REFERENCES

COLONIAL CONUNDRUM: DIVINING THE DIAGNOSIS OF A MYSTERIOUS FEVER

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> In 1793, synchronous with an epidemic of yellow fever at Philadelphia, this then small village was attacked, by a disease that so closely resembled it, that a writer of the time, Alexander Graydon, esq., in his *Memoirs*, remarks upon it. Quartan ague also prevailed at the time.
>
> —Hugh Hamilton, *The Sanitary Condition of Harrisburg, Pennsylvania* (1866)

Alexander Graydon (1752–1818) was appointed prothonotary of Dauphin County in 1785, a position he occupied for the next fourteen years after which he retired to a small farm near Harrisburg. He moved back to Philadelphia in 1816 and passed away at the age of sixty-six.[1] In his *Memoirs* in a chapter subtitled "Yellow Fever," Graydon reports that "a malady not less fatal than that in Philadelphia was raging" in Harrisburg in 1793. The mortality of the two was comparable. The symptoms of the Harrisburg disease included affection of the stomach or nausea with violent retching, yellowness of the skin, and black vomit in some cases. Illness duration was perhaps a week, sometimes

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longer, and some died in two to three days. Other ambulatory victims with symptoms only of ague suddenly became quite ill and expired. Graydon himself was ill with a quartan ague in mid-September but had no other symptoms. He attributed the origin of the illness to marsh effluvia caused by "torrid sun acting upon moist soil, or upon impure and stagnant water."[2]

In addition to Graydon's first-hand account of the illness, several other sources reported accounts of both the fever and circumstances surrounding it.[3] George H. Morgan's *Annals* describes a sickness in Harrisburg in 1793 characterized by "a fever of violent character, similar to the yellow fever" that was especially prevalent among new settlers. High fatalities were reported among Irish immigrants and some residents as well; most families were touched by the epidemic. Philadelphia was experiencing yellow fever during this same time and patrols were "established at the lower end of the town to prevent infected persons from Philadelphia from coming into it."[4]

The approximate population of Harrisburg, as listed in the census of 1790 was 875; it rose to about 1,300 in 1792–94.[5] According to the census of 1790, Pennsylvania's population of European origin was as follows: 35.5 percent English, 8.6 percent Scot, 14.5 percent Irish, 33.3 percent German, 1.8 percent Dutch, 1.8 percent French, 0.8 percent Swedish, and 3.9 percent "unassigned."[6]

Several sources reported on temperature and weather for the time period surrounding the illness, but none are specific to Harrisburg. (Harrisburg is located in southcentral Pennsylvania along the Susquehanna River at latitude 40°16′ N and longitude 76°53′ W. Its nearest colonial neighbors in 1793 were Middletown, Manheim, Lancaster, York, and Carlisle.) A daily weather and temperature table for Philadelphia covering January to November 1793 is included in Rush's "Account of the Bilious Remitting Fever of 1793" (see appendix).[7] Webster in *Epidemic and Pestilential Diseases* reported general weather conditions of the world including the following notes for Philadelphia: In 1792 winter was "Cold"; in 1793 summer was "Dry & Very Hot" and winter was "Mild"; in 1794 winter was "Mild."[8]

Benjamin F. Royer, Graydon, and Morgan all report that Peter and Abraham Landis's mill dam on the Paxton Creek (near Harrisburg) was the cause of the great fever or sickness. The dam spread water over eight to ten acres within a few hundred yards of the middle of town and provided an excellent source for marsh effluvia. Fearing further infection, irate village residents subsequently tore down the dam and confiscated the land.[9]

Countless vectors are associated with fever in humans. By far the most common is the mosquito, known to transmit malaria, yellow fever, and dengue. Lice and fleas are associated with typhus and ticks with spotted fevers. Plague and brucellosis are passed through rodents and other animals. Leptospirosis may be contracted from spirochetes by swimming in fresh water.

Differential Diagnosis

Malaria

Darrett Rutman and Anita Rutman define malaria as "a febrile disease arising as a reaction of the body to invasion by parasites of the genus *Plasmodium*." Colonial descriptors are imprecise as is the disease itself, but the word *ague* (meaning a combination of chills and fever) is commonly thought to be indicative of malaria. Chills and fever frequently herald a great company of infectious diseases. "Intermittent" or "remittent" fever may have also described malaria, although these, too, are inexact terms. Successful treatment with "the Peruvian Bark" (quinine) might signify malaria but it probably was used universally for many varieties of fever.[10]

There are four *Plasmodium* species: *vivax, ovale, malariae*, and *falciparum*. *Vivax* was probably imported to America by Europeans, while *falciparum* originated in tropical and subtropical regions. Untreated *falciparum* is the most lethal, accounting for 20 to 40 percent mortality. Symptoms of malaria include intermittent high fevers, chills, rigors, severe headache, body ache, nausea, weakness, and prostration. Anemia, cerebral malaria, wasting, and jaundice may follow. Malarial fevers tend to follow characteristic cyclic patterns of tertian (every third day), quartan (every fourth day), or malignant tertian (every third day with grave illness).[11]

Falciparum, the most severe form of malaria, occurred primarily south of the thirty-fifth parallel and almost never north of the thirty-eighth parallel. North and South Carolina, located between the twenty-ninth and thirty-sixth parallels, experienced high malarial fatality between August and November when conditions for transmission were ideal. *Vivax* was seen as far north as southern Canada because it tolerated wider temperature variation. The *vivax* parasite was able to survive winter in a dormant state and re-emerge the following spring. Boundaries of transmission rates are defined by the mosquito, levels of population mobility of infected individuals,

temperature (since cold inhibits mosquito activity), and latent activity (ability to winter over).[12]

Yellow Fever

Jari Vainio and Felicity Cutts define yellow fever as an arthropod-borne "viral hemorrhagic fever" of the family *Flavivirdae*. The female *Aedes aegypti* mosquito is the main vector in transmitting the virus to humans. Incubation in the human host is three to six days; an attack of yellow fever brings lifelong immunity against reinfection.[13]

Mathew Carey, a medical writer and publisher who resided in colonial Philadelphia, described initial symptoms as chills, headache, myalgia, inflamed eye, bellyache, and vomiting. These continued for three to five days and then abated, leaving a "yellow tinge in the white of the eyes" and skin, along with "constant puking." Vomited matter resembled coffee grounds, hence "black vomit." Hemorrhaging from other body parts, delirium, and death between the fifth and eighth days followed.[14]

It is remarkable how closely Carey's contemporary account mirrors those of today. According to Vaino and Cutts, yellow fever "is characterized by sudden onset of fever, headache, backache, general muscle pain, nausea, and vomiting." Jaundice may not be present in mild cases. About 15 percent develop a serious triphasic illness: acute three days with "sudden onset of fever, headache, myalgia, nausea, and vomiting" followed by remission of perhaps twenty-four hours and then onset of a toxic phase with jaundice and black vomiting, hemorrhaging from other parts of the body, progressing to diarrhea, tachycardia, and shock. "At least half of the individuals who reach the toxic phase do not survive."[15] Death occurs between seven and ten days.

Rene La Roche noted in 1855 that the "atmospheric heat" was "indispensably necessary," thus limiting northern geographic boundaries of yellow fever.[16] From Brazil to Charleston, South Carolina, and from Barbados to Tampico, plus the West Indies, are normal borders. Yellow fever visited north of Charleston along the coastal cities of the Middle Atlantic states, and even as far north as Boston; it was recorded in the Mississippi Valley as far north as Memphis. Thus, yellow fever may be seen between the twenty-second and twenty-third parallel south of the equator (just north of Rio de Janeiro, Brazil) to the forty-second parallel north on the Atlantic coast (near Plymouth, Massachusetts). A paper presented to the American Public

Health Association in 1873 expanded the yellow fever boundaries, noting that other factors such as extremes of heat and cold, mean temperature, wind direction, humidity, and annual precipitation contribute to favorable disease conditions. Population density (i.e., crowding) was also observed to have an influence.[17]

Leptospirosis

Leptospirosis is a spirochetal disease caused by human contact with an animal-contaminated water environment. Symptoms are fever, chills, headache, and severe myalgias. In about 10 percent of cases the disease progresses to severe in a multisystem fashion typified by renal insufficiency, bleeding, respiratory insufficiency, altered mental status, and jaundice. The mortality rate in those with severe disease may approach 15 percent.[18]

Leptospirosis, usually a tropical disease, occurs in a rural environment where there is a lack of sanitation. But the causative organism can exist in slow-moving water in temperate summers. It would be difficult, based on symptoms, to differentiate among dengue, malaria, typhoid fever, or hepatitis A.[19]

Typhoid Fever

Typhoid fever is a systemic infection caused by *Salmonella enterica typhi*, acquired through ingestion of food or water contaminated with fecal material. Incubation is five to twenty-one days until fulminant infection.[20] Onset is characterized by nonspecific symptoms including fever, malaise, chills, headache, diarrhea, nausea, belly pain, anorexia, cough, vomiting, and myalgia. Fever rises progressively and is often high and sustained by the second week. Classic "rose" spots occur in about 80 percent of patients. Complications (e.g., bowel hemorrhage and perforation) occur in 10 to 15 percent of patients. The fatality rate reported by Sir William Osler in 1900 was approximately 7.5 percent; both relapse and reinfection are recognized.[21] Other febrile diseases that resemble typhoid are malaria, tuberculosis, flu, dengue, leptospirosis, brucellosis, and typhus.[22]

Dengue

Dengue, a febrile illness characterized by fever and rheumatic symptoms, was known to the colonials as "breakbone fever" because of the particularly severe pain in the back, neck, and hips and was so named by Noah Webster

in 1780. Dengue occurred as an epidemic fever characterized by "headache with intolerance of light, general uneasiness, restlessness, sometimes more or less chilliness, a sense of great debility, and violent pains in the back, limbs and joints." A skin rash lasting about twenty-four hours accompanied the disease; some reported overall redness, like scarlet fever, while others reported similarity to measles or rubella.[23] Dengue is a tropical or subtropical *Flavivirus* disease that is spread by mosquitoes. Most cases resolve without treatment and life-long immunity ensues. George B. Wood notes that the prognosis is almost always favorable: "Perhaps no disease with so much severity of symptoms is so seldom fatal." However, in some cases the fever progresses to dengue hemorrhagic fever or dengue shock during which hepatic damage, cardiomyopathy, encephalopathy, and encephalitis may occur. In such cases, mortality may be high. Dengue may look a lot like yellow fever, scarlet fever, malaria, rheumatic fever, or measles; it was reported in Philadelphia in 1780.[24]

Hepatitis A

Hepatitis A is a viral illness acquired by contact, either personal or through contaminated water or food. It is passed by the fecal-oral route among individuals and has an incubation period of about twenty-eight days. Presenting symptoms include fever, malaise, nausea, anorexia, abdominal pain, and dark urine. Jaundice occurs in more than 70 percent of patients. Hepatitis A is a self-limited, short-lived disease usually followed by a full recovery in a few weeks. Care of afflicted individuals is supportive. About 20 percent of patients do not have a typical course and go on to carrier, recurrent, or chronic states. Fewer than 1 percent develop fulminant fatal hepatitis.[25]

Discussion

Lacking modern laboratory and imaging diagnostic tools, the colonials relied chiefly upon observance of symptoms to differentiate among diseases.[26] Some were easier to identify, like breakbone or spotted fevers, but many febrile illnesses presented with identical and quite nonspecific constellations of symptoms: fever, headache, chills, and generalized achiness. Colonial physicians tried to describe, sometimes in excruciating detail,

those aspects of one disease that made it different from another; for example, La Roche wrote 615 pages on yellow fever.[27] Consequently, it is difficult to distinguish among bilious, remitting, and enteric fevers even with their exacting accounts.

Royer, drawing from the contemporary description of the "Great sickness at Harrisburg," advanced a hypothesis that the fever was malarial in nature, citing the symptoms of severe vomiting and yellow skin as not inconsistent with malaria and general malarial debility. In support of this diagnosis, he reasoned that the Landis mill dam provided a stagnant source of pooled water in which *anopheles* mosquitoes could breed. He further hypothesized that immigrants from malarial areas may have carried *Plasmodium* to the region. Royer explained that the warm, late summer months provided the perfect combination of source, vector, breeding ground and susceptible population to sustain a fever outbreak. Harrisburg residents believed that the cause was a miasmatic contagion arising from the swamp created by the Landis brothers' mill dam.[28] The miasma theory, a noxious or foul-smelling vapor believed to contain poisonous particles that cause disease, was a popular explanation of disease causation and was often associated with malaria.[29]

Noting the appearance of fever in three consecutive years, Royer wrote that the malignant fever of August and September of 1793 brought a severe sickness "accompanied by chills, violent retchings, fever, severe vomiting and bloody flux and sometimes was characterized by yellow skin."[30] In addition to the features of the illness described in Graydon's contemporary account, Royer added bloody flux to the symptomatology. He attributed this to enteric disease commonly contracted from wells polluted by privies and thus postulated coexisting diseases—simultaneous diarrheal disease and malaria.

Osler noted in 1909 that dysentery and typhoid are probably contracted in the same way. He confirmed that typhoid and malaria "may co-exist in the same patient," but in 1,500 cases of typhoid only three patients had *Plasmodium*.[31] Jaundice, a prominent symptom in the Harrisburg malady, is rare in typhoid fever, uncommon in dysentery, and slight and rather late in the course of malaria. Skin rash is present in typhoid fever, but was not seen in the Harrisburg fever. Medical historian John Duffy of Tulane University agreed that "malaria was present in all American colonies during the 17th century" and that its incidence rose in the early eighteenth century

especially in the coastal plains along the Atlantic seaboard. He further noted, "The case fatality rate among malaria patients was considerably lower than that for yellow fever or small pox, but malaria was more widespread." *Falciparum* malaria with a fatality rate somewhat higher than the Harrisburg fever could be a possibility, but Professor Margaret Humphreys of Duke University reports that it almost never occurred north of the thirty-eighth parallel (southern border of Maryland).[32]

Both dengue and hepatitis A exhibit features in common with the Harrisburg fever, but neither carries a high fatality rate. Hepatitis A is associated with jaundice in nearly three-quarters of patients, but most recover in a few weeks. Additionally, dengue is accompanied by a skin rash that was not noted in the Harrisburg fever.

Leptospirosis is frequently associated with jaundice and has a fatality rate (15 percent) high enough to be considered a diagnostic possibility. It can be contracted by swimming in fresh water and has an intermediate ten- to twenty-one-day incubation period. It is primarily a tropical disease today, but the summer of 1793 was noted to have been "very hot." The Harrisburg population, between 875 (1790) and 1,472 (1800) along with numerous domestic animals, may have been sufficient to create an unsanitary environment in which the spirochetes could flourish. Still, it is difficult to imagine sufficient numbers of local residents swimming in the "swamp" created by the mill dam. Additionally, leptospirosis lacks several of the prominent symptoms (nausea, violent retching, and black vomit) attributed to the Harrisburg fever.

In his *Memoir* chapter, "Yellow Fever—Marsh Effluvia . . ." Graydon described the Harrisburg fever, although it seems apparent that he was initially referring to Philadelphia. He explained that, during the summer of 1793, "the metropolis of Pennsylvania . . . was visited with a calamity. . . . A disease that was soon recognized to be the pestilential yellow fever, carried off several persons early in the month of August; and gradually spreading in all directions, raged with the most fatal malignancy until the close of October. . . . Although the ravages of the disease were yet confined to Philadelphia, it was not supposed they would remain within these limits." Yellow fever was clearly recognized as the cause of the Philadelphia fever. Graydon continued, "Some of the people of Harrisburg were following the example of their neighbors [guarding the entry to town], though a malady not less fatal than that in Philadelphia was raging among themselves.

But the difference was, that one was called a plague, but the other a simple fever."[33]

The American plague to which Graydon and Noah Webster referred is a synonym for yellow fever, but Graydon seems to imply that some felt the Harrisburg malady was a "simple fever." He reported in his autobiography that he suffered from an attack of quartan ague in September but had none of the symptoms of the malignant fever *which prevailed* [emphasis in original]. Quartan ague was most likely *Plasmodium malariae* malaria, a chronic persistent disease with a long incubation period of about thirty days. Duffy reported that fever and ague were perennial complaints in the eighteenth century, with sections of Pennsylvania and Delaware among the major trouble spots, but he also commented that this disease was more morbid than mortal. The Drinker family diary entry for 1795 reveals, "No member of the Drinker family escaped malaria."[34]

Graydon continued his narrative, debating the origins of yellow fever and considering whether the disease could have progressed 100 miles up the Susquehanna River, before moving on to describe the symptoms and mortality of the Harrisburg malady. "With respect to the mortality produced by the two diseases, that at Harrisburg was, I believe, in proportion to the population of the place, as great as that at Philadelphia." The general description of the Harrisburg disease was

> an affection of the stomach, or nausea with violent retchings and a yellowness of the skin. Some were ill a week, some longer, some died in two or three days from the time of their being seized, and others, who were walking about with symptoms only of the ague, suddenly took ill and expired. The black vomit, which has sometimes been supposed peculiar to the yellow fever, appeared in some cases.[35]

The mortality rate reported for the 1793 yellow fever epidemic in Philadelphia approached 10 percent.[36] The symptoms Graydon described are consistent with yellow fever, particularly those of early jaundice, black vomit, rapidity of death, and relatively high mortality rate. The vector for both malaria and yellow fever is the mosquito, but it was not recognized as such in the 1790s. Instead, the marsh effluvia mentioned by Graydon was blamed, therefore initiating the public outcry against the Landises' mill dam. The subsequent repossession of the land and destruction of the dam was one of those happy circumstances where the right action was undertaken for the wrong reason.

Conclusion

Although an exact diagnosis of the Harrisburg fever may never be established, it seems likely that the malady Graydon described was yellow fever. It occurred during late summer when atmospheric conditions were favorable for mosquito breeding, induced jaundice early in the course of the fever, caused the black vomit so characteristic of yellow fever, had a high fatality rate in a short period of time, and a relatively close infection source in Philadelphia.[37] Another outbreak of yellow fever was reported in 1803 at Lisburn, Cumberland County, on the Yellow Breeches Creek, about nine miles from Harrisburg, adding credence to the presence of yellow fever along Pennsylvania's inland waterways.[38]

The presence of malaria should not be discounted. Although malaria does not fit the epidemic nature of the Harrisburg fever, evidence suggests that it existed in background. Vainio and Cutts observe that malaria and yellow fever coexist, and that "malaria usually shows clinical symptoms almost identical with those of the early stages of yellow fever."[39] The course and prognosis differentiate the two. "Yellow fever has no second week. It and the plague are the shortest of all febrile diseases, as they are also the most fatal."[40]

APPENDIX. Temperature and Weather for Philadelphia, June–September 1793

	JUNE			JULY			AUGUST			SEPTEMBER		
	TEMP		WEATHER	TEMP		WEATHER	TEMP		WEATHER	TEMP		WEATHER
DAY	7 AM	2 PM	AM, PM	6 AM	3 PM	AM, PM	6 AM	3 PM	AM, PM	6 am	3 PM	AM, PM
1	53	61	Rain, showery	77	88	Fair	65	77	Cloudy, fair	71	86	Fog, fair
2	54	64	Clouds, showers	77	81	Fair, showers	63	81	Fair, fair	73	86	Fair, fair
3	55	62	Cloudy, rain, fair	74	80	Cloudy	62	82	Fair, fair	60	—	Fair, fair
4	54	60	Rain, do. Cloudy	70	83	Cloudy, fair, rain	65	87	Fair, fair	55	75	Fair, fair
5	58	72	Cloudy, fair, rain	76	90	Fair, ditto	73	90	Fair, fair	62	80	Fair, cloudy
6	—	71	Cloudy, rain	78	91	Cloudy, thunder	77	87	Cloudy, fair	70	89	Fair, cloudy
7	68	78	Fair, ditto	73	88	Fair, clouds	68	83	Fair, fair	65	77	Fair, fair
8	65	—	Fair, ditto	72	85	Cloudy, fair	69	86	Fair, rain	64	70	Cloudy, cloudy
9	70	88	Fog, fair	73	81	Cloudy, ditto	75	85	Cloudy, fair	66	80	Rain, fair
10	74	90	Fair, ditto	70	84	Fair, ditto	67	82	Fair, fair	64	72	Fair, cloudy
11	76	90	Fair, ditto	74	88	Fair, clouds	70	84	Cloudy, cloudy	62	72	Cloudy, fair
12	75	88	Fair, showers	70	84	Fair, ditto	70	87	Fair, fair	58	76	Fair, fair
13	74	81	Cloudy, rain	68	83	Fair, ditto	71	89	Fair, fair	57	72	Fair, fair
14	63	77	Fair, ditto	65	80	Fair, hazy	75	82	Fair, rain	58	79	Fair, fair
15	63	82	Fair, hazy	66	75	Cloudy, ditto	72	75	Fair, cloudy	65	80	Fair, fair

16	67	85	Fair, ditto	70	83	Rain, fair	70	83	Fair, fair	70	84	Cloudy, fair
17	74	89	Fair, showers	68	81	Fair, ditto	71	86	Fair, fair	66	67	Cloudy, cloudy
18	73	88	Fair, ditto	66	86	Fair, ditto	73	89	Fair, fair	44	—	Fair,
19	77	91	Fair, ditto	75	85	Fair, cloudy, rain	72	82	Fair, cloudy	45	70	Fair, fair
20	79	88	Fair, rain, fair	72	87	Fair, ditto, shower	69	82	Fair, fair	54	69	Hazy, hazy
21	75	85	Cloudy, rain	70	86	Fair, ditto	62	83	Fair, fair	59	78	Cloudy, fair
22	58	78	Cloudy, fair, rain	72	87	Fair, ditto	63	86	Fair, fair	63	83	Cloudy, fair
23	58	78	Fair, ditto	73	91	Fair, cloudy, rain	63	85	Fair, fair	62	—	Cloudy, cloudy
24	60	79	Fair, ditto	75	89	Cloudy, fair	73	81	Cloudy, rain	65	70	Cloudy, fair
25	67	74	Cloudy, rain	71	83	Fair, ditto	71	66	Rain, Gr rain	61	68	Cloudy, cloudy
26	66	69	Cloudy, rain	63	82	Fair, ditto	59	69	Cloudy, cloudy	58	79	Cloudy, fair
27	68	80	Cloudy, fair	64	81	Fair, cloudy	65	73	Cloudy, cloudy	64	—	Cloudy, fair
28	71	85	Cloudy, fair	72	85	Cloudy, fair	67	80	Cloudy, clearing	54	73	Fair, fair
29	77	88	Cloudy, ditto	74	85	Cloudy, ditto, rain	72	86	Cloudy, fair	56	74	Cloudy, fair
30	74	90	Fair, ditto	73	86	Cloudy, fair	74	87	Fair, fair	57	75	Foggy, fair
31	—	—	—	76	80	Cloudy, rain, fair	74	84	Rain, fair	—	—	—

Note: The data for this table was extracted from Benjamin Rush, "An Account of the Bilious Remitting Yellow Fever as it appeared in Philadelphia in the year 1793," in *Medical Inquiries and Observations*, 4th ed. (Philadelphia: Griggs and Dickinsons, 1815), 3:19–22. Rush probably used the Meteorological Observations made by David Rittenhouse, esq., as his source of information.

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