Temporal Trends and Climatic Factors Associated with Bacterial Enteric Diseases in Vietnam, 1991–2001

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OBJECTIVE: In Vietnam, shigellosis/dysentery, typhoid fever, and cholera are important enteric diseases. To better understand their epidemiology, we determined temporal trends, seasonal patterns, and climatic factors associated with high risk periods in eight regions across Vietnam.

METHODS: We quantified monthly cases and incidence rates (IR) for each region from national surveillance data (1991–2001). High- and low-disease periods were defined from the highest and lowest IRs (1 SD above and below the mean) and from outbreaks from positive outliers (4 SDs higher in 1 month or 2 SDs higher in ≥ 2 consecutive months). We used general linear models to compare precipitation, temperature, and humidity between high- and low-risk periods.

RESULTS: Shigellosis/dysentery was widespread and increased 2.5 times during the study period, with the highest average IRs found between June and August (2.1/100,000–26.2/100,000). Typhoid fever was endemic in the Mekong River Delta and emerged in the Northwest in the mid-1990s, with peaks between April and August (0.38–8.6). Cholera was mostly epidemic along the central coast between May and November (0.07–2.7), and then decreased dramatically nationwide from 1997 onward. Significant climate differences were found only between high- and low-disease periods. We were able to define 4 shigellosis/dysentery, 14 typhoid fever, and 8 cholera outbreaks, with minimal geotemporal overlap and no significant climatic associations.

CONCLUSIONS: In Vietnam, bacterial enteric diseases have distinct temporal trends and seasonal patterns. Climate plays a role in defining high- and low-disease periods, but it does not appear to be an important factor influencing outbreaks.

Key words: cholera, climate, dysentery, enteric disease, epidemiology, outbreaks, seasonality, shigellosis, typhoid fever, Vietnam. Environ Health Perspect 116:7–12 (2008). doi:10.1289/ehp.9658 available via http://dx.doi.org/ [Online 16 October 2007]

In Vietnam, shigellosis (bacillary dysentery), typhoid fever, and cholera are important diseases of significant public health concern (DeRoek et al. 2005). They are primarily caused by the bacterial pathogens Shigella spp., Salmonella typhi, and Vibrio cholerae, respectively, and transmission occurs through fecal contamination of food or water or by person-to-person contact (Bhan et al. 2005; Crump et al. 2004; Kindhauser 2003; Kotloff et al. 1999; Lanata et al. 2002). Infection rates and outbreaks are highest where the standards of living, water supply, and human behaviors related to personal hygiene and food preparation are poor. The distinction between these diseases is difficult and may be influenced by climatic factors (DeRoek et al. 2005; Kovats et al. 2003; World Health Organization (WHO) 2004). Although climate is one aspect of the complex epidemiology of these enteric diseases, it can help to define high-risk periods. Few studies conducted in Asia have described the temporal patterns and outbreaks of shigellosis/dysentery and typhoid fever, and no study has specifically examined the impact of climate on these diseases. In general, cholera has been studied more widely, and formal and informal listings of outbreaks and putative risk factors are available from various sources (Griffith et al. 2006; Kelly-Hope et al. 2007; WHO 2003, 2005, 2006). Studies have shown associations of V. cholerae with climate, including rainfall, flooding, water temperature and depth, sea surface temperatures, and the El Niño Southern Oscillation (ENSO) (Huq et al. 2005; Koelle et al. 2005b; Lipp et al. 2002; Lobriz et al. 2000; Pascual et al. 2000; Rodo et al. 2002).

In Vietnam, monthly shigellosis/dysentery, typhoid fever, and cholera surveillance data have been collated for 1991–2001. We used these national data to determine the long-term temporal trends and seasonal patterns of shigellosis/dysentery, typhoid fever, and cholera in eight geographic regions of Vietnam, and to examine climatic factors associated with high-risk periods.

Methods

Study location. Vietnam is a narrow, densely populated country in southeastern Asia bordering China, Laos, and Cambodia (General Statistics Office of Vietnam 2005). It has approximately 85 million people living in an area of 330,000 km², with > 3,000 km of coastline. In the south the climate is tropical, whereas in the north, the two main seasons are a warm, wet summer and a cool, humid winter. The terrain is diverse with low, flat deltas in the south and north; highlands in the center; and hilly mountains in the northwestern region. Vietnam experiences occasional typhoons with extensive flooding, especially in the southern Mekong River Delta. Vietnam currently is divided into 64 provinces and eight agro-ecologic regions (Figure 1): Northeast, Northwest, Red River Delta, North Central Coast, South Central Coast, Central Highlands, Southeast, and Mekong River Delta. We used the eight geographic regions as the basis of our temporal and climatic analyses.

Disease data. We obtained data on shigellosis/dysentery, typhoid fever, and cholera for each province in Vietnam from 1991 to 2001 from the Epidemiology Department, National Institute of Hygiene and Epidemiology (Hanoi), and from a central database collected by the International Vaccine Institute (Korea). Data were primarily (≥ 90%) based on treated episodes, which are routinely collected by district health centers as part of the surveillance system of the Vietnam Ministry of Health; these episodes were supplemented with cases reported in the published scientific literature and unpublished national health reports. Thus, the database comprised a combination of cases that were diagnosed clinically...
and confirmed by serology and stool culture. Provincial data were pooled to provide estimates for each of the eight study regions.

Temporal trends and seasonal patterns. To determine long-term temporal trends and seasonal patterns of shigellosis/dysentery, typhoid fever, and cholera, we quantified the monthly number of cases and average incidence rates (IRs) per 100,000 population for each region. Population data for 1995–2001 were obtained from the General Statistics Office of Vietnam (2005), and population estimates for 1991–1994 were extrapolated from the fitted cubic spline of the known years (Eubank 1999) in order to obtain regional population estimates and crude IRs for each study year.

To identify distinct seasonal variations, we detrended (with a fourth-degree polynomial) and log-transformed monthly IRs in each region for each disease, and defined “high” and “low” disease periods based on the months with the highest and lowest rates (months with values at least 1 SD above and below the mean, respectively). Outbreak periods were detected similarly, but we defined them empirically as the positive outliers that were 4 SDs higher in 1 month or 2 SDs higher in ≥ 2 consecutive months from the modeled Fourier function of the time series (Bloomfield 2000; Pollock 1999), which was performed on each time series, accounting for disease seasonality.

Climate data and analysis. Monthly climatic data were obtained from worldwide climate maps generated by the interpolation of data from ground-based meteorologic stations with a monthly temporal resolution and 0.5° latitude by 0.5° longitude spatial resolution (Mitchell and Jones 2005). The climatic variables used were precipitation; average daily minimum, maximum, and mean temperatures; vapor pressure; and number of wet days. Monthly climate data during 1991–2001 were extracted from the pixels containing the centroid of each province and clustered according to the eight regional divisions of Vietnam. To calculate climatic averages for the eight regions, we used the climatic values for each province weighted by its respective population (to account for the proportional relevance of the diseases of each province within the regions, so the climatology of places where few people live would, in fact, account proportionally less in the regional analyses than places with a large demographic concentration).

To explore climatic factors associated with high-risk times, we examined differences between high- and low-disease periods and outbreak and non-outbreak periods. First, we used a general linear model to test significant differences between high- and low-disease periods with time lags from 0 to 2 months. Because multiple tests were conducted (four climatic variables tested at three time lags of 0, 1, and 2 months, thus yielding 12 tests for each disease at each region), significance levels were adjusted with the Bonferroni correction (Sokol and Rohlf 1995); we considered p-values < 0.05/12 significant.

Second, we compared climatic data corresponding to the outbreak period in each region with climate data for the same months in previous years when outbreaks did not occur (i.e., the non-outbreak period), with time lags from 0 to 2 months. We used general linear models with the climatic variables as dependent variables, outbreak presence as a fixed factor, and region as a random factor. All analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA), ArcGIS 9.1 (ESRI, Redlands, CA, USA), and MATLAB software (The MathWorks, Inc., Natick, MA, USA).

Results

Temporal trends and seasonal patterns. The monthly numbers of shigellosis/dysentery, typhoid fever, and cholera cases reported in Vietnam during 1991–2001 are shown in Figure 2. Shigellosis/dysentery was the most prevalent disease and increased approximately 2.5 times during the study period, with 16,976 cases (annual IR of 25.3 per 100,000) reported in 1991 compared with 46,292 cases (IR, 58.8) in 2001. The annual number of typhoid fever cases was similar at the beginning (7,592 cases; IR, 11.3) and end (9,614 cases; IR, 12.2) of the study period; however, there was a 3-fold increase during 1994 to 1997, with an average of 24,553 cases (IR, 33.8) reported annually. Overall, there were fewer cholera cases, which appeared episodically during 1991–1996, with four main peaks in May 1992 (1,851 cases; IR, 2.7), August–September 1993 (943–1,054 cases; IR, 1.4–1.5), May 1994 (1,127 cases; IR, 1.6), and June–July 1995 (1,097–1,492 cases; IR, 1.5–2.1). From January 1997 onward, the number of cholera cases reported nationwide decreased significantly, with only two minor peaks reported in January–February 1999 (188 cases; IR, 0.25) and September–October 2000 (166 cases; IR, 0.21).

Figure 3A shows the monthly IRs of shigellosis/dysentery, typhoid fever, and cholera for each region during 1991–2001. This figure highlights the widespread incidence of shigellosis/dysentery and its increase in the Central Highlands and the South Central Coast, the endemicity of typhoid fever in the Mekong River Delta and its emergence in the Northwest region, and the significant decline of cholera nationwide.

Overall, we found distinct seasonal variations in each region, as shown by the average monthly IRs in Figure 4. Shigellosis/dysentery peaks rates in the northern regions of the country (Northeast, Northwest, Red River Delta, North Central Coast) between June and August (IR range, 2.1–7.8), and in the southern regions (South Central Coast, Central Highlands, Southeast, Mekong River Delta)
between May and July (IR range, 8.2–26.2); the highest monthly IR occurred in the Central Highlands in June (IR, 26.2). Typhoid fever rates peaked in the northern regions between May and September (IR range, 0.38–5.2) and in the southern regions between April and July (IR range, 0.43–8.6); the highest monthly IRs occurred in the Northwest in July (IR, 5.2) and the Mekong River Delta in April (IR, 8.6). Cholera rates peaked in the northern regions between May and November (IR range, 0.07–2.7) and in the southern regions between May and July (IR range, 0.51–2.6). No cholera cases were reported in the Northwest, whereas the highest monthly IRs occurred in the North Central Coast in May (IR, 2.7) and in the South Central Coast in July (IR, 2.6).

In total, 26 enteric outbreaks were identified—4 shigellosis/dysentery, 14 typhoid fever, and 8 cholera—during 1991–2001 (Figure 3B). Apart from typhoid and cholera in the Mekong River Delta in June 1995, no disease outbreak coincided temporally with any other disease outbreak in any region. However, typhoid outbreaks in the Northeast, Red River Delta, North Central Coast, South Central Coast, and Southeast regions in 1996 overlapped temporally, with outbreak months ranging from March to July. Overall, outbreaks occurred most commonly in the months of May, June, and July, followed by April, August, and September. No outbreaks occurred in December, and only one to three outbreaks occurred in October–March.

**Climate associations.** The climatic measures during high- and low-disease periods at 0-month lag are shown in Table 1. The data highlight that, in most regions, conditions were warmer, wetter, and more humid in high-disease periods than in low-disease periods. Overall, we found significant differences in precipitation and the number of wet days between the high and low periods. For shigellosis/dysentery and cholera, precipitation was significantly different ($F_{1,11} = 14.7, p = 0.002, r^2_{adj} = 47.7\%$; and $F_{1,10} = 15.7, p = 0.002, r^2_{adj} = 53.1\%$, respectively), as was the number of wet days ($F_{1,11} = 18, p = 0.001, r^2_{adj} = 53.2\%$; and $F_{1,10}$...
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= 14.4, \( p = 0.003, r^2_{adj} = 50.7\% \), respectively) at the 0-month time lag. Similarly, for typhoid fever, precipitation was significantly different at the 0-month time lag (\( F_{1,11} = 40.1, p < 0.001, r^2_{adj} = 72.3\% \)), as was the number of wet days at the 0- and 1-month time lags (\( F_{1,11} = 24.8, p < 0.001, r^2_{adj} = 61.4\% \); and \( F_{1,11} = 28.1, p < 0.001, r^2_{adj} = 64.3\% \), respectively). No significant climatic differences were found at the 2-month time lag for any of the diseases, even when tests were not Bonferroni adjusted.

In our climate analyses we found no significant differences in the climatic conditions between the months during or preceding each outbreak period compared with non-outbreak periods in previous years. The data in Table 2 highlight the range of climate conditions under which enteric outbreaks occurred. Overall, precipitation ranged from 37 to 311 mm; for the majority (> 80%) of the outbreaks, > 100 mm was recorded. All mean temperatures were > 21.9°C (majority > 25°C); the number of wet days ranged from 4.9 to 20.3 (majority > 11); and most outbreaks occurred in months with an average vapor pressure > 26 hPa.

Discussion

This is the first time that temporal patterns of endemic and epidemic shigellosis/dysentery, typhoid fever, and cholera have been defined concurrently on such a large scale. In the present study we used surveillance data to highlight the different magnitudes and epidemiologic patterns of each disease in Vietnam during 1991–2001, and we offer some insight into the patterns of each disease in Vietnam during the different magnitudes and epidemiologic settings.

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Table 1. Differences in climatic factors during high- and low-disease periods in Vietnam during 1991–2001.

| Region               | Precipitation (mm) | Temperature (°C) | Wet Days | Vapor Pressure (hPa) | Precipitation (mm) | Temperature (°C) | Wet Days | Vapor Pressure (hPa) | Precipitation (mm) | Temperature (°C) | Wet Days | Vapor Pressure (hPa) |
|----------------------|--------------------|------------------|----------|----------------------|--------------------|------------------|----------|----------------------|--------------------|------------------|----------|----------------------|
| Northeast            |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 236.7              | 26.5             | 12.8     | 25.8                 | 172.7             | 26.5             | 12.1     | 25.1                 | 149.7              | 25.0             | 10.7     | 23.2                 |
| Low                  | 61.5               | 20.0             | 10.5     | 17.5                 | 97.5              | 21.4             | 10.6     | 19.2                 | 103.8              | 22.8             | 10.1     | 20.6                 |
| Northwest            |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 272.0              | 26.0             | 17.0     | 25.2                 | 226.3             | 24.7             | 16.5     | 23.5                 | NR                 | NR               | NR       | NR                   |
| Low                  | 60.2               | 19.7             | 10.7     | 16.5                 | 118.7             | 22.11            | 12.8     | 19.7                 | NR                 | NR               | NR       | NR                   |
| Red River Delta      |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 117.7              | 23.6             | 11.5     | 22.3                 | 228.5             | 28.0             | 13.0     | 28.4                 | 297.4              | 29.1             | 16.6     | 30.9                 |
| Low                  | 111.7              | 23.7             | 10.9     | 22.4                 | 38.0              | 19.1             | 8.2      | 16.2                 | 141.4              | 23.8             | 11.0     | 22.7                 |
| North Central Coast  |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 187.4              | 25.4             | 12.1     | 24.5                 | 170.3             | 25.4             | 13.6     | 24.4                 | 245.7              | 26.1             | 15.2     | 26.1                 |
| Low                  | 113.7              | 22.0             | 10.5     | 20.2                 | 85.7              | 21.7             | 11.1     | 19.8                 | 168.7              | 23.5             | 11.5     | 22.3                 |
| South Central Coast  |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 158.5              | 25.3             | 13.8     | 25.4                 | 199.5             | 26.5             | 13.8     | 27.2                 | 185.8              | 26.3             | 19.1     | 26.1                 |
| Low                  | 187.6              | 24.3             | 12.2     | 24.6                 | 161.3             | 24.4             | 12.0     | 24.5                 | 134.2              | 24.2             | 11.6     | 24.2                 |
| Central Highlands    |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 168.6              | 25.7             | 14.8     | 25.7                 | 185.6             | 26.3             | 15.7     | 26.2                 | 233.8              | 25.6             | 19.3     | 26.6                 |
| Low                  | 92.8               | 23.5             | 8.5      | 23.1                 | 133.6             | 23.8             | 9.8      | 23.7                 | 122.2              | 24.1             | 11.3     | 23.8                 |
| Southeast            |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 202.1              | 27.9             | 14.5     | 28.6                 | 221.8             | 27.6             | 15.7     | 28.8                 | 224.6              | 27.1             | 15.3     | 28.1                 |
| Low                  | 59.1               | 26.4             | 7.2      | 24.9                 | 66.3              | 26.3             | 8.0      | 24.7                 | 136.7              | 26.9             | 11.5     | 26.7                 |
| Mekong River Delta   |                    |                  |          |                      |                    |                  |          |                      |                    |                  |          |                      |
| High                 | 204.6              | 28.7             | 14.2     | 30.2                 | 209.0             | 28.2             | 13.9     | 28.8                 | 186.0              | 29.0             | 14.1     | 30.1                 |
| Low                  | 145.4              | 27.7             | 11.6     | 27.5                 | 102.9             | 27.2             | 9.5      | 11.2                 | 159.1              | 27.5             | 12.6     | 27.6                 |

NR, not reported; PREC, precipitation (mm); TEMP, mean temperature (°C); VAP, vapor pressure (hPa); WET, wet days (number in month).
Identifying peak periods of disease helps to focus local interventions. We were able to better define the seasonality of each disease and found that, on average, the highest IRs of shigellosis/dysentery occurred between May and August; of typhoid fever between April and September; and of cholera between May and November. For all diseases, the highest monthly IRs occurred earlier (April/May to July) in the southern regions than in the northern regions (May/June to November) of the country, which may be indicative of the different climatic patterns of the north and south. In particular, the tropical conditions of the south may help local health authorities implement timely interventions because peak periods of disease coincided with the onset of the wet season.

Distinct climatic differences were evident between the high- and low-disease periods, with hotter, wetter, and more humid conditions associated with an increased incidence of disease. Climatic associations, however, were not strong, and we found significant differences mainly when we compared the high- and low-disease periods (0-month lags) and not the months leading up to (2-month lag) each specific period. This may be because high and low periods occurred during more extreme climate conditions (i.e., wet and dry seasons) and because climate conditions outside these parameters are more variable and not specific enough to dramatically increase or decrease disease transmission.

The overall weak association with climate could also be related to the quality of surveillance data, which are inevitably flawed because of underreporting, misdiagnosis, and misclassification. In Vietnam, adequate diagnostic facilities are not universally available, and detection can be difficult and may be biased to those individuals with severe symptoms or better access to health centers (Dalsgaard et al. 1999; Hong et al. 2003). Further, other factors such as poor socioeconomic conditions play a role (Fewtrell et al. 2005; Kelly-Hope et al. 2007) and are also likely to be as important, if not more important, than climate. This theory is supported by our analysis of outbreaks, which found no significant climatic differences in the same months between years with outbreaks and years without outbreaks.

Using a robust method, we were able to define statistically 4 outbreaks of shigellosis/dysentery, 14 of typhoid fever, and 8 of cholera. We found little or no overlap between outbreaks of the three diseases within each region, which suggests that a combination of different factors triggered each event in each region, and that competition may have occurred between these enteric microbes for available hosts (Rabbani and Greenough 1999). Comparisons of climatic factors between outbreak and non-outbreak periods indicated that no specific or unusual climate conditions preceded any outbreak. However, most outbreaks occurred within certain periods and climatic parameters, with May, June, and July being the most common outbreak months, followed by April, August, and September.

We acknowledge that climate is only one aspect of a multitude of complex interactions that cause disease. Although the role of climate is limited, we believe that climate factors help define high- and low-risk periods and potentially provide some clues into the ecology and epidemiology of these enteric diseases. It is reasonable to expect that the different pathogens, as well as humans, respond to seasonal changes in the environment and that some conditions are more favorable than others for disease transmission.

### Table 2. Region, year, month, and average climate measures for shigellosis/dysentery, typhoid fever, and cholera outbreaks.

| Region              | Year/month | Disease | Climate measures |
|---------------------|------------|---------|-----------------|
|                     |            |         | PREC TEMP WET VAP |
| Northeast           | 1998/Jan–Mar | Typhoid | 116.3 24.1 10.7 21.9 |
|                     | 1998/Nov   | Cholera | 46.9 21.9 4.9 18.3 |
|                     | 2000/Aug   | Typhoid | 192.2 28.7 11.4 28.8 |
| North Central Coast | 1991/May–Jul | Shigellosis | 249.4 26.6 16.0 26.0 |
|                     | 1997/Sept–Oct | Typhoid | 327.2 24.7 11.7 23.0 |
|                     | 1999/May–Aug | Typhoid | 252.2 26.7 18.6 26.1 |
| Red River Delta     | 1998/Jan–Jun | Cholera | 311.4 28.7 18.2 30.4 |
|                     | 1998/May–Jul | Typhoid | 213.0 28.9 12.5 29.3 |
|                     | 1996/Jan–Jul | Typhoid | 177.0 26.2 15.1 25.9 |
| South Central Coast | 1995/May–Aug | Cholera | 142.0 27.0 19.3 26.4 |
|                     | 1996/May–Apr | Typhoid | 71.2 25.1 10.5 25.6 |
|                     | 1997/May–Jul | Typhoid | 121.5 28.5 15.2 28.2 |
|                     | 1998/Aug–Sep | Shigellosis | 238.2 27.3 20.3 27.1 |
| Central Highlands  | 1994/May–Jul | Cholera | 135.7 26.0 18.7 26.8 |
|                     | 1997/Jun–Sep | Typhoid | 230.6 28.8 19.8 29.4 |
| Southeast           | 1991/Jul–Aug | Shigellosis | 258.5 27.8 16.9 29.8 |
|                     | 1993/Jan    | Cholera | 60.5 25.1 5.6 22.6 |
|                     | 1993/Nov    | Shigellosis | 123.3 27.2 12.9 27.8 |
|                     | 1994/May–Jul | Cholera | 191.3 28.0 15.5 29.6 |
|                     | 1995/Jun–Sep | Typhoid | 298.7 27.6 18.4 29.1 |
|                     | 1996/Apr–Jun | Typhoid | 159.0 27.6 12.1 28.2 |
| Mekong River Delta  | 1993/Apr    | Typhoid | 37.0 29.2 5.7 28.2 |
|                     | 1993/Jun–Jul | Cholera | 250.8 28.1 16.1 29.8 |
|                     | 1995/Jan–Mar | Typhoid | 40.2 27.3 5.8 24.9 |
|                     | 1995/Apr–Jun | Cholera | 161.38 28.5 11.5 29.4 |
|                     | 1995/Jun–Jul | Typhoid | 280.7 28.4 15.9 30.3 |

**PRÉC**, precipitation (mm); **TEMP**, mean temperature (°C); **VAP**, vapor pressure (hPa); **WET**, wet days (number in month).
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