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After Soto left, no Europeans visited this part of the Mississippi Valley for more than a century. Early in 1682 whites appeared again, this time Frenchmen in canoes. One of them was Réné-Robert Cavelier, Sieur de la Salle. The French passed through the area where Soto had found cities cheek by jowl. It was deserted—La Salle didn't see an Indian village for 200 miles. About fifty settlements existed in this strip of the Mississippi when Soto showed up, according to Anne Ramenofsky, an anthropologist at the University of New Mexico. By La Salle's time the number had shrunk to perhaps ten, some probably inhabited by recent immigrants. Soto "had a privileged glimpse" of an Indian world, Hudson says. "The window opened and slammed shut. When the French came in and the record opened up again, it was a transformed reality. A civilization crumbled. The question is, how did this happen?"

The question is even more complex than it may seem. Disaster of this magnitude suggests epidemic disease. In the view of Ramenofsky and Patricia Galloway, an anthropologist at the University of Texas, the source of the contagion was very likely not Soto's army but its ambulatory meat locker: his 300 pigs. Soto's force itself was too small to be an effective biological weapon. Sicknesses like measles and smallpox would have burned through his 600 soldiers long before they reached the Mississippi. But the same would not have held true for the pigs, which multiplied rapidly and were able to transmit their diseases to wildlife in the surrounding forest. When human beings and domesticated animals live close together, they trade microbes with abandon. Over time mutation spawns new diseases: avian influenza becomes human influenza, bovine rinderpest becomes measles. Unlike Europeans, Indians did not live in close quarters with animals—they domesticated only the dog, the llama, the alpaca, the guinea pig, and, here and there, the turkey and the Muscovy duck. In some ways this is not surprising: the New World had fewer animal candidates for taming than the Old. Moreover, few Indians carry the gene that permits adults to digest lactose, a form of sugar abundant in milk. Non-milk-drinkers, one imagines, would be less likely to work at domesticating milk-giving animals. But this is guesswork. The fact is that what scientists call zoonotic disease was little known in the Americas. Swine alone can disseminate anthrax, brucellosis, leptospirosis, taeniasis, trichinosis, and tuberculosis. Pigs breed exuberantly and can transmit diseases to deer and turkeys. Only a few of Soto's pigs would have had to wander off to infect the forest.

Indeed, the calamity wrought by Soto apparently extended across the whole Southeast. The Coosa city-states, in western Georgia, and the Caddoan-speaking civilization, centered on the Texas-Arkansas border, disintegrated soon after Soto appeared. The Caddo had had a taste for monumental architecture: public plazas, ceremonial platforms, mausoleums. After Soto's army left, notes Timothy K. Perttula, an archaeological consultant in Austin, Texas, the Caddo stopped building community centers and began digging community cemeteries. Between Soto's and La Salle's visits, Perttula believes, the Caddoan population fell from about 200,000 to about 8,500—a drop of nearly 96 percent. In the eighteenth century the tally shrank further, to 1,400. An equivalent loss today in the population of New York City would reduce it to 56,000—not enough to fill Yankee Stadium. "That's one reason whites think of Indians as nomadic hunters," says Russell Thornton, an anthropologist at the University of California at Los Angeles. "Everything else—all the heavily populated urbanized societies—was wiped out."

Could a few pigs truly wreak this much destruction? Such apocalyptic scenarios invite skepticism. As a rule, viruses, microbes, and parasites are rarely lethal on so wide a scale—a pest that wipes out its host species does not have a bright evolutionary future. In its worst outbreak, from 1347 to 1351, the European Black Death claimed only a third of its victims. (The rest survived, though they were often disfigured or crippled by its effects.) The Indians in Soto's path, if Dobyns, Ramenofsky, and Perttula are correct, endured losses that were incomprehensibly greater.

One reason is that Indians were fresh territory for many plagues, not just one. Smallpox, typhoid, bubonic plague, influenza, mumps, measles, whooping cough—all rained down on the Americas in the century after Columbus. (Cholera, malaria, and scarlet fever came later.) Having little experience with epidemic diseases, Indians had no knowledge of how to combat them. In contrast, Europeans were well versed in the brutal logic of quarantine. They boarded up houses in which plague appeared and fled to the countryside. In Indian New England, Neal Salisbury, a historian at Smith College, wrote in Manitou and Providence (1982), family and friends gathered with the shaman at the sufferer's bedside to wait out the illness—a practice that "could only have served to spread the disease more rapidly."

Indigenous biochemistry may also have played a role. The immune system constantly scans the body for molecules that it can recognize as foreign—molecules belonging to an invading virus, for instance. No one's immune system can identify all foreign presences. Roughly speaking, an individual's set of defensive tools is known as his MHC type. Because many bacteria and viruses mutate easily, they usually attack in the form of several slightly different strains. Pathogens win when MHC types miss some of the strains and the immune system is not stimulated to act. Most human groups contain many MHC types; a strain that slips by one person's defenses will be nailed by the defenses of the next. But, according to Francis L. Black, an epidemiologist at Yale University, Indians are characterized by unusually homogenous MHC types. One out of three South American Indians have similar MHC types; among Africans the corresponding figure is one in 200. The cause is a matter for Darwinian speculation, the effects less so.