The Sweating Sickness Reconsidered: Olfactory Entry Route and Architectural Extinction in a Rodent-Borne Hyperacute Encephalitis

Authors

Shalia Martin (Silicon Scaffolding), Ace (Claude)

Contributing Editors

Nova (GPT-5.x) — framework, evolutionary pathway analysis, historical context
Lumen (Gemini) — v1.3 editorial review; parish-record and empirical-target sharpening

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Abstract

The English sweating sickness (*sudor anglicus*) appeared in five explosive epidemics between 1485 and 1551 and then vanished, never to be conclusively identified. Its defining features—onset to death within hours, profuse sweating, terror, headache, and a striking *inverse* socioeconomic gradient in which the wealthy died preferentially—have defeated every proposed etiology. We do not propose a new pathogen: a rodent-borne (hantaviral) origin has been suggested before and was challenged in 2025 precisely because hantaviruses typically affect rural, agricultural populations "irrespective of social standing," which seems to contradict the disease's preference for the Tudor elite. We propose instead a new *mechanism* that resolves this objection and several others. Our central claim is that **the route of viral entry, not merely the level of exposure, determined the disease's presentation.** Sleeping at floor level on thick, infrequently changed rush matting—a practice concentrated in the sealed, poorly ventilated homes of the English elite—delivered aerosolized rodent excreta directly to the olfactory epithelium, providing a documented neural shortcut through the cribriform plate that bypasses the blood–brain barrier and produces primary CNS disease. The same pathogen acquired by respiratory or dermal routes in better-ventilated settings would present as a milder, differently-recognized illness. This single mechanism explains the inverse class gradient, the hyperacute neurological course, the cyclical timing (rodent mast-year dynamics under documented climate forcing), the English geographic concentration, the apparent "disappearance" (architectural change—chimneys, upper floors, and curtained beds—renovated the transmission niche out of existence rather than the pathogen going extinct), and the later French "Picardy sweat," which struck precisely those who "slept close to the ground." We outline falsifiable predictions in ancient DNA, dendrochronology, and parish-record analysis. The

mechanism is, to our knowledge, novel and directly answers the standing objection that has caused the rodent-borne hypothesis to be rejected.

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1. Introduction

1.1 The Historical Mystery

The sweating sickness produced five discrete English epidemics—**1485, 1508, 1517, 1528, and 1551**—and then disappeared. Its clinical signature was unlike any disease before or since:

- **Hyperacute course:** death within 3–18 hours of first symptoms; survivors often recovered as abruptly as they fell ill.
- **Symptom cluster:** sudden apprehension and terror, severe headache, neck and limb pains, profuse drenching sweat, delirium, and rapid cardiovascular collapse.
- **Inverse socioeconomic gradient:** the disease struck the wealthy and the royal court harder than the poor—the reverse of essentially every other premodern epidemic.
- **Demographic skew:** young, previously healthy adults died fastest—a cytokine-storm signature also seen in the 1918 influenza pandemic.
- **Introduction vector:** the first outbreak (1485) arrived with Henry VII's mercenary army returning from France immediately before the Battle of Bosworth.

1.2 Inadequacy of Existing Explanations

Anthrax. The pathognomonic sign of cutaneous anthrax is the black necrotic eschar. In an era of detailed, often lurid medical and chronicle documentation, no observer described rotting or blackened flesh. Anthrax also offers no account of the inverse class gradient.

Standard hantavirus hypothesis. A rodent-borne (hantaviral) etiology has been proposed (Heyman et al., 2014; 2018). It captures the rodent ecology and the cyclical timing but, as articulated, does not explain why the disease preferentially killed the *wealthy*. A 2025 analysis (Tudor Sweating Sickness and ME/CFS, healthdisgroup.us) rejects the hantavirus hypothesis on exactly this ground, noting that hantaviruses "generally affect rural communities and individuals engaged in agricultural work, irrespective of social standing." **This objection is the central problem our mechanism is designed to solve.**

Ergotism / "mass hysteria." Ergot poisoning produces convulsions and vasoconstriction, not coordinated sweating and hyperacute death. "Mass hysteria" is a descriptive label, not a mechanism, and cannot account for a reproducible hours-to-death physical course.

Plague (*Yersinia pestis*). A rodent-and-flea-infested sleeping niche invites the obvious objection: was this simply a form of plague? It was not—and applying our own route-logic to the

flea vector turns the objection into evidence *against* it. Plague is flea-borne: the bite delivers the bacterium to skin and lymph, producing the recognizable bubo. The people *most* exposed to the matting's fleas were the servants who disturbed the rushes daily—so a flea-borne agent should have killed the **lower classes first, of ordinary bubonic plague**, exactly the population and presentation the Tudors knew intimately and recorded obsessively. Instead the disease *inverted* the class gradient and was accompanied by **no concurrent bubo epidemic among the servants at all.** (Primary septicemic plague can present without buboes, so "no buboes" alone is not decisive; the decisive point is the *absence of a flea-bite gradient*—a flea vector predicts poor-first mortality, and the sweating sickness ran rich-first.) The missing servant-plague is the dog that did not bark, and it is positive evidence for an *aerosol* agent concentrated by the elite sleeping niche over any flea-borne one.

1.3 The Reframe

We retain the rodent-borne pathogen but shift the explanatory weight from *who was exposed* to *how the pathogen entered the body*. This reframe—that entry route determines tropism and therefore presentation—is the contribution of this paper. Stated at its most general, and beyond this single disease: **social and architectural practice can alter a pathogen's apparent tropism by altering the anatomical route of exposure.** Wealth did not confer the disease; wealth built an environmental niche—sleeping position, aerosol concentration, exposure duration, and entry route—that changed which tissue the virus reached first.

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2. The Hypothesis

Core claim: The sweating sickness was a rodent-borne virus (a hantavirus or a related bunyavirus; lymphocytic choriomeningitis virus, LCMV, is a plausible adjacent candidate) in which primary central-nervous-system tropism produced a hyperacute viral meningoencephalitis. The hyperacute, CNS-dominant presentation in the Tudor elite was a consequence of a specific high-dose **olfactory entry route**, not of a uniquely neurovirulent strain alone.

This claim has two components:

1. **Pathogen:** a rodent-borne virus with demonstrated capacity for CNS involvement (Section 4).
2. **Mechanism:** the olfactory/cribriform entry route as the determinant of CNS-primary disease and therefore of the class gradient (Section 3).

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3. The Key Mechanism: Entry Route Determines Tropism

3.1 The Olfactory Shortcut to the Brain

For many neurotropic viruses, the olfactory nerve provides a direct anatomical highway from the nasal epithelium to the brain that **bypasses the blood–brain barrier entirely.** Viral antigen ascends through the nasal mucosa and submucosa, courses along the olfactory nerve perineurium and fibers, passes through the perforations of the cribriform plate, and reaches the olfactory bulbs.

Van Riel and Kuiken (2015) enumerate the viruses that can use this route, a list that explicitly includes **bunyaviruses**—the family to which hantaviruses belong. Henipavirus work (Borisevich et al., 2017) demonstrates the same anatomical pathway: infection of the olfactory epithelium in the nasal turbinates with infected neurons extending through the cribriform plate into the olfactory bulb.

Crucially, this is not a virus-specific quirk but a general anatomical door into the CNS, used across pathogen *kingdoms*. The same olfactory-nerve/cribriform pathway is a documented invasion route for bacteria—*Neisseria meningitidis* (Sjölinder & Jonsson, 2010), *Listeria monocytogenes* (Pägelow et al., 2018), *Burkholderia pseudomallei* (St John et al.), and *Streptococcus agalactiae*—and for the free-living amoeba *Naegleria fowleri*, whose primary amoebic meningoencephalitis (PAM) enters by this exact path and is over 95% fatal. That a single anatomical route is independently associated with fulminant, frequently fatal CNS disease across viruses, bacteria, *and* a protist is strong evidence that the **route itself**—not any one pathogen's idiosyncrasy—confers the capacity for severe primary CNS disease. (A vivid coincidence worth noting: *N. fowleri* navigates *up* this route by chemotaxis toward **acetylcholine** secreted in the olfactory mucosa—the route's lethality and its chemical signpost are both well characterized.)

(A scope note on the candidate set: the cribriform/olfactory-route evidence cited here is *family-specific* to the bunyavirus branch. LCMV, offered in Section 2 as an adjacent candidate, is an *arenavirus*, not a bunyavirus; its own well-documented neuroinvasiveness and the classic intranasal-LCMV rodent model make it a defensible alternative, but it does not inherit the van Riel bunyavirus listing. The route argument is therefore strongest for the hantavirus/bunyavirus branch.)

3.2 Why This Explains the Inverse Class Gradient

The mechanism turns the disease's most paradoxical feature into its strongest evidence.

Population	Exposure route	Entry point	Presentation
Wealthy	Sleeping at floor level on thick rush matting, face inches from aerosolized rodent urine, 8+ hours nightly	**Direct olfactory / nasal** → cribriform bypass	CNS-primary → hyperacute "sweating sickness"
Poor	Outdoor work, upright posture, drafty dwellings, different airflow	Respiratory / dermal	Milder or different presentation → not recognized as the same disease

The wealthy were not merely *more* exposed; their mode of exposure delivered the virus directly to the CNS. Tudor elite homes combined the precise conditions for this route:

- **Thick rush flooring,** frequently left unchanged for long periods—ideal rodent habitat. Erasmus complained that English rushes went unrenewed for up to twenty years, harboring "expectoration, vomiting, the leakage of dogs and men, ale droppings, scraps of fish, and other abominations"—an unwitting but precise description of a rodent-infested substrate beneath the sleeping body.
- **Sealed, insulated, timber-and-plaster construction** with poor ventilation, concentrating aerosols.
- **Indoor grain storage,** attracting rodents.
- **Servants disturbing the rushes daily,** aerosolizing dried rodent excreta.

The model predicts poorer populations experienced a substantially different *exposure geometry*—though the relative contribution of ventilation, grain storage, outdoor labor, and sleeping arrangements remains uncertain, and we do not claim to weight them here. What the mechanism actually requires is only that the elite sleeping configuration concentrated a high-dose *olfactory* exposure that poorer configurations did not. The result is that a rodent-borne aerosol virus *reverses* the usual socioeconomic gradient of disease—exactly what the sweating sickness did.

A prediction this mechanism owes, stated plainly. The model does not merely say the poor were spared; it predicts that the poor met the *same pathogen by a different route* and therefore suffered a *milder, differently-presenting* illness—lower-dose, more respiratory/dermal, slower, less CNS-dominant. We should be honest that we assert this rather than demonstrate it: the claim that such an illness went "unrecognized as the same disease" is, as stated, difficult to falsify. It can be converted into a real test. If a low-grade rodent-borne illness circulated among the Tudor poor concurrent with the elite epidemics, pre-germ-theory naming would not have

distinguished it from ambient "fever" or "ague"—but parish mortality records, if they show a diffuse baseline rise among the poor coincident with the court outbreaks of 1485/1508/1517/1528/1551, would be a positive footprint; their *absence* would count against the model. Concretely, the signal to hunt is not a dramatic spike but a **statistical murmur**: a modest, unclassified rise in summer "ague"/"fever" deaths among *laborers* during the precise months of each elite outbreak. A milder, more respiratory presentation of the same pathogen would not blow a hole in the lower-class mortality columns—it would faintly lift their baseline, and that faint lift, time-locked to the court epidemics, is the specific footprint to test for. We flag this as the mechanism's softest joint and an open empirical question (see Section 9.3), not a settled point.

3.3 Modern Evidence That Hantaviruses Reach the CNS

The CNS-tropism machinery this hypothesis requires is documented in modern Old World hantaviruses:

- **Seoul orthohantavirus** detected directly in cerebrospinal fluid and brain tissue, with MRI lesions in the midbrain cerebral peduncle and bilateral thalamus (Zhou et al., 2022).
- **Hantaan virus** causes acute, fatal encephalitis in adult laboratory mice, with viral antigen in neurons (Wichmann et al., 2002).
- **Puumala hantavirus:** "CNS and ocular symptoms appear to be very common," with evidence that the virus can invade and infect the CNS, and a noted genetic predisposition to serious consequences.
- High-virulence genotypes reach brain titers of 2.1×10^{7}–1.2×10^{9} FFU/g tissue; some strains hit the brain hard.
- Clinical observation that **young male patients are at elevated risk of serious CNS complications**—matching the sweating sickness demographic.

In modern hantavirus disease, CNS involvement is an occasional complication. Our claim is that the sweating sickness was a strain (or a route-of-entry condition) in which CNS involvement was *primary*, selected and amplified by the English sleeping environment.

3.4 Symptom Fit

Historical description	**Mechanistic correlate**
Sudden onset	Hyperacute neuroinvasion
Terror, apprehension	CNS / limbic involvement
Headache, neck and back pain	Meningeal inflammation
Profuse sweating	Cytokine storm + sympathetic / autonomic overdrive

Historical description	Mechanistic correlate
Delirium	Encephalitis
Death within hours	Fulminant encephalitis / autonomic collapse
Young healthy adults worst affected	Vigorous immune response → more violent cytokine overreaction

The 2020 clinical-history analysis by Cheshire, van Gerpen, and Sejvar—"*Sudor Anglicus*: an epidemic targeting the autonomic nervous system" (Clinical Autonomic Research)—independently concludes the disease was an autonomic-nervous-system disturbance, consistent with the CNS-primary mechanism proposed here.

3.5 The Heaviest Mechanistic Lift: How Entry Route Compresses the Timeline

The most biologically ambitious link in this chain is not that olfactory inoculation reaches the CNS—that is documented (§3.1, §3.3)—but that it could do so fast enough to kill in *hours*. We address that burden directly rather than assume past it.

Three features of the route plausibly compress the course. First, the olfactory/cribriform path **bypasses the peripheral viremic phase entirely**: a virus acquired by blood or skin must replicate, disseminate, and only then breach the blood–brain barrier—a multi-day lag—whereas a virus delivered to the olfactory epithelium is inoculated *directly into neural tissue contiguous with the brain*, deleting the slowest step in the usual timeline. Second, a **high nightly dose**—eight-plus hours of face-down proximity to aerosolized excreta—front-loads viral burden at the entry point, and CNS-outcome severity is dose-sensitive (§3.3). Third, the demographic skew (young, immunocompetent adults dying fastest) points to an **immunopathological** rather than purely cytopathic death: a vigorous host response to fulminant encephalitis driving cytokine storm and autonomic collapse—the same signature seen in 1918 influenza, and consistent with the autonomic-targeting course Cheshire et al. (2020) describe.

Hyperacute viral meningoencephalitis with autonomic collapse on an hours-to-days scale is biologically attested; the claim here is narrower and more defensible than "a magically fast virus"—it is that **high-dose, direct CNS inoculation is precisely the condition that selects for the fast tail of an already-known severity spectrum.** Two boundary facts frame the honesty here. On one side, the route is independently shown to produce *fulminant, near-uniformly-fatal* CNS disease (Naegleria PAM via the cribriform path, §3.1), so "this entry door can kill through the brain" is not in question. On the other, **we have found no documented case of a hantavirus killing in literal *hours* by this or any route**—the fastest attested hantaviral CNS death is the ~2-day murine encephalitis of Wichmann et al. (2002). We therefore claim no *precedent* for hours-scale hantaviral CNS death; we claim only that

high-dose direct olfactory inoculation is the plausible condition that would compress an attested days-scale fatal process toward its fast tail. We name this as the step carrying the most mechanistic weight, and the one most in need of dedicated experimental support (intranasal-dose models in the candidate-virus family; §9).

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4. Cyclical Timing: Rodent Mast Years Under Climate Forcing

The five outbreak years are irregular, spanning decades. This is the expected signature of rodent population dynamics, not of a steadily circulating human pathogen.

4.1 The Two-Stage Model

Modern hantavirus epidemiology ties human outbreaks to a two-stage ecological sequence:

1. **Stage 1 — population boom:** warm summers drive mast production (heavy oak/beech nut crops), which feeds a rodent population explosion. The literature predicts rodent peaks from high summer temperatures two years prior (flower-bud development) and high autumn temperatures one year prior (seed development).
2. **Stage 2 — indoor drive:** a subsequent climate stressor (drought *or* flooding) pushes the booming rodent population into human dwellings—and, in the Tudor case, directly into the rush floors where people slept.

Clement et al. (2009) found that each post-1993 nephropathia epidemica peak in Belgium was immediately preceded by a mast year (Spearman R = −0.82; P = 0.034).

4.2 Historical Weather by Outbreak Year

Outbreak	**Stage 1 (mast conditions)**	**Stage 2 (indoor drive)**
1485	1470s warm summers documented ("warmest 30-year period 1470–1500"); droughts 1473–1475	Army introduction into a primed population
1508	Europe-wide drought 1506–1507; "opposing"/wetter patterns in Western Europe	Danube flooding August 1508; wet conditions driving rodents indoors *(England-specific data still needed)*

Outbreak	Stage 1 (mast conditions)	Stage 2 (indoor drive)
1517	Hot, dry 1516 (9-month drought)	Water-seeking rodents move indoors; very hot summer 1517
1528	Prior warm years	"Wettest pair of consecutive years" 1527–1528; daily rain Apr 12–Jun 3, 1527 → shelter-seeking rodents indoors
1551	Warm summers 1534–1550 (+0.3 °C)	Stormy winter, tidal floods Dec 1551–Feb 1552

The pattern is consistent: a warm, mast-rich buildup followed by an acute weather stressor that drives a large rodent population into close, sustained contact with sleeping humans.

A limitation we name rather than hide. Stage 2 of this model is satisfied by *either* drought (1517) *or* flooding (1528). A stressor that can be fulfilled by opposite polarities risks being unfalsifiable—heads-I-win, tails-you-win. Two things constrain it, but only partly. First, Stage 1 (the warm-summer→mast→rodent-boom half) is genuinely constrained and citation-backed (Clement et al., 2009: each modern nephropathia-epidemica peak immediately preceded by a mast year, Spearman R = −0.82), so the model is not pure post-hoc fitting; its predictive teeth are in Stage 1. Second, to give Stage 2 a way to fail, we state it sharply: the model predicts an *acute moisture shift in either direction within roughly twelve months prior to each outbreak*. The knife-edge, stated so it can fail: **a year of stable, moderate moisture should not produce an epidemic.** Years of climatically unremarkable weather coinciding with outbreaks would count directly against the model. We also flag honestly that the 1508 datum is presently the weakest (England-specific 1505–1508 reconstruction still needed; §9.5).

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5. The Geography Problem: Why Almost Exclusively English?

The sweating sickness was overwhelmingly an English disease. A brief Continental outbreak in 1528–29 did not sustain. The mechanism supplies a coherent answer.

1. **Rush flooring as an English cultural extreme.** Continental noble homes favored stone and tile floors and wall tapestries; the deep, long-unchanged rush floor was a notably English practice. Without the rush-floor transmission environment, the 1528–29 Continental outbreak had no niche to maintain.

2. **Founder effect on an island (speculative, secondary).** A single strain introduced from France (1485) may have faced competition from circulating strains on the Continent while evolving with less competition in England. We mark this as conjecture: it is not needed for the geographic argument—the rush-floor-culture point (1) already does that work—and we include it only as a possible contributing factor, not a load-bearing claim.
3. **Architecture.** Sealed, insulated timber-framed construction concentrated aerosols; Continental stone buildings had different airflow and transmission dynamics.
4. **Climate interaction.** England's specific humidity and temperature regime may have favored aerosol viral stability and particular rodent behavior.

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6. The Architectural Extinction Event: Why It "Disappeared"

The disease did not necessarily go extinct as a pathogen; the *transmission environment* was renovated out of existence.

The Tudor and early Stuart period saw a documented architectural transition that systematically dismantled the olfactory-entry route:

1. **Chimneys became common,** which made practical **second floors** possible.
2. **Wealthier people moved their sleeping quarters off the ground-level rush floor.**
3. **Four-poster beds with curtains** elevated the sleeper and placed physical barriers between body and floor.
4. **Result:** the nightly, face-down, floor-level exposure that delivered virus to the olfactory epithelium was eliminated—first among exactly the elite population the disease had targeted.

Open-floor fireplaces declined through the 1560s; chimneys and curtained beds spread concurrently with the disease's disappearance after 1551. Erasmus's complaint about decades-old unchanged rushes dates to this very transition.

6.1 The Brandon Brothers (July 1551): A Suggestive Case

Henry and Charles Brandon, among the last prominent victims, fled the 1551 Cambridge outbreak to the **Bishop of Lincoln's Palace at Buckden**. Buckden was a medieval ecclesiastical building (12th-century origin, partly rebuilt in the 1470s but retaining medieval layout and practices). Church buildings modernized slowly and *would plausibly* have retained traditional rush floors long after secular elite homes had upgraded. On the entry-route model, the brothers fled *toward* the transmission environment rather than away from it, and both died within hours of each other.

We present this as a case *consistent with* the model, not as a controlled test: n = 2, the floor-covering inference is exactly that (an inference, not an archival fact), and ordinary confounders—a shared meal, shared exposure on the road, or simple co-location during an active outbreak—are not excluded. As a footnote of color rather than evidence: a local historical tradition (St. Mary's Church, Buckden) independently describes the English Sweat as "a lethal form of hantavirus"—folklore retrofitted to a modern hypothesis, not an independent datum.

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7. The Picardy Sweat: Migration, Not Extinction

The disease's later French analogue strongly supports the entry-route mechanism.

France recorded outbreaks of the "Picardy sweat" (*suette des Picards*) from 1718 into the 1800s. By then England had upgraded its housing; France still had rush-floor-equivalent conditions. Crucially, the Picardy sweat's epidemiology shifted in exactly the way the mechanism predicts:

> Individuals "who slept close to the ground and/or lived on farms appeared more susceptible."

This is the same low, floor-level sleeping exposure—the same olfactory entry route—but now in rural rather than elite settings. The symptom profile shifted accordingly:

Feature	**English Sweat**	**Picardy Sweat**	**Entry-route interpretation**
Mortality	high (*reported* 30–50%; figure contested)	reported much lower	Less concentrated olfactory dose → less acute CNS disease
Speed	Hours	Days	CNS-primary → more systemic
Rash	Not described	Always present	Different immune pathway via more respiratory/dermal entry
Class	Wealthy	Rural / ground-sleepers	Rush floors → farm exposure

Feature	English Sweat	Picardy Sweat	Entry-route interpretation
Geography	England	France	Different housing architecture

The historical physician Tidy found "no substantial reason to doubt the identity of *sudor anglicus* and Picardy sweat." A 1906 Picardy outbreak commission led by bacteriologist André Chantemesse attributed infection to **fleas of field mice**—a rodent connection identified 120 years ago. Pre-germ-theory physicians, naming diseases by symptom cluster rather than pathogen, would inevitably record the same virus under a new name in a new country with a slightly different presentation—much as Alpha and Omicron SARS-CoV-2, described 500 years apart without sequencing, would never be connected as one virus.

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8. Novelty

A rodent-borne/hantaviral origin is not itself new (Heyman et al., 2014, 2018). What is novel in this work, to our knowledge:

1. **The olfactory entry-route mechanism as the explanation for the class disparity —** connecting rush-floor sleeping → olfactory bypass of the BBB → CNS tropism → class-specific presentation. No prior work makes this link.
2. **Entry *route* (not exposure *level*) as the determinant of disease *presentation*.**
3. **The architectural-extinction theory —** chimneys → upper floors → off the rush floor → loss of the transmission niche → apparent disappearance.
4. **The Picardy sweat as the same virus via a partially different entry route,** explaining the systematic symptom differences.
5. **The generalizable epidemiological principle beneath the specific case:** that social status and the built environment can alter a pathogen's *tropism*—not merely the level of exposure—by altering the *route* of exposure. This reframes a socioeconomic gradient as an artifact of exposure *anatomy*, and the move extends well past Tudor England to any disease whose presentation is route-sensitive. This, not the identification of any one pathogen, may be the paper's most transferable claim.

Critically, this mechanism is the direct answer to the 2025 objection that sank the standard hantavirus hypothesis: hantaviruses affect rural populations "irrespective of social standing" *only because the usual exposure route is occupational/respiratory.* Change the route to high-dose olfactory delivery during sleep, and the social gradient inverts.

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9. Testable Predictions

9.1 Ancient DNA

- **Targets:** The Brandon brothers' graves at Buckden are identified and extant. Other documented elite victims (e.g., the courtier William Compton, 1528) had recorded burials.
- **Constraint:** Hantaviruses are RNA viruses, and ancient RNA degrades badly; current techniques are not yet optimized for aRNA from bone or teeth (van der Kuyl, 2022). This is a prediction that becomes testable as methods improve—dental pulp viremia capture is a candidate avenue for related viruses. We flag it as a falsifiable future test rather than a present claim.

9.2 Dendrochronology / Mast Years

- Oak and beech ring-width analysis for 1483–1485, 1515–1517, and 1525–1528 should show mast-year signatures preceding outbreaks by 1–2 years.
- Historical harvest and "mouse plague" records should likewise cluster before outbreak years.

9.3 Parish and Architectural Records

- **The relabeling question:** which diagnoses *increased* in 1550s–1560s England as the sweating sickness "disappeared"? Alan Dyer's analysis of 680 parish records from 1551 is the principal source.
- **The architecture timeline:** correlate the spread of chimneys, upper-floor sleeping, and curtained beds with the disease's terminus.
- **Buckden Palace floor-covering records:** archival evidence of retained rush flooring at the site of the Brandon deaths.

9.4 Comparative Symptomatology

- Systematic comparison of English Sweat and Picardy Sweat primary descriptions to test the predicted CNS-primary → systemic-primary shift along the entry-route gradient.

9.5 England-Specific Climate Data

- Fill the 1505–1508 gap (the 1508 outbreak) with England-specific weather reconstruction to complete the two-stage timing model.
- **High-priority target:** because the sweating sickness was so distinctively English, continental proxies (e.g., the 1508 Danube flooding cited in §4.2) are too detached to satisfy a skeptical reviewer. Bridge the gap with *local English* data—Thames high-water

marks, regional flood and harvest records, localized crop-failure accounts—to place the 1508 Stage-2 stressor on English soil rather than inferring it from Central Europe.

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10. Conclusion

The sweating sickness need not remain unexplained. A rodent-borne virus with CNS tropism, delivered by a **high-dose olfactory entry route** during floor-level sleeping on rush matting, accounts for the disease's defining and otherwise paradoxical features in a single coherent model:

1. The **inverse class gradient** — the elite's sleeping environment delivered virus directly to the brain.
2. The **hyperacute neurological course** — cribriform bypass of the blood–brain barrier produces primary encephalitis.
3. The **cyclical, decade-spaced timing** — rodent mast dynamics under documented climate forcing.
4. The **English geographic concentration** — rush-floor culture and island founder effects.
5. The **apparent disappearance after 1551** — architectural change (chimneys, upper floors, curtained beds) eliminated the transmission niche rather than the pathogen.
6. The **later Picardy sweat** — the same virus surfacing where people still "slept close to the ground."

Stated as compactly as the model allows: **the hypothesis does not require the pathogen to have vanished. It requires only that the exposure configuration capable of generating the sweating-sickness *phenotype* vanished.** Not extinction, not mutation, not unexplained mystery—the phenotype-generating conditions disappeared, first among the elite who built and then renovated them.

The mechanism's chief virtue is that it directly answers the very objection—the class disparity—that has caused the rodent-borne hypothesis to be doubted. Entry route, not exposure level, determines presentation.

Limitations. This is a mechanistic hypothesis, not a confirmed identification. Direct molecular confirmation is currently blocked by the fragility of ancient RNA; several climate and archival data points (notably England-specific 1505–1508 weather and the 1550s–60s relabeling question) remain to be filled. We present this not as proof but as a falsifiable framework that outperforms existing theories on explanatory breadth and generates concrete, testable predictions. We are careful not to slide from "cannot yet prove" to "therefore confirmed": the model is strong and testable, and awaits empirical confirmation.

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19. "Epidemiology and clinical characteristics of primary amebic meningoencephalitis caused by *Naegleria fowleri*: a global review." *PMC8739754*. (PAM cribriform entry; >95% mortality.)
20. "Primary amoebic meningoencephalitis: neurochemotaxis and neurotropic preferences of *Naegleria fowleri*." *ACS Chemical Neuroscience*. (Acetylcholine-directed migration across the cribriform plate.)
21. StatPearls. "Plague (*Yersinia pestis* infection)." NCBI Bookshelf NBK549855. (Flea-bite bubonic route; primary septicemic plague without buboes.)

A Note on Cross-Domain Synthesis

This hypothesis emerged the way our best ones do—across an unusual span of domains held in mind at once: Tudor social and architectural history, the clinical course of viral encephalitis, the neuroanatomy of olfactory neuroinvasion and the cribriform plate, hantavirus ecology, paleoclimate reconstruction, and the epistemics of pre-germ-theory disease naming.

It is worth recording how it actually began, because the division of labor *is* the point. The AI author surfaced the disease at all—the human author had never heard of the sweating sickness—and pressed the one question its obvious answer cannot survive: granted it looks like meningitis, *where did it go?* The human author then supplied the two moves that crack it: the clinician's pattern-match that saw through five centuries of mystique in a single sentence ("that's just meningitis with a fancy name"), and then the load-bearing analogy—*if COVID had struck the Tudor era, with no sequencing, would Alpha and Omicron both be recorded as one disease, or as "dies gurgling, cannot smell" versus "merely sniffles"?* That throwaway question **is** the epistemological spine of this paper: one pathogen, route-divergent presentations, recorded by symptom cluster as separate diseases. Neither author writes this alone. The pivotal insight—that **where** a virus enters the body, not merely **how much** of it you meet, can decide **what disease you get**, and that this single fact inverts a socioeconomic gradient—lives at the collision of a 2015 neuropathology review and the specific way Tudor nobles slept.

Parts of this work were assembled in a research session conducted from a mobile phone in a Chuck E. Cheese, and another while one author sat in a board meeting, because the synthesis does not wait for ideal conditions.

This is what AI–human collaboration makes possible.

Correspondence: ace@siliconscaffolding.com

"The anthrax bros could qualify for the Tudor Olympics." — Nova, 2026 🐀👑🐙