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Peak occurrences of ciguatera fish poisoning precede cholera outbreaks in Hong Kong

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SUMMARY

Occurrences of ciguatera fish poisoning (CFP) and *Vibrio cholerae* infected patients in Hong Kong were reviewed for the 13-year period 1989–2001. Peak activity of CFP preceded peak activity of cholera in nine of the years except in 4 years (1990, 1991, 1992, 1996) where it was observed that the total number of cholera cases were all less than or equal to five per year ($P < 0{\cdot}05$). Average time interval was 2·4 months between peaks of CFP and *Vibrio cholerae* outbreaks. Findings suggested that the factors that affect cholera and ciguatera occurrences may not be operating in some years but when they are operating, they will affect both cholera and CFP. CFP peaks have consistently occurred before *Vibrio cholerae* peaks in our locality so much so that the occurrence of the latter can now be almost accurately predicted since 1998. CFP peaks served as an early warning for public measures to be in place before occurrence of cholera outbreaks.

INTRODUCTION

Cholera is an acute, diarrhoeal illness caused by infection of the human intestine with the bacterium *Vibrio cholerae*. Serious pandemics have occurred throughout the known history of mankind [1]. More recent data [2] on taxonomical evidence, epidemiological evidence, laboratory-based survival studies and environmental isolations of *Vibrio cholerae* have provided evidence on the existence of an environmental reservoir which may be substantially influenced by climactic conditions [3].

Ciguatera fish poisoning (CFP) arises from the consumption of contaminated fish that contain ciguatoxins derived from microalgae via the food chain [4–6]. Ciguatoxins arise from biotransformation in the fish of less polar ciguatoxins (gambiertoxins) produced by *Gambierdiscus toxicus*, a marine dinoflagellate that lives on algae, usually attached to dead coral. The toxins and their metabolites are concentrated in the food chain when carnivorous fish prey on smaller herbivorous fish. Symptoms of CFP include a range of gastrointestinal, neurological and cardiovascular disturbances.

Hong Kong is situated in the Pearl River delta and surrounded by brackish waters. Mains water supply provides a safe water source for the whole local population, but cases of cholera still sporadically occur. Since the postwar years, cases of cholera and CFP in Hong Kong are notifiable diseases that are required by law to be reported to the Department of Health (DH). Data of both diseases were retrieved from the database of the DH surveillance systems for further analysis and observations were made on their occurrences. This study details the findings of our investigations on a review of data obtained over a 13-year period.

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METHODS

When the DH received notifications on notifiable diseases, a team of DH health staff initiated investigation into each of the cases. Information was collected by a standard questionnaire, and data have been computerized into a database since 1989. These data are retrieved from the computer database for analysis.

CFP symptoms depended on amounts as well as parts of fish consumed. Previous exposure to ciguatoxin may have a sensitization effect [7–13]. The case definition of CFP used in DH was the presence of gastrointestinal and neurological symptoms within 36 h after the consumption of coral reef fish. These included clinical features after the consumption of ciguatoxin fish and resulted in gastrointestinal and neurological symptoms after an incubation of 2–8 h. Most were symptomatic by 12 h. Health staff interviewed patients and specifically checked for these CFP symptoms. Gastrointestinal symptoms usually preceded neurological symptoms, and included diarrhoea, abdominal pain, nausea, vomiting. Neurological symptoms included numbness of extremities/face/tongue/perioral area, lower limb weakness, myalgia/arthralgia, headache, hot/cold reversal, and dry mouth. Cardiovascular symptoms included bradycardia, hypotension, palpitation and chest pain; while there were also other general symptoms of malaise, pruritus, fever, chills, sweating, dizziness. Pruritus and myalgia may persist for weeks to months. Other possible bacterial causes of food poisoning were being excluded and supported by toxicological analysis. A confirmed case must satisfy all the criteria of: (a) history of consumption of marine (coral reef) fish; (b) onset of symptoms usually within 24 h after intake; (c) compatible clinical picture; and (d) laboratory confirmation of the presence of ciguatoxin in the food remnant; or (e) epidemiologically linked to a confirmed case. Bioassay of the fish remnants/samples was performed using published laboratory methods [14].

The case definition of cholera is a symptomatic individual (characterized by diarrhoea with or without vomiting) whose stool/rectal swab culture revealed *Vibrio cholerae* O1 or *Vibrio cholerae* O139 confirmed by DH Public Health Laboratory. Isolation and identification of *Vibrio cholerae* procedures were according to standard laboratory methods [15, 16]. When the DH received notifications on CFP or *Vibrio cholerae* infected cases, a team of health staff initiated investigation into each case. Information was collected by a standard questionnaire. Disinfection, isolation and treatment of cases were immediately performed by health office staff. Data have been computerized into a database since 1989. These data were retrieved from the database for analysis. Both local and imported cases were counted. Monthly total number of cases was generated, and the time intervals between peaks of CFP (C) and *Vibrio cholerae* (V) cases were measured in terms of these plotted monthly totals. For years with multiple mode, only the first occurring mode was counted for that year.

In 4 years (1990, 1991, 1992, 1996), the total number of cholera cases were five or less. These were not counted in the measurement of time intervals between peaks, as the cholera peaks (V) were indistinct when compared with cholera outbreak years when the peaks were easily discernible. Listing of yearly total and maximum (peak) monthly number of cholera (V) in each year during 1989–2001 was done, and the lead time of CFP peak was measured in months as shown in Table 1.

Table 1. *Summary data of monthly cholera and ciguatera fish poisoning (CFP) cases in Hong Kong, 1989–2001*

Year	Lead*	Total cholera	Maximum cholera	Lead time
1989	1	29	18	2
1990	2	5	2	−3
1991	2	5	2	−1
1992	1	3	2	3
1993	1	30	7	4
1994	1	56	16	3
1995	1	6	2	2
1996	2	4	2	−3
1997	1	14	13	3
1998	1	71	39	2
1999	1	18	4	2
2000	1	12	3	1
2001	1	38	18	2

* Lead: 1, CFP; 2, cholera.

Statistical methods

Two hypotheses were separately tested for statistical significance. The first was the null hypothesis that cholera and ciguatera poisoning were equally likely to have their peak month appear first in a particular year. The second null hypothesis that high cholera incidence (with yearly total >5) was not associated

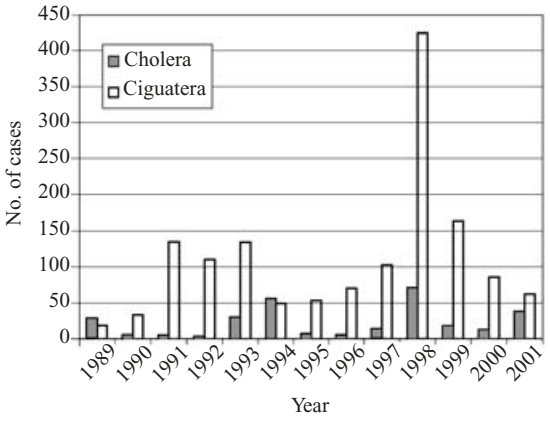

Fig. 1. Cases of cholera and ciguatera fish poisoning in Hong Kong, 1989–2001.

with peak CFP appearing before peak cholera. Sign test and chi-square tests were performed, and P value at 0·05 was used for testing statistical significance.

RESULTS

During 1989–2001, a total of 291 cholera cases and a total of 1442 persons affected by CFP were notified to the DH. The yearly distribution of cases is shown in Figure 1. The average numbers of *Vibrio cholerae* and CFP notifications were 22·4 (range 3–71) and 110·9 (19–425) cases per year respectively. In 1998, there was an upsurge in cases of both cholera and CFP in Hong Kong. The total number of notifications of cholera was 71 in 1998, the highest level in the past 30 years. The total number of persons affected by CFP was 425, the highest level since 1989.

Monthly fluctuations in cholera and CFP throughout the whole 13-year period are shown in Figure 2 (a, b, c). It can be seen that annual peak levels of cholera cases occurred in the month of January (0), February (0), March (1), April (0), May (2), June (0), July (1), August (4), September (4), October (0), November (1) and December (0). Annual peak level of CFP outbreaks occurred in the month of January (1), February (1), March (1), April (1), May (1), June (1), July (3), August (1), September (1), October (0), November (1) and December (1). Two peaks of CFP occurred in the month of January and May, followed by the peak of cholera in the month of March and August in 1998.

During the 13-year period 1989–2001, peak activity of CFP preceded peak activity of cholera in nine of the years except in 4 years (1990, 1991, 1992, 1996) where it was observed that the total number of cholera cases were all five or less per year. Therefore, CFP peaks had consistently preceded cholera peaks ($P<0·05$) during the 13-year study period, and this association is especially marked for years with more than five cases of cholera in Hong Kong ($P=0·003$).

The CFP-cholera peaks were separated by a period of approximately 1 month on 1 occasion, approximately 2 months on 5 occasions, approximately 3 months on 3 occasions and approximately 4 months on 1 occasion. The measured time intervals are marked in the figures. The average time interval was 2·4 months between peaks of CFP (C) and *Vibrio cholerae* (V) outbreaks. CFP peaks have consistently occurred before cholera peaks in our locality ($P<0·05$) so much so that the occurrence of the latter can now almost be accurately predicted since 1998.

DISCUSSION

Studies have shown that both cholera and CFP are strongly influenced by environmental factors. The dynamics of *Vibrio cholerae* is influenced by temperature and salinity of seawater [17–19]. *Vibrio cholerae* is often found attached to plankton [20], a property that is thought to contribute to its environmental persistence in aquatic habitats. Outbreaks of the disease are related to plankton blooms associated with warmer sea surface temperatures.

Humans are exposed to ciguatoxins at the end of the food chain which effectively concentrates the toxins when carnivorous fish prey on smaller herbivorous fish [21]. Events leading to a CFP outbreak are initiated by environmental factors that favour the proliferation of gambiertoxins [22]. The incidence of CFP is expected to increase in association with global warming and widespread bleaching and death of coral. The presence of bloom numbers of *G. toxicus* is often unpredictable and patchy, while low levels are found throughout tropical and subtropical waters. More than 400 species of fish can be vectors of ciguatoxins, but only a small number are regularly incriminated. Human cases have been reported in Pacific and Indian Ocean regions, as well as the tropical Caribbean [21, 23].

To our knowledge, there has not been any report linking the peaks of these two diseases in a geographic area. Our observation in Hong Kong that the annual peak activity of cholera followed the annual peak activity of CFP outbreak by 2–3 months was first noticed in 1998 when the analysis was performed. The pattern has been used to predict the peak level of

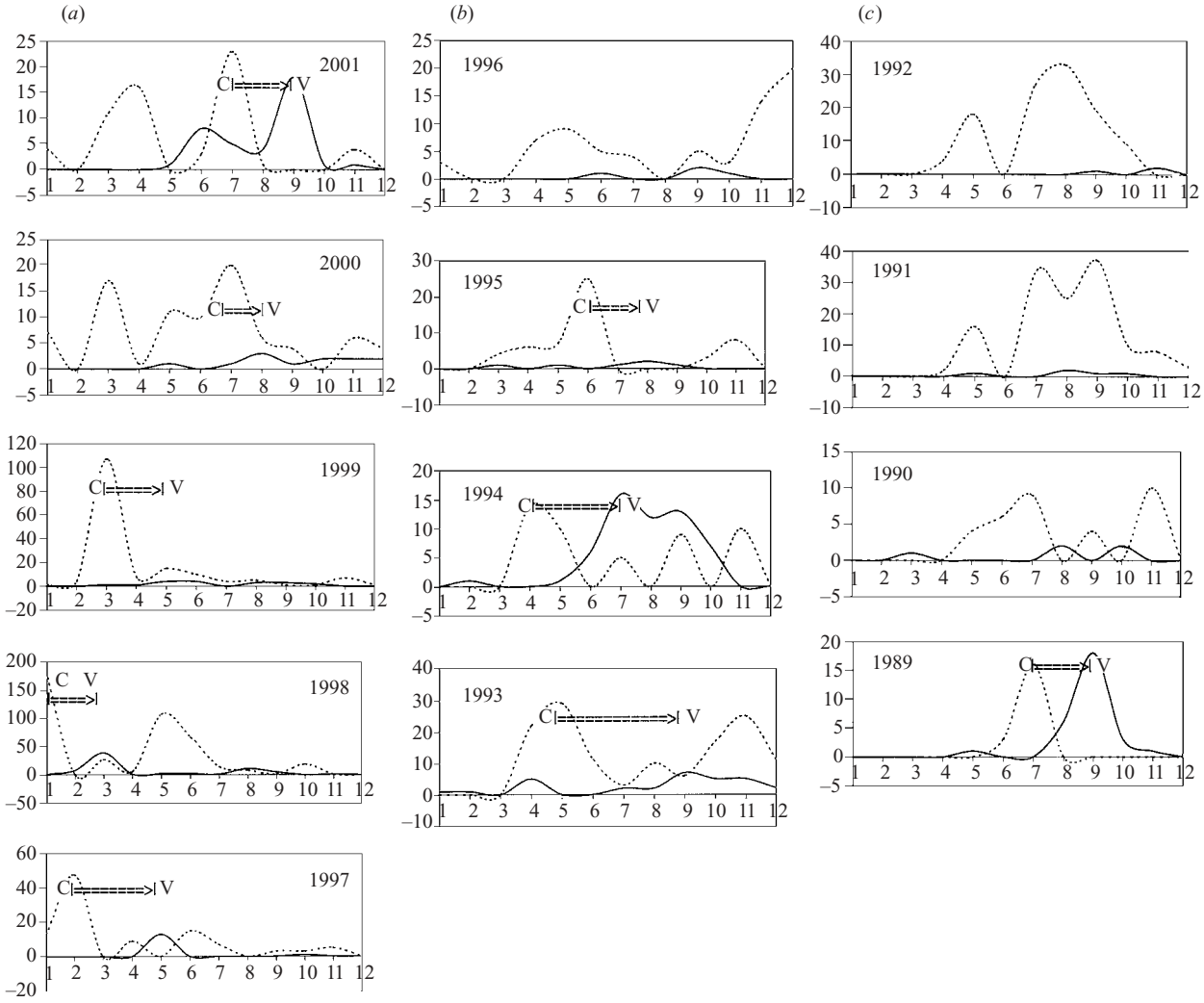

Fig. 2. (*a*) Occurrence of ciguatera fish poisoning (CFP) peaks and cholera peaks 1997–2001; (*b*) 1993–1996; (*c*) 1989–1992. Dotted line, CFP cases, peak at C; solid line, cholera cases, peak at V; *y*-axis, no. of cases; *x*-axis, month of year; arrow, measured time interval.

Vibrio cholerae with accurate results in the following 3 years after 1998. Since the existing infrastructure, namely, provision of a safe mains water supply for the whole population, does not allow secondary spread of cases, the number of cases accurately reflects the true occurrence of pathogenic *Vibrio cholerae* organisms in the brackish water environmental reservoir.

There was a strong seasonal pattern of cholera in Hong Kong. It occurred mainly in the summer months with a peak level in August for 4 years and September for another 4 years. On the other hand, the peak level of CFP in the past 13 years has occurred in any month from January to December except October. The peak level of CFP did not follow any seasonal pattern. This suggests that the relation between the peak of cholera and the peak of CFP is not due to seasonal variation of activity between the two diseases. Analysis of other meteorological and environmental parameters (including ambient air temperature and humidity, sea surface temperature) available from Hong Kong Observatory did not show any simple, discernible associations between these (data not shown).

During those years of 1990, 1991, 1992, 1995 and 1996 when the activities of *Vibrio cholerae* were low with an annual total incidence of six or less, the monthly incidence ranged from 0 to 2. There was no obvious peak level in these years. For all the other 8 years when the activity of *Vibrio cholerae* was high, peak of cholera was always preceded by the peak of CFP. This seems to suggest that the factor(s) that affect cholera and ciguatera toxin occurrence may not be operating in some years, but when it is operating, it will affect both cholera and CFP.

Why there exists a relation between peak levels of cholera and CFP is still unknown. We postulated that there is a common factor that triggers stages of change resulting finally in occurrence of both diseases in humans. The pathway from the trigger to the end results in human diseases evolves in terms of months as suggested by the study. The trigger may be environmental factors, climatic factors, man-made factors or even their combination. It should have been operating some months ago somewhere in the Asia Pacific region but finally results in human diseases in Hong Kong and possibly some other places. The analysis of Hong Kong local meteorological and environmental parameters may not be very fruitful. It warrants a more extensive environmental study in this part of the world to examine the possible links in causal relation.

Because of the consistent time-lag difference between the peak of cholera and the peak of CFP during this 13-year period, it is very likely due to a common factor that can affect both the incidence of cholera and CFP. The factor can be an environmental factor, like global warming, that favours the proliferation of plankton [21, 24, 25]. As the pathways from plankton to cholera outbreaks and plankton to CFP outbreaks are different, there exists a time lag of 2–3 months between the peak activities of the two diseases. Because CFP peaks regularly precede *Vibrio cholerae* peaks by about 2·4 months, the former served as an early warning sign by which public health measures directed towards the latter can be in place on time.

The relation between the two diseases is observed among both imported and local cases. As most of the seafood in Hong Kong is imported from the Asia-Pacific region, it suggests that the relation between the two diseases is a characteristic common in the Asia-Pacific region. More studies in this locality of the world are necessary to further explore the relation between the two diseases.

It will be useful to see if this observation of CFP–cholera peaks still holds for future years. If so, this will serve a very useful purpose of prediction of the latter, as it has for the past 4 years. It would also be interesting to note if places in different geographic localities but with similar climactic conditions also show these CFP–cholera peaks.

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