

REVIEW

Anisakiasis – Is the Sushi Bar Guilty?

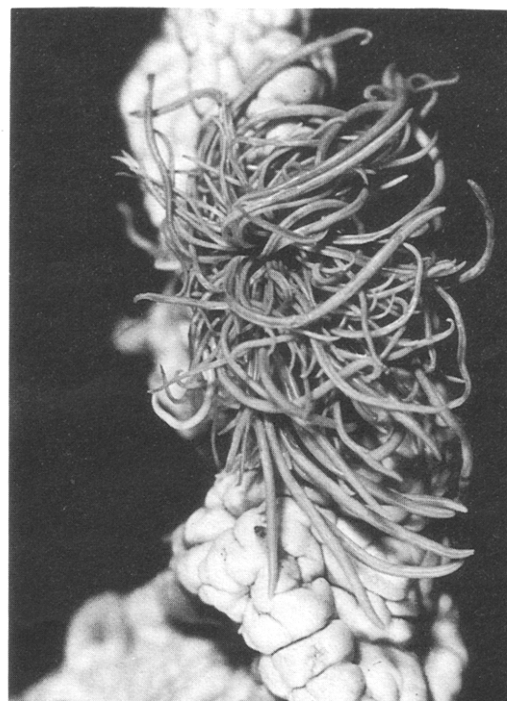
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Since 1972, Japan and some other countries such as the USA have seen a sudden increase in cases of anisakiasis (infection with *Anisakis* sp.) and codworm anisakiasis (infection with the codworm, *Pseudoterranova* [= *Phocanema*] *decipiens*). Larval stages of these nematodes occur in the muscles of a variety of fish and squid, and ingestion of raw and undercooked fish or squid is the prime route of human infection. Thus the Japanese style of eating sashimi (sliced raw fish fillet) and the increasing popularity of sushi bars where such dishes are served, has often been suggested as contributing to the spread of anisakid infections.

In this article, Tomoo Oshima discusses the current status of anisakiasis and codworm anisakiasis, showing that the apparent increase in human cases is related more to advances in diagnosis than to the commercialization of sushi.

The codworm or sealworm (*Pseudoterranova decipiens*) is a ubiquitous parasitic nematode of pinipedia (seals, sealions, walrus, etc.), and is also abundant in marine fish such as cod and pollock, which migrate in cold waters. Human infection with this parasite is known as codworm anisakiasis (Box 1); in contrast, true anisakiasis due to infection with *Anisakis* spp. is usually associated with other fish such as mackerel and herring (*Anisakis* is sometimes referred to as herring-worm). The sudden increase



Dr Kikuchi

Fig. 1. Adult *Anisakis simplex* in the first stomach of a bottle-nosed dolphin caught in coastal waters of Japan. The worms are aggregated like a chrysanthemum flower forming a crater-like ulcer on the stomach wall. Populations of dolphins and porpoise are increasing in coastal waters of Japan, due to protection measures; this can increase the contamination of waters with *Anisakis* larvae, leading to heavy infections in marine fish such as mackerel.

In the Netherlands, freezing regulations were introduced in 1968 to prevent anisakiasis; herring must be frozen within 12h and kept frozen for at least 24h. Such legislation would be impractical and culturally unacceptable in Japan.

Box 1. Nomenclature of 'Codworm'

Over the past 50 years, the specific name of 'codworm' or 'sealworm' has changed several times. Once it was called *Ascaris decipiens* (*decipiens* means deceiving); it later became *Porrocaecum decipiens*, then *Terranova decipiens*. Myers created a new genus for this worm, proposing the name *Phocanema decipiens*, but reexamination of the concept and validity of anisakid genera^{1,2} decided that *Phocanema* was a synonym of *Pseudoterranova* Mosgovoi, 1951. This criterion has been gradually accepted and *Pseudoterranova decipiens* (Krabbe, 1878) is found in current literature. *Terranova* sp. larvae Type A, as referred in Japanese literature, is definitely the third stage larva of this *P. decipiens*, which is commonly called codworm³.

Similarly, various names have been applied to the human disease caused by codworm. Margolis⁴ suggested restriction of 'anisakiasis' to denote infection with larvae of the genus *Anisakis*, using 'non-specific anisakiasis' when the larva has not been identified to genus or as a collective term for infection with anisakid larva, and 'phocanemal (or terranova) anisakiasis' for infections with larvae of genus *Phocanema*. But genus *Terranova* is now restricted to the parasites of elasmobranchs, teleosts, and aquatic reptiles, and genus *Phocanema* is abandoned. However, 'pseudoterranova anisakiasis' would be an impractical name for clinicians, so the term 'codworm anisakiasis' is preferred.

in human infections of both types in Japan since 1972 has been primarily due to the development of high performance endoscopes and radiology for the diagnosis of stomach diseases. A further factor may have been the protection movement for marine mammals which has led to an increase in the population of seals and porpoises in the coastal waters of Japan; this can increase the contamination of seawater with *Anisakis* larvae (Fig. 1), causing heavy anisakid infections in marine fish such as mackerel.

Human Codworm Infection

Codworms are abundant in coldwater fish such as cod, pollock, halibut, flatfish and others; these are the fish dwelling in the bottom of continental shelf waters of the North Sea, Atlantic, Pacific, Arctic and Antarctic waters (Box 2). Cod are regarded as the most frequent host of codworm. Early experimental infections with codworms in the laboratory animals had suggested that acute abdominal

syndrome might be caused in man with this worm. In 1967, natural infection of codworm in the stomach of dog was reported in Hokkaido⁵, but only 3 human cases were reported worldwide from 1921 to 1971. They were accidental and transient infections of no public health concern.

Codworm occurs primarily in the muscle of fish, with very few worms found in the viscera. Thus, if people consume raw fillet of fish infected with codworm, they should easily become infected. Raw fillet of cod, halibut and flatfish has long been important in the diet of people living in Hokkaido and coastal areas of Honshu Island, so why was abundant human infection not noticed in Japan before 1972?

New Tool for Diagnosis

The gastrofibrescope was devised in 1960 by Hirshowitz; it appeared in Japan soon after, equipped with miniature camera and manipulators for the diagnosis of stomach disease. In 1970, Namiki *et al.*⁶ first succeeded in diagnosis and treatment of stomach anisakiasis in Hokkaido using the new endoscope. Since then endoscopy has become the most important and effective diagnostic measure of stomach anisakiasis in Japan; as a result, the apparent number of patients abruptly increased and led to a rash of clinical papers on stomach anisakiasis in Japan. The advantage of endoscopy is not just to see directly the penetrating worm in the stomach and remove it with biopsy forceps (Fig. 2) but also to be able to identify the removed worm morphologically. In addition, advances in radiological techniques of double-contrast also aided recognition of the worm in the stomach – codworm is larger than anisakis larva and easy to find radiologically.

Endemic Codworm Anisakiasis

Following the report of Namiki *et al.*⁶ in 1970, in a hospital in Asahikawa City, Hokkaido, endoscopy was tried for those patients who complained of gastric disorder; 30 cases of non-specific anisakiasis were found – worms removed from five patients were identified as codworms (Fig. 3) and the rest were *Anisakis* Type I larvae^{7,8}. Further cases of codworm anisakiasis were diagnosed by endoscopy in 1972 in Hakodate City^{9,10} and Bihoro Town, Hokkaido. The ratios of codworm anisakiasis to anisakiasis in Hokkaido were 5:31 (Ref. 7), 10:24 (Ref. 11) and 9:10 (Ref. 12).

By 1979, a total of 132 cases of codworm anisakiasis were known in Hokkaido, but only a single case reported from elsewhere



Fig. 2. *Anisakis* larva caught by the biopsy forcep of the endoscope, just on the point of removing it from the stomach mucosa.

(O. O. Koyama, unpublished). All these cases had stomach involvement.

After 1980, the number of case reports of codworm anisakiasis gradually increased in northern Honshu Island, especially at the coastal area of Japan sea. In Aomori Prefecture, six cases in 1981 and another 14 cases in 1983 were found^{13,14}. The ratios of codworm anisakiasis to anisakiasis were 6:2 and 14:7 respectively – much higher than those in Hokkaido. Further cases were reported in Ishikawa, Toyama and Fukuoka in 1982.

Epidemiology of Codworm Anisakiasis

The sudden increase in reports of codworm anisakiasis in northern Japan after 1972 was not an epidemiological outbreak, but simply due to increased diagnosis by endoscopy. We suspect that the disease has been prevalent in northern Japan for a long time because consumption of raw fillet of cold water fish is the traditional food habit.

The type of fish consumed by patients just before the onset of disease (Box 3) was clearly remembered in 52 cases (Table 1). Among them, the most important causative fish were cod, halibut, greenling and squid.

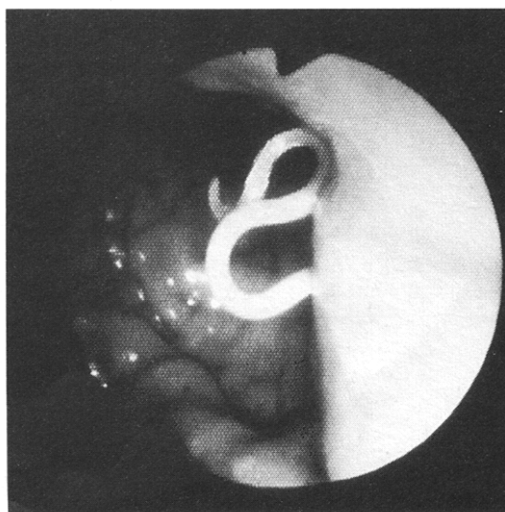
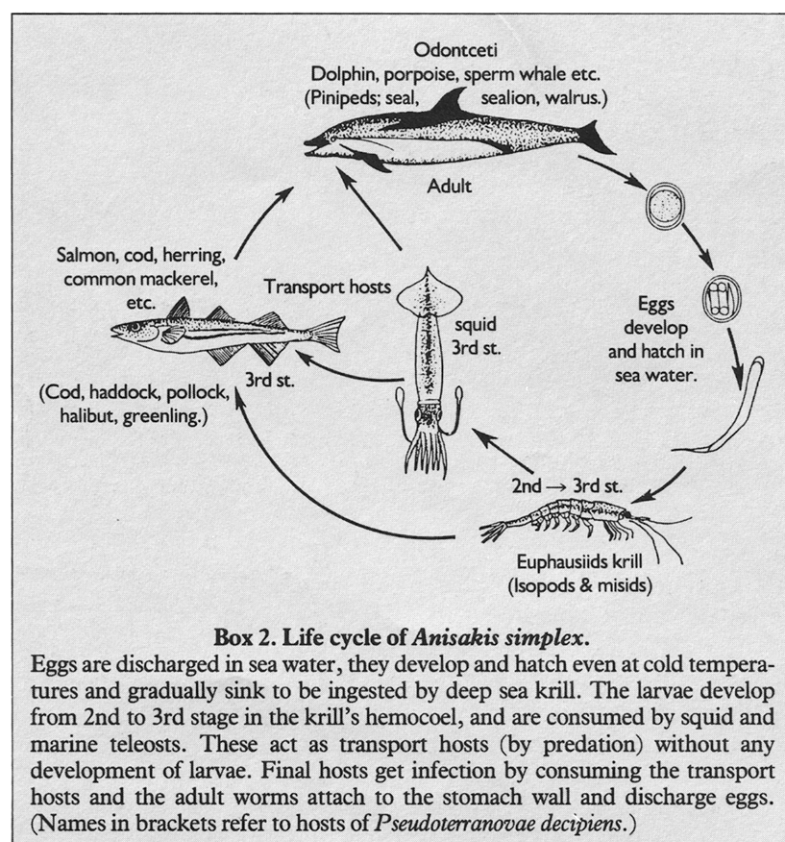


Fig. 3. Codworm just penetrating into the stomach mucosa. The worm appears yellowish and bigger than *Anisakis* larva.



These were primarily prepared in the home and served as sashimi and sushi dishes to the family. In Bihoro, where people purchased fresh halibut from the market and prepared them at home, the infections occurred from March to July. In Hakodate, the infection source was mainly raw cod fillet, with the occurrence of disease from January to July. In Aomori Prefecture, the causative fish were greenling and cod, with infections occurring from January to April.

In contrast, no codworm anisakiasis has ever been reported from the Pacific side of

Box 3. Clinical Codworm Anisakiasis

Codworm anisakiasis occurs mainly in the stomach; unlike infection with *Anisakis* which often causes intestinal problems (see Box 4), only one intestinal case of codworm anisakiasis has been reported¹⁵. Codworm seem to be better able than *Anisakis* to invade the mucous membrane of the digestive tract. One to seven hours after ingesting infected fish, most patients complain of severe epigastric pain which repeats every 5–10 minutes with nausea and vomiting. Some of them have urticaria and tingling throat. At this moment actively moving codworm just invading the stomach mucosa can be seen by endoscopy; invasion of the worm is frequently observed at the posterior wall of stomach. The site of invasion is swollen and haemorrhagic, and the codworm appears as a yellowish thick piece of string – quite different from the fine white-coloured *Anisakis* larva. (Although larvae should be removed for morphological identification, it is not difficult to differentiate codworm from *Anisakis* larvae under the endoscope.) Sometimes codworm try to invade the mucosa repeatedly, giving rise to multiple haemorrhagic lesions of the stomach wall. In rare cases, a patient may report no symptoms at all, even as the invading codworm is recognized by endoscopy.

Treatment is just to remove the invading codworm from the mucous membrane by using the endoscope biopsy forcep. But if the larva is free and actively moving on the surface of mucosa it is difficult to catch the worm. As a rule, when the codworm is removed, the symptoms improve instantly and completely disappear after 2–7 days.

Honshu Island, Shikoku Island or Kyushu Island.

Present Situation of Anisakiasis

Anisakiasis due to infection with *Anisakis* spp. (mainly *A. simplex*) has been comprehensively reviewed^{16–21} but the recent pattern of disease occurrence has dramatically changed.

Intensive research on clinical anisakiasis in Japan was originated by Ishikura²² in Hokkaido in 1967, and Hokkaido was believed to be the most heavy endemic focus. However, at the 27th meeting of the Japanese Society of Digestive-tract Endoscopy in 1984, a total of 3141 cases of stomach anisakiasis were reported, including 2236 cases from Kyushu Island, 489 cases from Hokkaido, 336 cases from southwest Honshu Island, 49 cases from Nagano Prefecture and 22 cases from Tokyo.

After 1976, the number of reported cases of stomach and intestinal anisakiasis in Kyushu Island gradually increased, with 1041 cases reported in 1981. Many cases have been reported subsequently^{23,24} but, as with codworm anisakiasis in Hokkaido, the sudden increase was not due to an epidemiological outbreak, but primarily due to the wide use of routine endoscopy. Worms removed from patients in southwest Japan were exclusively *Anisakis simplex* larvae, and the main causative fish was the common mackerel *Scomber japonicus* in each case^{23–26}.

Common mackerel are the most important source of anisakiasis in Japan at the moment. Several other fish in Japanese coastal waters, such as walleye pollock, chum salmon, herring and squid, have *Anisakis* larvae in their edible portion, but they play a relatively small role in the epidemiology of the disease. On the other hand, common mackerel is a cheap and popular market fish, often prepared in the home and served as vinegar-pickled sashimi or sushi especially in southwestern Japan.

Symptoms, pathology, diagnostics and treatment of stomach anisakiasis are almost identical with codworm anisakiasis, but the symptom of tingling throat is not observed. Unlike codworm however, *Anisakis* larvae often migrate to the intestine to cause intestinal anisakiasis (Box 4).

Anisakiasis in the USA

In the past 13 years, 14 cases of codworm anisakiasis and 11 cases of anisakiasis have been reported in the USA. In contrast to the situation in Japan and Holland, codworm anisakiasis is more prevalent than anisakiasis and its clinical appearance is

much milder without symptoms attributable to gastrointestinal invasion. Most of the codworm recovered from patients are fourth stage, but sometimes adult worms are removed from the mouth. Similarly, out of 10 cases of anisakiasis, only two showed gastrointestinal involvement. Why are there such differences in the clinical picture? Kliks³⁰ and Desowitz³¹ proposed there may be different strains of worm, but no morphological distinction has been found between the worms collected in Japan and the USA. And it seems unlikely that both codworm and *Anisakis simplex* would exhibit parallel strain difference in the two countries. This question remains enigmatic.

In the USA, consumption of raw salmon has been the main source of anisakiasis infection, with red snapper thought to be the main source of codworm anisakiasis. Both types of larvae are present in a wide variety of commercialized fish in the USA, but rarely in the edible portions of the fish. However, it may be that as the oriental dishes become more common in the USA, the chance of infection with codworm and anisakis larvae may increase in the future.

Table 1. Fish consumed by patients in northern Japan just before the onset of stomach disorders subsequently diagnosed as codworm anisakiasis

Common name	Scientific name	No. cases
Pacific cod	<i>Gadus morhua macrocephala</i>	20
Halibut	<i>Hippoglossus stenolepis</i>	16
Japanese greenling	<i>Hexagrammos otakii</i>	5
Surumeika squid	<i>Todarodes pacificus</i>	4
Flatfish	<i>Hippoglossus dubius</i>	3
Atka mackerel	<i>Pleurogrammus monoptyerygius</i>	2
large Rockfish	<i>Sebastes</i> sp.	1
Sardine	<i>Engraulis japonica</i>	1

Is the Sushi Shop Guilty?

Sushi is now a world famous Japanese dish and people can enjoy its taste in sushi shops in most major cities in the world. In Japan however, the sushi shops contribute very little to cases of anisakiasis and codworm anisakiasis. The most infected fish – halibut, cod, pollock, greenling, salmon, herring and common mackerel – are cheap and normally consumed only in the home. In contrast, commercial sushi shops use high class and expensive fish, such as raw fillet of blue-fin tuna, big-eye tuna, striped marlin, broadbill swordfish, skipjack, flounder, porgy or seabream and horse mackerel. Most of these have no codworm

Anisakis larvae occasionally occur outside the human gastrointestinal tract, in the peritoneum^{32,33}, and subcutaneously³⁴. A case of probable pulmonary anisakiasis has also been reported³⁵.

Box 4. Intestinal Anisakiasis

Codworm anisakiasis seldom produces intestinal lesions, but *Anisakis simplex* larvae often migrate to the level of the ileum to cause intestinal anisakiasis, or migrate out of the digestive tract and cause peritonitis. Ishikura *et al.* summarize 1523 cases of stomach anisakiasis and 223 intestinal cases in Japan in 1983.

Typically, patients complain of sudden abdominal pain 1–5 days after ingesting raw infected fish, usually with nausea, vomiting and retention of ascitic fluid, but without marked leukocytosis and fever. Endoscopy is rarely used in intestinal anisakiasis, but radiology shows irregular thickening of the jejunum, ileum or colon, with mucosal oedema and luminal narrowing with dilatation of the proximal intestine. An ex-

perienced physician can usually diagnose intestinal anisakiasis from the patient's history of ingesting raw fish just before the onset of disease and careful observation of the clinical signs. If the diagnosis is correctly established, conservative treatment without surgery usually results in complete cure^{27,28}. Experimentally, immunological diagnosis has given good results²⁹, but is not yet practically applicable.

Kliks³⁰ reported an interesting case of intestinal anisakiasis in Hawaii in 1986. The adult worm was found at the duodenum and removed by the aid of endoscopy (Fig. 5). This was the first case of duodenal anisakiasis with adult *Anisakis simplex*, which has not yet been found in Japan. From now on, endoscopy of the duodenum must be tried in anisakiasis.

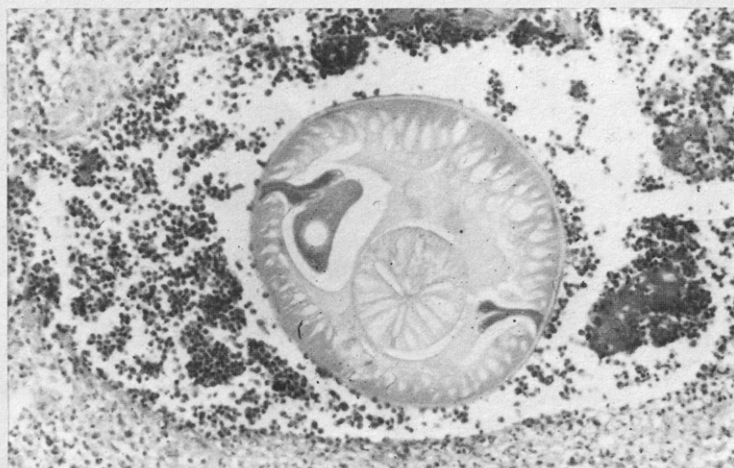


Fig. 4. Intestinal anisakiasis. Acute eosinophilic exudative inflammation around the invaded worm at the level of the terminal ileum. In the cross section of the larva, the lateral chord, renette cell and ventricles are clearly seen.

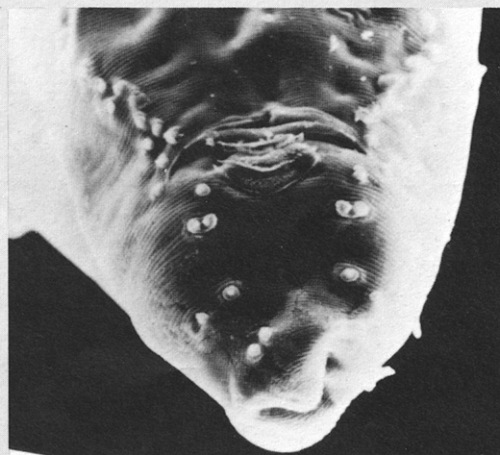


Fig. 5. Adult male *Anisakis simplex* recovered from human duodenum 10 days after infection. The worm was 33mm long and the arrangement of caudal papillae can be clearly seen.

M. Kliks

or anisakis larva in their edible portion. Sushi shops also use sea urchin, abalone, prawn, ark-shell, clam and scallop, which are quite safe when eaten raw.

The sushi shop industry has a long history in Japan and sushi cooks know how to avoid hazardous material for their customers. Also in other countries, professional sushi chefs rarely serve sushi cake plastered with fillet of cod, salmon, herring, halibut or squid. To avoid the delicious sushi in fear of anisakiasis or codworm disease would seem quite unnecessary at the present moment.

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