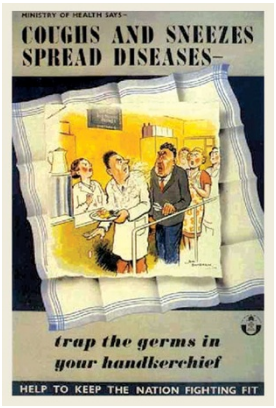
nature structural & molecular biology

Don't catch me if you can

Colds are a nuisance that we all suffer from. They go way back in history, and the Egyptians even had a hieroglyph for them—a nose followed by a symbol representing something coming out. In modern society, the many different cold remedies on drugstore shelves are a testimony to how desperate we are to overcome the unpleasantness these illnesses bring. Unfortunately, these remedies treat only the symptoms but not the source, and there are >200 viruses that cause colds. Adults will, on average, have two to five each year, and children four to seven. Although symptoms last only about a week, a cold can be quite debilitating. In addition, there is a risk for developing complications, such as asthma or bronchial and ear infections. Developing ways to prevent common colds is thus a much sought after goal.



H.M. Bateman, circa 1942

To this end, it is important to understand how viruses get into the cells in the first place, and the article on page 429 of this issue of *Nature Structural & Molecular Biology* presents the structure of a cold virus bound to a fragment of its cell surface receptor (an accompanying News and Views commentary discusses how this structure contributes to the understanding of the entry mechanisms of cold viruses). The results are better appreciated in the context of a recent book by David Tyrrell and Michael Fielder entitled "Cold wars: The fight against the common cold", which outlines the rich history of research on the common cold.

Throughout the ages, there have been numerous misguided ideas about colds. In ancient times, people imagined they were caused by evil spirits and later, it was thought that an 'imbalance' of the four humors—blood, black and yellow bile, and phlegm—led to 'leakage' from the nose. There are many myths surrounding the common cold, but the most enduring one is that the illness is caused by getting too chilled, leading to what used to be termed 'inappropriate sweating' through the nasal passages instead of through the skin. Treatments in the past have ranged from drinking brews of various herbal concoctions to stuffing rolled orange peels up one's nose. Modern sufferers still stand by chicken soup and hot tea, often on top of decongestants and pain relievers.

In the 1890s, researchers began investigating colds more scientifically, with an eye toward finding infectious agents. It had just been shown that diseases like cholera and dysentery were caused by bacteria. So, convinced that bacteria were also the culprits in colds, researchers swabbed noses and collected sputum from sniffling, coughing patients. While they did find a large number of bacteria, the same types were found in equal numbers in healthy individuals. Researchers were left confused.

In 1914, Walter Kruse, the German who had discovered the dysentery bacillus, conducted a critical experiment. He collected nose secretions from a colleague sick with a cold, passed them through a filter that would hold back bacteria and other large microbes, and inoculated volunteers. A full one-third developed colds within three days—an impressive outcome even though only 12 volunteers participated. Another slightly larger study replicated these results. Kruse believed that "filter-passing viruses" (where 'virus' is Latin for poison) were to blame. He planned to follow-up his work in this area but was waylaid by the start of World War I.

During the 1920s, the microbiological group at the medical school of Columbia University took this research to the next level. They used isolated chimpanzees as subjects and showed that inoculating them with bacteria-free nasal filtrates from sick individuals could indeed cause them to have colds. They also conducted well-controlled human experiments with similar outcomes. Their work convinced the scientific world at large that viruses did in fact cause colds. The next step was to grow the cold viruses reproducibly in culture—a feat that was finally accomplished in the 1950s and 1960s at the Common Cold Research Unit in Britain.

We now know that hundreds of viruses in numerous families cause the well-known coughing, sneezing and fever symptoms, making it impossible to envision a single vaccine that would be effective against the common cold. In addition, because the perpetrators are viruses, not bacteria, antibiotics are helpless and can only be used to defend against the complications resulting from bacterial infections. Nevertheless, many miserable people sick with colds continue to demand antibiotics, and overprescription of antibiotics contributes to the rise of multidrug resistant bacteria around the world.

Perhaps one day there will be safe and effective antiviral compounds to stop colds in their tracks. Many basic biology research projects contribute to this goal. For example, stopping the virus from entering the cells, from releasing its genetic material in the cytoplasm or from replicating its genome are all reasonable therapy targets. Nevertheless, an effective treatment is likely still many years away. Until then, the best practice is to try to prevent them. As they say, "coughs and sneezes spread diseases" (see the British wartime poster promoting good hygiene, from http://www.wkac.ac.uk/poster/imagebank/Coughs&Sneezes.htm), and the best measure against spreading colds is still good old fashioned hygiene. ■