Cholera and the Environment: An Introduction to Climate Change

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"The effects of environmental change may be analogous to those of nuclear war, which although it basically involves political, economic, and military issues, has the potential to harm human health to an unprecedented and intolerable degree" [1].

"Hay momentos en la vida de un pueblo en los que toda su historia puede verse al trasluz de una enfermedad" [2].

The accumulation of anthropogenic greenhouse gases in the troposphere and the depletion of ozone in the stratosphere are the major threats to the global environment. Changes in atmospheric and soil chemistry, in the distribution of water and vegetation, have major implications for human health, in particular the distribution of water-based and vector-borne diseases.

In 1991, cholera struck Peru, penetrating its poor communities, from multiple epicenters, with "unexpected breadth and intensity." Absent from the Americas for over 100 years, this severe form of gastroenteritis spread rapidly in societies whose water and sanitation systems had grown increasingly vulnerable, as the result of economic hardship and the stress of rapid urbanization. The means of transmission of Vibrio cholerae were described in the mid-nineteenth century, but a source and a reservoir have been matters for speculation.

Researchers have long associated the seasonality of cholera with the yearly blooms of algae, plankton, and sea plants in coastal waters. Using fluorescent antibody (FA) techniques, microbiologists have now identified a viable, nonculturable form of V. cholerae in a wide range of surface marine life. In unfavorable conditions, organisms "hibernate"; with warming and proper nutrients, they revert to a readily transmissible and infectious state. Plankton and algal populations respond to environmental conditions, and climatologists now report unusually large blooms of algae at sea. In the harbor near Lima, Peru, plankton is contaminated with cholera organisms.

It is argued that V. cholerae, having possibly arrived in the bilge of a Chinese freighter, found a competent reservoir in abundant coastal sea life, undergoing fertilization by increased atmospheric and coastal nitrate deposition; that the colonies were amplified, generating a heavy "inoculum"; and that infected carriers—fish, molluscs, and crustacea—carried V. cholerae into several ports, creating multiple epicenters along the Latin American Pacific coast. Finally, it is argued that it is unnecessary to await proof that global warming is occurring to assert that the by-products of known atmospheric and oceanographic changes are in the process of altering the distribution and impact of a gastrointestinal disease.

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BACKGROUND

In the nineteenth century progressive elements of the scientific community associated epidemics with environmental factors, such as sanitation and population density. The World Health Organization [3] and members of the medical profession [1] are now projecting the potential health effects of global climate change. These scientists warn of the direct consequences of increased ultraviolet B (UVB) rays and warming; of possible damage to agriculture and nutrition; and of the impact on habitats, which can alter reservoirs and the distribution of vector-borne and water-based infectious diseases. Eutrophication (algae growth due to increased nitrogen and phosphorus) and fertilizers by acid rain, air-borne dust, agricultural fertilizers, industrial waste, domestic sewage, and soil erosion due to agricultural practices, deforestation, and fire in the presence of dissolved carbonate and bicarbonate are already affecting marine microflora and aquatic plants, and there is now clear evidence that algae and plankton are a reservoir for enteric pathogens. The pattern of cholera in this hemisphere suggests that environmental changes have already begun to influence the epidemiology of infectious disease.

Cholera, Plankton, and Fluctuations in the Environment

In December 1991, it was reported that V. cholerae was present in sea and river water, in sewage, and in samples of plankton off the coast of Peru [4]. Cholera researchers have long sought to identify an environmental reservoir for this persistent, ancient pathogen [5–8]. In Bangladesh, there are two peaks of cholera incidence: the hot season (March to June) and the postmonsoon season (September to December) [9]. As early as 1960, Cockburn and Cassanos [5] reported that the peak incidence of cholera in endemic areas of Bangladesh occurred together with the bloom of blue-green algae [5]

In 1968, Dastidar and Narayanaswami [10] isolated a chitinase in V. cholerae 01, and in 1975, Kaneko and Colwell [11] described the adsorption of Vibrio parahaemolyticus onto the chitin of copepods, a zooplankton. In 1979, Nalin and colleagues [12] determined that adsorption of V. cholerae 01 onto chitinous fauna (including crabs, shrimp, and zooplankton) occurred more readily at lower pHs (6.2 versus 7.3). Nalin et al. found bacterial counts lower than those necessary for infection in volunteers with normal levels of gastric acid, but they speculated that chitin particles might provide a substrate for vibrio multiplication and provide protection against the acidic medium. In addition, V. cholerae secretes a mucinase [13] active in degrading mucin and mucin-like substances in plant cells.

V. cholerae organisms survive in water for four to seven days, faring slightly better in brackish water. Prolonged survival of V. cholerae 01 has now been associated with a wide taxonomic range of vascular aquatic plants, including water hyacinths, duckweeds, and a variety of phytoplankton and zooplankton [14–18] In the mucilaginous sheaths of a blue-green algae, Anabaena variabilis, V. cholerae can reach concentrations 1,000 to 5,000 times higher than in the aquatic environment [16,18] and can remain viable for as long as 15 months. Lemna minor, a common duckweed [19], harbors cholera on its surface. V. cholerae is found in laboratory control solutions that lack plants for only a few days. The improved survival of V. cholerae on L. minor may be due to the "utilization of dissolved organic carbon (DOC) excreted by L. minor. . ." or could be nonspecific and commensal (the plant merely providing a physical surface for the bacterial colonies).

Environmental conditions, e.g., sunlight, pH, temperature, salinity, and availability of nutrients, interact to affect both marine microflora and the physiological state, virulence, and survival of V. cholerae. Slime and surface films produced by some algae create turbulence-free microhavens, which can enhance growth of organisms (as well as retard the vertical flux of carbon return to the atmosphere) [20] (see below). On one species of green filamentous algae, Rhizoclonium fontanum, V. cholerae multiplies rapidly and releases a high level of toxins under conditions similar to those found during algal blooms (pH changing from 8 to 9) [5,8,21–25]. Species predilection has been studied: In comparison to four other species, (A. variabilis, Cladophora sp., Fontinalis antipyretica, and Elodea canadensis), R. fontanum showed the best attachment [26] and served as the nidus for substantial production of V. cholerae toxin [27].

A Dormant Form of V. cholerae

In searching for an environmental reservoir for cholera, Colwell and others have now refined their

microbiological techniques [28] Using FA techniques and the polymerase chain reaction (PCR) method of DNA replication, researchers have now uncovered previously undetected survival strategies of bacteria [29–35]. Nonculturable but viable forms of bacteria are detectable in a variety of environmental niches. Studying marine life in the waters of Bangladesh, these researchers found that four of five strains of V. cholerae 01 (and other bacteria, including other enteric pathogens) attach preferentially to zooplankton molts or exoskeletons (exuviae); one strain attaches to both exuviae and whole specimens [36,37]. Copepods, a common zooplankter, feed on V. cholerae, and 10^4 to 10^6 bacteria are found on the egg sacs V. cholerae also attaches to three species of phytoplankton studied, with high concentrations on Volvox sp., a colonial formation prominent in phytoplankton biomass.

Spore formation is one survival strategy of microorganisms [30]. (The general importance of refuges---of prey from predators or environmental changes or both---to the survival of agents and hosts was highlighted by a recent study involving parasitic insects [38].) V. cholerae (and other bacteria) revert to a microcyst, quiescent, or "somnicell" stage. The "round body" phenomenon, in which the volume of the organism decreases 15- to 300-fold, was described as early as 1969 [39]. In this "hibernating" stage, organisms reduce their rate of respiration, metabolism, and degradation of macromolecules. This strategy enables the bacteria to withstand environmental shifts in temperature, nutrient availability, pH, and salinity. When conditions are favorable to growth, the organisms return to a culturable, infectious state. The conditions favoring the culturable state are consistent with those created during algal blooms. Additional study is needed to determine species predilections, the relationship to contaminated carriers (molluscs, crustacea, and fish), and whether infective doses are maintained or, indeed, required. That the life cycles of V. cholerae and other water-borne enteric pathogens are intimately related to other marine organisms, in particular bacterial plankton, is consistent with the evolutionary development of life at sea.

CLIMATE CHANGE

The primary greenhouse gases include water vapor, carbon dioxide and monoxide, methane, nitrous oxides, and chlorofluorocarbons (CFCs). Excluding H_2O, CO_2 contributes 61%, CO 8%, CH_4 17%, nitrous oxides 3%, and CFCs 11%, in terms of 100-year global warming potential (GWP) [40]. The eight major anthropogenic sources include fossil fuel combustion, CFC use, landfills, land use changes, livestock production, rice cultivation, and fertilizer consumption. In the First Assessment Report of the U.N. Intergovernmental Panel of Climate Change (IPCC), the broadly representative panel concluded that increased greenhouse gas concentrations will "certainly" enhance the greenhouse effect and result, on average, in an additional warming of the earth's surface. "The main greenhouse gas—water vapor—will increase in response to global warming and further enhance it" [41]. In its national report for the 1992 U.N. Conference on the Environment and Development (UNCED), the U.S. claims that its "share amounts to approximately one-fifth of the total net greenhouse gas emissions" (net emissions are defined as the difference between emissions from "sources" and storage in "sinks") [40].

The Carbon Cycle

When self-replicating molecules first emerged on Earth approximately 4 billion years ago, 95% to 98% of the atmosphere was CO_2, as it is today on Mars, Venus, and Mercury With photosynthesis by cyanobacteria and subsequent generations of photosynthesizers, levels of CO_2 fell to 0.03% [42]. Ice core records demonstrate that between A.D. 1000 and A.D. 1850, atmospheric CO_2 remained nearly constant at 280 parts per million (ppm) by volume [43] Over the next century, levels steadily rose; and from 1958 to 1988, the concentration of CO_2 in the atmosphere increased from 315 to 353 ppm [44]. In 1988, the burning of fossil fuels (oil, coal, and gas) released an estimated 5.89 billion metric tons (gigatons) of carbon [45], or more than one ton for each human being on earth. Another one to two gigatons were released by the cutting and burning of forests. (Each ton of carbon results in 3.7 tons of CO_2 [46].) Of the seven gigatons of carbon emitted, 3.4 stay in the atmosphere, two are taken up by the ocean "sink," and the rest, most likely, by terrestrial plants [47,48]. Last year researchers proposed adding iron to further fertilize the algal blooms, in an effort to increase the absorption of atmospheric CO_2 [49] This idea is no longer in vogue, because of the uncertainty in evaluating the "side effects."

The Joint Global Ocean Flux Study (JGOFS) is the marine component of the International Geosphere

Biosphere Program, and it initiated field studies in 1989. JGOFS research has shown that variations in the absorption of carbon are directly related to the distribution of plankton [50]. During ice ages, "carbon apparently went into deep oceans," and "data from marine sediments have shown that the biological pump, acting via photosynthesis and surface waters, became stronger and deep water circulation more sluggish" [51]. Carbon settles as organisms die, and the rate at which it rises to the surface varies directly with temperature.

MARINE LIFE AND CLIMATE

Plankton and sea plants affect climate in three ways: 1) most important, they participate in the global carbon cycle by capturing CO_2, feeding carbon (in organic compounds) to larger marine life, and storing it when organisms die and sink to the ocean floor [52,53]; 2) they absorb and scatter light, warming the surface layers of the ocean [53a]; and 3) they produce volatile organic compounds, such as dimethylsulfide (DMS), which help to form nuclei for cloud formation [51,54,55].

Plankton and Algae

Plankton (drifting, minute organisms), and algae (nonvascular aquatic plants) live in the surface habitat that blankets more than 71% of the earth [56]. Some microbiologists divide plankton and algae into two kingdoms: Monera (i.e , bacteria), which are prokaryotic (lacking intracellular membranes), and Protista or Protoctistas (unicellular, multicellular, and colonial organisms, which are nonphotosynthesizers—zooplankton—and photosynthesizers—phytoplankton). Fossils of rod-like bacteria and forms suggesting blue-green and green algae found in South Africa suggest that such organisms originated 3.1 billion years ago [57]. (The other kingdoms of earth's biota are Animalia, Fungi, and Plantae.)

Bacteria, Protoctistas, and vascular aquatic plants occupy the sunlit photic zone of the oceans, which extends to depths of 50 to 100 m in clear and open seas, and inhabit inland waters: ponds, lakes, riverways, estuaries, wetlands, and bays. Plankton excretes organic compounds that serve as nutrients for other organisms. Metal ions bind with the organic compounds and together create a subsurface microenvironment very different from that at deeper levels. Growth of plankton and aquatic vascular plants depends on temperature, pH, and salinity [58,59], as well as nutrients. The chief nutrients, nitrogen and phosphorus, are found in sewage effluents, fertilizers, organic and inorganic pollutants, and combined by-products, together considered to be the primary causes of eutrophication or coastal algae overgrowth. Pesticides, on the other hand, as well as algae-induced deoxygenation, can kill off populations of grazers and reinforce algae and plankton growth [60]. The government of Morocco has successfully achieved biological control of excess algae growth due to eutrophication in one of its reservoirs; with the introduction of silver carp, phytoplankton biomass is significantly reduced [61].

Plankton comprise the "primary producers" of organic compounds [56], combining carbon and water by harnessing photosynthetically active radiation (PAR; 400 to 700 nm). (Cyanobacteria, blue-green in color, are the chief candidates for the earth's first photosynthesizers, predecessors of chloroplasts, and thus all plant life [62,63].) Ocean microflora today supply 70% of our oxygen, which in turn maintains the protective ozone layer in the stratosphere (altitude 9 to 30 miles) [42].

Plankton is the primary constituent in the food chain, itself the nourishment for many fish (basking shark and baleen whales), molluscs, crustaceans, and birds [59,64]. "Net plankters" measure 20 to 500 μm and are those caught in common, number 20 nets; nannoplankton and ultranannoplankton, which include bacteria and small chlorophyllous algae, filter through such nets. Red and brown pigments help create the variety of hues of plankton. Cyanobacteria contain chlorophyll type a; golden brown algae contain a and c; and blue-green algae contain chlorophyll types a, b, and c. Below the sediment surface lie anaerobic "consumers," the fermenters and methanogens, which decompose and "recycle" compounds and elements in a set of interrelated biogeochemical cycles necessary to sustain a complex ecosystem.

Plankton: Participants in Climate Control?

Photosynthetically driven growth of marine organisms cools the atmosphere by removing CO_2. Large CO_2 "drawdowns" through this biological pump (measured by pCO_2 gradients) occur in biological spring in polar regions. As the ice melts, illumination increases, nutrients become abundant, and fish and zooplankter grazers have not yet mobilized to consume the phytoplankton and algae [65].

In 1987, Bates, Charlson, and Gammon found additional evidence for the climatic role of marine life through the generation of biogenic sulphur [54]. Phytoplankton and algae produce DMS, the most abundant organic sulphur compound in the open ocean surface waters, which, when aerosolized, contributes directly to cooling through the backscatter of solar radiation. Sulfates also serve as cloud condensation nuclei (CCN). Dense, low clouds cool by reflecting sunlight and by delivering rain to the earth's oceans and landmasses. (Thinner clouds, at higher altitudes, can deflect heat back toward the earth's surface and thus contribute to warming.) In all, one-half of solar energy reaching the earth's atmosphere is reflected or radiated back into space. (Warm equatorial air, in opposition to cold polar air, drives much of the earth's wind systems, thus driving atmospheric circulation and the ocean currents. The Coriolus effect contributes a rotational force, in opposite directions in each hemisphere.)

Proponents of the Gaia hypothesis[1] argue that cooling from clouds reduces the populations of phytoplankton and diminishes DMS production and, therefore, cloud formation. They argue that such a feedback cycle or "rheostat" system has helped maintain biospheric temperatures within hospitable ranges over centuries [54,55]

While the theories of complex global interactions are disputed, the idea that feedback mechanisms are at work is gaining credence [66]. Schwartz [67] downplays the role of marine photosynthesizers, arguing that half of the world's SO_2 is anthropogenic (one-fourth originates from terrestrial plants, one-fourth from marine life), that there is no detectable hemispherical (north/south) asymmetry to the rate of temperature change, and that there is no observable influence of emissions of biogenic sulphur compounds on climate. "Nonetheless," he continues, "the potential for substantial human influence on global climate . . . makes it mandatory to gain a thorough understanding of the processes that control cloud albedo[2] and its influence on global climate." Calculations must also include the impact of volcanic eruptions, such as Mt. Pinatubo, which contain sulphur compounds and particles. These elements contribute to cloud formation and may be mitigating the warming impact of greenhouse gases in the short run [68].

Irrespective of the rheostat hypothesis and uncertainties in scientific modeling, the inherent relationship between marine life and the carbon cycle remains. How warming, increased CO_2, and sulfates and nitrates (which acidify rain) will combine to affect all plant (and animal) life is a matter of conjecture. With the manual clearing of terrestrial forests, the "fertilization" effect of additional CO_2, nutrient deposition, and warming may stimulate other terrestrial and marine plant life and alter its distribution and species composition. And while increased evaporation and precipitation may offset warming in the short run (5 to 10 years), the long-term prognosis is clouded by "convincing evidence that the deposition of sulfates, nitrates, and ammonium has significantly altered plant nutrition, soil, and freshwater chemistry" [69].

Ocean Currents

Ocean currents also influence regional weather patterns and concentrations of marine life. Large ocean streams—the "ocean's rivers"—have been shown to carry plankton over large distances [50]. Upwelling currents, like that off the Peruvian Coast, are rich in nutrients and can alter plankton and algae concentrations as well as shift them inward toward coasts [70].

The Continuous Plankton Recorder (CPR) survey, established by Sir Alister Hardy in the 1930s, has surveyed the northeast Atlantic each month from 1948 to the present [50]. Plankton populations are concentrated primarily along continental and island coasts but appear in the open ocean, their patterns determined by water currents and winds. CPR records demonstrate that from 1948 to 1980 phytoplankton and zooplankton in the northeastern Atlantic declined; the population of copepods, the primary component (in terms of biomass) of zooplankton, diminished sixfold. Since 1980 the trend has reversed. In the 1980s, the increase in copepods followed the Gulf Stream, and large increases appeared in areas west and northeast of Britain. At the Plymouth Marine Laboratory and the Ministry of Agriculture, Fisheries and Food, in Lowestoft, Eng-

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[1] Gaia hypotheses: that biospheric conditions such as temperature (15°C), atmospheric oxygen (20.9%), ocean salinity (0.4 M/l), and ambient pH (8.2) are maintained within ranges conducive to life; that the larger ecosystem depends on positive and negative feedback systems among the diverse biological and inert components, which generate the world's environment [42,62]. A proponent of this theory, microbiologist Lynn Margulis, argues that: "Biodiversity is not just a luxury; it is a necessity" [63].

[2] Albedo: reflective power, measured from 0 (100% absorbent) to 1 (100% reflective).

land, researchers concluded that the abundance of plankton in the North Atlantic responded to subtle climatic and oceanographic factors, which were operating over many thousands of kilometers. They "expect global warming of a few degrees to have a great effect on plankton patterns" [50].

Harmful Algae Blooms

At the Fifth International Conference on Toxic Marine Phytoplankton held in Newport, Rhode Island, in October 1991, algae blooms, surpassing the usual spring blooms, were reported from points as diverse as "North Carolina, California, Iceland, Finland, Japan, Thailand and Tasmania" [71]. Limnologists (researching inland bodies of water, in which, lacking carbonates, direct fertilization by atmospheric CO_2 may occur) also report outbreaks of algae and plant weed blooms in ponds and riverways [71,72]. Whether these blooms truly present an increase above normal background oscillations is a matter of intense study.

The 1972 New England red tide that extended the range of paralytic shellfish poisoning (PSP) caused by saxitoxin, the 1978 Florida outbreak of ciguatera poisoning linked to a dinoflagellate, and a series of papers in 1985 on diarrhetic shellfish poisoning (DSP) aroused the attention of oceanographers. In 1987, extensive work on the toxicology, ecology, taxonomy, and life cycles of several important fish-killing species of algae was presented at a meeting in Takamatsu, Japan. That meeting generated the first public discussion and speculation that harmful algae blooms might be increasing on a global scale and led to formation of the International Oceanographic Commission (IOC) program on Harmful Algae Blooms (HAB) [73].

Reports of HABs have continued [74–76]. In 1987, an outbreak of PSP acutely poisoned 153 and killed three people on Prince Edward Island, Canada [74]. In 1988, proliferation of a poisonous gelatinous algae (Chrysochromulina polyepsis) devastated Norwegian fishgrounds, costing the industry approximately U.S. $250 million, including the loss of 500 tons of salmon [73]. Pollution carried from rivers of eastern Germany was blamed, though other factors may have contributed. In 1989, on the beaches of Cape Cod, 13 humpback whales died from phytoplankton toxins, and, in September 1991, hundreds of pelicans and cormorants were poisoned in Monterey Bay, California by eating fish contaminated with domoic acid, an algae-produced toxin [71]. In 1991, a toxic algae bloom in Guatemala resulted in 185 reports of illness with 26 deaths [71]; and in December and January of 1991 to 1992, the contamination of the Aegean Sea with a high level of PCBs, blankets of algae, and possibly a "virus" were implicated in the deaths of 260 dolphins [77]. Finally, in 1991 in the U.S., an outbreak of diarrheal illness associated with cyanobacteria-like bodies (CLB) was reported in a Chicago hospital [78].

This series of reports has provided the impetus for the IOC and the World Meteorological Organization (WMO) to establish a Global Ocean Observing System (GOOS) under Agenda 21 of UNCED. The work of GOOS will involve oceanography, taxonomy, and the monitoring of public health and seafood safety.

Many climatologists have abandoned the view that these outbreaks are merely localized episodic nuisances. Such views are supported by fossil sediments suggesting large algae concentrations during a 1,000-year warming period that began around the first century A.D. [50] and are challenged by others who consider the recent rise in blooms to be part of natural cycles, perhaps bidecadal, dating back at least 2,000 years [53,79].

El Niño

El Niño (EN) events, the invasion of warm water from the western equatorial Pacific Ocean into the central and/or eastern equatorial Pacific, have a cyclic period of three to five years. Acting in tandem with the Southern Oscillation (SO) of air masses between eastern and western hemispheres, ENSO is felt all along the Pacific coast of the Americas and is related to temperature and precipitation, floods, and droughts in the U.S., Africa, Europe, and Asia [79a]. El Niño peaked in 1982 to 1983, warmed mildly in 1986 to 1987, and began a moderate rise (changing California coastal water about 0.5°C) in 1991 [80]. Warm and cold (Laniña) events, like that of 1988, are both associated with changes in algae populations. Modeling of ocean heat transfers is under study by the Tropical Oceans and Global Atmosphere (TOGA) and the newer group, TOGA Coupled Ocean/Atmosphere Response Experiment (TOGA COARE). Thermohaline ocean circulation involves warm surface currents flowing polewards, sinking, and returning at depths to tropical latitudes, with salinity changes reflecting the quantity of melting ice, and, locally, the difference between precipitation and evaporation [81,82]. Today's models of

ENSO do not yet take into account the concentration of greenhouse gases, and the study of ENSO's impact on large marine ecosystems (LMEs) is to be a main focus of GOOS.

Ozone and Phytoplankton

Stratospheric ozone loss, the other major component of global atmospheric change, has a negative impact on surface plankton, by allowing the increased penetration of harmful UVBs (280- to 320-nm short waves). Total Ozone Mapping Spectrometer (TOMS) surveys demonstrate that levels of ozone have been dropping approximately 3% per annum over the last decade in the latitude of New York and approximately 5% in the areas over Buenos Aires, Argentina, and Sydney, Australia [83].

Ozone's protective level is measured in Dobson units. The Antarctic ozone "holes" of 1987, 1989, 1990, and 1991 involved decreases from the norm of 500 to approximately 110 Dobson units. Harvard atmospheric chemist James Anderson, on the basis of research by the Airborne Arctic Stratospheric Expedition and NASA's Upper Atmosphere Research Satellite (UARS), calculated that the combination of stratospheric chlorine, bromine, and nitric acid trihydrate ice crystals would increase the breakdown of ozone during the spring of 1992 over densely populated areas of Europe [84]. By May 1, the predicted Arctic "hole" had reached only 20% diminution in ozone levels; the impact was decreased by unusually warm winter temperatures, which reduced from the average 66 to just 37 days on which there were sufficiently low temperatures for crystallization [85].

Scientists from the American Society of Limnology and Oceanography, working in the Antarctic region, have found that "ozone induced loss to . . . phytoplankton . . . is measurable" [86]. Since 1987, they record a reduction of 6% to 12% in total phytoplankton mass (notably krill, the shrimp-like food for penguins, seals, squid, and whales). Phytoplankton appear to have their own defense mechanisms; they increase the internal concentration of pigments (such as β-carotene), which block some of the harmful UVB rays.

The potential impact of this complex set of events on the food chain and on the global carbon cycle is a matter for speculation.

CHOLERA IN HISTORICAL PERSPECTIVE

Until the 19th century, cholera was confined to Asia, and almost exclusively to the Ganges and Brahmaputra River basins in India [87]. From 1817 to 1923, "Asiatic cholera" spread in six major pandemics to involve the European subcontinent, England, and the United States. International spread paralleled trade routes, reaching Great Britain in 1831 and the New York harbor in 1832. By the end of 1832, America's railways, canals, and steamboats had carried cholera to every large urban center, save Boston, Massachusetts, and Charleston, South Carolina [88]. The "poor man's plague" engulfed the cities, and populations (with the means to do so) fled to the countryside. In the 1848 outbreak, immigrants from Europe, having left famine and social turmoil behind, were blamed for its reemergence. The common people's belief in contagion and quarantine was considered medieval, and "anticontagionist" physicians (such as Rudolf Virchow) led the charge for social and environmental reform [89].

After 1895, with faster sea transport, cholera spread internationally with even greater rapidity, and, in the modern era, outbreaks have accompanied air transport [90]. Throughout history, migrations and changing population demographics have contributed to spread.

In 1849, John Snow argued in a brief pamphlet ("On the Mode of Communication of Cholera") that a "reproducing toxin" caused the disease. When cholera again surfaced in London in 1854, Snow conducted his famous epidemiological observations indicting contaminated water sources. In 1883, Robert Koch identified the bacteria, calling it Vibrio comma, after its curved shape [91]. V. cholerae is a gram-negative, flagellated and mobile, nonencapsulated, facultative anaerobe, its serotypes identified by two sets of antigens. The H antigens are flagellar and heat-labile proteins; the three O antigens (A, B, and C) are somatic and heat-stable polysaccharides. Ogawa (with A, B) and Inaba (with A, C) are the primary serotypes. Hikojima (A, B, C) is a third; a fourth (A only) is dubbed "unusual" [87,91,92].

In 1906, a hemolytic biotype was identified at the El Tor quarantine station in Egypt. The El Tor biotype, which evolved into a nonhemolytic form, is the agent responsible for the present pandemic. El Tor disease is of lower severity than classical cholera,

with 30 to 100 asymptomatic infections per severe case, in contrast to 2 to 10 infections per case of classical biotype. The El Tor biotype is more persistently excreted, is associated with a carrier state, and survives longer in the environment. In 1969, El Tor replaced classical as the dominant biotype in the Ganges River delta [92]. Drifts and shifts in types, strains, and virulence of microorganisms can be related to the environmental and evolutionary pressures on host and agent and the efficiency of transmission. (See the work of Ewald, May, and Anderson [93–96] for an extended discussion of host-parasite coevolutionary dynamics.)

Cholera in the Americas

The seventh world pandemic of cholera began in 1961 in the Celebes (Sulawesi), Indonesia, and soon spread throughout Asia and southern Russia [97, 98]. In 1970, cholera appeared in western Africa, in Mediterranean Africa, and in eastern Europe. By 1971, southern Europe and southern Africa were affected. Its initial course in Africa followed coastlines and waterways (being carried by fishermen and tradesmen) and later spread along land routes. During the 1980s, the number of cases reported worldwide declined, but the number of countries affected rose threefold (Fig 1).

At the end of January 1991, an outbreak of acute diarrhea was reported in the city of Chancay, 60 km north of Lima [97,98–100]. A day later the same occurred in Chimbote, a seaport 400 km north of Chancay. On January 31, cholera was confirmed in both cities; over the next two weeks, 12,000 cases were recorded. Moving with "unexpected speed and intensity," the epidemic spread 2,000 km along the Peruvian coast and appeared in all coastal departments (Figs 2 and 3). By the fourth week, cases were reported in the central mountainous regions (consistent with the movement of persons) but continued to gather greater strength along the coast. In one month (February 17 through March 20), 2,550 cases were occurring each day, a pace that heavily taxed the health resources of the region. Since January 1991, 441,000 cases (with over 4,000 deaths as of February 1992) have been reported in the Americas, 81% of those in Peru. The attack rate in the coastal departments was 1.1% as of May 91, while inland it was 0.16%. Case fatality, however, has been almost 12 times higher inland (4.6% versus 0.4%) than along the coast, reflecting most likely the relative lack of health services in the countryside.

Cholera appeared first in nations contiguous with Peru, reaching Ecuador on February 28 and Colombia on March 8. On April 16 Chile began reporting cases. In Colombia and Chile, the first regions affected were not on the borders with Peru but were located 800 km and 1,700 km, respectively, from the previous epicenters. On April 22, cholera appeared in western Brazil, in regions sharing waterways with Peru. In Venezuela, cases appeared only this winter and occurred in the western regions and in the capital but spared the rest of the Caribbean coast. (Venezuela is separated from the Pacific Ocean by Central America, and its primary waterway—the Orinoco— flows into the Brazilian Amazon.)

Although alternative explanations are possible, the epidemiological pattern of the cholera pandemic in the Americas is consistent with inoculum from multiple entry points along the Pacific coastline.

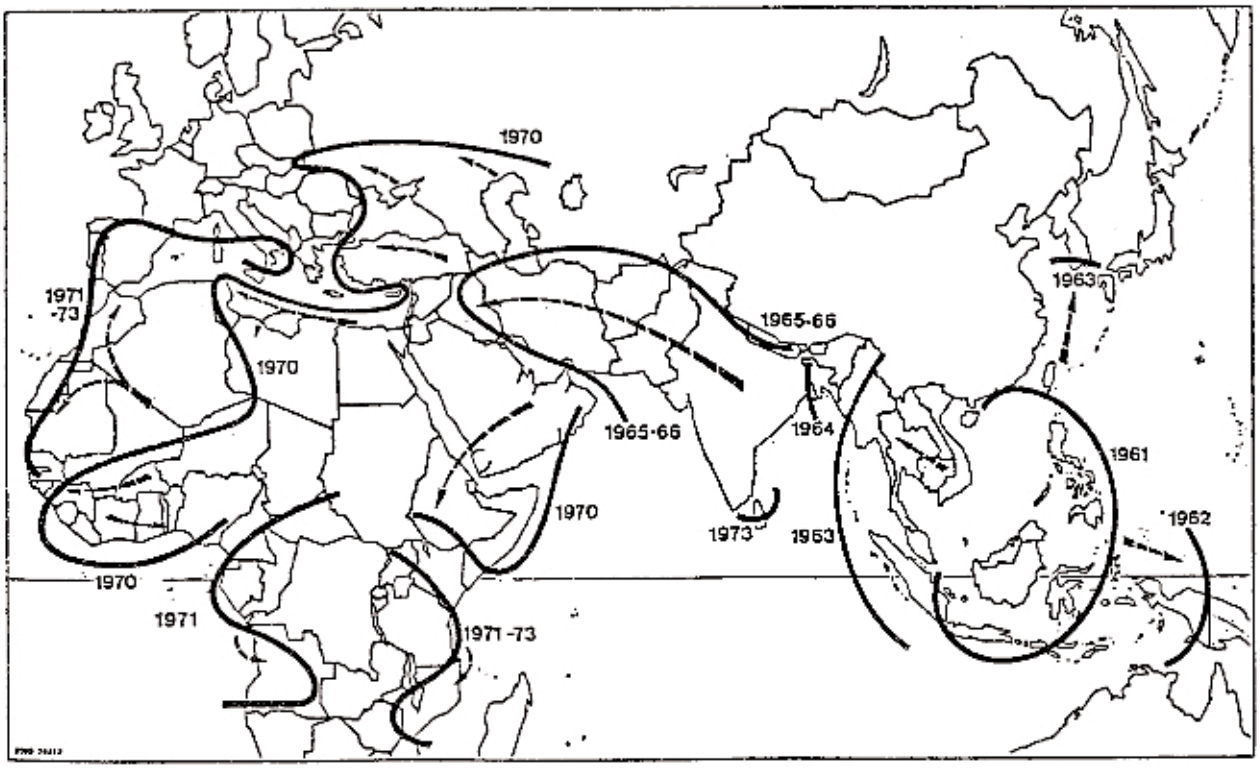
By the end of 1991 cholera was reported in Peru (300,000 cases, with 3,000 deaths), Ecuador (42,173 cases), Colombia (11,218), Guatemala (3,530), Mexico (2,605), and Panama (1,177); Chile, Nicaragua, El Salvador, and Brazil had fewer than 100 cases [88,89]. The worldwide total for 1991 reached 500,000, with 138,000 cases (and 12,500 deaths) in Africa [101].

The appearance of cholera in Peru in 1991 was the first such occurrence in the Americas in over 100 years [102–104], excluding sporadic cases in the U.S. and possibly Mexico (1973 and 1978). The etiologic agent in over 99% of the cases has been V. cholerae 01, biotype El Tor, serotype Inaba. (Costa Rica reported one case of serotype Ogawa, originating from Ecuador [105].) Chromosomal DNA probing suggests "genetic identity for V. cholerae 01 (biotype El Tor, serotype Inaba) strains causing epidemics in Bangladesh and" Latin America [9]. Throughout the spring of 1992, cholera continued unabated in Latin America, with 120,000 new cases and 700 deaths reported to WHO in 1992 by April 24.

The Host: Populations at Risk

Pan American Health Organization (PAHO) officials believe that cholera may have arrived in Peru with the contaminated bilge water of a Chinese

Map 1 **Global spread of cholera, 1961-1973** Carte 1 **Extension mondiale du choléra, 1961-1973**



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory city or area or of its authorities or concerning the delimitation of its frontiers or boundaries

Les designations utilisées sur cette carte et la présentation des données qui y figurent n'impliquent, de la part de l'Organisation mondiale de la Santé, aucune prise de position quant au statut juridique de tel ou tel pays, territoire, ville ou zone ou de ses autorités, ni quant au tracé de ses frontières

FIGURE 1. Weekly Epidemiological Record No. 9, March 1, 1991; 66:61.

freighter docked in the Lima harbor [106]. Once introduced, the vulnerability of the host—the societies and populations in the nations affected—played a crucial role in dissemination.

Despite the impressive achievement of the United Nations during the 1980s through the International Drinking Water Supply and Sanitation Decade, 2.7 billion people worldwide still lack safe water or sanitary toilet facilities or both [107]. Anastomoses between sewage and water supplies are commonplace, and their severity is sensitive to minor fluctuations in the water table. Urban centers throughout the third world have outgrown their infrastructures, and local economies, stymied by insurmountable foreign debts, are unable to assure maintenance, let alone make fundamental improvements to keep pace with periurban growth. From 1950 to 1980, many third world cities grew approximately sevenfold. Peru's capital was no exception; today 4 million people live in Lima's 2,000 shantytowns.

A sophisticated network of aqueducts and irrigation canals once latticed the Inca Empire (encompassing Peru), also famous for its cooperative, terraced farming and the rich (now threatened) fishing grounds. Five hundred years ago, the Incas were driven underground to mine the rich stores of copper, zinc, lead, and silver. By 1796, their population, once numbering 18 million, was reduced by European diseases and conditions of enslavement to 1 million. In the mid-1980s, the economy of Peru, now a nation of 22 million, collapsed. Structural Adjustment Programs (SAPs), introduced during the same period, compounded economic stresses on the poor. Government spending on infrastructure and, in some instances, supplies of chlorine were drastically reduced. Between 1985 and 1990 the inflation was 2 million percent. These disruptions left an estimated 12 million people in "extreme poverty" [108] and generated waves of internal migration. In 1990 and 1992 urbanization in Peru accelerated, the population uprooted by civil war and a U.S.-aided drug war in the countryside. (On April 7, 1992, a

Map 1 **The spread of cholera in Peru, 1991** Carte 1 **L'extension du choléra au Pérou, 1991**

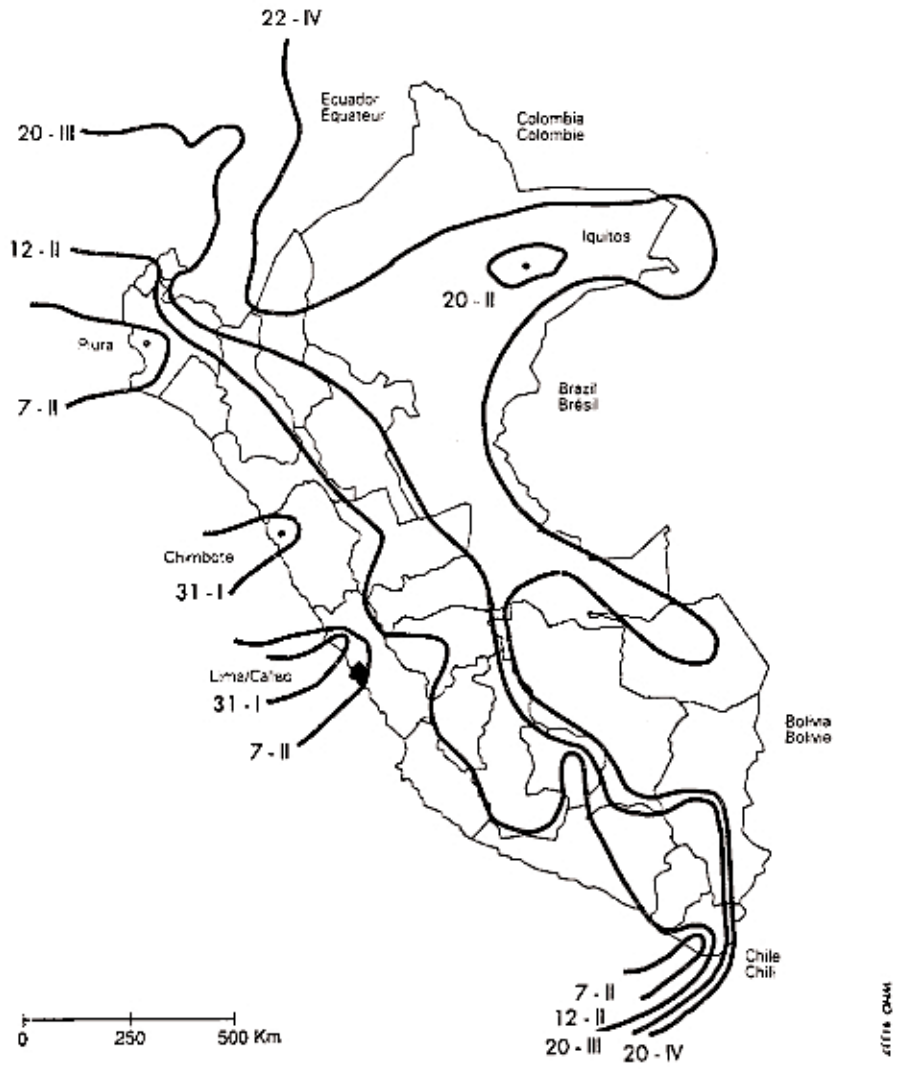


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FIGURE 2. Weekly Epidemiological Record No. 20, May 17, 1991; 66:142.

"civil-military" coup occurred in response to growing instability) Population shifts have put added strains on sanitation, water supplies, and housing. Every day ". . . 20% of Lima's population eats in neighborhood soup kitchens. . ." [109].

The poor are particularly vulnerable to cholera, and the periurban barrios have suffered inordinately from the cholera epidemic. Cultural habits, a focus of international attention (e.g., the "ceviche" wars), cannot be separated from economic status and social conditions. The poor tend to eat small fish, caught off harbor piers, near sewage effluents. Large fish, caught further out at sea, are not generally contaminated. (Elizabeth Evans, EDUCA, Lima, personal communication, February 1992.) Water collected from taps is delivered in trucks and sold in the barrios. Well water, tap water, commercial ice, and household containers have all grown cholera and have demonstrated progressive levels of contamination from distribution through storage There are

Map 2 **Cholera epidemic in Peru, attack rate as at 2 May 1991** Carte 2 **Epidémie de choléra au Pérou, taux d'attaque au 2 mai 1991**

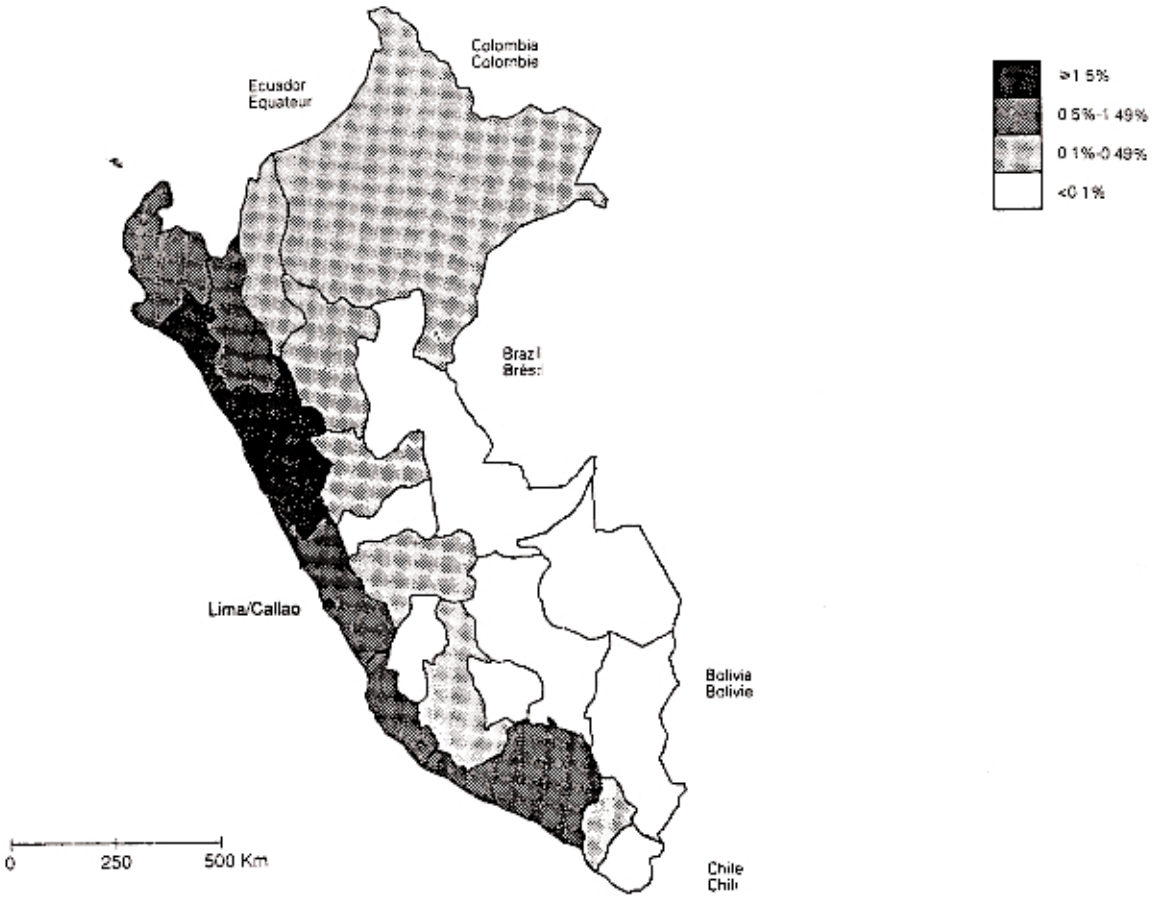

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FIGURE 3. Weekly Epidemiological Record No. 20, May 17, 1991; 66:144.

few bathrooms, chlorine is shunned (because of the smell), and fuel is scarce. The increased search for wood for fuel adds to the growing problem of deforestation, and some families in Lima have resorted to using school desks and chairs as fuel to burn to boil water. Peruvian government assistance is inadequate; the new year brought monetary charges for health services, and nongovernmental agencies have struggled to educate families in poor communities. Foreign aid has fallen, and there is, as yet, little evidence that the "cholera scare" is mobilizing substantial international resources [110].

The U S., although lacking the conditions conducive to sustaining an epidemic of cholera, is not immune to sporadic penetration. Over a two-year period (1989–1990), 26 waterborne-disease outbreaks (WBDOs) associated with deficiencies in well (50%), surface (38%), and spring (12%) water distribution systems were reported from 16 states [111]. V. cholerae 01, biotype El Tor, serotype Inaba has been recovered from the ballast, bilge, and sewage of three ships docked in the Gulf of Mexico; the previous ports of call were in Brazil, Colombia, and Chile [112,113]. There remains the possibility of future international spread by ships, currents, and storms, given the apparent establishment of a maintenance reservoir for cholera in the Americas.

CONCLUSION

The earth's biosystem is threatened primarily by the current methods of energy conversion and wide-

spread deforestation. These patterns of "development" are accelerating, driven by debt and unequal terms of trade in the global market. The current international financial arrangements are generating the local economic activities such as forest clear-cutting and export-based monocropping that pit immediate needs against long-term survival. "The global economy's engines are out of tune and sputtering" [114], and the by-product is uncoordinated attacks on its invaluable resources. (The impact is not all negative, however, for CO_2 emissions dropped from 1989 to 1990, as a result of the world economic downturn; and CO_2 emissions would have fallen further, save for the oil well fires in Kuwait [115].)

There is growing evidence that the populations of bacteria and Protoctistas are being altered by climatic changes, and it is now known that these marine microflora, lying at the heart of the food web, provide a reservoir for V. cholerae and other enteric pathogens. The rapid dissemination of cholera in the Americas may reflect both a large "inoculum effect" of the assaulting organism and the vulnerabilities in host immunity. The toll of infectious diseases in animals and plants depends upon the overall community of organisms; the interrelationships range from commensalism, symbiosis, and synergism to competition and parasitism, across the five kingdoms of biota. The multiplicity of environmental changes, while some may be self-correcting through intricate feedback cycles, could be setting the stage for multiple shifts along the spectrum of these interactions. Climate is controlled by the interaction of the atmosphere, oceans, land systems, and ice cover. "A change in any one of these aspects will affect the entire system," explained Bert Bolin, head of the IPCC, speaking in Rio. Habitat fragmentation and disruptions in predator-prey relationships may drastically alter disease reservoirs and vectors, and we can expect the redistribution of old diseases and, indeed, the emergence of new ones.

We cannot afford to await proof that human activities are warming the globe. The Framework on Climate Change Convention (FCCC), signed at UNCED, calls for decreased greenhouse gas emissions, though strict targets and timetables were eliminated. Largely escaping public attention is that the goal of stabilizing emissions is in itself inadequate; an *immediate* 40% to 60% reduction in emissions is needed according to the IPCC to reduce the crucial value—the aggregate atmospheric concentrations of greenhouse gases. On the positive side, the FCCC does provide an international legal framework, which can be amended as scientific information becomes more certain or as climate changes dictate.

The medical profession has an important role to play in evaluating the health impacts of climate change. It can also join an interdisciplinary effort to monitor the accuracy of climate model projections, by conducting case studies, by participating in international monitoring teams, and through construction of a disease database, constructed around a Geographic Information System that interdigitates with climate models. Physicians can also work with nongovernmental organizations and legislators to regulate environmental impacts, to implement international accords, and to help translate the impact of global changes to the public.

"Epidemics," wrote Rudolf Virchow in 1848, "are like sign-posts from which the statesman of stature can read that a disturbance has occurred in the development of his nation that not even careless politics can overlook"; [116] and they require interventions that address their underlying causes. ❧

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