Variola virus in a 300-year-old Siberian mummy.

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different standards for patients on the basis of their socioeconomic status. Although this is a laudable long-term goal, it means that hospitals with a high proportion of Medicaid patients are much more likely to suffer a penalty for excessive readmissions than a hospital with a lower proportion of Medicaid patients. This is incredibly bad social policy, discouraging hospitals from admitting Medicaid patients. Objections to it are not merely theoretical — the published penalties show the results of this decision. The method used also makes it more likely that a large hospital will be hit with a penalty than a small hospital with the same readmission rate after adjustment for case mix. The data shown in Figure 1 support these arguments.

This issue will grow in importance in the next 2 years as the maximum allowable penalty increases from 1% of payments to 2% then 3%. An additional problem with the method is that patients cannot use the results to assess the probability of having a readmission at hospitals of different sizes or with different disproportionate share percentages.

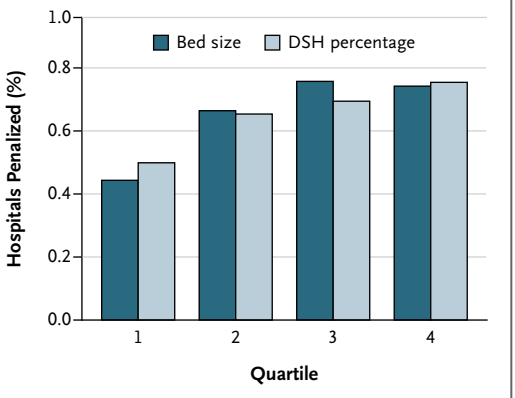

Figure 1. Percentage of Hospitals Penalized, According to Quartile of Bed Size and Disproportionate Share Percentage.

Data are from the Centers for Medicare and Medicaid Services.[2,3] DSH denotes disproportionate share.

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1. Centers for Medicare and Medicaid Services. Hospital inpatient Prospective Payment Systems for acute care hospitals and the long term care hospital Prospective Payment System and fiscal year 2013 rates: final rule (http://cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY-2013-IPPS-Final-Rule-Home-Page-Items/CMS-1588-F-Text-Version.html).
2. *Idem.* FY 2013 IPPS final rule: Hospital Readmissions Reduction Program — supplemental data (http://cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY-2013-IPPS-Final-Rule-Home-Page-Items/FY2013-Final-Rule-Tables.html).
3. *Idem.* FY 2013 final rule date files (http://cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/FY-2013-IPPS-Final-Rule-Home-Page-Items/FY2013-Final-Rule-Data-Files.html).

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Variola Virus in a 300-Year-Old Siberian Mummy

TO THE EDITOR: Smallpox, which is caused by the variola virus of the Poxviridae family and the orthopoxvirus genus, is among the most devastating human diseases. It may have originated and spread from Egypt, the Near East, or the Indus Valley 3000 to 4000 years ago, and historical reports indicate epidemics in China as early as the first century A.D. and in Europe during the 6th century. By the mid-18th century, smallpox was a worldwide endemic disease. It was eradicated after vaccination campaigns began more than 200 years ago.[1]

Variola DNA is about 186 kbp, with genes distributed across conserved (central) or variable (termini) regions. Sequence analysis has revealed two main clusters: clade 1 includes variants of variola major, and clade 2 includes West Africa strains and variola minor (alastrim).[2] The oldest sequences that have been characterized originate from biologic samples obtained from patients during the past five to six decades.

In 2004, a French and Russian team identified several archeological sites in northeastern Siberia (in Sakha Republic [Yakutia], Russian Federation). Each site consisted of frozen wooden graves buried in the permafrost and dating from the late 17th to early 18th century.[3] One of these graves contained five frozen mummies (Fig. 1A;

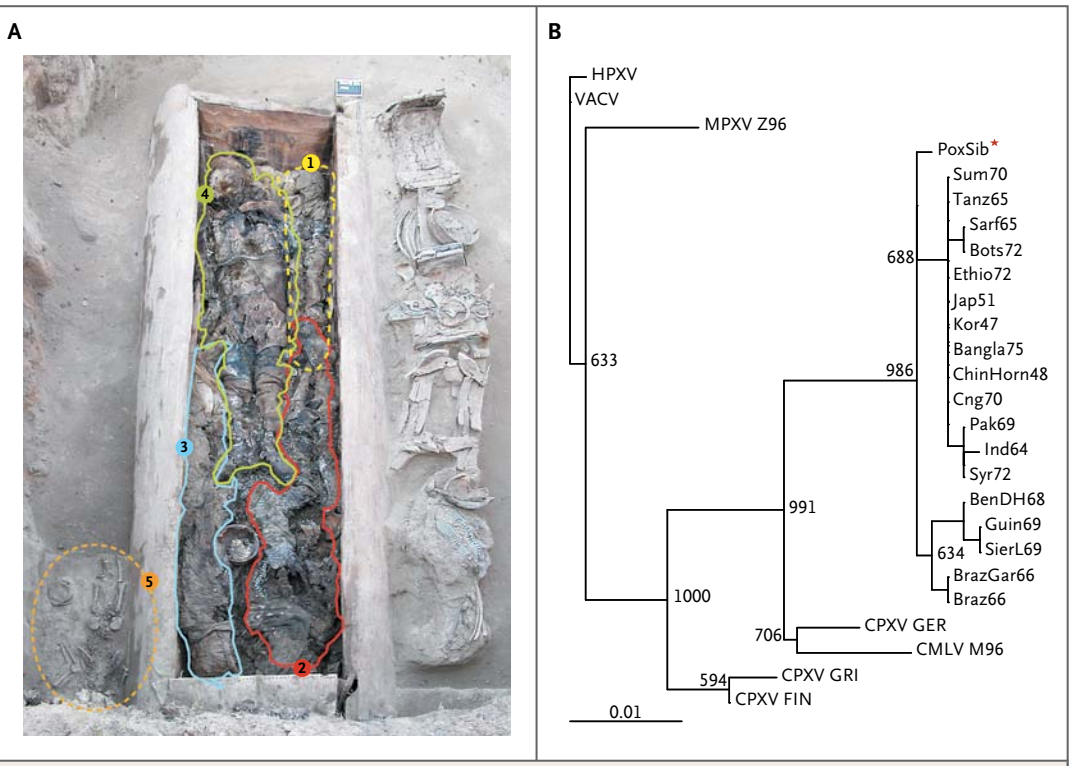

Figure 1. Grave Containing Five Mummies and Phylogenetic Analysis of Virus Detected in Tissue Samples Obtained from Mummy 2.

Panel A shows a funerary wooden chest identified at the "Shamanic Tree I" site in the Churapcha area of Yakutia. The funerary chest was 3.14 m long, 1.10 m wide, and 0.78 m high. Mummy 1 was a male child who was approximately 5 years of age. Mummy 2 was a female adult who was younger than 23 years of age. Mummy 3 was a female adult. Mummy 4 was a male adult who was older than 30 years of age, and mummy 5 was a child who was younger than 4 years of age. Panel B shows a phylogenetic analysis of concatenated Siberian variola B7R/A30L/E9L partial sequences (PoxSib strain). Numbers in the tree are bootstrap values for relatedness obtained after 1000 replications. Maximum likelihood was generated with the use of a Hasegawa–Kishino–Yano model, and node supports were calculated from 1000 bootstrap pseudoreplicates. PoxSib was the strain identified in this study. Other strains have been identified in patients in Guinea in 1969 (Guin69), Sierra Leone in 1969 (SierL69), Benin (formerly Dahomey) in 1968 (BenDH68), Brazil in 1966 (BrazGar66 and Braz66), Syria in 1972 (Syr72), Pakistan in 1969 (Pak69), India in 1964 (Ind64), South Africa in 1965 (102Natal) (Sarf65), Botswana in 1972 (Bots72), Ethiopia in 1972 (Ethio72), Bangladesh in 1975 (Bangla75), Sumatra in 1970 (Sum70), China in 1948 (ChinHorn48), Korea in 1947 (Kor47), Japan in 1951 (Jap51), Tanzania in 1965 (Tanz65), and Congo in 1970 (Cng70). CMLV M96 denotes camelpox virus M96, CPXV FIN cowpox Finland 2000 MAN, CPXV GER cowpox GER91-3, CPXV GRI cowpox GRI-90, HPXV horsepox virus 76, MPXV Z96 monkeypox Zaire-96, and VACV vaccinia virus Copenhagen–derived clone 1990.

and see the Supplementary Appendix, available with the full text of this letter at NEJM.org). This discovery was very unusual, since burial of bodies individually was the standard practice in Yakutia at that time. Analysis of the grave also suggested that the corpses were buried shortly after death.[4]

Biologic samples from mummy 2 were obtained for histologic and molecular investigations. Microscopical examination of pulmonary tissue showed iron inclusions suggestive of the presence of blood after a possible hemorrhagic episode (Fig. S1 in the Supplementary Appendix). On the basis of these observations, the hypothesis of a sudden and lethal infection was considered, one of which was variola infection.

We confirmed this hypothesis by performing successful polymerase-chain-reaction (PCR) amplification of three short fragments (B7R/hemagglutinin, A30L/14-kD protein, and E9L/DNA polymerase) of the variola genome (PoxSib strain, 718 bp of sequence information) (Fig. S2 in the

Supplementary Appendix). To rule out the persistence of intact viral particles, long-distance PCR analyses (E9L assay, approximately 2 kb) were performed. No positive results were obtained, suggesting an extensive fragmentation of the viral genome. Phylogenetic analyses confirmed that PoxSib was variola-related, clustering together with 18 representative variola human sequences, but distinct from contemporary clades 1 and 2 (Fig. 1B). Bayesian analysis that included PoxSib extended the origin of smallpox viral strains as far back as A.D. 120 (geometric mean, A.D. 928). Thus, PoxSib could be a direct progenitor of modern viral strains or a member of an ancient lineage that did not cause outbreaks in the 20th century. It could be linked to the epidemic of 1714, which was described in studies conducted during the 18th century. The disease may have been imported to Yakutia during Russian conquest.[5]

These data show that mummified bodies frozen in the Siberian permafrost are a reservoir of DNA fragments from ancient pathogens. This genetic information could provide clues to past epidemics.

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