, there is less known about human infections, but they are discussed based on known genetic information [70]. Two human cases of *C. osculatum* sensu lato have been reported from Hokkaido, Japan [80].

Species of *Contracaecum* from birds appear to be phylogenetically separate from the seal species and confused taxonomically. Each of the well-known species actually comprises a separate complex [81]. Members of the genus were not originally thought to infect humans, but at least two human cases of unidentified species from a bird or seal have been reported [82], and at least fourth-stage juveniles of a member of the *Contracaecum multipapillatum* complex (Fig. 15.15) can infect and mature in experimentally infected kittens but not rats, ducks, and chickens [83]. The worms, some attached, were in the intestine, causing hemorrhaging and associated with small ulcers.

Because members of *Hysterothylacium*, many of which were originally placed into the genus *Contracaecum*, mature in fishes, no one expected them to infect humans. Juveniles of *Hysterothylacium aduncum* have been suspected as the cause for eosinophilic granuloma in humans [84, 85], and *Hysterothylacium* type MB larva can produce pathological alterations, including eosinophilic granuloma, consistently in rodents (mice and rats) and rhesus monkey (*Macaca mulatta*) (Figs. 15.16 and 15.17) and probably humans [86]. The juvenile is small (1.4–3.1 mm long) but occurs in large numbers in some of its several secondary intermediate

Fig. 15.15 Red drum,
Sciaenops ocellatus,
exhibiting infective juveniles
of *Contracaecum
multipapillatum* sensu lato in
mesentery. The same species
is also common in fillets or
viscera of other fish species in
coastal Mississippi

Fig. 15.16 Stomach of
rhesus monkey, *Macaca
mulatta*, 5 h post-feeding with
juveniles of *Hysterothylacium*
type MB showing
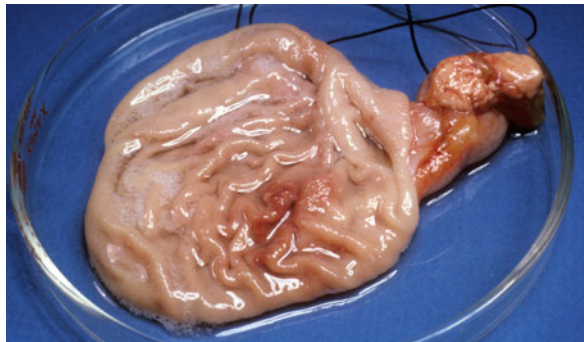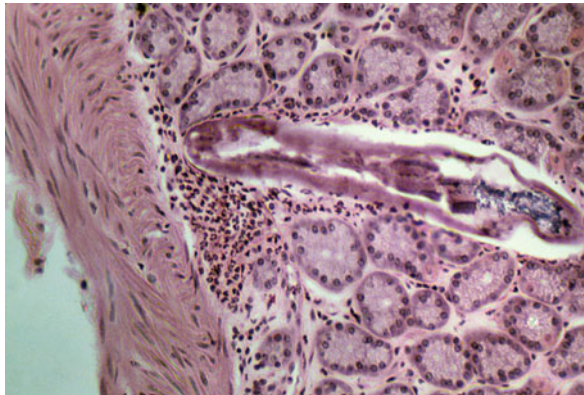hemorrhagic lesions where
juveniles penetrated

Fig. 15.17 Section showing
juvenile of *Hysterothylacium*
type MB penetrating near
muscularis mucosae of rhesus
monkey stomach surrounded
by eosinophils at 1.5 h post-
feeding

or paratenic fish and invertebrate hosts [87]. Worms penetrated the stomach or
duodenum within an hour or so, with the attraction of an abundance of eosinophils
accompanied by an apparent decrease of those leukocytes in the peripheral blood.
Not all species of *Hysterothylacium* will penetrate the alimentary tract or cause
lesions in mammals [87, 88], and juveniles of some species approach 3 cm long.
A Japanese male passed a living young adult female specimen of *H. aduncum* after

suffering chronic abdominal pain and diarrhea for a month. Whether the worm was acquired as a juvenile or an adult was not clear, but he had eaten raw fish, *Gadus macrocephalus* fillet pressed against kelp (Tara no kobujime) a month before onset of symptoms and *Oncorhynchus nerka* sliced and quick frozen (Ruibe), a week before onset [89]; both the cod and salmon host *H. aduncum*. The symptoms cleared following excretion of the worm. Whether *Terranova* type HA juveniles from Hawaiian bony fishes mature in sharks or in a marine mammal is not known, but, when gavaged into the laboratory rat, it migrates into the submucosa and forms a granuloma but does not pass through muscularis mucosae [90].

Other Nematodes

Gnathostomatidae (Spirurina, Gnathostomatomorpha). Gnathostome nematodes are easily recognized by their spiny anterior swelling in both juveniles and adults. They are best known as public health risks of freshwater species but are mentioned here because the fishes that host the infective juveniles move into estuarine and marine habitats where they infect mammals and humans in coastal areas. *Gnathostoma spinigerum* occurs throughout Asia with infected humans primarily in Thailand and Japan, but *Gnathostoma hispidum, Gnathostoma doloresi*, and *Gnathostoma nipponicum* have all been identified from human cases in Japan [4, 91]. *Gnathostoma binucleatum* infects humans eating seviche made with estuarine fish in Sinaloa, Mexico [92], as do other species. With infections of *G. spinigerum* and *G. binucleatum*, the juveniles usually produce a migrating erythema (larval migrans) on the peripheral portions of the body for a few days to several years. Juveniles of the three other species usually migrate into surface skin, forming a serpiginous eruption on the trunk before disappearing spontaneously within 3 months. The juvenile can migrate into the central nervous system (CNS) and other vital organs such as lungs, intestine, genital organs, ear, and nose, occasionally producing a fatal disease, especially when involving the CNS [93, 94].

The typical life cycle starts with adults within a tumor-like mass in the stomach wall and serosa (Fig. 15.18) of the mammal host. Eggs extrude into the stomach and pass out with the feces. First-stage juveniles hatch within 12 days and develop when eaten by *Cyclops* sp. or presumably some other cyclopoid copepods. Development progresses in the copepod hemocoel to the third-stage juvenile and are infective to a variety of fishes, amphibians, reptiles, birds, and mammals, including humans. Perhaps in some species, a specific fish serves as a second intermediate host, but fish serve as a primary paratenic host (Fig. 15.19), allowing the juvenile to migrate or encapsulate in any of the previously indicted paratenic hosts necessary to maintain the population until eaten by the proper definitive host. Human infections can come from any of the paratenic hosts and probably from drinking freshwater containing infective copepods. The importance of marine or estuarine hosts depends on the area, since infections can occur in freshwater or estuaries and freshwater hosts can migrate into estuarine or marine habitats.

Fig. 15.18 Tumor-like mass containing a few adult individuals of *Gnathostoma* sp. in the serosa of the stomach of the raccoon in Mississippi
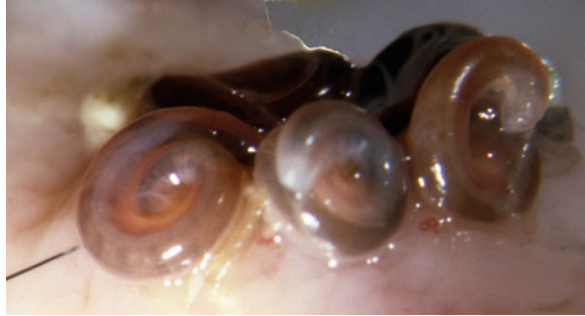

Fig. 15.19 Infective third-stage juvenile of *Gnathostoma* sp. in mesentery of the Gulf killifish, *Fundulus grandis*, in open marine lagoon of offshore barrier island, Horn Island, Mississippi

The true marine counterpart of *Gnathostoma* is *Echinocephalus*, and at least *Echinocephalus sinensis* can probably infect humans. It matures in rays and sharks in the South Pacific and is transmitted by at least the oyster *Crassostrea gigas* and scallops. It was observed throughout the year in Hong Kong, but juveniles administered to kittens, monkeys, and puppies were infective to those mammals from August through October only [95]. When a dose of 600 worms was given to a kitten, most were apparently vomited, but the host died at 16 h. A total of 134 worms were recovered in various visceral organs. All but one of nine other kittens administered with fewer juvenile worms, 130–350, survived, but exhibited visceral larval migrans during the first 40 h. Kittens examined at days 3, 4, and 9 revealed no juvenile worm. The two different monkey species given 80 or 200 juveniles and dogs given larger doses each showed similar results of worms located throughout various visceral organs for the first 40 h post-feeding and no worm after 3 days. Substantial infections were also achieved at 18 h in kittens when fed additional worms acclimated in oysters at 28°C and 33°C [96]. Humans are potentially at risk, especially if eating heavily infected mollusks and any worms enter the CNS. There are several other species of *Echinocephalus*, and some may also have the ability to

Fig. 15.20 Section of adult female of *Angiostrongylus cantonensis* associated with other males and females in pulmonary artery of rat definitive host. The paired creamy-white uterine branches spiral around the hematin-filled intestine giving a diagnostic barber-pole appearance to this 20–30-mm-long worm when alive
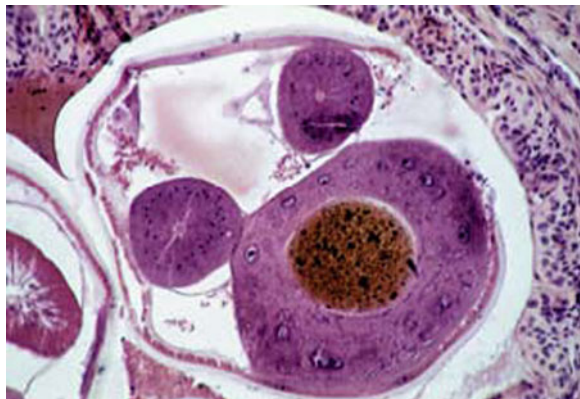

penetrate the alimentary tract of mammals and undergo a visceral or cutaneous migration. Gnathostomes cause both cutaneous and visceral migration, and human cases are probably much more common than diagnosed because specimens of the fast-moving worms are difficult to collect or biopsy; a refined serological method should be able to determine the presence of gnathostomes, and specific diagnoses should allow for a better understanding of marine associations.

A related unidentified juvenile spiruroid nematode known as suborder Spirurina type X has been known to cause creeping eruption in at least 28 Japanese [97]. The juvenile is acquired by eating raw tiny squid (*Watasenia scintillans*) as sashimi in Japan; the serpiginous erythematous eruption along the abdomen took 4 weeks to become apparent. All infections were confirmed with an indirect immunofluorescence test.

Metastrongyloidea (Rhabditina, Strongyloidea). *Angiostrongylus cantonensis* is usually considered a freshwater or terrestrial disease, even though it was originally thought to be acquired from improperly prepared marine fishes. There are several ways that this rat metastrongyle nematode can infect humans that involve estuarine or fully marine situations, and they have been reviewed [98]. The species matures in the pulmonary arteries of rats (Fig. 15.20) and has a rather complicated life cycle. Eggs lodge in the arteries and capillaries of the rat lung where they hatch (Fig. 15.21); the first-stage juvenile migrates through the alveoli and up the trachea before being swallowed and ultimately passed out in the feces. The juvenile develops to a third stage in a molluscan intermediate host. When the juvenile in the mollusk, its slime trail, or a paratenic host feeding on the host or the free juvenile is eaten by the rat, it migrates to the subarachnoid space adjacent to the brain (Fig. 15.22). After a couple of weeks, it forces its way into the venous system to be carried to the pulmonary arteries. Humans are accidental hosts, and the infective juvenile still goes into the brain cavity, but it remains there and often enters the brain tissue (Fig. 15.23) and causes behavior problems and even death in the patient. Because of abnormal behavior in infected humans, many never receive medical attention. Even though the infective juveniles do not necessarily survive as long in marine waters or in marine invertebrate or vertebrate hosts as freshwater

Fig. 15.21 Section of rat lung showing deposited eggs and hatching juveniles of *Angiostrongylus cantonensis* infective to mollusks
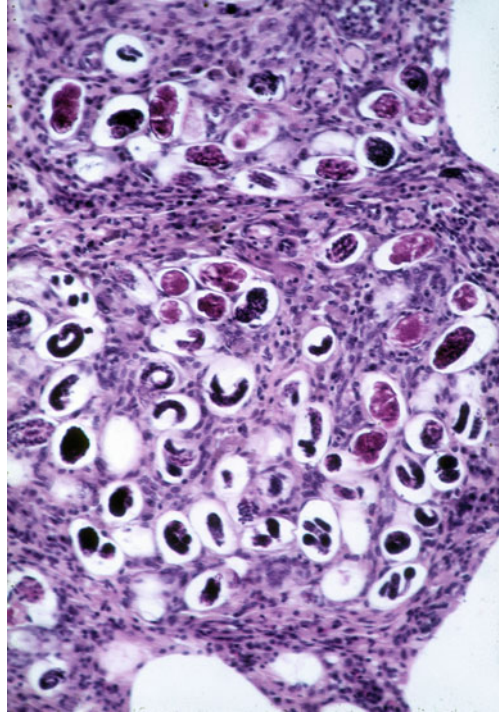

counterparts, they survive long enough to transmit the infections. The eastern oyster, *Crassostrea virginica*, and northern quahog, *Mercenaria mercenaria*, can serve as intermediate hosts in 15 ppt, and large amounts of the oyster are eaten raw. There are many possible ways for humans to acquire the infection, but it is difficult to discern individual cases. In Tahiti, special dishes involve a sauce prepared from uncooked shrimp hepatopancreas (liver/digestive gland) often containing infective juveniles mixed with grated coconut and "coconut milk." Infections originated in the Indo-Pacific, but have spread by rats aboard ships to the Northern Hemisphere. Infections have become recognized in Hawaii, Cuba, Puerto Rico, and the USA through Louisiana.

Dioctophymatidae (Dorylaimia, Dioctophymatida). Juveniles of *Eustrongylides* spp., like those of *Dioctophyme renale*, are relatively large and red, making ingestion seem unlikely. However, when fish intermediate or paratenic hosts are eaten alive whole, a severe peritoneal infection can occur. In the USA, eating live fish is usually a behavior to gain attention or a hazing ritual. Consequently, fishermen eating their bait, tavern clientele taking a wager, and students being initiated as well as unaware consumers eating homemade sushi are likely victims [99]. Unlike *D. renale*, which matures in mammals, all species of *Eustrongylides* mature in birds. Three well-known species are recognized, *Eustrongylides ignotus* from North and South America plus New Zealand, usually infecting herons and egrets; *Eustrongylides tubifex* from North and South America, Europe, and into Asia in ducks, loons, and cormorants; and

Fig. 15.22 Section of fourth-stage juvenile of *Angiostrongylus cantonensis* developing normally in meninges of brain of rat after 29 days without any apparent inflammatory response

Fig. 15.23 Section of juvenile of *Angiostrongylus cantonensis* after abnormal migration into brain of a Thai, showing atypical inflammatory response in human brain
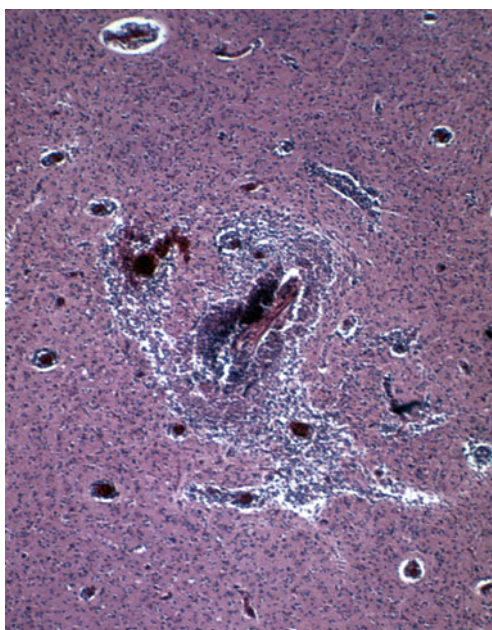
Eustrongylides excisus from Europe, Asia, and Australia in ducks, cormorants, and herons [100]. Juveniles of all should be regarded as a health risk, and all occur in both freshwater and estuaries. In Mississippi, *E. ignotus* occurs mostly in estuarine conditions and commonly spreads to its second intermediate mosquito fish and *Fundulus* hosts by a variety of tubificid and other oligochaete first intermediate hosts. Because paratenic hosts such as largemouth bass and striped bass commonly eat mosquito fish and fundulids and are preferred seafood products, humans dining on these and other fishes wild or in culture [101] in an uncooked state are at a high risk for infection.

Dracunculidae (Spirurina, Spiruromorpha, Dracunculoidea). *Dracunculus insignis*, once thought to be a synonym of *Dracunculus medinensis*, the "fiery serpent" of the Bible and possibly the "snakes" in the caduceus of the American Medical Association and many other medically related societies, constitutes a public health risk. It occurs in the hind legs of the raccoon in the brackish marshes of the northern Gulf of Mexico [1] as well as freshwater habitats throughout North America and presumably is transmitted by paratenic fish and frog hosts. Consequently, *D. insignis* could be acquired by someone eating raw fish, not presently the habit of most persons living in a region abundant in seafood typically eaten in a cooked state.

Other Parasites

Acanthocephala (Spiny-Headed Worms)   Acanthocephalans, especially those that mature in the alimentary tract of marine mammals, pose a threat to those who eat raw fishes. Two palaeacanthocephalans were discussed above as species that occur in the intestine of humans, even though they did not mature in the patients. They also did not penetrate the human digestive tract. Another case of what was tentatively identified as *Bolbosoma* sp., presumably the same marine mammal parasite species mentioned earlier [63], penetrated through the intestine and became encapsulated in a granulomatous mass on the serosa of the ileum in the peritoneal cavity of a 16-year-old boy in Japan [102]. Another species, one that matures in a fish, *Acanthocephalus rauschi*, was discovered in the peritoneum of a native in Alaska. The frequency of acanthocephalan infections in humans, especially native groups from the Arctic where fishes containing infective juveniles are eaten raw, is difficult to discern but is probably substantial [18, 62].

The spiny-headed worm with hooks on the everting proboscis can produce severe lesions if it penetrates through the intestine or occurs in large numbers. An experimental study feeding rats with *Centrorhynchus* sp. from a paratenic host resulted in the worms penetrating the intestine on day 1, entering the muscles by day 5, and producing granulomas on day 20 [103]. When captive primates feed on intermediate hosts or are fed paratenic hosts, they can die when the worms invade beyond the serosa but otherwise produce a focal inflammatory response without harming the host [104]; when large die-offs occur, the invading worms are usually associated with secondary bacterial involvement.

Fig. 15.24 Nymphs of
Sebekia mississippiensis
partially pulled from body
cavity of intermediate host,
the western mosquito fish,
Gambusia affinis, which is
infective to paratenic fish,
turtle, and mammalian hosts,
including humans, or to the
alligator definitive host

Members of the Archiacanthocephala, *Moniliformis moniliformis* from rats and
Macracanthorhynchus hirudinaceus from pig have been reported from man through-
out much of the world, sometimes with serious complications. They are acquired
from terrestrial arthropods such as roaches or paratenic hosts. Nine specimens of the
relatively large related *Macracanthorhynchus ingens*, known from the raccoon,
Procyon lotor, and a few other carnivores, was reported from the intestine of a 1-
year-old child in Texas [105]. The worm is common in coastal areas, so it could be
transmitted to humans in estuarine, freshwater, or terrestrial paratenic hosts as well
as from wood roaches and millipedes, if eaten raw.

Sebekidae (Crustacea, Pentastomida, Porocephalida). Nymphs of pentastomes,
a crustacean group perhaps derived from and of equal status as Branchiura (argulid
parasites of fish and amphibians) also can migrate in and become encapsulated in
human visceral organs. A marine threat would be *Sebekia mississippiensis*, a parasite
from the lungs of the American alligator. Nymphs are abundant in the western
mosquito fish (*Gambusia affinis*) (Figs. 15.24 and 15.25) and present in the Atlantic
croaker and gulf killifish, which may or may not have acquired the infection from the
mosquito fish from estuarine and marine habitats, like its alligator final host. When any
of the intermediate or paratenic fish, snake, or turtle hosts and possibly eggs is eaten by
a mammal, the nymphs migrate and usually become encapsulated by the mammal. The
opossum and river otter were infected in Mississippi, suggesting a human potential host
[106], since humans are known to host nymphs of other pentastomes. This and related
species infect other crocodilians. At least one case report for a related species of

Fig. 15.25 Anterior end of
Sebekia mississippiensis,
a pentastome from the lung of
the American alligator in
Mississippi

Sebekia involved skin dermatitis in a woman in Costa Rica [107]. An autopsy of a woman from Georgia, USA, with presumptive acquired immunodeficiency syndrome (AIDS) revealed the cuticle of an unidentifiable pentastome in her pericardial sac and epicardium associated with tuberculous pericarditis [108]. Non-marine-inhabiting pentastome species of several genera present an equal risk to infect people.

Protozoans   Sarcocystidae (Alveolata, Apicomplexa). The coccidian *Toxoplasma gondii* has final hosts that contain a sexual, coccidian-like phase, restricted to cats and other felines, all terrestrial mammals. Human infection results from shed oocysts in feline feces, by ingesting tissue cysts in warm-blooded mammals and birds, by eating passive vector hosts, and by congenital transmission. Infected humans, predominantly immunocompromised patients or transplant recipients on immunosuppressive therapy, can develop encephalitis, mental retardation, and blindness. If infection occurs for the first time during pregnancy, the parasite can cross the placenta into the brain or eye, and possibly cause miscarriage. The reason for the large number of human infections, perhaps a significant portion in some geographic regions, in the marine environment, may be the low number of oocysts necessary to establish a human infection. As an example, a pet cat sheds oocysts for only a few days during its lifetime, and it produces about 25 g of feces per day. However, in each fecal deposit, tens of millions of oocysts may be produced, and as few as one oocyst can infect a mouse or pig [109]. The small floating oocyst can sporulate into the infectious agent at 15 or 32 ppt and remain infectious for long periods, up to 6 months at 15 ppt [110]. These oocysts, resistant to most disinfectants, however, have not been reported from coastal waters even though present in marine and coastal animals [111, 112]. When experimentally exposed to the eastern oyster, the agent in oyster tissue was infectious to mice for 6 days [113], but, even though experimentally exposed mussels (*Mytilus galloprovincialis*) tested

positive by PCR assay, mice fed with various PCR-positive tissues as old as 21 days demonstrated infections for at least 3 days only when fed digestive gland tissue [114]. At least 13 marine mammals, including dolphins, have shown a positive reaction by agglutinations and indirect fluorescent antibody tests [111, 115]. The California sea otter (*Enhydra lutris nereis*) has been studied most extensively because *T. gondii* has been associated with meningoencephalitis and extensive mortalities in the California population. There are three dominant genotypes, two of which have been identified from human infections; the otter had two genotype isolates in the brain and heart, and one of those was one that was known from humans and the other a rare one [111]. The otter feeds on mollusks, and evidence indicates land-based runoff as the source of the otter infections, suggesting "potent implications for human health" [116]. Perhaps crustaceans also serve as vectors. Additional epidemiological evidence deals with Inuit women of childbearing age in Northern Quebec, Canada, where seals are infected [117]. About half were seropositive to *T. gondii*, and seropositive women were at least four times more likely to have eaten dried seal meat or seal liver than seronegative counterparts. Seronegative women during pregnancy are now instructed to avoid all uncooked or dried meat, particularly seal and caribou, and to refrain from skinning animals.

Microspora. Microspora is a large phylum with obligate intracellular members that infect and obtain their energy from primarily invertebrates and lower vertebrates, cold-blooded vertebrates. The life cycles of microsporidans include several patterns including a direct cycle, a cycle that needs a true intermediate host, a transovarian cycle, and a cycle that passes through a vector without undergoing any development. Members of few genera infect mammals, with *Encephalitozoon cuniculi* being the best known. A few species have been reported from humans, and most of those represent immunologically incompetent individuals [118]. These include *Encephalitozoon intestinalis* and *Encephalitozoon hellem*. Others, such as *Pleistophora ronneafiei*, *Trachipleistophora hominis*, and *Anncaliia vesicularium*, involve species with fish or other cold-blooded hosts. These species are named for material taken from human AIDS or otherwise immunologically incompetent patients, and they may have already been named earlier from a cold-blooded host, even a marine one. *Pleistophora ronneafiei* was suspected to have been injected into a prisoner in Florida with a syringe containing infective material from a fish [1, 118]. A study conducted on other microsporidans to determine human risk from spores reaching coastal and marine waters tested the viability of the three indicated species of *Encephalitozoon* [119]. As expected for spores of species that can infect humans, the viability decreased as temperature increased from 10°C to 20°C. More proliferation of the parasites tested at 0, 10, 20, and 30 ppt occurred at the lower salinity concentrations, with *E. hellem* and *E. intestinalis* surviving better than *E. cuniculi*, in which survival lasted 1–2 weeks at 10 ppt. Those former two still proliferated at 4 weeks, with some proliferation of *E. intestinalis* at 10 ppt at 12 weeks. Consequently, all three species could infect humans and marine mammals or contaminate shellfishes. At least *E. hellem* and *E. intestinalis* can contaminate water with spores passed by aquatic birds [120]. *Enterocytozoon*

bieneusi may be the most common microsporan of man. A total of 81 different genotypes with 111 different genotype names have been identified, with 26 exclusively in humans, but with none from marine animals [121]. The species without a characterized genotype was identified with PCR from an ill bottlenose dolphin (*Tursiops truncatus*) [122].

Myxozoa. Myxozoans, actually multicellular parasites that get placed in most textbooks as protozoans, seem to be bilaterian metazoans, possibly in a sister group to the Nematoda [123], or a trachylinan Cnidaria; members are not thought to infect humans. Spores occur primarily in fishes and amphibians, but atypical species have been reported from a variety of other hosts. Sexual development takes place in oligochaetes and a variety of other invertebrates. Because people often eat fish infected by myxosporidians, they can exhibit spores from the product passed in their feces. There is no indication that any myxosporan has actually infected healthy humans and undergone vegetative reproduction. Two patients were reported to exhibit spores and diarrhea, but at least one of those was an immunosuppressed, HIV-positive patient infected with the human coccidian *Isospora belli* and the other had human helminths *Strongyloides stercoralis, Hymenolepis nana*, and *Ascaris lumbricoides* [124]. Other case reports, such as some in Australia involving eating fish that had been frozen, exist but probably do not represent human infections [125]. Spores of *Henneguya salminicola* also have been reported from human diarrheic feces [126, 127]. Patients had been eating salmon, and, in one case, the spores were misdiagnosed as human sperm, resulting in scandalous consequences [126].

Parasites Acquired When People Have Direct or Indirect Contact with Them

Parasites acquired by contact consist of both helminths and protozoans, but helminths usually actively enter humans by direct contact. In some cases, difficulty exists distinguishing between active and passive contact. Also diseases acquired from agents in marine water fit into different groups. Some originate from estuaries and marine habitats, but most seem to have a freshwater origin but can tolerate marine or estuarine conditions.

Direct (Active) Contact with Disease-Causing Agents

Trematoda

Schistosomatidae. Members of the Schistosomatidae exhibit atypical features among trematodes such as having separate male and female individuals rather than being hermaphroditic and living in blood. They also do not have a distinctive second

intermediate host, but there occurs a juvenile stage, schistosomula, that develops from the cercaria after it penetrates the definitive host. Those species that mature in humans use as their first intermediate host freshwater snails only, but some members in marine snails occurring throughout much of the world that infect birds and mammals produce cercariae that accidentally penetrate humans and establish a hypersensitivity dermatitis.

Dermatitis, known as "swimmer's itch," "clam digger's itch," and other terms, results when humans are challenged by epithelial penetration of the cercariae of some specific schistosome species occurring in the mesenteric blood vessels of the avian and mammalian marine and freshwater hosts. Swimmer's itch is best known for freshwater species; however, several marine species result in similar human responses. Some freshwater cercariae can survive well in low-salinity conditions, but salt usually kills the snail hosts. For example, the cercariae of *Bolbophorus damnificus* can tolerate 2.5 ppt sodium chloride, a concentration toxic for the freshwater snail host *Planorbella trivolvis* that sheds it [128].

For cases of most dermatitis caused by schistosome cercariae, the cercaria hangs in or near the surface of the water where it comes into contact with the appropriate bird or mammalian (such as raccoon) host. Consequently, a pruritic maculopapular rash occurs on the human body in contact with the surface, often around the knees or ankles for those occurring in shallow water. Typically, when the cercaria penetrates human skin that it had previously penetrated with no or limited discernment by the patient, it produces a more apparent prickling sensation for several minutes. Depending on the number of cercariae and the host immune system, this condition may be associated with "macular eruption" (color change in 5–10 mm focal area without elevation or depression) with diffuse erythema or urticaria. Later in the day an itchy "macropapular eruption" (elevated colored area, 5–10 mm) develops and the papules "progress" to fluid-filled vesicles that may become secondarily infected because of the tendency to scratch them. Over the next week to month, the lesions become pigmented and apparent. The "hypersensitivity" reaction is not a true allergic one, and, when the same cercarial species or one with cross-reactivity penetrates the skin in the future, it produces a more severe dermatitis. Occasionally, systemic signs such as fever lymphadenopathy and edema develop [129].

A large number of marine schistosome species probably produce human dermatitis. The number of reported species, however, has remained low because of the inability until now with molecular tools to identify the species, the paucity of studies associating specific species with dermatitis, and the lower likelihood of human contact with cercariae in the marine environment when compared with infective species in freshwater. Swimmers in several freshwater lakes are more prone to continual visits to cercarial/snail-laden portions of the lake. Moreover, the fact that a variety of agents in marine habitats can produce a rash, apparently including non-schistosome cercariae, makes diagnosis of the cause of the rash difficult.

Austrobilharzia variglandis is probably the best known marine cause of the dermatitis, but what is identified as *A. variglandis* probably consists of a complex

of several species from California [130], Hawaii [131], Australia [129], and elsewhere as well as the clam beds of Rhode Island [132] and Connecticut [133] where it is transmitted by *Ilyanassa obsoleta* to a variety of gulls plus the double-crested cormorant and Canada goose. At least *Austrobilharzia terrigalensis* in the silver gull *Larus novaehollandiae* and *Batillaria australis* (as *Pyrazus australis*) in South Australia and Western Australia [134] has been distinguished from misidentified Australian *A. variglandis*. The snail *I. obsoleta* ranges along the Atlantic coast to Florida. *Austrobilharzia variglandis* was reported from the migratory American white pelican in Mississippi [135]. A second species from the northern Gulf of Mexico, *Austrobilharzia penneri*, occurs in *Cerithidea scalariformis*. Gulls are important definitive hosts of marine schistosomes, especially species of *Austrobilharzia*, and since gulls and shorebirds commonly occur in close association with humans, there is a tendency for infections in Hawaii, Australia, and China [129, 136]. There is need to accurately differentiate species worldwide because most or all produce dermatitis.

Members of other blood fluke genera also produce dermatitis. *Gigantobilharzia huttoni* in both the brown pelican and American white pelican and the Antilles glassy-bubble, *Haminoea antillarum* (Cephalaspidea), occurs in Florida [135, 137, 138]; *Gigantobilharzia acotylea* caused dermatitis in the Venice Canal, Italy [139]; *Ornithobilharzia* cf. *canalicula* infects terns, and *Batillaria minima* from the Gulf of Mexico in Florida, USA [140, 141], although the dermatitis attributed to this cercariae was rightfully questioned [138]. Unidentified species producing dermatitis were reported from southern California in *Littorina keehae* (as *L. planaxis*) [142], from eastern Australia in the limpet *Siphonaria denticulate* on rocky shores [143], and from other regions such as Japan [144]. One from California occurs in the Japanese bubble snail (*Haminoea japonica*), which was introduced into San Francisco Bay in about 1999 [136]. Comparative sequence data did not allow information on whether the blood fluke was native to California, introduced from Asia in the snail, or a species from Asia acquired from migrating birds.

As indicated above, most schistosome species responsible for dermatitis are shed from freshwater snails in freshwater. Ten genera contain these species and are cited [145] compared with just three genera from salt or brackish waters. Studies on species of *Trichobilharzia* have provided some information that may relate to human infections. When bird species are experimentally exposed to a mouse, rather than mammalian skin trapping and eliminating the cercariae, it allows some to produce schistosomula. In the case of *Trichobilharzia regenti*, the agent typically penetrates the skin of the bird host and migrates to and becomes established in nasal tissues after passage through the peripheral and central nervous system [146]. When in a mouse, even a small number of the agent in the CNS can produce severe responses [147]. Members of *Trichobilharzia* as well as of *Gigantobilharzia* and *Ornithobilharzia*, especially on the initial exposure to experimental mammals, can progress to the lungs and CNS where they can produce severe pathological alterations [145].

Fig. 15.26 Juveniles of
Strongyloides stercoralis
passing from human intestinal
crypts and representing
zoonotic species, some
released as eggs and others as
hatched juveniles
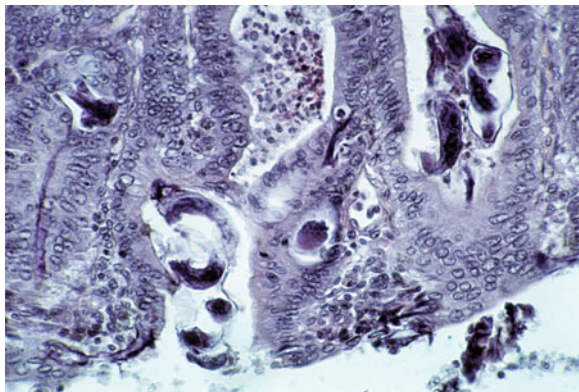
Nematoda

Strongyloididae (Rhabditina, Rhabditoidea). Some members of the nematode genus *Strongyloides* cause a creeping eruption (larval migrans) or rash in people exposed to juveniles and then challenged at a later date. Two species proven to cause the dermatitis in man are *Strongyloides myopotami* from the nutria (*Myocastor coypus*) and *Strongyloides procyonis* from the raccoon (*Procyon lotor*). These are probably the principal agents of what trappers, hunters, fishermen, and oil workers in the northern Gulf of Mexico call "marsh itch." A human volunteer was exposed in his arm to a relatively small number of third-stage juveniles of *S. myopotami* on seven occasions over 11 months before a minor rash (pruritus with small papules) erupted and lasted about 5 days [148]. Following that time, the volunteer was sensitized and juveniles of both species produced a reaction. Those from the raccoon allowed to penetrate the opposite arm produced more extensive reaction at the site of penetration for a few days, but, after disappearing for several days, it reappeared 5 cm from the site. Future exposures responded similarly but the recurrence resulted in a sinuous creeping eruption that spread from the arm to the chest. The juveniles migrating near the surface differs from the reaction by the larvae of blood flukes mentioned earlier. The species from the raccoon is morphologically similar to the human species, *Strongyloides stercoralis* (Fig. 15.26), which can undergo autoinfection. When a challenge dose of 185 juveniles of the raccoon species were exposed, at least one was able to mature and produce juveniles for a few days. The normal life cycle of species of *Stronglyloides* differs from that of most nematodes. The threadlike parasitic female in the mucosa of the intestine deposits eggs passed in the feces as either eggs or first-stage juveniles. In the external environment, the juvenile develops into a feeding rhabditiform juvenile, which in turn develops into an infective third-stage filariform juvenile. The non-feeding filariform can invade the definitive host or develop further into a single free-living generation of both males and females. These mate and produce infective juveniles, even though under optimal conditions, the offspring may develop into a second free-living generation. Infective juveniles penetrate the skin and pass by the cutaneous blood vessels to the lungs, where they break out of the alveoli and migrate by the respiratory tree to the pharynx and intestine, maturing in

mucosal epithelium in about 2 weeks. The parasitic female produces juveniles without being fertilized and is parthenogenic. Most species of *Stronglyloides* infect one or few related amphibian, reptile, mammal, and bird hosts. Probably few species would be capable of producing creeping eruption in humans, but at least two from mammals in the Southern US do. Unpublished research in Mississippi showed that the free-living infective filariform juveniles of *S. myopotami* and *S. procyonis* can tolerate seawater well.

Miscellaneous agents. Unusual circumstances can result in involvement by a parasite not expected to affect humans. For example, a diving accident resulted in such a case with an adult philometrid (Dracunculoidea) nematode, a parasite that matures in non-intestinal sites in fishes. A scuba diver in Hawaii accidently stabbed himself when reloading a spear gun and then later cleaned a fish to eat. He noticed some parasites and discarded the fish, but 3 h later he sensed a 1-cm portion of a red worm protruding from the stab wound. He tried to kill and remove this firmly still-attached worm with vinegar, rubbing alcohol, and forceps. Because of the pain, he had the worm surgically removed by a physician [149]. Other parasites or free-living marine invertebrates can also take advantage of wounds or create their own. Isopods (Crustacea, Peracarida) in the Aegidae, Cymothoidae, Cirolanidae, and other flabelliferan families can produce lesions and urticaria, and are especially annoying. Even an amphipod has produced acute urticaria in a diver in Hawaii [1].

Protozoans

Acanthamoebidae (Amoebozoa). A few different free-living amoebae can cause severe disease if they can enter a human. Best known is *Naegleria fowleri* (Excavata, Heterolobosea, Vahlkampfiidae), which causes fatal "primary amoebic meningoencephalitis (PAM)," but it is restricted to freshwater habitats and moist soil throughout the world. Several species of *Acanthamoeba*, however, occur in marine waters or along marine beaches as well as in freshwater habitats. Species are known to cause chronic granulomatous amoebic encephalitis (GAE), granuloma-tous skin and lung lesions, and amoebic keratitis. The life cycle of *N. fowleri* consists of an amoeboid, feeding, and replicating trophozoite. During periods of low nutrients or desiccation, the motile amoeboid stage forms either a biflagellated, non-feeding, non-replicating trophozoite or a cyst until conditions improve. Human tissues contain only the amoeboid stage. The trophozoite apparently enters through the nasal cavity and migrates into the brain and central nervous system (CNS) along the olfactory nerve. The PAM typically progresses rapidly from a sudden headache and fever to coma and death, without much possibility of diagnosis before death. Species of *Acanthamoeba* do not have a flagellated trophozoite, the amoeboid trophozoite has spike-like pseudopodia and is more sluggish, and three-layered cysts can occur in human tissues. The portal of entry may differ for different species. Invasion appears to be from a primary focus in the skin, lower respiratory tract, or nasopharynx, with dissemination of the trophozoite reaching the CNS through the circulatory system and possibly by crawling along the outside of

blood vessels [150]. Signs of GAE progress much slower and initially are less severe than for PAM; they take weeks or months to result in death, and infections are difficult to diagnose. In contrast with PAM, which affects healthy people, GAE is usually associated with chronically ill, immunocompromised, or otherwise debilitated patients. Predisposing factors for infections include broad-spectrum antibiotics, steroid or antineoplastic therapy, radiation therapy, alcoholism, pregnancy, and bone marrow or renal transplantation. Many of the earlier diagnosed infections, especially in non-compromised patients, were associated with *Balamuthis mandrillaris*, a morphologically similar free-living but genetically different species that has been considered a soil-inhabiting species.

Which species of *Acanthamoeba* infect humans in the marine environment and how they infect the people have not been established. Several isolates of the *Acanthamoeba* complex have been cultured from marine waters or beaches [151–153], and eight strains are pathogenic to mice and potentially to humans. Of 17 species of free-living amoeba cultured from salt water in Northwest Spain, only *Acanthamoeba polyphaga* was pathogenic to mice [154]. Seven species have been associated with human disease, and of these, *Acanthamoeba castellanii, Acanthamoeba culbertsoni, Acanthamoeba hatchetti, Acanthamoeba rhysodes, A. polyphaga*, and *Acanthamoeba griffini* have been identified from amoebic keratitis, a hard-to-treat disease of the cornea [155]. This disease causes severe ocular pain, photophobia, recurrent epithelial breakdown, and edema, and confirmed by trophozoites and cysts in a corneal scrape or biopsy. It was recognized in 1973 and not common until 1985 when contact lenses became popular. Lenses are maintained in a saline or tap water solution in a reusable storage case that can get contaminated.

Members of *Acanthamoeba* also have the ability to harbor viruses and bacteria, perhaps serving as vectors or reservoir hosts for a variety of agents. Isolates of *Acanthamoeba* from water sources in the Canary Islands revealed four different serotypes of adenoviruses, one related to ocular disease and the others unknown, probably respiratory, gastroenteritis, or neurologic [156]. A large DNA mimivirus was identified from *A. polyphaga*. Experimental studies [157] have shown that coxsackie B3 viruses can be adsorbed on the surface and accumulated within *A. castellanii*. The same marine amoeba can also host the bacteria *Chlamydia pneumoniae* and *Legionella pneumophila*. It did not prey on *Vibrio parahaemolyticus*, but it secreted a factor that promoted survival of the bacterium in coculture, suggesting the amoeba provides a survival to the extracellular pathogen in the environment [158]. These and other facultative parasites probably contribute greatly to transmission of microbial disease agents as can obligate parasites [159].

Nonparasitic: But Confused with Parasites

In the marine environment, there are, in addition to schistosome cercariae, a variety of nonparasitic agents that cause similar appearing rashes. The stinging nematocysts of several members of the phylum Cnidaria (previously called

Fig. 15.27 Visiting, teaching marine biologist at San Salvador, The Bahamas, exhibiting back with hypersensitive rash developed after and presumably caused by exposure to challenge dose of planula larvae of the thimble jelly, *Linuche unguiculata*

Coelenterata) have been held responsible for "seabather's rash" or "seabather's eruption." Members usually go through an alteration of generations with asexual polyploidy and sexual medusoid generations, but there are variations of this life cycle. Divers can brush against the nematocysts of fire corals (Hydrozoa, Anthomedusae, *Millepora* spp.) with their encrusting calcareous coral-like skeletons, while bathers can become entwined in expandable fishing tentacles lined by batteries of nematocysts of the "man-of-war" (Hydrozoa, Siphonophora, *Physalia* spp.) hanging from the gastrozooid, maintained on the surface by a gas-filled float. This floating colony appears like a medusa but is actually a highly modified polyp. When the long, up to 13 m, tentacle of the Atlantic *Physalia physalis* washes onto sandy beaches, it gets ground up in the surf, leaving minute pieces with undischarged batteries of nematocysts to get into bathing suits or work gear. Medusa of several jellyfishes (Scyphozoa) have been associated with stings and rashes. Moreover, some sea wasps and box jellyfishes (Cubozoa), exhibiting square cross sections of their medusa, have been shown to cause human fatalities. The planula larvae of true jellyfishes, such as the thimble jelly, *Linuche unguiculata*, get under swimsuits, and challenge exposures produce a hypersensitive rash reaction (Fig. 15.27). Cases are common along the Southeastern Atlantic US, Mexico, and the Caribbean Sea, but exact identifications and prevalence of these and other cases worldwide require study. Systemic symptoms from the planulae are considered more common than with schistosome dermatitis [129]. The sting from the planula larva of the burrowing anemone (e.g., Anthozoa, *Edwardsia lineata* as *E. leidyi*), appearing as a "tiny pink egg" [160] attached to the inner lining of bathing suits, has been associated with seabather's eruption in Long Island, New York, from mid-August through early September. The planula also parasitizes ctenophores, which can get caught in swimming apparel and transmit the condition. Not all rashes attributed to blood flukes or cnidarians come from those agents. Many cases also result not from ejected toxins but from rubbing between the bathing suits and human skin of molluscan opisthobranch gastropod shells, sponge spicules, and spines of zoea and megalops larvae of crabs and shrimps, swarms of

which can occur seasonally in heavy concentrations. Rashes attributed to "sea lice" are misleading; the term "sea lice" is a common name usually attributed to a variety of parasitic copepods but primarily *Lepeophtheirus salmonis* infesting salmon. None of these copepods produces human rashes, but some marine dermatitis caused by cnidarians has been referred to as caused by sea lice. Some polychaetes (Annelida) produce an irritating rash as does contact with the excrement of some sea cucumbers (Holothuroidea) or eating some inadequately cooked species. Contact with Cyanobacteria (previously referred to as blue-green algae), such as *Lyngbya majuscula* growing on sea grasses in Hawaiian waters, has been identified as causing "swimmer's itch" or "seaweed dermatitis." The agent is called fireweed in Australia. Rashes also result from some "harmful algal blooms" (red tide) throughout the world. The Internet includes some incorrect or misleading information, but researchers are tackling some of the cases, especially since they have a large impact on recreational and occupational activities in the marine and coastal environments.

Indirect (Passive) Contact with Disease-Causing Agents

Eating products contaminated with an agent or drinking contaminated water are herein considered differently than eating infected products because the food or water contaminated with the organism serves as a mechanical or passive vector of the agent rather than as a host that the organism requires for its survival. Also, the agent does not actively penetrate the skin as achieved by an agent of swimmer's itch or marsh itch.

Trematodes

Humans occasionally get infected with trematodes in a passive process. A person does not knowingly eat a product, and the parasite does not actively penetrate a host. For example, a seafood handler who came in contact with an abundance of fresh killed coho salmon (*Oncorhynchus kisutch*) known to be heavily infected with the trematode *Nanophyetus salmincola* developed an infection exhibiting acute clinical signs. He denied eating raw or cold-smoked fish and rarely ate any seafood products. Alternatively, he could have transferred the minute metacercariae on his hand to his mouth while smoking [1, 43].

Protozoans

Giardiinae (Excavata, Diplomonadida). Species of the flagellate *Giardia* have long been associated with severe diarrheal disease in humans. They are typically considered as freshwater or terrestrial species acquired when people drink contaminated water, but they have recently been found to be abundant in marine waters. The agents were thought to be confined to those discharged in raw sewage disposal and

from recreational swimmers throughout the world, both raising public health risks. Consequently, infectious cysts or the trophozoites of the flagellates have been detected along some marine beaches near sewage outfall and canals influenced by runoff, where bathing is common in Hawaii [161], as well as in Panama and Hong Kong [111]. The trophozoite is a microscopic pear-shaped organism with four pairs of flagella. Two of these occur within the resistant cyst, and when the vertebrate host acquires the cyst, it excysts, releasing the trophozoites which reproduce asexually by binary fission and remain in the lumen or attach to the mucosa of the small intestine. Under the appropriate conditions, encystment occurs and both the cysts and trophozoites pass out with the feces. The taxonomic classification of members in the genus is not well established, but there are five recognized species (e.g., [162]), and the genetic characterization of *Giardia duodenalis*, also referred to as *Giardia intestinalis* or *Giardia lamblia* and the species with the widest host-specificity, groups at least seven genetic assemblages (genotypes) including Assemblage A, the one most commonly found in humans [163]. *Giardia* sp. occurs widespread in the river otter (*Lontra canadensis*) from the marine waters of Puget Sound Georgia Basin of Washington [164], but species also occur abundantly in the feces of a variety of temperate and Arctic marine mammals such as the right whale (*Eubalaena glacialis*, 71% prevalence), bowhead whale (*Balaena mysticetus*), ringed seal (*Phoca hispida*, 65%), California sea lion (*Zalophus californianus*), and harbor seal (*Phoca vitulina*) but not the beluga whale (*Delphinapterus leucas*) or bearded seal. Assemblage A occurred in the harp seal (*Phoca groenlandica*), gray seal (*Halichoerus grypus*), and harbor seal (*Phoca vitulina*) but not the beluga whale [165]. Moreover, despite the common occurrence of infections in adult seals and cyst contamination on ice floes, cysts were not encountered in seal pups less than 1 year of age. However, the epidemiology and potential for zoonotic transmission in marine systems remains virtually unknown [164], but the genotypes of *G. duodenalis* in the harbor seal in Puget Sound, Washington, were the same as from a canine, from other sites, and were mostly novel genotypes [166]. Cysts remain infective for about 56 days in relatively deep freshwater cool lake water, but at least those of *Giardia muris* become inactivated by the combination of salinity and sunlight in warm Hawaiian marine beach water within 3–6 h [167]. In the Netherlands where the salinity remains stable at 28–31 ppt, *Giardia* cysts were detected in what was considered to be a low estimate of 12% of oysters, where viability was presumed to be preserved, representing some public health risk to those consumers who ate the oysters raw [168]. Cysts have also been filtered out of the water and concentrated by the blue mussel, *Mytilus edulis*, and other bivalves, and this tool has been used to monitor *G. lamblia* in Ireland [169] and for that and other species or genotypes elsewhere [112, 170]. Depending on the size and species of bivalve, it can filter as much as 20–100 l of water per day. Much information on human health risks from beaches and marine waters, animal health, source of agents, dispersal of agents, and primary vectors can be established by a variety of surveillance programs. For example, a survey of live and dead, stranded and bycatch, birds, dolphins, seals, and fishes was conducted in the Northwest Atlantic using PCR techniques [171]. With the exception of infections in seals,

those of *Giardia* spp. were more frequent than those of *Cryptosporidium* spp., to be discussed next.

Coccidiasina (Chromalveolata, [Alveolata, Apicomplexan]). Coccidian species in the genus *Cryptosporidium* pose a stronger human risk for infections than those in *Giardia* [112], especially species in estuaries compared with freshwater [169]. Typically, marine mammals, invertebrates, and marine water are examined for the agents concurrently with *Giardia* because the agents are transmitted by the fecal-oral route from humans and other mammals. Thick-walled oocysts are passed in the feces as a resting cyst, each with four sporozoites infective to the vertebrate host, where development occurs. Additionally, there is a thin-walled cyst that cannot survive long in a harsh environment, but it may lead to endogenous autoinfection. This seems to be especially true for persistent infections in immunocompromised patients. A total of 14–15 species are accepted [172, 173], and several are known to infect humans: *Cryptosporidium hominis* (previously *Cryptosporidium parvum* genotype 1), *C. parvum*, *Cryptosporidium meleagridis, Cryptosporidium felis, Cryptosporidium canis*, and *Cryptosporidium muris*, with most human infections from *C. hominis* and *C. parvum*. Human agents have been detected in more marine recreational areas than *Giardia*. They occurred in Hawaii, Panama, Puerto Rico, Australia (tidal area of Georges River), and Hong Kong [111]. In fresh deionized water, oocysts of *C. parvum* can survive for at least 6 months at 0–20°C, 3 months at 25–30°C, 1 week at 35°C [172]. As many as 10^9 to 10^{10} can be excreted from bovine calves or non-compromised humans per week, and as few as 30 oocysts have been known to infect a human volunteer [174]. Bioassays in mice show that oocysts of *C. parvum* can survive 12 weeks in 30 ppt at 10°C and at 20°C for 12 at 10 ppt, 8 weeks at 20 ppt, and 4 weeks at 30 ppt, which was long enough for the oocysts to be removed by filter feeding bivalves such as the eastern oyster (*Crassostrea virginica*) [170]. Literature reports consist of a variety of bivalve mollusks from seven countries that contained *Cryptosporidium* as detected by immunofluorescence microscopy, bioassay in mice, or molecular methods [111]. In North America, oocysts have been detected from New Brunswick to Texas. Gill washings from the oyster near a large cattle farm and septic tanks were positive for the oocysts and infective to mice [170]. The agents occur in hematocytes as well as on gill surfaces, and they were more abundant after rainfall events, with two of the four identified species (*C. hominis* and *C. parvum*) infective to humans [111]. The same two species plus *C. meleagridis* also occurred in North American commercial products [111]. Species have also accumulated in hard clams, bent mussels, and zebra mussels [175]. To date, no human cryptosporidiosis cases have been linked to eating raw shellfish [111], even though some human genotypes have been concentrated in various bivalves. There is a higher prevalence of infection of both *Cryptosporidium* spp. and *Giardia* spp. in the ringed seal and right whale than in reported terrestrial mammals, and those infections might result from ingestion of contaminated water or from prey that had concentrated oocysts [176]. Other hosts of *Cryptosporidium* spp. include the California sea lion, bowhead whale, dugong (*Dugong dugon* in Australia), and marine foraging river otter but not the bearded seal and beluga whale [164, 176]. Isolates from the ringed

seal from Nunavik, Quebec, were genetically characterized using two gene fragments and actin loci as *C. murus* plus two novel genotypes that were distantly related [177]. The risk for recreational bathers to come into contact with *C. parvum* was significantly greater on weekends than on weekdays, when the number of bathers was lower. The same was true in that Chesapeake Bay marine beach for *G. duodenalis* and *Enterocytozoon bieneusi*, a microsporidian to be discussed below [178]. The proportion of water containing the agents also correlated significantly with enterococci counts. The study suggested using those counts to indicate the presence of the parasites and recommended preventing diapered children from entering the water, restricting the number of bathers in the recreational areas, advising those with gastroenteritis to avoid bathing, and using showers prior to and after bathing.

Birds contract cryptosporidiosis with at least five avian species and numerous avian genotypes, and some of these have been investigated in regard to infecting mammals. They can also serve as vectors of *Cryptosporidium* spp., *Giardia* spp., and microsporidians infective to humans. In fact, aquatic birds seem to play a substantial role in contaminating water around the world, and managing water resources could benefit by incorporating protection measures for pathogens linked to these birds [120, 179]. In contrast, little research has been conducted to evaluate the public health threat of species of *Cryptosporidium* and related genera described from marine and freshwater fishes and from amphibians and reptiles. The various taxa and isolates have been reviewed [180].

Entamoebidae (Amoebozoa). Some strains or species of amoeba *Entamoeba histolytica* complex also are zoonotic threats. Poorly documented records of infections in the bottlenose dolphin (*Tursiops truncatus*) from Cuba, Mexico, and other locations suggest a relationship among the marine mammals, sewage, recreational beaches, and human infections. Researchers at the Gulf Coast Research Laboratory and the American Type Culture Collection have seen cysts but were unable to culture material from the bottlenose dolphin (*Tursiops truncatus*) from Mexico. Because there were slight morphological differences between it and *E. histolytica* sensu stricto, this subject deserves a critical investigation to determine if the dolphin form is restricted to marine mammals and whether it can cause fulminating dysentery, bloody diarrhea, fatigue, and abdominal pain in humans. Possibly, the agent was acquired by the dolphin from humans during associated recreational activities or from human sewage.

Parasites That Produce Excretions or Secretions That Result in an Immunological Response in People

Ascaridoid juvenile nematodes produce excretions and secretions (ES products) that elicit immunological responses. These responses include both the allergic response by the host to living worms migrating into or through tissues and true anaphylactic reactions triggered by dead or living worms by food-borne, airborne,

and skin contact routes [75]. Ascaridoids are unusual among nematodes to produce such reactions. Most concerning is that some sensitized individuals respond to infected cooked seafood products and even chicken that has been fed fish meal made from infected fish products [181].

The tissue migration by ascaridoids is made possible by potent proteolytic enzymes released from the esophageal gland and excretory cell through separate anterior openings. These contain hyaluronidase, serine proteases, anticoagulants, and numerous other identified and unidentified substances, but only specific ones probably produce the well-defined, erosive, hemorrhagic lesions in the gastric mucosa and these and others produce other effects in the human accidental host. Metabolic products released by the migrating juvenile also produce humeral and cellular responses, especially involving the acute lesions. These products, also including surface and somatic components of the juvenile, form insoluble immune responses with antibody. Some also cause direct IgE-independent degranulation of mast cells, at least in sensitized mice, and chemotaxis of eosinophils associated with thermolabile factors from the parasite, and produce the characteristic local response in the digestive tract but not systemically like in most other helminth infections [75]. When either living or dead individuals of *A. simplex* are ingested, cholinergic hyperactivity and adrenergic blockade can be rapidly induced, resulting in focal reactions associated with living worms but widespread along the entire bowel if the worm becomes ruptured or disintegrated. These activities may explain why 70% of the symptoms in *A. simplex*-induced anaphylactic reactions involve the digestive tract.

Anaphylaxis appears to be complex. Rodent studies demonstrate a mixed Th1/Th2 pattern of cytokines when the host is sensitized and challenged intravenously with certain parasites, but not when challenged orally. When the antigen is an extract of *A. simplex* proteins or a live worm, a strong Th2 response occurs, resulting in scratching, irritability, diarrhea, and puffiness around the eyes within 1 h. The multifaceted immune hypersensitivity reactions after induction by members of the *Anisakis simplex* complex have been investigated in terms of a wide range of parasite products and host cells; a concise helpful review treats all the known facets [75]. Hypersensitivity is usually diagnosed by skin prick tests and in vitro confirmation (specific IgE, histamine release, and basophil activation test). The skin prick test for *A. simplex* was first used in 1995 and now is used by physicians as an important test for cases of urticaria and anaphylaxis [75, 182, 183].

Recognition of allergic signs has been emphasized because of cases in Spain and South Africa. In Spain where fish is consumed abundantly, what was referred to as *A. simplex* is the most important hidden food allergen in the adult population suffering acute urticaria and anaphylaxis. It comprises as much as 10% of the anaphylaxis previously diagnosed as idiopathic [75], if the specific immunoglobulin E (IgE) detection by ImmunoCAP assay did not overestimate the number of sensitized subjects. Anisakiasis in Spain is caused primarily by eating pickled anchovy (*Engraulis encrasicholus*). That fish plus European hake (*Merluccius merluccius*) and cod (*Gadus morhua*, just in Atlantic Ocean rather than in both the

Mediterranean Sea and Atlantic Ocean) are eaten by allergic patients. Half the 64 allergic patients in one report required emergency treatment [184]. Half of the patients presenting signs of infection said they ingested raw fish, but the remainder ate cooked fish or, in rare cases, canned fish. Allergic cases requiring hospitalization demonstrated respiratory arrest, severe shock, and persistent angioedema.

In Spain, the matter of allergic responses in "gastroallergic anisakiasis" remains complicated and seems to be reported primarily from some regions in Spain. Patients entering the hospital emergency room with a severe acute epigastric pain and positive *Anisakis* prick tests plus total and specific IgE assays were divided into two groups. One group was diagnosed by the presence of at least one worm in the stomach, and the other group which had no worm seen in the stomach. Most patients had just eaten raw or pickled anchovies. Both groups averaged about 5 h, but up to 26 h, between intake of raw fish and onset of hypersensitivity symptoms, and no significant difference occurred between the two in their allergic symptoms of urticaria, angioedema, erythema, bronchospasm, and anaphylaxis, suggesting a borderline condition between a food allergy and parasitic disease supporting quick removal of the worm from the stomach. Moreover, only 26 of 40 patients required drug therapy to manage the allergic reaction, with only three requiring it for more than 1 day, suggesting an acute, self-limiting disease. In contrast, anaphylaxis can be life threatening, but abdominal symptoms disappeared within a few hours after removal of the worm [185]. When a portion of the *Anisakis*-sensitized groups with gastric worms, without gastric worms, and with no gastroscopy conducted (when symptoms did not persist for more than 8 h) were challenged with frozen worms from the blue whiting (*Micromesistius poutassou*, from either Atlantic or Mediterranean sources) and later from undocumented hosts on multiple occasions, there was no patient who suffered a reaction. This lack of a response to the thermostable proteins suggested that live worms had to be present for the allergic symptoms to occur [186]. Because the specimens from the Mediterranean Sea were from the anchovy, they were *A. pegreffii* [70] and not *A. simplex* as reported, even though if some material came from the Atlantic Ocean, both species could have been present. However, human infections with *A. pegreffii* are typically gastric in nature, and those of *A. simplex* are usually intestinal, based on findings from Japan, where 10% of healthy adults were seropositive against the *Anisakis* antigen [187]. The fact that some individuals exhibit allergic episodes when no viable nematode is present may express a difference between the effects of *A. pegreffii* and some other species of *Anisakis* or may be variation in responses by individual patients.

The cases in Western Cape Province, South Africa, involved workers in fish-processing plants. An epidemiological study of 578 workers from two large-scale plants reported 30 workers (5%), who said they had allergic symptoms to seafood. A total of 87% said symptoms occurred after eating fish, 40% after handling them, and 17% after smelling them. A prevalence of sensitization was tested as 6% with a higher value of 8% sensitive to *Anisakis* [188, 189]. *Anisakis*-specific IgE reactivity in the workers was determined to be associated with bronchial

hyperreactivity and dermatitis. In corresponding mice studies, the juvenile worm induced a striking Th2/type 2 response. The investigation suggested that consumers acquiring an infection most likely can acquire sensitization to anaphylaxis, but that exposure to *Anisakis* proteins alone may be enough to elicit allergic reactions in sensitized individuals. In other words, occupational exposure to infected fish or fish meal constitutes a risk factor for developing sensitization to *Anisakis* or other ascaridoid-related allergic disease.

Historically, eating fish fillets infected with the plerocercoids of trypanorhynchean cestodes has been considered harmless with rare exception. All members of the group mature in elasmobranchs. In fact, some infected intermediate host products are preferred over noninfected counterparts; one example is the flesh of the Atlantic pomfret, *Brama brama*, also known by a variety of other common names, infected with plerocercoids of *Gymnorhynchus gigas* and preferred by some Portuguese [99]. Recently, the rat and mouse were orally inoculated with plerocercoids of *G. gigas* to test for anti-worm IgG, M, and A (H + L) levels in intestinal fluids and serum as well as specific serum IgE levels by enzyme-linked immunosorbent assay (ELISA) [190]. Levels of all increased in the challenged mouse, producing distress. The rat had an increased expression of heat shock proteins in the intestine and spleen. Repeated exposure to the worm in the rodents produced clinical signs appearing progressively more rapid and lasting longer, suggesting that feeding on infected fish triggered production of anaphylactic-type antibodies in rat, mouse, and, by implication, human.

Management, Control, and Treatment of Parasites Affecting People

Management

Management starts with education about parasites. Parasites are or may be involved with a recognized or unrecognized problem but are not necessarily harmful or bad, if certain practices are recognized or followed by regulating agencies, funding agencies, the seafood industry, consumers, and those using marine waters for occupation or recreation. Harm can be done if partial data deludes people not to eat seafood or not to enter the water.

Being alerted to public health risks allows people to make choices about what product to eat, how it should be prepared, when to avoid a product, when not to enter specific bodies of water, and when to visit a physician. If the industry provides a safe and sanitary product to its customers, the number of customers will increase.

Control

The best way for processors and restaurants to control infections with most helminths and most protozoans is to freeze or heat the product. Some restaurants flash-freeze products sold as fresh to avoid infective products, and apparently few customers can detect the difference from the never frozen products. If products with few or no parasites can be provided to these groups by fishermen or fish farmers, that product will be in higher demand, able to meet regulations, and more valuable. Controlling infections by interrupting a parasite life history link and harvesting from a noninfected region are easy ways to avoid future problems.

Heating and Freezing

Historically, the US Food and Drug Administration (FDA) [191] has recommended food-service industries to cook fish products to an internal temperature of at least 63°C by conventional methods or to an internal temperature of 74°C by a microwave process rotated midway through the process and allowed to stand for 2 min afterward. Any process sufficient to kill bacterial pathogens also will kill parasites.

However, the FDA, under the seafood Hazard Analysis and Critical Control Point (HACCP) regulations, will allow for a facility to submit to it an alternative proposal with justification to modify the recommendations. When ten specimens of *Anisakis simplex* sensu lato were embedded into an approximate 1.8-cm-thick portion of a fillet of the arrowtooth flounder (*Atheresthes stomias*) and microwaved, the viability of the worms was assessed. Survival was determined as 31% at 60°C, 11% at 65°C, 3% at 74°C, and 0% at 77°C [192]. Thick salmon fillets with *Diphyllobothrium* spp. and *Anisakis* spp. require additional cooking. Microwaving pork chops with *Trichinella spiralis* still had active juveniles at 82°C, and microwaving can produce temperatures differing by 20°C when measured just 1 cm apart. The purpose of HACCP Regulation, as implemented in 1997, is for processors of fish and fisheries products to develop and implement reasonable plans for safe and sanitary procedures. Recommendations are established at each point that specific parasites can be detected, eliminated, or treated, and FDA will guide and work with those people and facilities in the industry to provide their specific appropriate plans and systems (www.fda.gov/Food/FoodSafety).

Freezing infected fisheries products is also not clear because the effectiveness depends on the temperature of the process, the length of time undergoing freezing, the length of time held frozen, the fat content of the product, and the species and stage of the parasite. For example, most cestode plerocercoids are more susceptible to freezing than nematode juveniles, which in turn are more susceptible than encysted trematode metacercariae. FDA recommends the following: freezing and storing at −20°C or below for 7 days, freezing at −31°C or below until solid and then storing at that temperature for 15 h, or at −4°C for 24 h. The fishing industry has used a process

called "blast freezing," which rapidly reduces the temperature to −40°C, and it has shown to effectively kill parasites and not have much influence on flavor or texture of the product. Also, most US sushi bars freeze their fish [1].

Other communities have different recommendations or regulations. The European Food Safety Authority presented a scientific opinion on food safety related to parasites in fishery products [193]. The presence of *Anisakis* was of major concern for products intended for marinating, salting, and eating fresh. Treatments should provide an equivalent level of protection as freezing at −20°C for ≥24 h, at −35°C for ≥15 h, or −15°C for ≥96 h at the product's core; heat treatment should be >60°C for at least 1 min. These are less rigorous than those in the USA but more than some other regulations. Emphasis focused on the insufficiency of many traditional marinating and cold-smoking methods to kill the juvenile worms. Some metacercariae can tolerate more-harsh temperatures and treatments than other parasites.

Detection of Parasites and Culling

Large parasites and those that contrast well with the infected seafood product are those most easy to detect. Many of these are not harmful to consumers, but they will have an influence on whether consumers will purchase the products or eat them in a "raw" state. Some, such as *Anisakis* spp. and *Pseudoterranova* spp., constitute a public health risk, and these have attracted research in detection methodology. The efficiency of successively more accurate methods for detecting these nematodes range from (1) gross visual inspection, (2) candling on a light table, (3) candling of belly flaps (ventral portion of fish), (4) ultraviolet illumination (UV) of frozen fillets, (5) pepsin/hydrochloric acid degradation, and (6) UV illumination of frozen remains [194]. Candling or passing a product over a light table, either sandwiched between two glass or plastic plates, sliced fillet, or whole fillet, has been a popular method for several decades and usually the recommended method during industrial processing of marine fish intended for human consumption. European Union regulation 91/493/EEC and Norwegian fish quality regulations require removal of any visible parasites seen in gross inspection of commercial products by spot checking [194]. The more efficient methods indicated above are occasionally used for scientific purposes, and in one article [194] examining Norwegian spawning herring, mackerel, and blue whiting from the Northeast Atlantic Ocean for nematode juveniles in fillets, the detection efficiency for candling was 10% or less. After testing with the other listed methods, the highest values were obtained with UV illumination of remains after enzymatic digestion. Size and thickness of fillet as well as texture and color of flesh influence the efficiency. Pressing 2–3 mm layers of fillet with a hydraulic and manual press between 12-mm-thick acryl glass sheets, deep-freezing the removed cake in a plastic bag, and examining the sample in the bag with UV light at 366 nm more than doubles the recovery rate of candling at 1,500 lx; this method is rapid and good for surveys [195]. Imaging spectroscopy provides a promising method to detect spectral and

spatial information from nematodes in cod as deep as 0.8 cm below the surface of the fillet. That is deeper than can be determined by manual inspection, but the instrumentation has not been perfected enough for commercial use [196].

Fish Farming Practices

In Europe, apart from farmed Atlantic salmon, sufficient monitoring data on marine products are not available [193]. A wealth of information occurs in the literature and on Internet sites about how to detect and treat parasites and control infections, usually with focus on health of the cultured product rather than on a human consuming or coming into contact with the product. This chapter does not recommend or discuss the numerous specific methods for use in fish farms and other aquaculture operations, but parasites are best managed in those facilities by breaking the link in the life cycle that can disrupt or eliminate the infections. Fish in culture can have more or fewer parasites than wild products, and the degree relates to several factors [1].

Treatment

This chapter mentions a few chemotherapeutic treatments for infected patients but purposely does not attempt to provide compounds for all taxa. People are becoming resistant to some compounds, some compounds have serious side effects, the Internet contains both good and poor or misleading advice, and new compounds are continually being tested or made available. Because a reader should use or recommend the most reliable treatment for the agent or strain, the reader should seek professional advice. Recent information has been compiled such as that found in the most recent edition by Garcia listed in the "Books and Reviews" or some other recent source. The Centers for Disease Control and Prevention (CDC) has a website with much helpful information and a willingness to respond to individuals that contact it. On the other hand, methods to avoid infections by properly freezing or cooking a product occur above. Of course, because of well-entrenched customs, the wonderful flavor of raw or specially prepared seafood, and the lack of knowledge about most parasites, inadequately prepared and uncooked products will always pose a risk of infection.

Future Directions

As seen already in this chapter, a wealth of information has been acquired in the last few decades regarding parasites that pose a public health risk. Many questions remain unanswered and lifetimes of research will be required to answer these and additional questions regarding the risks and what to do about them. Some of the suggested paths for future research occur below in five overlapping categories:

1. Harmful parasites presently unknown or unrecognized still need to be discovered. Because of new cuisines, opportunities to get infected, methods to characterize agents, and methods to detect agents as well as variability in human responses to parasites, those parasites need to be determined that are capable of infecting humans. As seafood products are overfished or the consumers increase in number, seafood products need to come from new areas or new products. Consequently, the risk for acquiring an infection from a product historically recognized as safe increases without the consumer's knowledge. Protozoans cannot be seen without a microscope, and infections by marine species and freshwater species flushed into the marine environment are being recognized as important agents affecting human health, and the marine environment probably contains many more of these than recognized.

2. An improvement in taxonomy of many parasitic groups will allow the scientific community and public to know what species or genotypes are involved with diseases in different areas resulting from different parasite life histories. Morphologically similar species can elicit entirely different responses, and the knowledge of what specific agents are where and what signs of disease result from which of those agents comprises a fundamental cornerstone of biology and research. Taxonomic research will involve morphological treatment of quality specimens from both humans and natural hosts backed up with corresponding molecular characteristics. Molecular tools (PCR, quantitative PCR, sequence analysis, and other techniques) allow better detection and diagnosis of some of these parasites and consequently improve our understanding of the epidemiology of human infections, the geographic range of the agents, the hosts of the agents, and the longevity of the parasites. Taxonomic studies matching genetic sequences with corresponding morphological data help identify or establish sister and cryptic (closely related) species or strains. This is true for helminths as well as protozoan groups as indicated in the discussion of specific taxa. In addition to needing supplemental molecular research on taxonomy, identifications, and diagnoses, molecular tools will help determine/confirm life cycles, life histories, mechanisms of pathogenesis of infections, and approaches to manage, control, and treat the specific agents.

3. Once specific agents are characterized, methods to detect and diagnose them need improvement, especially by noninvasive means. This is especially important because many parasites do not mature in humans, thereby not allowing the detection of diagnostic eggs, cysts, and spores in the feces or blood. Even when parasites do mature in patients, they cannot always be specifically identified. For example, most heterophyids have very similar eggs, and biological variation occurs for each species. Cross-reactivity occurs in many of the present serological and molecular assays. In the case of *Paracapillaria philippinensis*, there is a need to identify juvenile stages as well as serologic or other diagnostic methods to assess infections when eggs and adult specimens are not apparent in fecal examinations. Improved molecular assays could also detect specific infected fishes in specific locations that are responsible for most of the resulting human infections. More sensitive methods are necessary to detect general and specific

isolates of *Cryptosporidium*, *Giardia*, and *T. gondii* in bivalves, where some unknown and nonremovable components inhibit the presently used PCR reactions [168]. As indicated above, many more protozoans probably infect humans, and new methods will allow their detection.

4. Surveillance methods of known agents require improvement so that infections can be reduced, and causes can be detected. In Europe, the EFSA recommends coordinated studies to improve and implement surveillance and diagnostic awareness of allergic reactions to parasites in fishery products and encourages epidemiological studies throughout Europe to assess the impact of *Anisakis* on human-associated disease, including all allergic forms [193]. All surveillance programs in the marine environment are in an early stage of research, and many could be implemented in conjunction with microbiological studies involved with maintaining healthy waters.

5. There is a need to create ways to avoid parasitic infections without having to reduce seafood consumption or reduce time spent in the water for recreation or occupation. The spread of information in a subtle manner should definitely reduce parasite infections in most countries today. On the other hand, this can be difficult when an improved economy in areas such as Vietnam have increased the social activities that are conducive to eating more raw seafood because it is "healthier when eaten raw" and acquiring more parasites. Also, global climate changes can affect infections as exemplified earlier for the peoples of Hokkaido Island, Japan, who understood parasitic infections and depended on their seafood products.

A few causes for human infection by zoonotic parasites that seem correctable by means other than spreading knowledge about specific parasites include unsanitary defecation habits, use of human excreta as fertilizer, inadequate sewerage systems, and inadequate aquaculture practices. New ideas associated with acquired knowledge about infective parasites and their life histories can contribute to modifications in sources of products and methods of complex food consumption and cooking habits. The latter include economic and sociocultural factors such as beliefs and tradition. Examples of traditional dishes in addition to those already mentioned include raw or partially cooked aquatic products such as raw crab soaked in soy sauce (ke-jang, Korea), raw drunken crabs and raw grass carp in China, and raw fish in Thailand (Koi-pla [raw fish with chopped garlic, lemon juice, chili, rice, and vegetables] and pla som). In contrast, in some industrialized countries like Japan, where eating raw fish is widespread, infections can be coupled with foreign travel and with eating imported foods or exotic delicacies.

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