ORIGINAL ARTICLE

Sushi in Pregnancy, Parasitic Diseases – Obstetrician Survey

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Impacts

- Most U.S. obstetricians do not recommend eating uncooked fish during pregnancy.
- Health providers and the public should be informed that proper freezing of fish kills parasites.
- The safety of treatment of parasitic infections during pregnancy varies with the type of infection, length of gestation and the medications prescribed.

Keywords:
Fish; parasite; food safety; pregnancy; obstetrician

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Summary

Parasites from raw fish can lead to a wide range of clinical manifestations and can be challenging to treat in pregnancy as result of medication exposure of the foetus. We surveyed obstetrician-gynecologists (ob-gyns) in the U.S. to determine their knowledge about the consumption of raw fish during pregnancy. In March 2007, a questionnaire was mailed to members of the American College of Obstetricians and Gynecologists (ACOG) randomly selected to represent all members. Non-responding physicians were sent two additional mailings. Of the 606 ACOG members surveyed, 305 (50%) responded. Most (82%) respondents indicated that eating raw fish is not safe during pregnancy. However, few (19%) knew that thorough freezing kills parasites in fish. Nearly all (94%) respondents thought that parasitic infections can be more challenging to treat in pregnancy. U.S. ob-gyns believe that eating raw fish during pregnancy is not safe; most would benefit from information about how to prevent infection and about treatment.

Introduction

Over 30 different parasites, principally roundworms, tapeworms and flukes can be acquired from raw sea- (or freshwater-) food, including undercooked fish (Deardorff, 1991; Pozio, 2003). Fishborne parasites are responsible for an estimated 18 million human infections worldwide from flukes alone (World Health Organization, 1995; Chai et al., 2005). Parasites such as *Anisakis* spp. (roundworm) and *Diphyllobothrium* spp. (tapeworm) occur worldwide, where as flukes such as *Clonorchis* spp., *Opisthorchis* spp., *Heterophyes* spp., *Nanophyetus* spp., and *Metagonimus* spp. are endemic in Asia. In the global market, fish are sometimes imported to areas without endemic disease. In addition, international travellers can be exposed to fishborne parasites in many areas of the world. However, fishborne parasitic diseases are not reportable in the United States, so there are no population-based estimates of cases reported nationally. The manifestations of these parasitic infections range from mild gastro-intestinal disease to nutritional deficiency, anaemia, liver disease and bowel obstruction, and are all potentially debilitating for pregnant women. When treating these infections in pregnancy, it is important to consider any potential impact on the foetus.

Raw or undercooked fish in the form of sushi, sashimi, ceviche or other dishes, is often eaten in the United States. Data from the 2002 FoodNet population survey conducted in nine states indicated that an estimated 3.7% of the population ate raw fish in the past week, and in California 9.8% of the population ate raw fish in the past week (FoodNet, 2004). In addition, some ethnically prepared dishes such as gefilte fish, or raw salted or marinated fillets, when tasted or eaten before fully cooked, can

lead to fish tapeworm infections (for example, with *Diphyllobothrium* spp.) (Scholz et al., 2009), traditionally called 'Jewish housewife's or 'Scandinavian housewife's disease. Because of the potential for parasitic infection and exposure of the foetus, there can be some risk if raw or undercooked fish is eaten during pregnancy. We surveyed obstetrician-gynaecologists in the United States to determine their opinions and knowledge about the parasitic disease-related implications of eating dishes containing raw or undercooked fish during pregnancy.

Materials and Methods

The survey questionnaire was developed by obstetricians, epidemiologists and scientists in the Department of Research, American College of Obstetricians and Gynecologists (ACOG) and reviewed by the Division of Parasitic Diseases, Centers for Disease Control and Prevention (CDC). Prior to implementation, the questionnaire was pilot tested by 10 obstetrician-gynecologists in ACOG and their feedback was incorporated into the final questionnaire. The questionnaire focused on parasitic infections and did not assess knowledge about bacterial or viral pathogens, or toxins such as mercury, which can also cause fish-related illnesses. The survey was mailed by ACOG in March 2007 to members of the ACOG Collaborative Ambulatory Research Network (CARN), a group of obstetrician-gynaecologists in practice who are identified by a stratified random sampling scheme that is representative of all ACOG members relative to geographical location, age and gender, and who are invited to participate in ACOG surveys. Non-responding physicians were sent two additional mailings in April and May. Respondents were excluded from the survey if they practised outside the United States ($n = 6$) or did not treat obstetric patients ($n = 85$). The survey project was reviewed and exempted by the institutional review boards at ACOG and CDC.

Data from returned surveys were electronically compiled without personal identifiers at the ACOG headquarters in Washington, DC. Data analysis was performed using SAS (SAS, 2003) software at the CDC in Atlanta. Demographic variables were compared with Student's *t*-test for continuous variables and the chi-square test for categorical variables ($P < 0.01$ significance level). Confidence intervals for the responses were calculated using binomial proportions.

Results

Of the 606 practising U.S. ACOG CARN members who were surveyed, 305 (50%) responded. The respondents were similar to ACOG members overall by geographical district and gender, and differed slightly by mean age (Table 1). Most (81.5%) respondents indicated that eating raw fish (sushi, sashimi, etc.) during pregnancy is not safe (Table 2). However, most (80.8%) respondents also indicated that raw fish can not be made safer to eat from a parasitic standpoint if it is well frozen before it is eaten.

In addition, most (81.3%) of the respondents were aware that all three of the major types of helminths (roundworms, tapeworms and flukes) could be present in undercooked fish. Nearly all (98.3%) of the surveyed obstetrician-gynaecologists correctly indicated that parasites present in fish are not always visible to the naked eye. However, a majority (50.4%) indicated that <5% of wild pacific salmon contain roundworms such as *Anisakis* spp. Nearly all (93.4%) of the respondents recognized that parasitic infections from raw or undercooked fish can present more challenges in pregnant women because some medications used for treatment could potentially harm the foetus, especially in the first trimester.

Table 1. Comparison of CARN* survey respondents and ACOG† members, United States, 2007

	CARN respondents (N = 305)	ACOG members (N = 32 441)	P-value‡
Mean age (years)	46.9	48.5	<0.01
Gender (%)			
Female	49.3	45.1	0.11
Male	50.7	54.9	
Geographical district (%)§			
I	7.5	6.6	0.03
II	5.2	7.9	
III	6.2	7.9	
IV	17.7	19.5	
V	5.2	10.1	
VI	9.5	9.0	
VII	23.9	17.7	
VIII	13.8	11.0	
IX	10.8	10.4	

*Collaborative Ambulatory Research Network.
†American College of Obstetricians and Gynecologists.
‡Student's *t*-test for means, chi-squared test for categorical data.
§District I: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Brunswick, Newfoundland, Nova Scotia, Prince Edward Island, Québec; District II: New York, Bermuda; District III: Delaware, New Jersey, Pennsylvania; District IV: District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia, Puerto Rico, West Indies; District V: Indiana, Kentucky, Ohio, Michigan and Ontario; District VI: Illinois, Iowa, Minnesota, Nebraska, North Dakota, South Dakota, Wisconsin, Manitoba, Saskatchewan; District VII: Alabama, Arkansas, Kansas, Louisiana, Mexico, Mississippi, Missouri, Oklahoma, Tennessee, Texas; District VIII: Alaska, Alberta, Arizona, British Columbia, Central America, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming, American Samoa, Guam, Northwest Territory, Yukon Territory; District IV: California. Note, only U.S. physicians in results.

Table 2. Responses from a sample of obstetrician-gynaecologists in the United States to a survey about parasites and eating raw or undercooked fish during pregnancy, 2007

Question	*N*	Number selecting answer	Percent selecting answer**	95% confidence limits
Regarding parasites, eating raw fish (sushi, sashimi, etc.) during pregnancy is safe				
True	297	55	18.5	14.3, 23.4
*False	297	242	81.5	76.6, 85.7
Regarding parasites, raw fish can be made safer to eat if it is well frozen before it is eaten				
*True	291	56	19.2	14.9, 24.3
False	291	235	80.8	75.8, 85.1
Parasites that may be present in raw fish in the United States are always easily visible to the naked eye				
True	303	5	1.7	0.5, 3.8
*False	303	298	98.3	96.2, 99.5
Parasites that can be present in raw or undercooked fish consumed in the United States include				
Tapeworms that can rob nutrients from pregnant women	305	9	3.0	1.4, 5.5
Roundworms that can cause bowel obstruction and perforation	305	18	5.9	3.5, 9.2
Flukes that can cause liver and biliary disease	305	26	8.5	5.6, 12.2
*All of the above	305	248	81.3	76.5, 85.3
In most studies, what percent of wild Pacific salmon contain roundworms (such as *Anisakis* spp.) that can cause illness in humans?				
<5%	266	134	50.4	44.2, 56.5
5–25%	266	110	41.4	35.4, 47.5
26–50%	266	13	4.9	2.6, 8.2
*>50%	266	9	3.4	1.6, 6.3
Parasitic infections from raw or undercooked fish can present more challenges in pregnant women because some medications used for the treatment can harm the foetus, especially in the first trimester				
*True	289	270	93.4	89.9, 96.0
False	289	19	6.6	4.0, 10.1

*Correct answer.

**Total percentages for each question may not add to 100% due to rounding.

Discussion

In our survey, most obstetrician-gynaecologists indicated that raw fish is not safe to eat during pregnancy. This is understandable considering the risk of parasitic infections and potential exposure of the foetus to treatment during pregnancy. However, in contrast to scientific evidence, most obstetrician-gynaecologists indicated that raw fish could not be made safer to eat from a parasitic standpoint by freezing. Freezing of fish has been shown to kill potentially infectious parasites including the most frequently encountered helminths in the United States. The U.S. Food and Drug Administration (FDA) indicate that fish intended to be consumed raw should be: 1) frozen and stored at a temperature of −20°C (−4°F) or below for a minimum of 168 h (7 days) in a freezer; 2) frozen at −35°C (−31°F) or below until solid and stored at −35°C (−31°F) or below for a minimum of 15 h; or 3) frozen at −35°C (−31°F) or below until solid and stored at −20°C (−4°F) or below for a minimum of 24 h (FDA, 1997–2005, 2005). However, some home freezers may not be sufficiently cold to meet the FDA recommendations. An audit of 874 home freezers throughout the United States by EcoSure in 2007 found that nearly 60% of home freezers produced a frozen product (ice cream ½ gallon) temperature of −17.2°C (1°F) or higher (EcoSure, 2007), nearly 30% produced −14.4°C (−6°F or higher) and 1.8% produced −6.1°C (21°F) or higher, so consumers relying on home freezing fish to kill parasites should check their freezer temperature.

Good food safety preparation practice by sushi chefs includes adequately freezing all fish that is going to be served raw, but some connoisseurs feel that freezing can degrade the flavour of fish and those preparing raw fish dishes at home are not always informed about parasitic disease prevention practices. Visible inspection of fish flesh, sometimes with back lighting (termed candling), can often identify parasites. However, this method cannot reliably identify all parasites because in some cases the larvae are too small to be consistently visible to the naked eye, especially when the cut of fish is thick or the flesh is dark. In addition, cold smoking, marinating, brining or salting of fish cannot always be relied on to kill parasites (Hauck, 1977; FDA, 2001). Gardiner found that cold smoking for 12 h did not reduce *Anisakis* spp. larvae in salmon (Gardiner, 1990). Karl et al. found that *Anisakis*

spp. larvae in herring were only killed after 5–6 weeks of marination in 8–9% salt, and 7 weeks in 4.3% salt (Karl et al., 1994), indicating that the typical water phase salt concentrations of 3–3.5% in cold smoked fish would not be sufficient to kill the organisms (FDA, 2001). Dry salting tends to kill the parasites on the fish surfaces, but generally does not kill those imbedded in the tissues (FDA, 2001). Salting or brining processes such as those used in lox preparation can kill parasite larvae if the salt concentration, fillet thickness (i.e. thin cuts) and contact times are sufficient. Commercially prepared lox (salmon) has often been frozen before preparation. Farmed fish fed only processed foods should be relatively free of nematode parasites such as *Anisakis simplex* (Deardorff and Kent, 1989). However, other types of parasite larva, such as those of the tape worm *Diphyllobothrium,* which involves land-dwelling animal hosts or humans in its life cycle, may be spread in nature and to humans by aquaculture of fish such as salmon in freshwater lakes (Cabello, 2007).

It is interesting that a majority of the respondents indicated that <5% of wild Pacific salmon are infected with roundworms such as *Anisakis* spp. Previous studies have shown that nearly all wild Pacific salmon contain these parasites (Deardorff and Kent, 1989), although other fish such as large tuna species are not so highly infected. *Anisakis* spp. and related organisms infect marine mammals (for example, seals or dolphins), which shed the parasite eggs in their faeces. When the parasite eggs hatch, the free-swimming larvae are ingested and infect crustations (for example, shrimp); the larvae are then passed to fish when they eat crustations or other fish that have been infected. Humans become incidental hosts for the larva through eating raw or undercooked fish (CDC, 2009). *Anisakis* spp. and related helminths can cause gastrointestinal disease when they invade the stomach or intestines and may require removal during endoscopy or by surgery (Pinkus and Coolidge, 1975; Valdiserra, 1981; Kilks, 1983; Deardorff et al., 1986; Couture et al., 2003). Adequate freezing will kill *Anisakis* spp. in fish (Gustafson, 1953; Hauck, 1977; Deardorff and Throm, 1988) and other parasites. Infection with the tape worm *Diphyllobothrium* (via larva in the fish flesh) has also been associated with undercooked fresh salmon in the Pacific Coast states (CDC, 1981; Ruttenber et al., 1984). In addition, Pacific salmon was the likely source of infection with *Diphyllobothrium* in Switzerland (Shimizu et al., 2008).

As indicated by the respondents, parasitic infections from ingestion of raw or undercooked fish can present more challenges in pregnant women because some medications used for treatment could harm the foetus, especially in the first trimester. Roundworm infections from undercooked fish, such as those caused by *Gnathostoma* spp. can be treated with albendazole or ivermectin (The Medical Letter on Drugs, Therapeutics, 2007). Albendazole and the related drug mebendazole are benzimidazole derivatives that disrupt cellular microtubules, and in theory could disrupt mitosis. Albendazole has been shown to cause embryotoxicity in rabbits and rats (Rossingnol et al., 1981; Whittaker and Faustman, 1991, 1992; Mantovani et al., 1995; Albenza, 2001), and mebendazole in rats (Vermox, 2000), both at similar or lower doses per unit weight than are used for humans. For this reason, these drugs should be used with caution during pregnancy and only if the risk of illness outweighs their potential toxicity (both are in FDA category C). As a general rule, they should not be given in the first trimester. However, a review of 49 cases of inadvertent use of albendazole in the first trimester of pregnancy found no adverse outcomes reported (Bradley and Horton, 2001); inadvertent exposure of 50 pregnant women to albendazole and ivermectin during mass drug treatment for lymphatic filariasis did not lead to an increased risk of spontaneous abortion or congenital malformations (Gyapong et al., 2003); and a randomized trial with 286 women (after study follow-up) given albendazole or albendazole and ivermectin in the second trimester did not increase the risk of severe adverse events (Ndyomugyenyi et al., 2008). In addition, a randomized trial in 1042 pregnant women given mebendazole after the first trimester found no differences in adverse birth outcomes between the mebendazole and placebo groups (Gyorkos et al., 2006).

Ivermectin is categorized as FDA category C and has been shown to be teratogenic in mice, rats and rabbits at 0.2, 8.1 and 4.5 times the maximum recommended human dose respectively (Stromectol, 2008). Poul (1988) found ivermectin given during pregnancy to be neurotoxic in newborn rats. Although there are no well controlled studies of ivermectin in pregnant women, Pacque et al. (1990) compared 203 children born to women inadvertently treated with ivermectin during pregnancy (one half estimated to be in the first trimester) to untreated women in a onchocerciasis mass drug treatment programme in Liberia and found no major effects on pregnancy outcome. The study by Pacque et al. (1990) is supported by data from a study by Chippaux et al. (1993) who evaluated 97 women inadvertently treated in the first trimester of pregnancy (compared with 142 untreated women) and found no increased risk of specific congenital malformations or miscarriage. Nevertheless, the studies of benzimidazole drugs and ivermectin in pregnancy have sample sizes that are too small to fully assess adverse pregnancy outcomes.

Pyrantel pamoate, a drug that can be used for some roundworm infections, is poorly absorbed from the gastrointestinal tract, but it has not been well studied in

pregnant women for fishborne parasite therapy. Studies in rats and rabbits did not show that it caused congenital or postnatal effects (Owaki et al., 1971).

Praziquantel, used for tapeworms such as *Diphyllobothrium latum* and many fishborne fluke infections, such as those caused by *Clonorchis sinensis,* an Asian fluke that may be in raw or undercooked freshwater fish (The Medical Letter on Drugs, Therapeutics, 2007), is relatively safe in pregnancy. Praziquantel is classified as belonging to pregnancy category B; studies in mice, rats and rabbits at doses up to 40 times the human dose revealed no evidence of harm to the foetus (Frohberg, 1984; Biltricide, 1999). A World Health Organization consultation in 2002 concluded that praziquantel is safe to use in pregnancy and lactation and poses little risk to the health of a women or foetus (Allen et al., 2002; World Health Organization, 2002). In a retrospective study, Adam et al. (2004) compared 88 women treated with praziquantel during pregnancy from four villages in Sudan with 549 women who had not received praziquantel and found no differences in the rate of abortion or preterm deliveries. In addition, Adam et al. (2005) reported that in a small prospective study of pregnant women treated with praziquantel for schistosomiasis (6, 12 and 7 women treated during their first, second and third trimesters respectively), no increase in expected rates of adverse pregnancy outcomes occurred. However, there are no large controlled studies of praziquantel use in pregnancy. It would seem advisable to prescribe praziquantel during pregnancy only when the clinical condition is severe enough to warrant its use. Niclosamide is an alternative that is not absorbed well and therefore has little impact on the foetus. Niclosamide kills adult tapeworms, but not their eggs and can be difficult to find in local pharmacies.

Nitazoxanide has been shown to have activity against some helminthic infections (for example, *Fasciola hepatica*, *Taenia saginata*, *Trichuris trichiura*, *Strongyloides stercoralis*) as reviewed by Anderson and Curran (2007)), and Fox and Saravolatz (2005). However, there has been minimal evaluation of nitazoxanide for fishborne helminthic infections. There are no studies of pregnant women using nitazoxanide, but the drug is labelled as FDA category B, has not shown teratogenic effects in rats at 26 times the adjusted human dose or rabbits at two times the adjusted human dose (Alinia, 2005), and tested negative in the Ames *Salmonella* assay (Murphy and Friedmann, 1985).

Our survey is subject to several limitations. The response rate was 50%; although this is relatively good for a physician survey and the respondents represented ACOG overall by geographical location and gender, we cannot be certain that the responses are representative of all ACOG members. It is possible that some respondents may have indicated that eating raw fish during pregnancy is not safe (the first question) after reading subsequent questions that ask about making fish safer by freezing, visualizing parasites, and types of parasites that can be present. In addition, the responses to the first, second, third and sixth questions were limited to 'true' and 'false', (without a 'don't know' option), so some participants may have guessed at the answers. Finally, ACOG members who agreed to participate in the CARN group and responded to the survey might be more knowledgeable in public health related issues such as foodborne illnesses.

In conclusion, most U.S. obstetricians would inform pregnant women that they are not advised to eat dishes containing raw and undercooked fish because of the risk of parasitic infection. The risk can be minimized by thorough freezing of fish before it is eaten, but one cannot always be certain that fish has been thoroughly frozen, especially when 'home' chefs do not know it is necessary. Adequately cooking fish [internal temperature of 60°C (140°F)] kills parasites and renders it safe to eat. To provide fish- and other foodborne disease-related information to the public and health professionals the Division of Parasitic Diseases at CDC is developing a food-related diseases web site.

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Disclaimer

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