

## Why do smokers catch colds more easily?

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*Recent studies have shown that, following exposure to cigarette smoke, the cells of the respiratory tract respond to this oxidative stress by decreasing the effectiveness of antiviral defenses, which facilitates infection by the rhinoviruses responsible for colds.*

### VIRAL ATTACK

The epithelial cells that line the respiratory tracts represent our first line of defense against numerous aggressors present in the external environment, whether they are tiny particles of atmospheric pollution, toxic agents (smoke, solvents) or some of the many respiratory viruses.

In the case of viruses, there are about 100 distinct species of rhinovirus responsible for colds, representing one of the most common threats: following their entry into the respiratory cells, these viruses multiply rapidly and cause the characteristic symptoms of a cold, most notably a runny nose, sneezing, coughing, congestion and headaches. Though they are usually not dangerous to one's health, colds nevertheless lead to important direct and indirect health costs, estimated at 40 billion dollars annually in the United States<sup>1</sup>.

### ANTIVIRAL DEFENSES

The presence of viruses in the respiratory tracts is much more frequent than is commonly thought: for example, one study, which continuously measured the presence of respiratory viruses in the nasal passages, found that the average person carries these viruses for about seven weeks of the year. On the other hand, although this cohabitation is certainly involuntary, about half of these infections are completely asymptomatic, which suggests that the respiratory passages possess a front-line defense mechanism which significantly reduces the infectious potential of these viruses.

To better understand the mechanisms involved in the defense of the respiratory tracts against viruses, a team at Yale University (New Haven, CT) exposed cells removed from the nasal passages and bronchi to a common rhinovirus (RV-1B) and then examined the response triggered by the infection<sup>2</sup>. They noticed that the virus activated two types of responses: 1) an antiviral response, characterized by the strong production of type III interferon (a class of proteins whose function is to stimulate the immune system) and 2) an antioxidant response, with the expression of several neutralizers of free radicals. The antiviral response is principally located in the nose, which is logical as it acts as the entry location for the virus, whereas the antioxidant response is predominantly found within the lungs, which is also logical due to the constant presence of potentially toxic aggressors in the air we breathe.



### MAKE A COMPROMISE

According to the authors of the study, this separation of the antiviral and antioxidant defenses at distinct locations (nose and lung) suggests that the cells of the respiratory tract cannot employ these two approaches simultaneously and must choose either to use an antiviral defense or to protect against oxidative stress. This compromise is well illustrated by the observation that the nasal cells, when exposed to cigarette smoke, are much more susceptible to becoming infected by a rhinovirus. In these cells, activation of a transcription factor responsible for the antioxidant response (NRF2) induces a series of adaptations which favour survival, but which also lead to a decreased level of interferon and thus of the antiviral response. In other words, the respiratory tracts are very effective at defending against viruses and other types of toxic aggressors present in the air, but become much more susceptible to viral infection when they are simultaneously exposed to two attacks.

These observations explain why people who are chronically exposed to an oxidative stress, such as smokers, patients with chronic obstructive pulmonary disease or even asthmatics, are much more susceptible to the cold virus and more often develop complications following infection.

- (1) Fendrick AM et al. The economic burden of non-influenza-related viral respiratory tract infection in the United States. *Arch. Intern. Med.* 2003; 163: 487-494.
- (2) Mihaylova VT et al. Regional differences in airway epithelial cells reveal tradeoff between defense against oxidative stress and defense against rhinovirus. *Cell Rep.* 2018; 24: 3000-3007.