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A large outbreak of scombroid fish poisoning associated with eating escolar fish (*Lepidocybium flavobrunneum*)

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SUMMARY

In August 2003, an outbreak of scombroid fish poisoning occurred at a retreat centre in California, USA. In a retrospective cohort study, 42 (75%) of the 56 dinner attendees who ate escolar fish (*Lepidocybium flavobrunneum*) met the case definition. Individuals who ate at least 2 oz of fish were 1·5 times more likely to develop symptoms than those who ate less (relative risk 1·5, 95% confidence interval 0·9–2·6), and to develop more symptoms (median 7 *vs.* 3 symptoms, $P=0·03$). Patients who took medicine had a longer duration of symptoms than those who did not (median 4 *vs.* 1·5 h, $P=0·05$), and experienced a greater number of symptoms (median 8 *vs.* 3 symptoms, $P=0·0002$). Samples of fish contained markedly elevated histamine levels (from 2000 to 3800 ppm). This is one of the largest reported outbreaks of scombroid fish poisoning in the United States and was associated with a rare vehicle for scombroid fish poisoning, escolar.

INTRODUCTION

In August 2003, individuals attending a workshop at a retreat centre in Marin County, California, USA, became ill after eating escolar fish (*Lepidocybium flavobrunneum*) served at dinner. The dinner started around 18:30 hours; shortly thereafter, several attendees experienced symptoms including a peppery taste, numbness of the tongue, headache, flushing and sweating, dizziness, nausea, diarrhoea, and shortness of breath. The retreat centre requested urgent medical assistance. Paramedics assessed over 20 symptomatic individuals. A clinical diagnosis of scombroid fish poisoning was subsequently laboratory-confirmed.

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The Marin County Department of Health and Human Services, the California Department of Health Services (CDHS), and the California Emerging Infections Program investigated this outbreak to identify its source and extent.

METHODS

Epidemiological investigation

We conducted a retrospective cohort study of all dinner attendees. We defined a case as an attendee at the dinner held on 11 August 2003, who developed at least one symptom listed in Table 1 within 2 h of eating fish. Preliminary interviews were conducted with several cases, retreat centre staff, and the event caterer to develop a questionnaire on food items served at dinner, the amount of fish eaten, the

Table 1. *Symptoms reported by case-patients* ($n=42$)

Symptom	No.	%
Headache	28	67
Facial flushing	26	62
Palpitations or rapid pulse rate	24	57
Nausea	20	48
Dizziness	20	48
Diarrhoea	17	41
Sweating	14	33
Abdominal cramps	13	31
Full body flushing	13	31
Anxiety	11	26
Tingling or burning, mouth or throat	10	24
Metallic taste	10	24
Shortness of breath	10	24
Other symptoms*	9	21
Vomiting	8	19
Respiratory distress	8	19
Peppery taste	7	17
Numbness of the mouth or tongue	6	14
Generalized rash	5	12
General itchiness	5	12
Difficulty swallowing	4	10
Localized rash	3	7
Hives or wheals	2	5

* Nine case-patients reported other symptoms than those listed. These included: light-headedness, feeling 'spacey' or disoriented ($n=5$), puffy face, slight swelling in the throat, increased blood pressure, and 'queasy' stomach.

incubation period and duration of symptoms, the range of symptoms, treatment, and underlying medical conditions including allergies. A questionnaire was sent by e-mail on 21 August to each workshop attendee with instructions to complete it electronically and return by e-mail or to print it, complete it, and return it by fax or U.S. mail. At least two follow-up phone calls were made to all non-responders. For case-patients treated at an emergency room, we abstracted their medical records for medicines administered or prescribed. For case-patients not seen at an emergency room, we relied on the patients' self-reports of which medicines they took. Data were analysed using Epi-Info, version 6.04 [1]; we considered a P value of 0·05 or less as significant.

Environmental investigation

The CDHS Food and Drug Branch and Marin County Environmental Health conducted an investigation of the caterer and the kitchen facilities at the retreat centre, and the Food and Drug Branch conducted a traceback investigation of the fish. Leftover samples of fish served at the dinner on 11 August were collected and tested for histamine by the CDHS Food and Drug Laboratory Branch using the Food and Drug Laboratory Method 64, a combination of three published methods [2–4]. In brief, representative uniformly ground fish samples were homogenized in extraction solvent, centrifuged, and filtered prior to injecting onto the high performance liquid chromatography (HPLC). Filtrates were analysed by ion-paired HPLC with post-column derivatization and fluorescence detection.

RESULTS

Epidemiological investigation

The retreat centre provided a list of all workshop attendees ($n=79$). Questionnaires were sent by e-mail to 79 attendees in 20 states and one Canadian province on 21 August. From 22 August to 9 September we received 72 (91%) completed questionnaires, 51 (71%) of which were returned within 1 week. Fifty per cent of the respondents returned the questionnaire by e-mail, 24% by fax, 19% completed it over the phone, and 7% used the U.S. Postal Service. Of the respondents, 64 (89%) attended the dinner on 11 August and, of those, 56 (88%) ate fish. Forty-two (75%) of the 56 reported that symptoms began within 2 h of eating fish, and thus met the case definition. Case-patients ranged in age from 19 to 64 years (median 47 years). There were no significant differences between the 42 case-patients and the 14 well individuals who consumed fish in gender, race, allergy history, chronic medical conditions, or taking medicines other than medication for scombroid fish poisoning on 11 August.

Attack rates (the proportion of ill persons among those exposed) and relative risks for each food item served at the dinner (Table 2) show that only fish was positively associated with illness, and all case-patients ate some fish [relative risk (RR) undefined, Fisher exact two-tailed P value $<0·0001$]. Both dessert items (fruit tart and vanilla bean ice cream) had protective effects [RR 0·55, 95% confidence interval (CI) 0·35–0·86 and RR 0·60, 95% CI 0·38–0·94 respectively]. No other food item was significantly associated with illness.

Case-patients experienced from one to 18 symptoms (median, six) that started immediately after eating the fish to as long as 2 h afterwards (median,

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Table 2. *Food-specific attack rates and relative risks*

Exposure	Ill among exposed (%)	Ill among unexposed (%)	Relative risk	Confidence interval	Mantel–Haenszel *P* value
Mixed greens	34/52 (65)	2/4 (50)	1·3	0·5–3·6	0·54
Poppy seed roll	19/25 (76)	16/24 (67)	1·1	0·8–1·6	0·47
Butter	17/20 (85)	19/29 (66)	1·3	0·9–1·8	0·13
Corn on the cob	18/26 (69)	17/25 (68)	1·0	0·7–1·5	0·93
Escolar fish	42/56 (75)	0/8 (0)	Undefined		<0·0001
Baby carrots and broccoli	29/42 (69)	8/11 (73)	1·0	0·6–1·4	0·81
Brown rice	23/33 (70)	15/22 (68)	1·0	0·7–1·5	0·91
Nectarine and blueberry tart	12/26 (46)	26/31 (84)	0·6	0·4–0·9	0·003
Vanilla bean ice cream	11/23 (48)	28/35 (80)	0·6	0·4–0·9	0·01

30 min). Acute symptoms lasted from 15 min to 24 h after onset (median, 3 h). The most common symptoms reported were headache (67%), facial flushing (62%), palpitations or a rapid pulse rate (57%), nausea (48%), dizziness (48%), and diarrhoea (41%) (Table 1).

The fish was prepared and served in pieces that averaged 4 oz in weight. Nearly 75% of case-patients reported eating one whole piece or less. Individuals who ate at least half a piece (2 oz or more) were 1·5 times more likely to develop symptoms than those who ate less than half a piece, and this approached significance (RR 1·51, 95% CI 0·90–2·55, $P=0·07$). The incubation period and duration of symptoms were not significantly associated with the amount of fish consumed; however, patients who ate less than half a piece of fish experienced fewer symptoms than those who ate half a piece or more (median, three *vs.* seven symptoms, $P=0·03$).

Twenty-seven (64%) case-patients were attended by paramedics; eight went to local emergency rooms. Of the eight, five were treated with diphenhydramine, four with an H2-antagonist such as cimetidine or ranitidine, two were given acetaminophen, and several were prescribed anti-anxiety medication. Including those seen at an emergency room, 23 (55%) patients reported taking medicine for symptoms associated with this outbreak, either self-administered or administered by a health-care provider. Nearly all (96%) of these patients took diphenhydramine, 30% took acetaminophen, and 26% took both.

The incubation period was not significantly different between the patients who took medicine for their symptoms and those who did not; however, patients who took medicine reported a significantly longer duration of symptoms than those who did not (median, 4 *vs.* 1·5 h, $P=0·05$). Patients who took medicine also experienced a significantly greater number of symptoms than those who did not (median, eight *vs.* three symptoms, $P=0·0002$). Of the 42 case-patients, 23 (55%) reported having an allergy but this was not significantly associated with incubation period, duration of symptoms, or number of symptoms.

Environmental investigation

Traceback information indicated that the escolar was harvested, processed, and frozen in May 2003. The frozen fish was imported into California on 5 June 2003, and remained frozen until it was shipped to San Francisco in July. The escolar was defrosted under refrigeration between 10 and 11 August and subsequently filleted and distributed to the retreat centre on 11 August. A kitchen inspection was conducted on 13 August and two samples of leftover cooked fish were obtained and split into four subsamples for testing. The histamine levels in the fish subsamples were markedly elevated at 2000, 2700, 2800, and 3800 parts per million (ppm). No environmental health violations were identified in the kitchen, at the caterer's premises, or at either of the two processors.

For the implicated meal, the caterer received three fillets of escolar fish weighing a total of 21 pounds that were delivered in individual plastic bags on ice. Two of the fillets originated from a single fish. The fish was prepared and then stored in a walk-in refrigerator until it was grilled, plated, sauced, and served on two platters in pieces that averaged 4 oz. Attendees served themselves from the buffet. It was not possible to distinguish the different fillets based on the time the fish was served, and people became ill after eating fish from both platters.

DISCUSSION

We report a large outbreak of scombroid fish poisoning in which 42 out of 56 individuals became ill after consuming escolar fish. Of the 218 outbreaks of scombroid fish poisoning reported to the Centers for Disease Control and Prevention during the period 1990–2001, the two largest outbreaks reported 148 and 74 cases [5]. If these two outlying outbreaks are excluded and only the remaining 216 outbreaks are considered, a median of two and a mean of four persons were affected per outbreak.

Fish-associated attack rates are rarely reported in the scombroid fish poisoning literature. Given the 91% response rate to the survey, we can estimate the lowest possible attack rate for this outbreak. Seven questionnaires (out of 79) were not returned, and one of the individuals who did not return a questionnaire met our case definition based on abstraction of medical records. If we assume that the other six individuals who did not return the questionnaire *did* eat fish but did *not* develop symptoms, then the lowest possible attack rate was 68% (43 affected out of 63 who ate fish). Interestingly, workshop participants were given the assignment to go to bed hungry, and many individuals reported eating less than they would have otherwise. Based on data presented, had attendees eaten 'normally', the attack rate would probably have been greater. The protective effect seen with the dessert items is puzzling. It is possible that some feature of the dessert (e.g. high fat content) protected against illness. Alternatively, affected individuals possibly were beginning to feel sick by the time dessert was served and so were less likely to eat it.

Allergies or other underlying medical conditions, gender, race or taking other medications could not explain why certain individuals became ill while others did not. However, those who ate at least half a piece of fish were 1·5 times more likely to develop symptoms (this finding approached significance) and experienced significantly more symptoms than those who ate less than half a piece. It is known that histamine levels can vary considerably in the same cut of fish [6] and the fact that some ate small portions could explain why some individuals were unaffected despite eating highly contaminated fish. It is also possible that because the three fillets originated from two different fish, not all of the fish was contaminated; however, the two fish were harvested and processed as part of the same shipment and were probably both subjected to the same mishandling. This is the first report to show a dose response between the amount of fish consumed and severity of illness.

Although escolar is not a well-recognized vehicle for scombroid fish poisoning in the medical literature, it was reported in 15 out of 218 scombroid outbreaks in CDC's database for 1990–2001 [5]. Of these 15, 12 (80%) were reported in 2001. The recent increase in the number of escolar-associated outbreaks probably reflects the increasing popularity of this fish: according to the National Marine Fisheries Service, annual landings of escolar increased from 11·1 metric tons in 1991 to 65·6 metric tons in 2002 [7].

Fish of the Scombroidei suborder (including tuna and mackerel) are much more common vehicles for scombroid fish poisoning than escolar. Other fish that have been implicated in scombroid fish poisoning outbreaks include mahi mahi, bluefish, and marlin. When susceptible fish are not promptly and continuously refrigerated, bacteria can metabolize histidine and degrade the protein of fish flesh to produce scombrotoxin, which consists of histamine and other amines. The presence of 50 ppm or more of histamine is indicative of decomposition whether or not there is gross evidence of this, such as bad odour [8]. When illness results, histamine levels in implicated fish have commonly been at least 200 ppm and often greater than 500 ppm. Histamine is heat resistant and can, therefore, cause illness even when fish is properly canned or cooked thoroughly [9]. While some contaminated fish will not show any outward signs of spoilage, some will show such signs such as a bad smell. Cooked fish that has spoiled may have a 'honeycombed' appearance [9].

Escolar is a large deep-water fish often caught as a by-catch of tuna fishing; it, and the related oilfish (*Ruvettus pretiosus*) contain approximately 20% indigestible waxy esters (by body weight) which can have a laxative effect, called kerriorhoea, in those who eat them [10]. Associated symptoms can be varied and include mild and rapid passage of oily yellow or orange droplets, severe diarrhoea with nausea and vomiting, abdominal cramps and headache. A recent report describes a cluster of illness associated with escolar that was attributed to both its laxative effects and scombrotoxin ingestion [11].

To reduce the chances of scombroid fish poisoning, fish, especially of the Scombroidei suborder and escolar, should be appropriately refrigerated

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from the time caught to the time cooked. Fish with a 'honeycombed' appearance or a bad odour should not be consumed. To enable appropriate public health measures to be taken and prevent additional illness from occurring, all scombroid-like illness should be promptly reported to local public health authorities. Whenever possible, fish should be saved and kept frozen for laboratory determination of histamine concentrations when scombroid fish poisoning is suspected, particularly when it involves a commercial product that may need to be recalled.

In these times of increasing internet access, we were pleased that we could conduct our investigation of cases by e-mail. Despite the ease, simplicity, and quick response, there was still a need for labour-intensive data entry with its inherent potential for introducing errors. In future foodborne outbreak investigations, we would recommend, where possible, a web-based system in which individuals respond to a questionnaire at a secure website and data are automatically entered into a database.

In summary, outbreaks of scombroid fish poisoning associated with escolar fish have been increasingly recognized in the last decade, paralleling increases in escolar fish consumption. We describe a large outbreak of scombroid fish poisoning associated with escolar and have demonstrated an expected dose–response relationship between escolar consumption and the extent of subsequent disease.

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