

Widespread Foodborne Cyclosporiasis Outbreaks Present Major Challenges

To the Editor: The organism now named *Cyclospora cayetanensis* was first recognized as a cause of human illness in 1977. For several years, as its taxonomy was deliberated, it was referred to as "cyanobacterium-, or coccidia-like bodies" (CLBs), or considered to be blue-green algae. In 1993, *C. cayetanensis* was reported to be a protozoan parasite, a coccidian member of the family *Eimeriidae*. To be infectious, the spherical, chlorine-resistant oocyst (8µm to 10µm) found in the feces of infected persons must sporulate in the environment, a process that, depending on conditions, takes at least several days. Upon examination by ultraviolet microscopy, *Cyclospora* oocysts autofluoresce and upon staining, they are variably acid-fast. The incubation period between infection and onset of symptoms averages approximately 1 week. *Cyclospora* infects the small intestine and usually causes watery diarrhea, with frequent stools. It can also cause loss of appetite, weight loss, stomach cramps, nausea, vomiting, fatigue, increased flatus, and low-grade fever. The duration of symptoms is often several weeks, and remitting courses spanning 1 to 2 months, with several relapses, have been reported. Cyclosporiasis is effectively treated with trimethoprim/sulfamethoxazole; however, therapy for patients who are sulfa-intolerant has not been identified.

Before 1996, only three outbreaks of *Cyclospora* infection had been reported in the United States. However, between May 1 and mid-July 1996 almost 1,000 laboratory-confirmed cases were reported to the Centers for Disease Control and Prevention (CDC). A few hospitalizations (<20) were reported, but no *Cyclospora*-related deaths were confirmed. These infections occurred in at least 15 states and Canadian provinces and the District of Columbia. Investigations of approximately 50 event-related outbreaks of diarrheal illness due to *C. cayetanensis*, as well as case-control studies of sporadic, laboratory-confirmed cases by several states, now clearly implicate consumption of fresh raspberries. Complete, high confidence level

trace-backs of raspberry shipments related to more than 25 of the events have indicated that the raspberries responsible were imported from Guatemala between early May and mid-June 1996.

On June 17, 1996, CDC began hosting thrice-weekly conference calls to ensure close coordination among CDC, the U.S. Food and Drug Administration (FDA), and the many state and local health agencies investigating these widespread outbreaks and cases. The conference calls provided coordination in tracking and discussing this multifocal problem. In addition, on July 17, 1996, in Atlanta, CDC and FDA held a 1-day work-shop entitled "*cyclospora* - 1996," which was attended by more than 80 persons representing CDC, FDA, the U.S. Department of Agriculture, 16 states, one province, five cities, five universities, the Council of State and Territorial Epidemiologists, the Association of State and Territorial Public Health Laboratory Directors, the Pan American Health Organization, and the government of Canada. The participants in the investigations of *Cyclospora* shared the knowledge gained through their individual investigations of this multistate, multicountry outbreak. The goals of the workshop were to begin to formulate effective prevention strategies for *Cyclospora* infection, to discuss the strength of the evidence implicating Guatemalan raspberries, and to formulate research needs. The workshop allowed for discussions about the epidemiologic and trace-back studies conducted and speculation about where and how the raspberries became contaminated. Representatives from Texas, South Carolina, New York City, Florida, and New Jersey presented data from their respective case-control and cohort studies; CDC representatives provided an overview of the outbreaks and focused on multiple, specific trace-backs from more than 20 of the event-related outbreaks. FDA representatives discussed their roles and regulatory authority in foodborne investigations.

The workshop also addressed the array of scientific challenges concerning *C. cayetanensis*, such as clinical diagnostic techniques, protocols for detection of the organism on produce, and the basic biology of

this protozoon. We do not know the infectious dose, the proportion of infected persons who have diarrhea, the proportion of diarrheal illness caused in various settings by *Cyclospora*, the existence of animal reservoirs, or the viability of the organism in different environmental conditions. It can be transmitted by water and food, and its transmission is seasonal (late spring/early summer), at least where it has been studied (primarily temperate, seasonal climates).

The poor sensitivity and specificity of current methods for diagnosis and detection of *Cyclospora* were discussed. A photomicrographic demonstration convinced the participants that currently the foremost requirement for accurate clinical diagnosis is a skilled microscopist. The status of polymerase chain reaction technologies for detection and diagnosis of *Cyclospora* was presented and discussed, including the inhibitory aspects of berry juices and the difficulty in oocyst recoveries from spiked berry samples. Participants stated the need for a bank of *Cyclospora* organisms and their DNA (molecular libraries) from different locations and outbreaks. Currently, we may not be able to take full advantage of such epidemiologically well-documented specimens; however, the technologies and tools will continue to advance, and these specimens need to be centrally banked now, to be made available when the tools are up to the task. An animal model needs to be developed, or at least explored. The uses for such a model include providing material (oocysts and other life-cycle stages) for reagent development (monoclonal antibodies) to allow studies of the organisms, the disease, immune responses, and potential environmental transmission. Such a model will facilitate the development of prevention and treatment strategies.

Ongoing investigations into how the raspberries were contaminated were discussed. The lack of sensitive and reproducible detection assays for *Cyclospora*, which does not replicate outside the human host, remains the major stumbling block in providing proof of contamination of suspected transmission vehicles. Studies were too preliminary for conclusions. Both the government of Guatemala and the producer/

exporter associations were most helpful in the investigations and need to remain involved if we are to better understand what occurred in May and June of this year.

Throughout the workshop, a wider issue than the current situation with *Cyclospora* was discussed: the management of the emerging problem of widespread multistate and international foodborne outbreaks of both infectious and toxic nature. Such outbreaks are increasing and can be expected to worsen as the world moves toward a global food economy. What contaminates a particular food item on a farm, in a herd or crop, at a processing shed, or from a handler, can now cause widely distributed outbreaks, continents away, in a day. More coordination is needed on several fronts in the management of such outbreaks: 1) the development of a structured process for integration and coordination of epidemiologic studies; 2) more aggressive laboratory diagnostic training related to poorly recognized or understood emerging infections; 3) better coordination of press releases related to multistate outbreaks; 4) better understanding and clarification of the legal roles and responsibilities of federal, state, and local agencies; 5) and earlier involvement of industrial partners at all levels, including growing/processing, exporting/importing, transporting, and wholesale/retail sales. Because these types of outbreaks are likely to become international this aspect must be addressed in considering appropriate approaches.

The *Cyclospora* outbreaks of May and June 1996 underlined that without the ability to culture and grow the organisms, without a supply of the organism to develop expedient assays, without an established coordinating body to expedite agreed-upon means for dissemination of information, we, as public health officials, are called upon to provide guidance without the benefit of all the appropriate knowledge. The workshop engendered interchange and discussion on critical issues concerning what is known and unknown about *Cyclospora* and the outbreaks of cyclosporiasis during May and June 1996. The workshop also provided a forum in which it became apparent that public health officials must launch a committed effort to develop an established,

coordinating system among agencies at all levels and deal with the threat of widespread, multistate/international foodborne outbreaks caused by infectious or toxic agents.

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Identification of *Cyclospora* in Poultry

To the Editor: Human infection with the parasitic protozoa, *Cyclospora*, was first described in 1979 (1), and the organism was only recently categorized as an important gastrointestinal parasite. A single species, *Cyclospora cayetanensis*, has been described in humans (2), while most species in the genus *Cyclospora* have been described only in reptiles and rodents (3). The consumption of undercooked meat and exposure to contaminated water have been considered possible sources of human infection with *C. cayetanensis* (1,4). Coccidia were detected in drinking water in Nepal (5), and the parasite was identified in an animal species (one duck in Peru, by Zerpa et al. [6]) different from those in which it was described earlier. To determine whether a domestic animal is either a host or a reservoir for *C. cayetanensis*, we first examined feces from cats, which are hosts and reservoirs of *Toxoplasma gondii*, a coccidia causing human illness, but got negative results. Because *Cyclospora* were recently phylogenetically linked to *Eimeria mitis* and *E. tenella* (7), coccidial parasites of chickens, we investigated the presence of *Cyclospora* in poultry.

We pooled feces from approximately 600 4- to 6-week-old chickens from a poultry farm near Monterrey, Mexico, and extracted feces from the caecum of 50 6- to 8-week-old chickens from a poultry market at that location. By Percoll discontinuous-gradient centrifugation (Medina-De la Garza et al., submitted), both fecal pools were positive for coccidia, mainly *Eimeria* species and what we regarded as *C. cayetanensis* oocysts. Presence of *Cyclospora* was confirmed

by 1) characteristic morphology and size (8 μ m to 10 μ m), 2) positive staining with Kinyoun's acid-fast stain, 3) positive autofluorescence under ultraviolet light, and 4) sporulation of oocysts with formation of sporocysts after a 10-day incubation. All these are diagnostic features of *C. cayetanensis* (8) and to our knowledge are not described for any known poultry coccidia.

On the basis of these findings, we suggest that poultry may serve as a possible source for human infection with *Cyclospora*. Consumption of chicken has been reported in one infected patient in the original description by Ashford (1) and in a patient reported recently by Connor and Shlim (9). Moreover, the only existing report of *C. cayetanensis* found in feces from a domestic farm animal concerned a farm duck (6). Zerpa et al. suggest that besides consumption of contaminated water, other modes of transmission involving contact with domestic animals must be considered. So far, however, a possible infection route involving poultry, whether it may be direct consumption of undercooked chicken meat, contamination of food and water sources with chicken feces, or both, remains to be determined. It should be noted that sanitary standards in poultry-breeding facilities in developing countries may not be adequate. This would account for the fact that reports implicating chickens in the transmission of *Cyclospora* (1,9) have occurred in, or in relation to, developing countries. The *Cyclospora* found in the chickens in our study have the diagnostic features of *C. cayetanensis*. Nevertheless, the existence of another, not yet described, *Cyclospora* species infecting poultry, which has similar features but is different from *C. cayetanensis*, cannot be excluded at this stage. In addition, the number of oocysts recovered was not large and because feces were pooled, we could not calculate the number of oocysts passed by each bird. The possibility that oocysts were acquired as a contaminant from food or water sources and were only passing through the gut of the chickens (making the chickens a paratonic host) cannot be ruled out.

The increased recognition of *Cyclospora* as an important cause of diarrhea in both immunocompromised and immunocompetent

persons and the public health relevance of this emerging pathogen as a potential cause of diarrheal outbreaks (3,4) make prompt disclosure of the epidemiologic features and behavior of the parasite necessary. As we propose the possible participation of poultry in the epidemiologic cycle of the coccidia, we invite other *Cyclospora* working groups worldwide to confirm the so far putative reservoir described in this communication and to further study other possible hosts or reservoirs.

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PCR Confirmation of Infection with *Cyclospora cayetanensis*

To the Editor: *Cyclospora cayetanensis*, formerly known as cyanobacterium-like body, is a variably acid-fast microorganism. Recently, it was classified as a coccidian parasite (1) closely related to the genus *Eimeria* (2). Humans infected with *C. cayetanensis* typically have diarrheal illness with a variable number of stools per day and sometimes have nausea and vomiting (3,4). *Cyclospora* infection has been reported in many parts of the world as clustered or sporadic cases (1,3-5).

Variable success in diagnosing infection with this parasite underscores the need for using (as quality control) molecular methods, which do not rely on the level of expertise of laboratory personnel in microscopy. The key features for diagnosis by light microscopy are size (8 μ m to 10 μ m in diameter), internal features of stained and unstained oocysts, and autofluorescence of oocysts (1,6). The definitive diagnosis is understood as visualization of characteristic sporulated oocysts, which contain two sporocysts. However, sporulation typically requires incubating oocysts for up to 2 weeks, and this approach cannot be applied to Formalin or polyvinylalcohol-preserved stool smears.

Sporadic and clustered cases of *Cyclospora* infections were reported in the United States and Canada during May and June 1996 (5,7). From these outbreaks, more than 900 cases were diagnosed by examining stool specimens under light microscopy (Barbara Herwaldt, pers. comm.). Epidemiologic studies indicated risk for *Cyclospora* infection from consuming raspberries imported from Guatemala (7). Forty-two stool specimens supplied in 2.5% potassium dichromate from patients with intestinal symptoms were forwarded to the Centers for Disease Control and Prevention to be evaluated by microscopy and by polymerase chain reaction (PCR) amplification. In addition, one well-characterized positive stool specimen from Nepal was provided by John Cross, Armed Forces Research Institute of Medical Sciences,

Bangkok, Thailand, to use as the positive control.

Using techniques we developed for diagnosis of other protozoan parasites in stools, we extracted DNA from all stools. The techniques we used employ glass-bead disruption of oocysts in a buffer containing Laureth-12, purification with the RapidPrep Micro Genomic DNA Isolation Kit for Cells and Tissue (Pharmacia Biotech Inc., Piscataway, N.J.), followed by a final purification step employing the QIAquick PCR purification kit protocol (Qiagen, Inc., Chatsworth, Calif.) (8). The glass-bead disruption of oocysts was far more effective than sonication (2) or freeze-thawing techniques (9). We performed nested PCR in all stool specimens by using Relman et al. (2) primers CYCF1E and CYCR2B for the first step of nested amplification and primers CYCF3E and CYCR4B for the second (nested) step of the PCR. These are the only primers described for amplification of *Cyclospora* DNA. We found optimal conditions for the first step PCR to be denaturation at 94°C for 30 s, annealing at 55°C for 30 s, and extension at 72°C for 90 s, 45 cycles. The same conditions were used for the second step of the nested PCR, but the annealing temperature was 60°C.

By using this approach, we amplified the *Cyclospora*-specific DNA fragment in 16 (38%) of the 26 (62%) specimens reconfirmed as positive by light microscopy. The 10 specimens negative by PCR but positive by microscopy showed either few or moderate numbers of *Cyclospora* oocysts. None of the 16 (38%) specimens negative by microscopy generated positive results in the PCR *Cyclospora* test. Upon further examination by the PCR technique we developed (9), three of these samples were positive for another enteric coccidian, *Cryptosporidium parvum*.

Preliminary evaluation indicates that the sensitivity of PCR is 62%, and the specificity is 100%. Although the sensitivity of the technique should be evaluated further, these results indicate that PCR can be used to detect *Cyclospora*. We assessed the sensitivity of this PCR again by using the Nepalese specimen described above. This specimen, which was used as positive control in all reactions, was amplified even when the

extracted DNA was diluted at 10⁻⁵.

Lastly, a note of caution. As noted by Relman et al. (2) and confirmed by us through GenBank searches, the nested PCR *Cyclospora* primers cross-amplify other coccidians, especially those belonging to the genus *Eimeria* (because no molecular data exist for another human coccidian enteric parasite, *Isospora belli*, potential cross-amplification remains to be determined). This cross-amplification with *Eimeria* should not present a problem in diagnosing *Cyclospora* in human stool, as no human infections by *Eimeria* are known. However, when analyzing food or environmental specimens, this cross-amplification may complicate precise detection of *Cyclospora*.

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Emerging Infectious Diseases and the Depopulation of French Polynesia in the 19th Century

To the Editor: The same dynamics now considered factors in the emergence of infectious diseases may have been involved in the dramatic depopulation of French Polynesia in the 19th century. Temporal and geographic variation in the frequency and severity of infectious diseases are the result of the encounter and interaction of a population of parasites and a population of hosts. J. Musser reviewed the "bacterial side of the equation" (1). On the host side, there are two historical models that describe the influence of parasitism on human populations (2-4): 1) the South American model, in which new pathogens were introduced into native populations by the European conquistadores, causing the death of 50 million people; and 2) the African model, in which infectious diseases present in native populations protected them from the effects of colonization until modern times when the discovery of quinine and other efficient antipathogenic drugs provided added protection. The second model is well illustrated by the attempted colonization of Madagascar, where the French lost five men to war and 5,000 to malaria (2). This letter intends to illustrate the first model. We suggest that during their first contacts with European navigators in the very late 18th century and the 19th century, Polynesian islanders, much like populations in the South American model, were decimated by newly introduced infectious diseases.

It is difficult to know precisely which infectious diseases were present in Tahiti and the other French Polynesian islands before the arrival of the first Europeans. However, a study of Polynesian languages indicates that Bancroftian filariasis and leprosy were already present, while syphilis and other venereal diseases, influenza, and

tuberculosis (TB) were probably unknown. Epidemic diarrhea and dysenteriae could have existed, although first reports mentioned that the oldest Polynesians "never heard of dysenteriae before" (5). In the Marquesian language, names exist for leprosy, bronchitis, abscesses, and impetigo.

The number of inhabitants in Tahiti, as well as in the Marquesas and the Austral Archipelago, was at first only estimated by European explorers. However, a precise census was performed as soon as missionaries and French authorities noted the high death rates in most of the islands (5,7,15,16). Tahiti was annexed by France in 1843; the first census was performed in 1848, and the population size was assessed approximately every 5 years until 1911.

Four major epidemic diseases (TB, typhoid, influenza, and smallpox) devastated the Marquesas from 1791 to 1863/64; approximately 80% of the population died. During that period, exchange of populations between the Marquesas Islands also increased, as a consequence of colonization. Thus, leprosy increased dramatically during the second half of the 19th century, to a prevalence of 4.11% in 1884 (6).

In Rapa, the remote, southern island of the Austral Archipelago, at least three epidemics were reported, resulting in the loss of more than 90% of the population. Although the cause of the first epidemic remained unknown, dysenteriae and smallpox were identified as causes of the second and third epidemics, respectively.

From Rapa, a missionary went to Mangareva in 1831 or 1832, and his visit there was followed by an epidemic that the natives attributed "to his god." He had to flee back to Rapa. The second recorded epidemic disease was "Chinese scabies" in 1865, which decimated the child population. Then, the warship "La Zélée" brought an epidemic of influenza in 1908. In 1910, TB and leprosy were reported "to spread rapidly" (7), and in 1911, the ship "La Gauloise" brought whooping cough to Mangareva.

In Tahiti and the Society Islands, the number and diversity of international and interisland exchanges, involving numerous commercial ships and whalers, make the origin of epidemics more difficult to trace.

However, at least five were reported successively in the Leeward Islands in 1843, 1848, 1854, and 1864 (7), and at least 11 in Tahiti: influenza (1772 to 1774), pulmonary TB (1775), dysentery following the passage of the ship of Vancouver (1790), dysentery after the passage of the whaler "Britania" (1807), disastrous influenza in 1820, whooping cough in 1840, smallpox in 1841, dysentery again in 1843, scarlet fever in 1847, measles in 1852-1854 (800 deaths were recorded) and typhoid fever after the passage of "La Magicienne" in 1877 (8).

Almost without exception, authors attributed the dramatic depopulation of French Polynesia during the 19th century to infectious diseases. Other causes, such as alcohol, opium, local wars, infanticides, and even orgiastic behavior were also mentioned as possible causes. Depopulation occurred to a similar extent in other South Pacific countries (9), e.g., the Cook Islands, Hawaii, Tonga, Samoa, and particularly Fiji, where 50% of the population died. Thus, after limited initial contact with persons exposed to infectious diseases, most of the Polynesian populations died. Why did it happen? Why were epidemics so intense and so severe? It is unlikely that clones of bacteria, viruses, fungi, or parasites with particularly high virulence were introduced into native populations since the long crossing by sailing boats would have selected clones with lower virulence. Moreover, epidemics are also intense and severe in animal populations when new infectious agents are introduced. In Hawaii, the introduction of *Plasmodium* from birds had catastrophic consequences for the local fauna (10).

Host population factors that may influence the spread of an infectious agent (i.e., the intensity of an epidemic) are diverse: 1) social disruption was certainly a major cause for the increase of leprosy and TB in the Marquesas during the 19th century: pacification of the archipelago by Dupetit-Thouars changed traditional behavior and destroyed tribal barriers against leprosy by permitting the development of interisland exchanges, thus contributing to the spread of both leprosy (within the Marquesas) and TB (from Tahiti to one Marquesas island, then between the Marquesas) (11); 2) the absence

of most infectious diseases in Polynesia before the 18th century probably slowed the selection of behavioral methods of prevention and the development of traditional medicine; 3) a small population without exposure to infectious diseases would not have selected resistance genes against nonexistent infectious agents; and 4) the lack of population immunity probably had a major role in the spread of new infectious agents.

Host population factors that can influence the virulence of parasites (i.e., the severity of an epidemic) are less frequent. Successive epidemics of closely related viruses or bacteria can enhance the severity of the disease, as in dengue fever (12), or can inversely provide cross-protection, as was suggested between yaws and syphilis (13), whose causative organisms are almost indistinguishable. Reduced genetic polymorphism of 19th century Polynesians who had no immunity to infectious diseases could have contributed to the severity of epidemics in the South Pacific, as it was speculated for South America (4,14).

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Epidemic Zoster and AIDS

To the Editor: Zoster (exogenously reactivated varicella-zoster virus infection) may seem an unlikely candidate for emergence and epidemicity. A recent report, however, describes a zoster outbreak associated with epidemic HIV in injecting drug users in Manipur State, India (1). In addition to underscoring the variety of ways in which "old" diseases may reemerge under complex bio-ecologic conditions, this outbreak may also have implications for anticipating and diagnosing HIV infections and AIDS in developing countries. The Manipur outbreak was associated with a doubling of zoster frequency above background levels, with increased occurrence most notable in males 12-44 years old, who also had the highest HIV prevalence. In a separately studied group of 120 injecting drug users, 20 developed zoster and all were found to be HIV positive (1), a correlation substantially greater than for such other clinical predictors of HIV infection as persistent lymphadenopathy, weight loss, or recurrent dermatoses. Increased zoster occurrence associated with HIV transmission has also been seen in Ho Chi Minh City, Vietnam, and in other Southeast Asian countries, particularly in injecting drug using populations (unpublished). Zoster as a sentinel indicator of community HIV transmission is also sug-

gested by reports from Africa (2).

For over 150 years, it was believed that zoster occurred in local epidemics (3,4). By the 1950s, however, it was generally agreed that zoster represented reactivation of latent ganglionic varicella virus either sporadically, or in response to immunosuppression or trauma. Epidemics of "endogenous" immunosuppression, such as those associated with epidemic HIV infection, might thus be expected to produce outbreaks of zoster, as seems to have occurred in Manipur and Vietnam. In the Indian outbreak traumatic zoster seemed unlikely: truncal and facial dermatomes predominated, rather than dermatomes corresponding to drug injection sites (usually the hands or legs). Recognition of zoster outbreaks may be important in developing countries where HIV diagnosis is limited, CD4 cell counts are unavailable, and diagnosis of AIDS is delayed. Zoster is not currently accepted as an AIDS-defining condition (5), and the extent to which it may reflect immune collapse or predict HIV disease progression is uncertain. Nevertheless, greater awareness of zoster as a sentinel indicator of community HIV transmission may be of help not only in clinical diagnosis, but also in public health efforts to recognize epidemic HIV occurrence.

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Ancient Egypt and Today: Enough Scourges to Go Around

To the Editor: In a recent letter (1), Ablin conjectures that translation of the hieroglyphic symbol for \overline{AAA} in many ancient Egyptian papyri (Ebers, Berlin, Hearst, London, and Kahum), may be suggesting the existence of human immunodeficiency virus (HIV) or its prototype during the time of the pharaohs. While hieroglyphic interpretations remain challenging, the symbol cited in his letter has most commonly been translated as hematuria (2-4) and has most often been related to schistosomiasis haematobia. This infection, caused by the helminth *Schistosoma haematobium*, has been shown to have occurred in Egypt from early pharaonic times (3200 B.C.), by the demonstration of schistosome eggs (5) and circulating schistosome antigens (6,7) in mummies. Remedies for hematuria were recorded in papyri from many centuries (9 in Hearst, 11 in Berlin, 20 in Ebers), perhaps implying that the condition was serious and widespread. In giving one of the remedies in the Ebers papyrus (circa 1500 B.C.), the text actually mentions worms in the body (although it seems to state that the worms are caused by \overline{AAA} disease, perhaps inverting the true order of causality). In the Hearst papyrus one of the remedies cited for hematuria is antimony disulfide. Until only 25 years ago, antimonial compounds were the most effective drugs for schistosomiasis chemotherapy.

It seems likely that, over a period of many centuries in ancient Egypt, \overline{AAA} disease was a widespread condition of sufficient severity to require medical attention. I concur with many others in proposing that the translation of \overline{AAA} disease is hematuria, and that the relationship drawn between \overline{AAA} and worms in the body, antimonial-based remedies, and the knowledge that *S. haematobium* infections were

widely present at that time provide strong evidence that \overline{AAA} disease refers to schistosomiasis haematobia.

Schistosomiasis is still with us. In fact, through dispersions of both human populations and specific fresh-water snails (the intermediate hosts for schistosomes), this disease now infects some 200 million persons and is responsible for an estimated 800,000 deaths per year (8). While clearly ancient, schistosomiasis can emerge as a new infectious disease in a given location under certain man-made changes in environmental conditions and economic- or war-related migrations of people. For example, in the Senegal River basin, estuarine dams, irrigation systems, and an influx of people to work irrigation-intense crops led, over a period of only 3 years, to an increased prevalence of *S. mansoni* infection from 0% to >95% of the population of >50,000 (9). Even in modern-day Egypt, such interventions as the Aswan High Dam have significantly altered patterns of schistosomiasis (2,10). The Ministry of Health and Population of Egypt and the U.S. Agency for International Development are addressing this ancient scourge through the Schistosomiasis Research Project, a national schistosomiasis research and control program that attacks the disease with available tools, while it presses forward with research on much needed new tools, such as vaccines.

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AIDS and $\overline{\text{AAA}}$ in Egypt?

To the Editor: A recent letter concerning Egyptian hieroglyphs on the disease $\overline{\text{AAA}}$ asks if this disease could be AIDS or an HIV-associated condition prevalent in Egypt during the time of the pharaohs (1). We believe this possibility is highly unlikely. Aside from conflicts with current thought on the origin and evolution of lentiviruses, there is a problem of linguistic interpretation. The initial hieroglyph in the series of hieroglyphs comprising the word $\overline{\text{AAA}}$, a picture of a discharging phallus, is a "determinative," indicating the class or category to which the word belongs. Although scholars once took this determinative to indicate a phallic connection with disease, even suggesting that $\overline{\text{AAA}}$ meant hematuria, consistent with schistosomiasis (2,3), it was later proposed that the determinative meant semen or poison, reflecting the Egyptian concept that diseases may be transmitted by an evil spirit in the form of an incubus, impregnating a victim with poisonous semen.

This interpretation is now generally accepted (4,5). The phallus-with-discharge thus came to indicate a deadly disease, and $\overline{\text{AAA}}$ a poisonous disease-causing substance introduced into the body by magic. The word $\overline{\text{AAA}}$ is used elsewhere in the Egyptian medical papyri in other contexts, such as " $\overline{\text{AAA}}$ of the heart" and " $\overline{\text{AAA}}$ of the belly and heart," and is not known to have been used in connection with the bladder or genitalia. While the determinative meaning may not be absolutely established, it is clear from its usage in other contexts that the phallus-with-discharge determinative can indicate fatal or serious illness. The notion that the phallus-with-discharge determinative refers to sexually transmitted disease is not consistent with its usage. To further argue that $\overline{\text{AAA}}$ represents AIDS or HIV disease is not justified by the linguistic evidence. Without further archaeological or inscriptional evidence, we would doubt that HIV circulated in ancient Egypt.

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