BBC NEWS
HEALTH

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City life 'boosts bug resistance'

People from traditionally urban areas could be genetically better suited to fighting infection, say researchers.

The University of London team looked at how many people carried a specific gene variant known to give them resistance to TB and leprosy.

It was more common in those from areas with a longer history of urbanisation, where the diseases were more likely to have been rife at one point.

They described the discovery as an example of "evolution in action".

The phenomenon, reported in the journal Evolution, is suggested as an example of so-called "selective pressure" in relation to disease resistance.

It happens because, when a population is exposed to a killer illness, the people who are best placed to pass on their genes to the next generation are those whose genetic make-up helps them fight the infection.

In towns and cities, where people intermingle far more closely, the likelihood of being exposed to infectious disease is theoretically higher.

So, over the centuries, the greater the level of historical exposure, the more likely it is that these resistance genes will be spread widely among the population.

Disease resistance

The scientists, from University College London and Royal Holloway, part of the University of London, tested this by analysing DNA samples drawn from 17 different human populations living across Europe, Asia and Africa.

The results were cross checked against historical and archaeological data about the date of the first city or urban settlement in each region.

The protective gene variant was found in nearly everyone from the Middle East to India and in parts of Europe where cities have been established for thousands of years, but were less frequent in regions with a shorter history of urbanisation, such as Africa.

Dr Ian Barnes, one of the authors of the research, said: "This seems to be an elegant example of evolution in action.

"It flags up the importance of a very recent aspect of our evolution as a species, the development of cities as a selective force.

"It could also help explain some of the differences we observe in disease resistance around the world."

There are other examples of selective pressure in disease resistance - it has been suggested that one is the prevalence of the gene defect responsible for the lung disease cystic fibrosis.

Normally, the lethal nature of the condition across history would suggest that people carrying the gene defect were at a distinct evolutionary disadvantage, and their numbers would be fewer.

However, scientists believe that the gene gives carriers an advantage when faced with the cholera toxin - which, in early cities, could have significantly outweighed the disadvantage of some children developing cystic fibrosis.

Overcrowding

Professor Brian Spratt, chair of molecular microbiology at the Imperial College London School of Public Health, said: "Individuals who are more resistant to a pathogen that causes a disease with substantial mortality, such as malaria or TB, will survive better and will contribute more offspring to the next generation. As many of their children will have inherited increased resistance to the pathogen, they also will survive better.

"Thus frequencies of these genetic sequences that provide increased protection to a disease will be far more common in areas where the disease has been killing people for centuries or even millennia than those where the disease has never been endemic.

The same effect should occur for some diseases with populations who have lived for centuries within dense cities because diseases such as cholera and TB will have always been a problem in cities due to overcrowding and poor sanitation, compared to people living nomadic lives."

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Urban living helps people develop resistance to disease, say scientists

Scientists have discovered that generations of urban living develops resistance to TB, leprosy and other diseases

Press Association
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A leper colony north of Cairo. Living in cities over generations has helped people develop an immunity to such diseases. Photograph: Claudia Wiens

Living in urban areas has helped people develop an immunity to diseases, a study published today suggested. Researchers discovered that people who have a history of living in more populated regions are more likely to have a genetic variant which gives them a resistance to diseases such as tuberculosis and leprosy.

Poor sanitation and high population densities provided an ideal breeding ground for disease in ancient cities. Past exposure to pathogens led to disease resistance spreading through populations because ancestors passed it on to their descendants, scientists said. Dr Ian Barnes, from the School of Biological Sciences at Royal Holloway College, said: "This seems to be an elegant example of evolution in action.

"It flags up the importance of a very recent aspect of our evolution as a species, the development of cities as a selective force. It could also help to explain some of the differences we observe in disease resistance around the world."

Researchers analysed DNA samples from populations across Europe, Asia and Africa and compared rates of genetic disease resistance with urban history. They found that in the areas with a long history of urban settlements, today's inhabitants were more likely to possess the DNA variant which provides some resistance to infection.

The study, which was conducted by researchers at Royal Holloway, the University of London, University College London and Oxford University, is published in the journal Evolution.

City-dwelling helped us evolve resistance to disease

12:20 20 September 2010 by **John Cannon**

Living in a crowded city doesn't sound like a recipe for good health, but it may have helped our ancestors protect their descendants from disease.

Some people carry a genetic sequence, or allele, that provides immunity to leprosy and tuberculosis. Mark Thomas, an evolutionary biologist from University College London, and Ian Barnes, a molecular palaeobiologist from Royal Holloway, University of London, wondered whether this genetic immunity could have been gained when people began living in close proximity. Poor sanitation would have meant that disease was rife in ancient cities, but exposure to the pathogens would have led to resistance developing, which the inhabitants would have passed onto their descendants.

To test this idea, Thomas and colleagues analysed the DNA of people living in 12 regions in Europe, Asia and Africa. For each area, they combed the historical and anthropological records to work out when people first started living in close-knit groups. They found that the longer cities in the region had been established, the more likely it was that the current inhabitants carried the immunity allele.

Thank the cows

It had been thought that the allele became prevalent when cattle were first domesticated, as cows carry a strain of TB that humans can catch. But the team found a stronger correlation between the allele and urbanisation than with the onset of cattle farming.

It is likely that cattle domestication would have played a role in developing the immunity, because cattle farming would have been important in early city life, Barnes points out.

Thomas describes population dynamics as "an awesome, underplayed feature of our history" and thinks resistance to other diseases could also have evolved in this way.

John Odling-Smee, an evolutionary biologist at the University of Oxford who wasn't involved in the study, agrees. "This study could be regarded as the tip of the iceberg" in terms of the effects of urbanisation on disease immunity, he says.

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News

Evolution in the urban jungle

Tuberculosis resistance is most prevalent in city slickers.

Ewen Callaway

Survival of the fittest is more than just an apt metaphor for city living. Humans may have evolved disease resistance in response to urbanization.

Urban populations can evolve resistance to certain diseases over time.

Jacob Silberberg/Panos

An immune-system gene that protects against pathogens such as tuberculosis (TB) and leprosy is more prevalent in contemporary cultures with long histories of urbanization than in those where cities appeared more recently, finds a study published in the journal *Evolution*[1].

"There are pros and cons to starting to move into cities, and one of the downsides is you actually get higher disease rates — at least for the short term," says Ian Barnes, a geneticist at Royal Holloway University of London, who argues that those disease rates were high enough to lead to natural selection for resistance.

High population densities and regional trade help pathogens to shuttle between hosts and populations, and poor sanitation, standing water and domesticated animals all provide ample breeding grounds, he says.

To test whether this combination could propel natural selection on disease resistance, Barnes and his team compared the urbanization histories of 17 African, Asian and European populations with the prevalence of an allele of a gene linked to protection against TB, called *SLC11A1*, in the same populations.

They relied on archaeological evidence for the earliest urban settlements in each area, indicative of hundreds to thousands of people living stably in one place. These settlements appeared beginning from around 6000 BC for Anatolian Turks to the early twentieth centuries for the southern Sudanese and the Sami — a culture native to northern Scandinavia.

Members of such newly urbanized populations proved significantly less likely to possess a TB-protective version of *SLC11A1* than populations from the Middle East, India and parts of Europe, where the protective allele is found in nearly everyone and cities have been around for millennia.

Going with the flow

However, natural selection isn't the only explanation for such a pattern. Genes and ideas tend to flow together, so interbreeding and not evolution might instead explain why the TB-resistance allele is extremely prevalent in Italians and Greeks, for instance. Yet, even after accounting for shared ancestry, Barnes and his team still found a strong link between TB resistance and

urbanization.

Pardis Sabeti, a geneticist at Harvard University in Cambridge, Massachusetts, agrees that urbanization has probably influenced natural selection in humans. Her own lab recently scoured the human genome for natural selection within the past 30,000 years and identified numerous genes involved in fending off tuberculosis and leprosy.

If city life did influence the evolution of pathogen resistance in humans, ancient DNA samples could capture that process in action, says Mark Thomas, an evolutionary biologist at University College London, who collaborated with Barnes on the paper. Thomas and Barnes and their colleagues plan to look for signs of natural selection in other alleles of *SLC11A1*, as well as in other genes linked to infectious diseases.

References

1. Barnes, I., Duda, A., Pybus, O. & Thomas, M. G. *Evolution* advance online publication doi:10.1111/j.1558-5646.2010.01132.x (2010).

TIME Partners with CNN

Study: City Life Spreads Disease, But If It Doesn't Kill You...

By MEREDITH MELNICK Thursday, September 23, 2010

Following the news that the rise of cities contributed to the spread of HIV is a more heartening take on urbanity: a history of city living may have helped some populations develop resistance to tuberculosis (TB).

A new study published in *Evolution* this month found that modern-day residents of ancient cities (Rome and Damascus, for example) are more likely than others to have a genetic variant that lowers the risk of TB infection, the highly contagious bacterial respiratory disease that afflicts 11 million people worldwide each year.

Researchers from University College London (UCL) analyzed human DNA samples from the current populations of 17 different cities across Africa, Asia and Europe. They matched these samples to historical records of those cities' first settlements.

What they found was that the genetic variant was almost universally present in populations throughout the Middle East and India, and was also found in some of the older European settlements.

"Population density seems to play an important role in shaping so many aspects of our species," said Mark Thomas a professor in the department of genetics, evolution and environment at UCL in a statement. "It was a vital factor in our species maintaining the complex skills and culture that distinguish us from other primates. It drove many of the genetic differences we see today between different populations from around the world. And now, it seems, it also influenced how infectious diseases spread in the past and how we evolved to resist those diseases."

The authors of the study expressed excitement about the merging of scientific analysis and historical records, but this is also a potential limitation. Scientific and historical conclusions are different in nature and difficult to merge — that is, you can't necessarily extrapolate science from history. So it might be hasty to suggest that population density was the central contributing factor to the development of the anti-TB genetic mutation.

For one thing, the highest rates of the anti-TB variant occurred in Middle Eastern populations and in areas that were involved in prominent Arabic invasions — for example, Spain (711 to 1492) and India (in the 12th century) — and not in other areas that are home to ancient cities but were not subject to Arab invasion (China). So who's to say that immunity isn't a result of Arabic ancestry, rather than city life? Or that some other historical factor triangulated with urban centers to suggest this result?