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Megacity Megaquakes—Two Near Misses
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(Rpl38) is depleted, a subset of mRNAs that encode homeobox genes are not translated during mouse embryogenesis (*6*). Likewise, reduction of Rpl40 impairs translation of vesicular stomatitis virus mRNAs in cultured human cells (*7*). Indeed, the amounts of mRNA that encode ribosomal proteins also vary among tissues in the developing mouse embryo (*6*). It is not clear whether these differences are reflected in the constituents of the functioning ribosome. If so, this raises the question of "specialized" ribosomes, and one must look closely for whether ribosome composition influences the pathogenesis of ribosomopathies.

Another possible explanation for tissue proclivity is that mutations in ribosomal proteins or assembly factors result in reduced numbers of fully functional cytoplasmic ribosomes. Although ribosome amounts would be adequate for survival, a smaller number of ribosomes could alter the mRNAs that are translated. This may, in turn, inhibit normal cellular growth and differentiation in specific cell types. In Diamond-Blackfan anemia, a mutation in Rpsl9 results in defects in the processing of the pre-18*S* rRNA, thereby reducing the amount of the small subunit that is assembled (*1*, *2*). Indeed, in mouse erythroblasts with reduced amounts of Rpsl9, translation of a subset of mRNAs is decreased (*8*). Other ribosomopathies with proposed nucleolar dysfunction, such as North American Indian childhood cirrhosis, may similarly result in reduced amounts of ribosomal subunits (*9*).

Additionally, in some cases, mutations that disrupt ribosome assembly can cause the nucleolar stress response in some cell types. This response involves increased synthesis of the protein p53. This tumor suppressor protein arrests cell division in response to such stress, which leads to programmed cell death (apoptosis) (*10*). In a mouse model for Treacher-Collins syndrome, craniofacial dysmorphology was rescued when p53 expression was reduced (*11*). Treacher-Collins syndrome often results from haploinsufficiency in *TCOF1*, the gene that encodes Treacle, a nucleolar protein involved in pre-rRNA synthesis. Similarly, in mouse (haploinsufficiency in Rpsl9) and zebrafish (haploinsufficiency in Rps29) models for Diamond-Blackfan anemia, p53 inactivation rescued some of the red cell lineage abnormalities (*12*). However, in a zebrafish model for Shwachman-Bodian-Diamond syndrome, loss of p53 did not rescue the associated exocrine pancreas developmental defects (*13*). Do some cell types more readily succumb to nucleolar stress? Activation of p53 may contribute to the tissue proclivity of some ribosomopathies, but perhaps not all.

Mutations in ribosomal proteins and assembly factors confer a broad clinical spectrum. Although the mechanisms underlying the tissue proclivity in ribosomopathies are yet to be defined, these disorders do make it increasingly clear that the days of thinking of ribosomes as unchanging monoliths are coming to an end.

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GEOPHYSICS

Megacity Megaquakes—Two Near Misses

Seismicity patterns after large earthquakes suggest that the earthquake hazard can rise sharply in areas well beyond the mainshock rupture zone.

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Two recent earthquakes left their mark on Santiago de Chile and Tokyo, well beyond the rupture zones, raising questions about the future vulnerability of these and other cities that lie in seismically active regions. Though spared strong shaking, the megacities nevertheless lit up in small quakes, perhaps signaling an abrupt change in the condition for failure on the faults beneath the cities. To detect such changes in earthquake rate requires good seismic monitoring networks; to respond to such hazard increases with civic preparations requires good government.

When the moment magnitude $M_w = 8.8$ Maule earthquake struck the Chilean coast before dawn on 27 February 2010, its strong shaking and modest tsunami killed 550 people and led to the collapse of some large buildings. Chile's capital city Santiago lies 400 km from the high-slip portion of the rupture and 100 km beyond its edge. On the afternoon of 11 March 2011, the $M_w = 9.0$ Tohoku earthquake struck the coast of Japan, causing a massive tsunami that claimed most of the earthquake's 18,564 victims and wreaked great damage. Reminiscent of Santiago, Japan's capital city Tokyo lies 400 km from the high-slip portion of the rupture and 100 km beyond its edge. Because of this distance, both cities largely escaped the consequences of the quakes.

But it may not have been a clean getaway. Immediately after both megaquakes, the rate of small shocks beneath each city jumped by a factor of about 10. In Santiago, the quake rate remains twice as high today as it was before the Maule shock; at Tokyo it is three times as high (see the figure). What this higher rate of moderate ($M_w < 6$) quakes portends for the likelihood of large ones is difficult—but imperative—to answer, because Tokyo and Santiago are probably just the most striking recent cases of a common phenomenon: seismicity increases well beyond the rupture zone.

Tokyo and Santiago, both founded in about 1600, were all but destroyed twice by earthquakes, Santiago in 1647 and 1730, Tokyo in 1855 and 1923. Santiago's 6 million inhabitants constitute 38% of the Chil-

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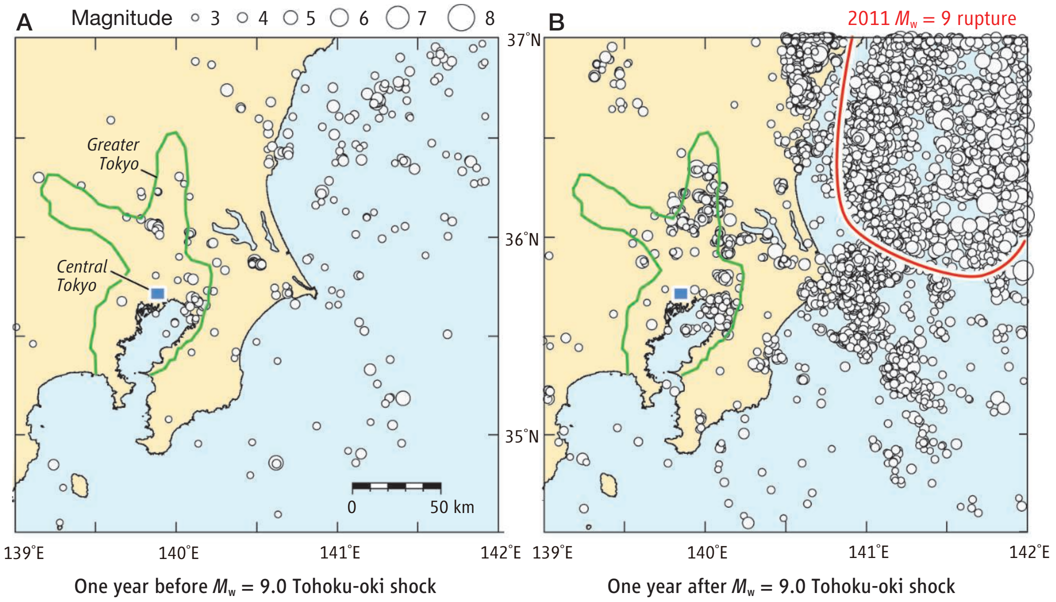
ean population; greater Tokyo's staggering 35.6 million inhabitants represent 28% of Japan's population. Fortunately, they are among the world's most earthquake-resilient cities, because they have regularly updated and strictly enforced construction codes. Nevertheless, the concentration of people, older buildings, wealth, and governmental functions renders the fate of these cities important not only for their nations, but for the world. Furthermore, other great cities within reach of megaquakes (M_w > 8), such as Vancouver, Taipei, Manila, Lima, and Jakarta, could suffer a similar fate; many are in developing nations that are far less well prepared for earthquakes (*1*).



Before and after. Seismicity 1 year before (**A**) and 1 year after (**B**) the 11 March 2011 M_w = 9.0 Tohoku-Oki, Japan, earthquake beyond the southwest edge of the rupture (*7*); shallower shocks are plotted atop deeper ones. The sharp jump in the rate of shocks beneath greater Tokyo was unexpected and continues today. In the figure, magnitude is the JMA magnitude (*12*).

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Following a crustal mainshock of any size, the rate of quakes smaller than the mainshock jumps and then rapidly decays over years to decades; these are termed aftershocks. The rate increase commonly occurs up to a distance equal to the rupture dimension (so, aftershocks could lie 100 km from the end of a 100-km-long rupture). But the aftershocks can sometimes extend much farther. Aftershocks just one magnitude unit smaller than their mainshock are common, and there is a small probability that an aftershock will be larger than its mainshock (*2*). They can thus not be dismissed as harmless, particularly in light of the damaging M = 7.1 Düzce shock that struck 3 months after the M_w = 7.6 Izmit, Turkey, mainshock (17 August 1999), and the M_w = 6.3 Christchurch quake that struck 5 months after the M_w = 7.1 Darfield, New Zealand, earthquake (4 September 2010), each 20 km beyond the initial rupture. Several countries issue short-term aftershock forecasts in the months after large earthquakes. But despite promising experiments and proposals (*3*–*5*), aftershock hazard has yet to be incorporated into national seismic hazard assessments. A hazard assessment that includes aftershocks will make its debut in the new U.S. Geological Survey–California Geological Survey–Southern California Earthquake Center model for California later this year (*6*). This will be based on seismicity observations and stress transfer calculations.

So, are the Tokyo and Santiago earthquakes, 100 km from the fault rupture, aftershocks? The seismicity beneath Santiago is occurring on the adjacent unruptured section of the Chile-Peru trench megathrust; most earthquake scientists would thus deem them off-fault aftershocks. The shocks beneath Tokyo, however, illuminate a deeper, separate fault system. Calculations suggest that the stress imparted by the nearby megaquakes brought the faults beneath Santiago and Tokyo closer to failure, as well as those to the south of the Tohoku rupture, where seismicity also increased (*7*, *8*). Thus, they are aftershocks in the sense that they are contingent on the mainshock and undergo decay.

Aftershocks do not necessarily signal a heightened likelihood of large shocks. They could simply accompany postseismic creep, with the creep shedding the stress imposed by the megaquakes. The aftershocks beneath Santiago and Tokyo are too deep for Global Positioning System observations to reveal unequivocally whether the faults are locked or creeping. But one clue is that the ratio of small to large shocks was not changed by the megaquakes. Given that we are not seeing a heightened rate of small shocks alone, large shocks may now indeed be more probable than before the megaquakes by a factor of at least 2, calling for seismic monitoring and civic preparedness. It is encouraging that Tokyo is already the best-monitored site in the world, and that Chile has just installed a new seismic network.

This view of seismic hazard, predicated on the behavior of the abundant small shocks and guided by stress calculations, contrasts with national and insurance industry hazard assessments. Hazard assessments and models tend to assume that after a great quake, the probability of large shocks first plummets as earthquakes relieve accumulated tectonic stress on the ruptured fault and then gradually rises as tectonic loading restresses the fault over centuries to millennia. This time-dependent hazard has proven difficult to validate and remains the subject of debate (*9*, *10*). The difficulty perhaps arises because the postmainshock hazard drop is not uniform over the rupture surface; pockets of high stress remain that could nucleate the next large earthquake, and stress increases near the edge of rupture can trigger overlapping events.

A further limitation of global seismic hazard modeling is that countries often employ independent approaches based on their seismic history, data quality, and scientific strategies. Differences are found not just in regions far apart, but even between Canada and the United States. The Global Earthquake Model (GEM) (*11*) was founded in 2009 as a public-private partnership to overcome this problem. In 2014, it will launch an open, public model of global earthquake risk that includes not just the hazard, but its consequences in terms of lives and money saved and damage diminished when protective measures are taken. GEM is also producing OpenQuake, a hub for earthquake risk assessment that aims to give scientists in all countries access to a common modeling resource.

In the years ahead, we hope that GEM also tackles the time and space dependencies seen in Tokyo and Santiago and after many other earthquakes. More broadly, we need to understand whether such seismicity rate increases indeed signal a greater chance that a large earthquake will strike, because without this knowledge, governments will be reluctant to act.

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GEOCHEMISTRY

An Arsenic Forecast for China

A map of possible arsenic contamination in China's aquifers may guide mitigation efforts.

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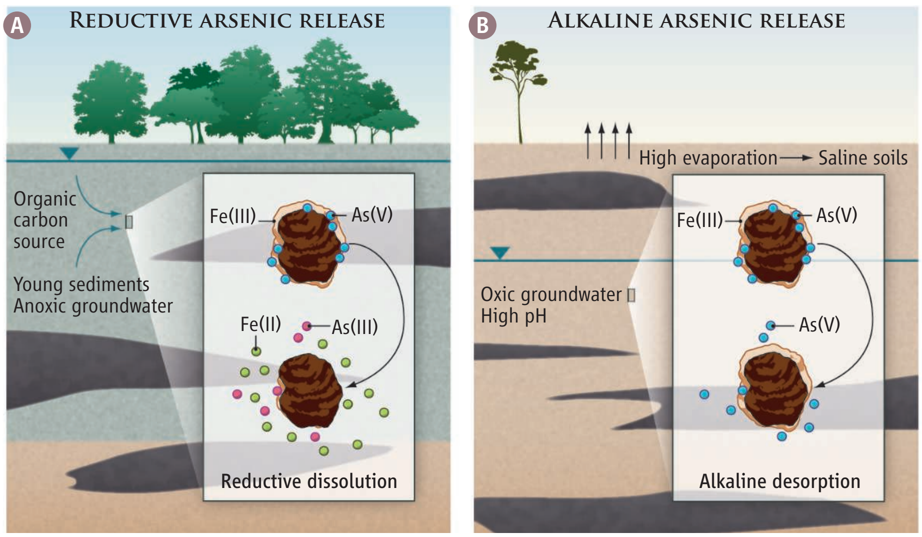
About 140 million people worldwide drink groundwater containing unsafe levels of arsenic (*1*). Chronic exposure to this tasteless, odorless poison leads to health effects such as skin lesions and cancer. In China, pollution is pervasive and anthropogenic groundwater contamination has attracted attention (*2*). Naturally-occurring arsenic is perhaps less widespread, yet equally dangerous to those exposed. Though the problem has been known for decades (*3*) and mitigation is ongoing (*4*), estimates of the exposed population differ widely (*5*, *6*). On page 866 of this issue, Rodríguez-Lado *et al.* (*7*) assess the probability of the occurrence of unsafe arsenic levels in China's groundwater and identify at-risk areas where data are sparse. They suggest that more than 19 million Chinese may be drinking water above the World Health Organization guideline of 10 μg/liter. Such predictive models could guide action toward minimizing the impact of this widespread threat to human health.

More than two decades of research on groundwater arsenic that occurs naturally in aquifers has laid the foundation for predicting conditions in which arsenic concentrations are likely to be high. Two hydrogeologic settings that promote release of arsenic from sediments to the dissolved forms that contaminate and move with groundwater are shown in the figure. In reducing environments (panel A) under anoxic conditions, organic carbon drives chemical reactions that dissolve iron minerals on which arsenic is bound. This reductive dissolution often occurs in wet, flat regions and is the main mechanism producing high arsenic concentrations in the large river basins of South and Southeast Asia (*8*, *9*). Arsenic release also happens in oxic, high-pH waters that promote desorption of arsenic from mineral oxides (see the figure, panel B). This generally occurs in arid regions; for example, in Argentina, Spain, and the southwest United States (*1*). High arsenic concentrations resulting from both conditions occur in localized areas of China (*10*, *11*).



How arsenic is mobilized. Rodríguez-Lado *et al*. use land surface attributes such as geology, soil texture, salinity, river density, and slope to predict areas where reductive (**A**) or alkaline (**B**) arsenic release into groundwater may occur, producing a map of probability of arsenic concentration above 10 μg/liter over all of China.

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Can arsenic-releasing environments be identified in areas where no testing has been done? Easily measurable characteristics of land surface that indicate conditions favoring release and build-up of high arsenic concentrations would be ideal predictors. However, identification of such proxies is challenging, because arsenic release is affected by complex, three-dimensional processes in the subsurface. Rodríguez-Lado *et al*. meet this challenge by first identifying land surface characteristics that can indicate arsenic release and then using statistical analysis to determine which proxies have predictive power for aquifers in China. A combination of eight factors explains much of the variability in known arsenic concentrations and could therefore be used as a reliable set of indicators to predict the probability of arsenic occurrence in areas without data.

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