among a number of meningococcal strains and that induce the production of bactericidal antibodies when injected into mice. The fact that these seven proteins are both highly conserved and exposed in the bacterial outer membrane makes them good candidate virulence factors.

It is likely that conserved regions of the meningococcal genome encode essential components of the pathogenesis pathway. Tettelin *et al.* report that 91% of the genome sequence of strain MC58 (serogroup B) is present in the genome of strain Z2491 (serogroup A). The 9% of the genome that differs between serogroups A and B may account for the different ways in which these two serogroups spread through human populations.

The *Neisseria* species include *Neisseria gonorrhoeae* (which colonizes and invades the epithelium of the urogenital tract, where it causes an inflammatory response) and *Neisseria lactamica* (which is not pathogenic). Subtractive hybridization has enabled the construction of a library of genes that are present in one species but not the other (*6*). In addition, comparison of the sequence of *N. meningitidis* with the partial sequence of *N. gonorrhoeae* (*7*) now allows the identification of chromosomal regions that are either specific for *N. meningitidis* or shared with *N. gonorrhoeae*. Those sequences specific to *N. meningitidis* are more likely to be involved in specific aspects of meningococcal pathogenesis, such as septicemia and invasion of the brain meninges. Genomic regions shared by *N. meningitidis* and *N. gonorrhoeae*, but absent in *N. lactamica*, are likely to be responsible for common aspects of the life cycle of pathogenic *Neisseria*, such as colonization of epithelia at the point of entry.

The success of the conjugate vaccine for protecting against *H. influenzae* serogroup B infection demonstrates that efficient protection against bacterial pathogens that cross the blood-brain barrier is possible. The goal of a meningococcal vaccine is not to prevent infection but to block bloodstream dissemination of the pathogen in asymptomatic carriers. Administration of a vaccine antigen such as purified coat polysaccharide early in life could result in the production of bactericidal antibodies that prevent bacteria from entering the bloodstream. Unfortunately, the serogroup B coat polysaccharide is structurally identical to a carbohydrate component of the N-cellular adhesion molecule expressed on the surface of brain cells and so it cannot be used in a vaccine. However, coat polysaccharides of serogroups A and C induce protective antibodies in children older than 2 years of age, and a new conjugate vaccine containing these polysaccharides is now being administered to infants.

Pizza *et al.* (*3*) systematically screened the *N. meningitidis* genome for surface proteins that are highly conserved. They identified 350 candidate vaccine antigens, expressed the genes in *Escherichia coli*, purified the proteins, and immunized mice with them. Of these they identified seven surface proteins that are highly conserved among 22 serogroup B pathogenic strains and are also highly conserved in serogroup A and C pathogens. All seven proteins, which include four lipoproteins and two outer membrane proteins, were accessible to antibodies and evoked efficient antibacterial antibody responses, suggesting that they hold promise as vaccine antigens.

Although the path that leads from finding a vaccine candidate to producing a working vaccine is seldom smooth, the reports by Tettelin, Pizza, and their colleagues stress the enormous potential of bacterial genomics for discovering new therapeutic strategies to fight infectious disease.

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PERSPECTIVES: PLANETARY SCIENCE

Glass Beads Tell a Tale of Lunar Bombardment

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By a little over 3 billion years ago, the heavy battering that the early moon and Earth had been receiving from projectiles had diminished to a level comparable with that of today (*1*). Has the bombardment been essentially constant over these past few billion years, or has it increased or declined? Have there been periodic or episodic variations? The answers to these questions contain clues to the source of bodies—asteroids or comets or both—that enter the inner solar system, the influence of impacts on Earth, the current hazard risk, and the dating of surfaces of other inner solar system planets. On page 1785 of this issue, Culler *et al.* (*2*) use radiogenic isotope analyses of lunar samples to persuasively argue that there has been a substantial increase in impacting in the Earth-moon system over the past few hundred million years, following a decline over the previous 3 billion years.

The present impact rate can be estimated from an inventory of Earth-crossing asteroids and comets (*3*). The average rate over the past 3 billion years can be determined by counting the lunar craters that have formed on the 3.1- and 3.3-billion-year-old lava flows sampled by the Apollo 12 and Apollo 15 missions, respectively (*1*). This average lunar rate can be compared with that estimated from Earth's own ~150 impact craters, with appropriate consideration of Earth's greater cross section for attracting projectiles and the greater impact velocities and different crater modification because of its higher gravity.

Earth's craters have the potential for reasonably accurate and precise absolute and stratigraphic ages. Estimates of both the present rate (based on observed Earth crossers) and that over the past 200 or so million years (based on impact structures on older continents and the younger Mississippi lowlands) suggest a rate twice that of the lunar average over the past 3 billion years (*4*). The anomalously high frequency of very large "young" craters on Earth (such as Chicxulub, 65 million years old) is consistent with such a higher rate. However, the uncertainties are high enough to allow the possibility of a fairly constant rate (*1*).

Erosion, sedimentation, and plate tectonics have eliminated much of the older record on Earth, and in the case of smaller craters, even relatively young ones are depleted. It is thus not likely that we can ever substantially improve our database from the terrestrial record. In contrast, the lunar record is superbly retained, and we have limited access to it. In particular, we do

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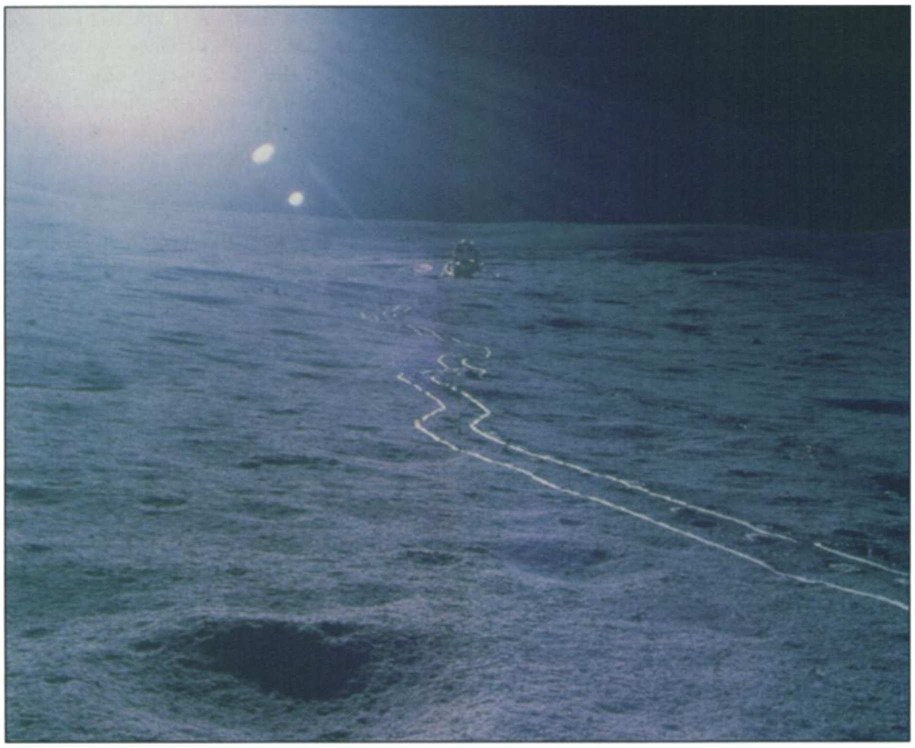
not have appropriate samples of a sufficient number of older craters. The few craters that have been directly dated are too young and too small, for example, North Ray crater (sampled by Apollo 16). Only a few dates, indirect and circumstantial, are available for larger craters (Tycho, 110 million years; Copernicus, 800 million years; Autolycus, 2.1 billion years) (*1*, *5*) on whose throwout deposits we can count even younger craters. If the first two ages are correct, the amount of younger cratering suggests an increase in the cratering rate over the past billion years. If the last is also correct, it suggests an earlier decrease in the cratering rate. The dating of samples of melt from many documented craters has been proposed as the solution (*6*), but this would require a substantial return to the moon.

Now Culler *et al.* (*2*) suggest a way forward, using the Apollo samples. Fast impactors, even small ones, produce glass droplets by melting the lunar regolith or "soil." Thus, the regolith contains numerous impact glass beads, most less than a few hundred micrometers across. The beads are a random selection from the lunar surface, and their age distribution should therefore mimic that of the impacts. It does not matter whether the impacts were large or small: The size distribution of craters seems to have been fairly constant over the past 4 billion years, suggesting that if large projectiles become more abundant, so do small ones.

These glass beads can in principle be dated, although it is not easy and not all beads give a reliable age. The dating method exploits the decay of radioactive potassium to argon. When regolith is melted, any argon in it degasses (if it stays hot enough for just a few seconds). After the glass solidifies, new argon formed by the decay of potassium is trapped. Culler *et al.* use a laser $^{40}Ar/^{39}Ar$ method in which the beads are pulse-heated by a laser, followed by isotopic analysis of the gas given off in each pulse. Among the many difficulties are the small amount of sample and the low concentrations of potassium and thus argon. Culler *et al.* chose beads in regolith samples from the Apollo 14 landing site, which contains somewhat more potassium than others and has been recording impacts for just over 3.8 billion years.



Tracks on the moon. This NASA photo, AS14-67-9367, taken during Apollo 14 against the sun back toward the Lunar Module, shows the nature of the soil surface. The rough texture has been imparted by little impacts of the kind that produced some of Culler *et al.*'s glass beads. A larger crater can be seen in the foreground. Highly reflective wheel marks have been left by the cart. See the Apollo 14 Digital Picture Library at www.hq.nasa.gov/alsj/a14/images14.html.

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The data of Culler *et al.* (*2*) are too imprecise to provide information on time scales of 30 million years but can elucidate trends at longer time scales. The data show an excess of glasses formed in the past 400 million years compared with the previous 3 billion years, corresponding to a rate increase of a factor of about four over the lowest point (*7*). This is consistent with the conclusions based on the terrestrial cratering record of an increase in projectile abundance in the inner solar system during the past 200 million years. The time frame overlaps with that of the Phanerozoic on Earth, during which complex life evolved, and Culler *et al.* suggest that this might not be coincidental.

Culler *et al.*'s data also suggest a substantial decrease in the lunar cratering rate from 3.5 billion years to about 400 million years ago, consistent with the stratigraphic lunar record, which indicates that the cratering rate in the Eratosthenian (2 to 3 billion years ago) was twice that in the succeeding Copernican era (*5*), although perhaps it is not clear where we should place the boundary. Thus, we now have some fairly hard evidence for the earlier tentative conclusion that cratering in the Earth-moon system has not been constant over the past 3 billion years. This leads to considerable uncertainties in the absolute dating of other planetary surfaces, such as Mars. And we still do not know how smooth or irregular the decline and subsequent increase were.

It remains unclear what caused the recent increase. Most dynamicists would argue that asteroids are not a possibility for such a change and that there must be a cometary source. But is it likely for the size-population distribution of projectiles to remain constant if the sources have changed? Data on the chemistry of the projectiles that produced the glass beads and dating of other samples should help answer these questions.

Culler *et al.*'s study emphasizes the need to collect samples from other planetary bodies. This work could not have been done remotely, nor could it have been done 30 years ago because the technique had not been invented. We can continuously deploy newly invented techniques to analyze the Apollo samples, whereas in situ planetary analyses, once performed, cannot be improved upon.

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