How likely is cholera in crowded quarters?

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Preliminary draft
For discussion only

Abstract

The number of severe cases of cholera may rise linearly with the number of mild cases. [JEL I12]

Cholera, a form of severe diarrhea, killed 370,000 in India alone between 1898 and 1907. It still threatens developing areas: A 1991 epidemic in Peru killed more than 4,200 there by 1994 and evidently spread to other countries in Latin America.[2]

Models to predict the incidence of cholera may have value, particularly in refugee camps and slums, where the infectious disease may spread too rapidly to be quickly contained.[3] In the inner city of Trujillo, Peru, the 1991 epidemic evidently began among poor residents who drank unboiled water.[4] Because they had access to tap water for only a few hours throughout the day, most had stored their drinking water in containers; these often also served as basins for washing hands.[5] The resulting epidemic soon overwhelmed labs with cases of cholera to identify.

Generally, only 7% to 15% of the cases that occur early in an epidemic can be identified readily.[6] Without early identification, however, cholera can easily kill. It can so dehydrate its victim – robbing her of a tenth of her weight, and thickening her blood – that she may die of shock in 12 hours.[7] Without treatment, a fifth to a half of the cholera patients may die.[8] While treatment is simple, a patient may not receive it in time, since cholera shows no symptoms before diarrhea.

This paper proposes a probability function based on conditions that can be observed before an epidemic. Conceivably, health officials might avoid many deaths by projecting the number of cholera cases that would occur, given the population density and the size of the region affected as well as its food and water sanitation.[9] Treatment need not cost much: In a refugee camp in Uganda, health workers found that fully immunizing a person cost 53 cents on average for an oral vaccine that was provided and stored for

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[2] Swerdlow *et al.*, 1994; *Morbidity*, 1991.

[3] *Britannica*, 1997.

[4] That finding was according to a study of 46 hospital cases – and of 65 controls with no symptoms.

[5] Swerdlow *et al.*, 1992.

[6] Vugia *et al.*, 1992. Denote as E the number of cases that workers normally associate with the start of an outbreak. Let r be the rate at which the cholera spreads over time. Let the actual number of cholera cases at time t be $C(t) = e^{rt}$. Then workers may mistakenly identify the start of the epidemic as time v, where $E = .11e^{rv}$ and .11 represents a typical share of cholera cases that are correctly identified. (That is, $(.07 + .15)/2 = .11$.) Workers should identify the start of the epidemic as the earlier time w, where $E = e^{rw}$. Solving this crude model suggests that $w = v + ln\ .11$, or a lag of 3 or 4 time units.

[7] Van Heyningen and Seal, 1983; CDC, 1991.

[8] Legros, *et al.*, 1999.

[9] Pascual *et al.* provide evidence that El Niño may also affect cholera epidemics.

free.[10] Conceivably, however, officials may not recognize an outbreak until well after it has begun, since most cases of cholera lack symptoms. In the El Tor variant of the bacterium, more than 99 percent of the infections may lack symptoms.[11] Once an outbreak has occurred, one may forecast the number of cholera cases from the number of existing cases; but this may not provide enough time for treatment. After 24 to 48 hours, the bacterium that causes cholera, *vibrio cholerae*, can resist a standard antibiotic, streptomycin.[12] One study found that, once severe diarrhea had begun, workers should provide intravenous therapy in less than 28 hours.[13] Supplies as well as time may be limited: Medical supplies of sterile bicarbonate, essential for replacing the bicarbonate lost in diarrhea, are often scarce.

Below, Section II sketches a probability model for cholera; Section III provides crude empirical estimates; and Section IV concludes.

II. *Model*

Definitions follow. A person infected by *vibrio cholerae* is a "carrier" until diarrhea begins. She is then a "cholera case" for the duration of the diarrhea. One must distinguish between carriers and cases, since high carrier rates often accompany low case rates.[14] In a populace of n, the number of cholera cases at time t is $m(t)$. The number of carriers of the *vibrio* bacteria is c.

In a crowded and unsanitary area, carriers and cases may transmit the disease to others. More carriers and cases connote more new cases. The change in cholera cases, dm, thus increases in m as well as in c.

When cases are many, they may transmit so many *vibrio* organisms to the carriers that these begin diarrhea, thus becoming new cases. Without this transmission, carriers may not turn ill. In a study of prisoners, none contracted cholera after ingesting 10^4 to 10^7 organisms of the O1 strain of *vibrio*; but five of nine did develop infections after ingesting 10^8 to 10^{11} organisms. One became so ill as to require intravenous fluids.[15] This suggests that the threshold number of organisms that must be ingested to develop cholera may be high -- especially in severe illnesses, for which the threshold may be 10^{11}.

In summary, the numbers of carriers and existing cases may interact to produce new cases:

Equation 1

$$dm = a(c)m.$$

Consider now the carriers. By replacing epithelial cells in the gastrointestinal tract at the rate of 250 grams per day, the body may flush out *vibrio* organisms within a week or so.[16] One may thus distinguish between carriers infected by *vibrio* several days

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[10] Legros *et al.*, 1999.

[11] Van Heyningen and Seal, 1983.

[12] Stewart, 1972.

[13] Cash, 1974.

[14] Stewart, 1972.

[15] Bennish, 1994; and Cash *et al.*, 1974.

[16] van Heyningen and Seal, 1983, page 218.

ago and those infected more recently. Denote the number of carriers infected days ago as c_0; the number of carriers infected recently is c_1.

The number c_0 may relate indirectly to income per capita, y, since it depends on the capacity of the populace to achieve and sustain good health. In effect, income correlates with the stock of health capital. Healthier workers produce more.

The number of recent carriers, c_1, relates instead to conditions that can give rise quickly to cholera infections: Untreated water, uncooked seafood and unwashed vegetables.[17] The standard of water treatment is w; it may be indexed by the percentage of dwellings with plumbing. The standard of food quality is f; it may be indexed by the average price of a restaurant meal, since diners who are willing to pay more for safer meals are also likely to handle food with more care at home.

The total number of carriers sums two functions:

Equation 2

$$c = c_0(y) + c_1(w, f).$$

Given: The number of carriers and cases is substantially smaller than the populace. Then one may take as roughly constant the probability that a given number of existing cases may convert an additional carrier into a new case. In that event, a given rise in the number of carriers is likely to lead to a proportional rise in the number of new cases. The coefficient function $a(c)$ in (1) is thus linear.

Define the probability of a cholera case, $p(t)$, as a relative frequency -- the ratio of existing and new cases to the populace:

Equation 3

$$p(t) = \frac{m(t) + dm}{n}.$$

Solving (3) with the use of (1) yields

Equation 4

$$p(t) = \frac{[1 + a(c)]Ae^{a(c)}}{n}.$$

Equations (2) and (4) define the probability of a cholera case. The analysis will treat a case as a “success” in a Bernoulli trial. It assumes that, early in an outbreak, the number of existing cholera cases is small compared to the populace. For simplicity, assume that the probability that one person may contract cholera is independent of the probability that another person would also contract it at time

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[17] Swerdlow *et al.*, 1992.

t.[18] In effect, one draws cholera cases from a bottomless urn. The probability p of another cholera case, then, determines the binomial distribution for the probability of k new cases of cholera in a populace of n:

$$b(p,k,n) = \binom{n}{k} p^{k}(1-p)^{n-k}.$$

III. Estimates

Preliminary estimates indicate that the accuracy of the model is sensitive to the specification of parameters. The estimates are based on published data from a 1969 study in which 111 prison volunteers received oral doses of *vibrio cholerae* that ranged from 10^4 to 10^{11} organisms.[19] Of the prisoners, 79 (71%) developed cases of cholera – i.e., where at least one stool culture was positive – accompanied by diarrhea. The study may thus indicate the characteristics of a small, contained epidemic. The outbreak was brief: The mean period from ingestion of 10^6 *vibrio* organisms to the first diarrheal stool was 53 hours for the main serotype used, Inaba 569B; and 36 hours for Ogawa 395. The brief, intense outbreak may provide an analogy to refugee camps.

The severity of cholera is measured in discrete categories. In Grade 2 cholera, at least one stool culture tests positive for *vibrio*, and at least one diarrheal stool occurs. In Grade 3 cholera, diarrhea is so severe that it requires intravenous treatment.

Assume a linear relation between the severity of the cholera, measured by the diarrheal response, and the log of the *vibrio* dose:

Equation 4

$$Severity = a + b\log dose.$$

The severity of cholera arises from an enzymatic reaction that floods the lumen and produces diarrhea. It is speculated that the amount of fluid may relate linearly to the log of the number of *vibrio* organisms that attach to the cell walls of the small intestine beneath the mucus layer. When more organisms colonize the intestinal wall, they may induce more enzymes. These, in turn, may provoke more diarrheal fluid -- but at a diminishing rate, since the intestinal capacity to support *vibrio*, as well as to produce diarrheal fluid, may be limited.

The expected number of victims of cholera of a given severity s, $E[N_s]$, sums already-existing cases, $N_{0,s}$, and the expected increase in cases that occurs because milder cases of cholera have worsened through larger ingestions. Consider this expected increase. Since the *vibrio* pool is common to all in the populace, each person may face the same probability of a large ingestion of bacteria. A larger population of *vibrio* in the pool connotes a higher probability of a large ingestion for each person. Denote this probability as p_1. Then

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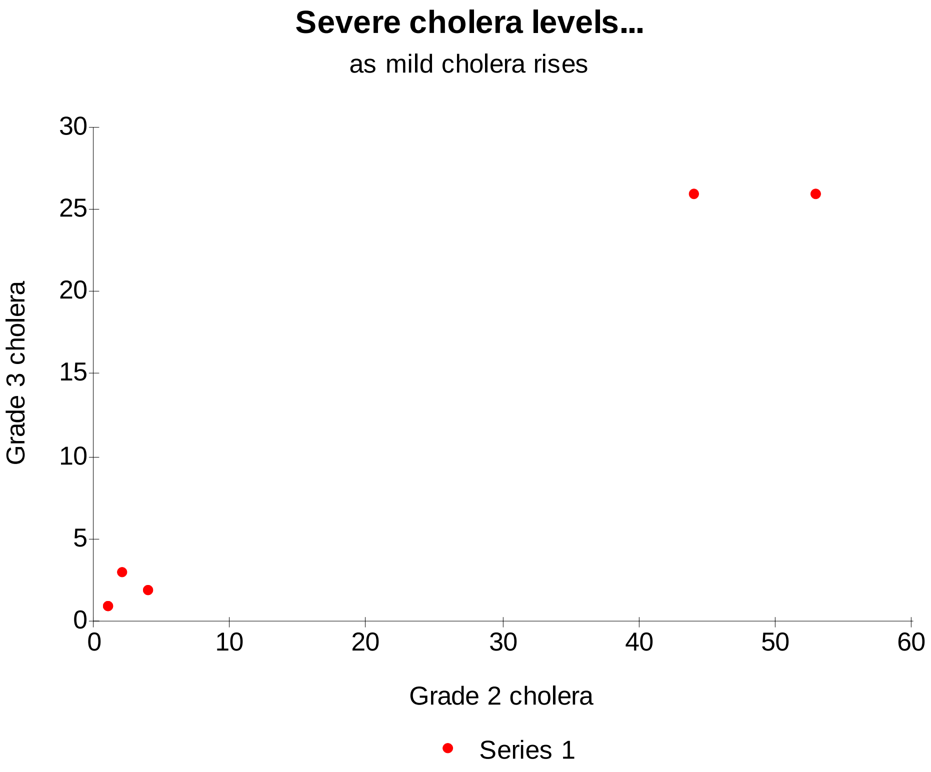
[18] Two persons may contract cholera at the same time, and independently of one another, yet not independently of the number of existing carriers.

[19] Cash, et al., 1974.

Equation 5

$$E[N_s] = N_{0,s} + p_1 N_{0,s-1}.$$

Equation (6) suggests that Equation (1) may be proxied by a linear relationship between the two more severe grades of cholera, Grades 2 and 3.[20] The number of Grade 3 cases is modeled as a function of the number of Grade 2 cases, for a given maximum dose of *vibrio*. The figure below shows the two series of cholera cases; the maximum dose associated with a point is not shown. For example, doses of up through 10^{10} *vibrio* organisms resulted in 44 cases of Grade 2 cholera and 26 cases of Grade 3 cholera; doses of up through 10^{11} *vibrio* organisms resulted in 53 cases of Grade 2 cholera and 26 cases of Grade 3 cholera. That is, increasing the dose from 10^{10} to 10^{11} organisms adds 9 cases of Grade 2 cholera but no new cases of Grade 3 cholera. The correlation coefficient, .99, suggests a linear relationship.[21]



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[20] The proxy may be suitable here because the choleric episode studied might have been too short to let one observe how the number of cholera cases may have related to the number of carriers.

[21] The linear regression model, estimated with Minitab, is *Grade 3 cases* = .35 + .52 *Grade 2 cases*, with t-statistics of .49 and 19.12 respectively on the two coefficients. Adjusted R^2 is .98. There are only seven observations, however.

While the data points are too few to permit much confidence in estimates, one can conjecture that a piecewise linear function may fit them. The implied linear slope coefficient between (4,2) and (44,26) is .6. This value is used for $a(c)$ in (1).

Estimating the probability function in (4) also requires a specification of A, where the number of cases is $m = Ae^a$. Setting m equal to the number of Grade 2 cases of cholera, 53, renders $A = 43.4$ and $p = .764$. This probability estimate is somewhat close to the actual relative frequency of .71.

The estimate, however, is sensitive to how one characterizes the equilibrium number of cholera cases. Setting m equal to the sum of Grade 2 and 3 cases yields an infeasible estimate for the probability, $p = 1.1$. One can conjecture this: Suppose that an equilibrium connotes no new cases of severe cholera; also suppose that severe cases would derive from milder cases of cholera. Then Grade 2 cases in themselves may represent an equilibrium.

IV. Conclusions

Preliminary estimates, based on too little data to permit much confidence, suggest that the number of cases of severe cholera may relate linearly to the number of cases of mild cholera. Conceivably, more robust estimates may someday enable health officials to use the number of mild cases of cholera, which occur early in an epidemic, to predict the number of severe cases that require emergency treatment. Future research may identify socioeconomic conditions that predate and predict epidemics.

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