

# An Explanation for the Seasonality of Acute Upper Respiratory Tract Viral Infections

R. Eccles

To cite this article: R. Eccles (2002) An Explanation for the Seasonality of Acute Upper Respiratory Tract Viral Infections, *Acta Oto-Laryngologica*, 122:2, 183-191, DOI: [10.1080/00016480252814207](https://doi.org/10.1080/00016480252814207)

To link to this article: <https://doi.org/10.1080/00016480252814207>



Published online: 08 Jul 2009.



Submit your article to this journal [↗](#)



Article views: 507



View related articles [↗](#)



Citing articles: 123 [View citing articles](#) [↗](#)

# An Explanation for the Seasonality of Acute Upper Respiratory Tract Viral Infections

R. ECCLES

From the Common Cold Centre, Cardiff School of Biosciences, Cardiff University, Cardiff, UK

**Eccles R.** *An explanation for the seasonality of acute upper respiratory tract viral infections.* Acta Otolaryngol 2002; 122: 183–191.

Despite a great increase in our understanding of the molecular biology of the viruses associated with acute upper respiratory tract viral infections (URTIs) there is a remarkable lack of knowledge and ideas about why URTI should exhibit a seasonal incidence. Most publications in this area either acknowledge a complete lack of any explanation for the seasonality of URTI or put forward an explanation relating to an increased “crowding” of susceptible persons in winter. This review will discuss some of the ideas concerning the seasonality of URTI and put forward a new hypothesis for discussion, namely that seasonal exposure to cold air causes an increase in the incidence of URTI due to cooling of the nasal airway. The hypothesis is supported by literature reports demonstrating that inhalation of cold air causes cooling of the nasal epithelium, and that this reduction in nasal temperature is sufficient to inhibit respiratory defences against infection such as mucociliary clearance and the phagocytic activity of leukocytes. A case is also made to suggest that warming of the nasal airway during fever and nasal congestion may help to resolve a current URTI. *Key words:* common cold, fever, infection, influenza, mucociliary clearance, nose, phagocytosis, season.

## INTRODUCTION

Seasonal changes in climate are associated with diverse changes in animals and plants. Humans are buffered from many of the seasonal climate changes by housing and clothing but are still subject to many seasonal changes, such as changes in mood and health (1). This review will focus on one seasonal change in human health that affects all populations exposed to a winter climate but which apparently has no generally accepted explanation, namely the seasonal change in the incidence of acute upper respiratory tract viral infections (URTIs).

It is common knowledge that the incidence of URTIs such as common cold and influenza exhibits seasonal fluctuations. In the more northerly and southerly parts of the hemispheres there is a peak in respiratory illness during the winter months. Winter seasonality has been reported for a wide range of URTIs caused by > 200 different viruses belonging to six families: orthomyxoviruses (influenza), paramyxoviruses (respiratory syncytial virus), parainfluenza, coronaviruses, picornaviruses (common cold), herpes viruses and adenoviruses (2). Viruses which may cause systemic illness but which gain entrance to the body via the upper respiratory tract, such as certain paramyxovirus infections (measles, mumps) and varicella-zoster infection (chickenpox), also show a similar winter seasonality (3–5). Lower respiratory tract diseases such as pneumonia, which may be of viral or bacterial aetiology, also show a similar seasonal pattern, with the peak of illness in winter (6, 7). The nose is the entrance to the lower airways and URTI predisposes to lower airway infection with viruses and bacteria. Life-threatening lower airway

infections often start as an URTI, especially in the elderly. Annual vaccination programmes against influenza can help to protect those at risk of lower airway infection, but there is at present no protection from the hundreds of viruses responsible for the common cold syndrome.

Every year in the UK the decrease in air temperature in winter is associated with a great increase in mortality and morbidity. For every degree Celsius decrease in average temperature there is an increase in the number of winter deaths by ≈ 8,000 (8). Respiratory infections are a major cause of this seasonality of death and illness and place a great seasonal burden on the health service. Around 33% of the seasonal increase in mortality is associated with respiratory disease associated with infection (9), and there is increasing evidence that some of the seasonal increase in mortality associated with cardiovascular disease may be related to respiratory infection (10, 11).

The common factor amongst the wide range of seasonal diseases, from common cold to measles and pneumonia, is a correlation between the incidence of the disease and air temperature (3, 7). As an example of the seasonality of respiratory infection the correlation between air temperature and the incidence of epidemic influenza and influenza-like illness in the UK is illustrated in Fig. 1. The incidence of epidemic influenza and influenza-like illness is based on reports from around 230 general practitioners in England and Wales for the period August 1970 to July 1991, and is given as the rate per 10,000 registered patients. The author of the Figure acknowledges that the data do not relate solely to influenza and are likely to

include other URTIs such as common cold. A clear relationship between air temperature and the incidence of influenza and influenza-like illness is apparent from the graph, with the peak of illness occurring at the period of lowest average temperature in February.

The clear seasonality illustrated for influenza and influenza-like illness is provided as one example of URTI, as seasonality has previously been described for many other viral infections which infect the nose and upper airways, such as common cold (12), RSV (13), measles and chickenpox (3).

Despite a great increase in our understanding of the molecular biology of the viruses associated with URTI there is a remarkable lack of knowledge and ideas about why it should exhibit a seasonal incidence. There is at present no hypothesis to explain the seasonality of URTI. Most publications in this area either acknowledge a complete lack of any explanation for the seasonality of URTI or put forward an explanation relating to an increased "crowding" of susceptible persons in winter (2).

The present article will review the development of some of the ideas concerning seasonality of respiratory infection and put forward a new hypothesis for discussion, namely that seasonal exposure to cold air causes an increase in the incidence of URTI due to cooling of the nasal airway.

## PAST AND PRESENT EXPLANATIONS FOR SEASONALITY

Acute upper respiratory viral infections such as the common cold have traditionally been associated with cold weather and this may be the origin of the term "common cold", which implies exposure to cold.

The idea that exposure to cold alone is sufficient to cause the symptoms described as catarrh (which would be described as URTI today) was widely be-

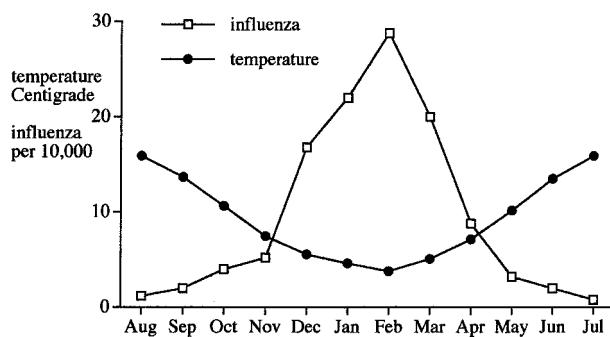


Fig. 1. Relationship between incidence of acute upper respiratory tract viral infections (epidemic influenza and influenza-like illness; rate per 10,000 registered patients) and average air temperature (°C). Redrawn from Curwen (9).

lieved in the 19th century. The description of the aetiology of acute catarrh in a standard clinical textbook of otolaryngology is typical of the period. Mackenzie, in 1884 (14), states that "Exposure to cold, under certain circumstances, is very apt to cause catarrh, but the exact mode of its operation is uncertain. Cold currents of air on the head are familiarly recognised as a cause of the disorder, and the bald are in this respect, of course, peculiarly vulnerable". He goes on to say that "Occasionally coryza appears to be due to epidemic influences, and several persons in the same house, the dwellers in a particular street, or even the inhabitants of a whole town, may be observed to suffer simultaneously". Mackenzie discusses how whole armies have developed symptoms of coryza when exposed to cold weather and goes on to conclude "In short, coryza can only be said to occur epidemically, in so far as a sudden lowering in the temperature, with increased humidity of the air, may cause the malady to be widespread".

The idea that exposure to cold weather in some way caused URTI was modified at the start of the 20th century to focus more on crowding as a factor. In a book published in 1929 Hill and Clemen (15) state that "if cold weather gives rise to an epidemic of 'colds' the cause is not to be sought in meteorological conditions, but rather in crowding in overheated and stuffy rooms". This idea of crowding indoors facilitating the spread of infection was generally accepted by scientists because there was no competing hypothesis to explain the seasonality of respiratory infections. In his textbook published in 1965, Andrewes (16) reluctantly accepts the idea that crowding indoors may explain the seasonality of colds but also raises the criticism that our cities are just as crowded in summer as in winter and states "Many people regard this (crowding) as the likeliest 'winter factor' to explain the facts. I have always had doubts about this. Indoor workers in towns spend their working hours in much the same way winter and summer; they are cheek-by-jowl in their offices or at the factory bench or canteen all through the year. There may be rather better ventilation in summer, but that is the only likely difference. If close contact were all, one would think that London Transport would ensure an all-the-year round epidemic". Andrewes goes on to conclude his discussion on colds and cold weather as follows: "So, as to why we get more colds in the winter, we must at present admit that we just do not know".

Our understanding of the seasonality of URTI has not progressed very far during the 20th century and in a textbook published in 1996 (17) the crowding theory is still put forward as the major explanation of seasonality: "There is no evidence to date to indicate

that cold weather *per se*, chilling, wet feet, or draughts play any role in the susceptibility of people to colds. Epidemiological data suggest that school attendance and other forms of crowding populations (particularly children) are the major factors influencing common cold virus transmission rates". However, the authors do acknowledge that "The underlying biological explanation for seasonal differences has remained elusive". At the start of the 21st century the crowding theory persists in textbooks of human virology as an explanation for the seasonality of respiratory infection and there are some signs that any link with climate has now been lost. In a summary on the seasonality of viral respiratory infections Collier and Oxford (2) state that "The precise conditions that result in seasonal spread are not known with certainty but may be attributed more to changes in social behaviour with the seasons e.g. overcrowding in cold weather, than with variations in humidity and temperature".

### THE HYPOTHESIS

The hypothesis that will be proposed in this review is that seasonal exposure to cold air causes an increase in the incidence of URTI due to cooling of the nasal airway.

A model of the hypothesis is shown in Fig. 2. This illustrates that breathing cold air during the winter season causes cooling of the nasal airway, which causes a fall in temperature of the respiratory epithelium and a decrease in the effectiveness of local respiratory defences, such as mucociliary clearance and leukocyte phagocytosis.

The scientific information which supports this hypothesis will be presented below and will establish that: (i) a decrease in air temperature causes a decrease in the temperature of the nasal airway; (ii) cooling of the nasal airway compromises respiratory defence against infection by slowing mucociliary clearance and inhibiting leukocyte phagocytosis; and (iii) warming of the body and airway associated with fever and nasal congestion are natural defences against infection.

### SEASONAL CHANGES IN AIRWAY TEMPERATURE

The air we inspire is warmed and humidified as it passes through the nose, so that by the time it reaches the lungs it is fully saturated with water vapour and warmed to body temperature (37°C). In most environments the temperature of the air we breathe is well below body temperature, and therefore the nasal airway is always exposed to a degree of heat loss and

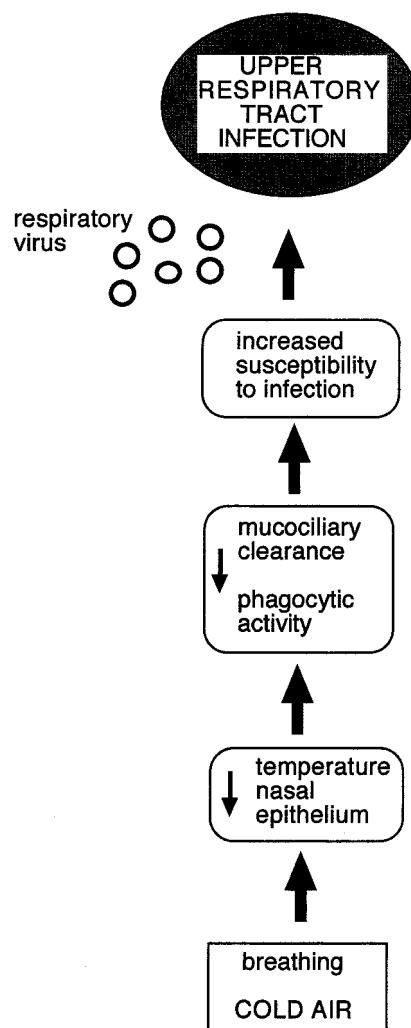


Fig. 2. A model illustrating the mechanism to explain the seasonal effects of cold air on the incidence of acute URTI.

cooling. Even in a temperate climate such as that of the UK, the annual extremes of air temperature can range as widely as from -13 to +34°C (Heathrow Airport, London) (18).

The nasal airway is subject to a temperature gradient during inspiration, with the anterior part of the nose being the coldest part of the airway (19). Thermal mapping studies of the airways in humans have demonstrated that in the course of conditioning the inspired air, the airways undergo thermal changes that extend well into the periphery of the lung (20).

The temperature gradient along the nasal airway on breathing air of different temperatures is illustrated in Fig. 3. The graph is based on experiments on 18 male subjects who were exposed to different ambient air temperatures (21). The temperature of the air passing through the nose was measured at fixed distances into the nasal passage by means of a small thermocouple. The Figure illustrates how the

inspired air is warmed as it passes through the nose, and clearly illustrates the different gradients for cold and warm air. The 2 ambient air temperatures used in the study ( $23\text{--}28^{\circ}\text{C}$  and  $5\text{--}8^{\circ}\text{C}$ ) could be considered as representative of summer and winter conditions, respectively and illustrate how airway temperature can be influenced by seasonal changes in air temperature. With an inspired air temperature of  $\approx 6^{\circ}\text{C}$  the anterior 5 cm of the nasal respiratory epithelium will be exposed to temperatures between 6 and  $20^{\circ}\text{C}$ . With lower ambient air temperatures one would expect an even greater temperature gradient.

The nasal air temperatures illustrated in Fig. 3 relate to the inspired air. However, during the respiratory cycle, the respiratory epithelium will be alternately exposed to cooling (during inspiration) and warming (during expiration). The surface temperature of the nasal epithelium will closely follow the temperature of the inspiratory and expiratory air, but the temperature deeper in the nasal epithelium will be an average of the inspired and expired air temperatures. It is not possible to measure this tissue temperature gradient without disrupting the gradient in some way, as any penetration of the nasal epithelium will cause bleeding and an inflammatory response. However, Cole in 1954 (19, 22) performed experiments in which a small thermistor in the tip of a hypodermic needle was pushed into the epithelium, and reported that on breathing room air (presumably at  $\approx 20^{\circ}\text{C}$ ) the submucosal temperature was several degrees lower than the surface temperature, and remained well below body temperature throughout the respiratory cycle.

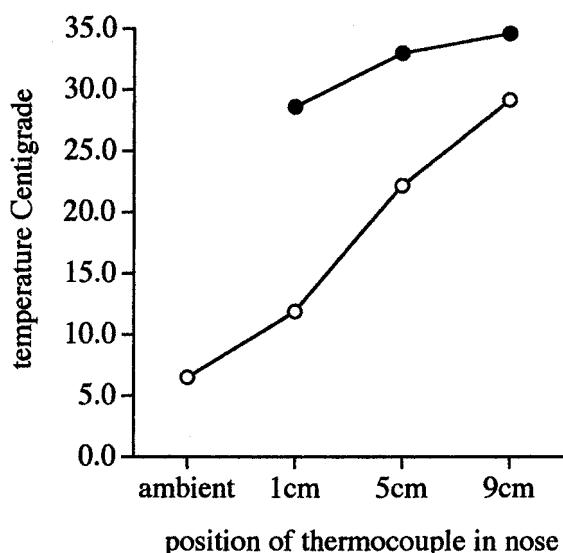


Fig. 3. Mean peak temperatures in the nasal airway in 18 resting subjects exposed to 2 different ambient air temperatures. Redrawn from Webb (21).

From the information presented above it is reasonable to assume that seasonal changes in air temperature will cause seasonal changes in the temperature of the nasal airway.

One argument that could be used against the idea of a seasonal change in nasal airway temperature is that as we spend most of our time in centrally heated homes and workplaces, the airway will not be exposed to cold air in winter. To counter this argument, a case can be made that periodic exposure to cold air is inevitable whenever one moves out of doors. Seasonal fluctuations in room temperatures also occur indoors, especially at night time when heating systems may be switched to a low level to conserve fuel. Mean monthly air temperatures in the bedrooms of UK elderly persons in their own homes or in residential homes show a seasonal fluctuation of  $>15^{\circ}\text{C}$  (10), and although the body may be protected from heat loss to some extent by clothing and blankets, the nasal airway is still directly exposed to the air temperature in the room.

#### EFFECTS OF AIRWAY COOLING ON RESPIRATORY DEFENCE

Every day each one of us warms, filters and humidifies  $\approx 14,000\text{ l}$  of air (19). This air contains suspended particulate matter that is contaminated with viruses, bacteria and fungi. The upper airways are the most commonly infected area of the body, with acute upper respiratory tract viral infections afflicting almost everyone on a regular basis. The nose and upper airways have two major defences against infection: firstly, the physical barrier of a continuously moving layer of mucus that lines the airway; and secondly, a local immune response involving phagocytic polymorphonuclear leukocytes and other leukocytes such as natural killer cells. Airway cooling is likely to compromise both these mechanisms of respiratory defence and predispose to respiratory infection.

#### *Effects of airway cooling on mucociliary clearance*

Particulate matter  $>10\text{ }\mu\text{m}$  in diameter is deposited in the nose, trapped on the thin mucus blanket that covers the nasal respiratory epithelium and then slowly moved by rapidly beating cilia to the nasopharynx, to be swallowed and then sterilized in the acid of the stomach (23). Mucociliary clearance comprises two components: the production of a thin blanket of mucus and the beating of cilia (23). Mucociliary clearance is the first line of respiratory defence against infection and anything which compromises mucociliary clearance leads to an increased incidence of respiratory infection (24). The rate of clearance of particles deposited on the surface

of the respiratory epithelium can be slowed by factors that slow the rate of beating of the cilia, and by factors that decrease the rate of secretion of mucus or increase the viscosity of the mucus (25). For example: (i) the beating of the cilia may be slowed by genetic diseases which predispose to ciliary dyskinesia, and these diseases invariably result in chronic infections of the nose, paranasal sinuses and lower airways (26); and (ii) the viscosity of the mucus blanket is increased by diseases such as cystic fibrosis, and this results in frequent and often chronic infection of the airway.

Human mucociliary clearance is slowed on exposure to cold air (23). The decrease in temperature, by slowing metabolic activity, is likely to influence the rate of mucociliary clearance by reducing both ciliary beat frequency and the rate of secretion of mucus. Depending on the magnitude of the decrease in temperature it is also likely to cause an increase in the viscosity of respiratory mucus.

Experiments on cilia in the paranasal sinuses of rabbits have shown that the beat frequency was greatest between 18 and 33°C, and that with a lowering of temperature the frequency gradually declined, until all motion ceased at temperatures between 7 and 12°C (27). Experiments on living chicks have demonstrated that mucociliary clearance of droplets injected into the lower trachea is slowed on breathing cold air (25). In a study on calves, mucociliary clearance was measured at ambient temperatures of 2–4°C and 16–18°C, with exposure periods of 3 days (28). Nasal mucus velocity was 24% lower during cold exposure. In addition, a direct relationship was found between mucosal temperature and tracheal mucus velocity in excised tracheas.

The evidence presented above indicates that exposure to cold air decreases the temperature of the nasal respiratory epithelium and that this causes a decrease in the rate of mucociliary clearance. Diesel et al. (28) have already speculated that the decrease in mucociliary clearance associated with cold exposure may be sufficient to predispose to respiratory infection.

#### *Effects of airway cooling on local immune response of the airway*

The immediate local immune response of the nasal respiratory epithelium to viral and bacterial infection involves a non-specific response of polymorphonuclear leukocytes and lymphocytes. The non-specific response involves phagocytosis, the generation of viricidal and bactericidal superoxides, the generation of complement factors and the generation of chemical mediators such as bradykinin and prostaglandins which play an active role in local defence (29). Like all biological processes that are dependent on metabolic activity, the local immune response of the

respiratory epithelium is likely to be slowed by a decrease in temperature.

The phagocyte is the most powerful and most important part of the host defences that can operate without delay against the invading viruses once they have penetrated the nasal mucus and breached the epithelial surface (30). Phagocytosis of viruses and bacteria is a major component of the non-specific immune response, and plays a vital role in preventing infection (29). A study on rats has shown that cold exposure to ambient temperatures of 4°C causes a decrease in phagocytic activity of macrophages and, in the same study, *in vitro* experiments showed that exposure of macrophages to a temperature of 24°C for 1 h also caused a decrease in phagocytic activity (31). The authors concluded that the results of the study "could contribute to understanding the predisposition to infections during exposure to cold". In these animal experiments the macrophages were sampled from the peritoneal cavity and although the average decrease in body temperature observed during cold exposure was only 1.5°C, exposure to this degree of body cooling was sufficient to alter phagocytic activity. *In vitro* exposure of peritoneal macrophages to temperatures of 4, 10, 24 and 37°C for 1 h showed a close inverse relationship between incubation temperature and the number of cells capable of phagocytosis (31).

The *in vitro* exposure of macrophages to a temperature of 24°C for 1 h is comparable to the degree of cooling that may be experienced by nasal polymorphonuclear phagocytes in cold weather. These studies indicate that the local immune response in the nose may be subject to seasonal changes due to seasonal changes in temperature.

#### ACUTE VERSUS CHRONIC EXPOSURE TO COLD AIR

The seasonality of URTI is related to long-term changes in the incidence of URTI measured on a monthly basis, but there is also a long-standing folkloric belief that rapid changes in air temperature associated with a short period of very cold weather are associated with a sudden epidemic of URTI. This belief is so widespread and has persisted for so long that it is difficult to dismiss the idea as having no credibility.

The occurrence of an epidemic of URTI immediately following a spell of cold weather may be explained by the conversion of many asymptomatic subclinical infections in the population into symptomatic clinical infections.

As respiratory viruses spread throughout the community during the winter there are likely to be many

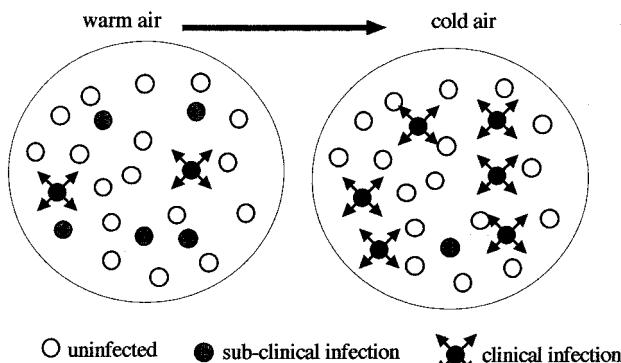


Fig. 4. Model to illustrate the effects of exposure to cold air associated with seasonal changes in air temperature and spells of cold weather in the winter period on the incidence of acute URTI.

subclinical infections. This is generally accepted as the "iceberg concept" of infection, with subclinical infections often greatly outnumbering clinical infections (32). Even in viral challenge studies in the laboratory, around one-third of those challenged with the corona virus develop subclinical, asymptomatic infections (33).

It is possible that in subjects who are harbouring a subclinical infection, exposure to cold air will lower nasal respiratory defences as discussed above, so that the infection is converted from a subclinical to a clinical form. The self-diagnosis of a respiratory infection is based solely on the symptoms and, as far as the subject is concerned, exposure to cold weather has caused the infection.

Studies in The Netherlands involving  $\approx 7,000$  participants have clearly demonstrated that periods of cold weather can cause simultaneous epidemics of colds across a large geographical area (12). Van Loghem (12) states that "there appears to be a connection in time between the colds-epidemics in our country and that their joint occurrence runs hand in hand with falls in the temperature of the air".

A model to illustrate how a sudden decrease in air temperature associated with a spell of cold weather can influence the incidence and spread of common cold is illustrated in Fig. 4. The population is shown to be made up of three categories: the uninfected; those with subclinical infections; and those with clinical infections. Only the symptomatic, clinical infections are associated with significant spread of infection, as illustrated by the arrows. Respiratory infections are spread primarily in air-borne droplets of respiratory mucus by coughs and sneezes, and by fomites contaminated with respiratory mucus (17). Although it is theoretically possible for infection to be spread by someone with a subclinical infection, this is far less likely as the subject will not be suffer-

ing from the symptoms that facilitate spread of infection, i.e. runny nose, coughing and sneezing. Figure 4 illustrates how a rapid decrease in air temperature associated with a spell of cold weather may cause conversion of subclinical infections to clinical infections. In addition, the cold air exposure is also likely to increase the susceptibility of the uninfected population to infection by changes in nasal respiratory defence as described above.

It is not difficult to see from the model how the rapid onset of cold weather will initially cause an increase in the apparent infections by converting subclinical to clinical infections. This acute effect of cold weather would explain the simultaneous epidemics of colds across a large geographical area that cannot be explained by person-to-person spread of infection (12). Although immediately following a spell of cold weather there may not be an actual increase in the number of infected persons, there will be an increase in clinical infections, which will promote the spread of infection by coughing and sneezing, etc. Cold weather will also facilitate an epidemic of colds by increasing the susceptibility of the population to infection.

## SEASONALITY OF URTI IN TROPICAL CLIMATES

One argument commonly raised against the idea that cold weather is responsible for the seasonality of URTI is that URTI is still seasonal in warm tropical climates. There is only one study in the literature that has examined the incidence of URTI in a tropical climate in a scientific way (34) and that study concluded that colds in the tropics were milder and less prevalent than in colder northern climates, and that the seasonal incidence curves were the same as those of more northern, colder areas. The study was conducted on one of the Virgin Islands in the West Indies. Despite the relatively small seasonal change in temperature the authors found evidence that convinced them that the seasonal decrease in air temperature was responsible for the seasonal increase in URTI and they concluded that "There is strong evidence that environmental factors, particularly reduction in atmospheric temperature, have some influence upon the incidence of colds".

## FACTORS THAT RAISE NASAL AIRWAY TEMPERATURE

The seasonality of URTI is explained above on the basis that cooling the nasal airway causes an increased susceptibility to infection. The opposite argument will be used below, namely that warming the

nasal airway during fever and nasal congestion may help to resolve a current URTI.

#### Fever

The natural response to infection is an elevation of body temperature, i.e. fever. Fever as a response to infection is found in a wide range of animals: amphibia, reptiles, fish, insects, crustacea, annelids and molluscs (35). Cabanac (35) states that "The converging evidence that fever occurs across a broad spectrum of the zoological kingdom conveys an overwhelming impression that fever must be a beneficial physiological response to infection, rather than a pathological consequence". The main benefit of fever can be considered to be an increase in the activity of the immune response by the enhancement of phagocytosis, neutrophil migration, T-cell proliferation and  $O_2$ -radical production, and the increased synthesis of interferon (36). Fever will increase the temperature of the nasal airway, by two mechanisms: firstly, by increasing the temperature of the blood circulated to the nasal airway; and secondly, by increasing the temperature of the expired air and therefore increasing the degree of heat transfer to the airway during expiration.

The presence of fever as a mechanism of defence against infection supports the idea that cooling the nasal airway and body will compromise the local and systemic immune responses.

In the adult, common cold infection is only infrequently accompanied by fever (17). The absence of fever in this very common infection could be used as an argument against the benefits of fever in combating infection. However, one could view this problem in another way. If fever is beneficial in combating viral infection then, by a process of natural selection, those viruses that do not induce fever are likely to proliferate, whereas those that do induce fever will be less successful. The common cold viruses may owe some of their success to the fact that they induce only a local immune response without fever. This could also explain why viruses which do induce fever and a systemic immune response, e.g. influenza, are not as common as those which cause a mainly local immune response without fever, e.g. rhinoviruses.

#### Nasal congestion

In a study on volunteers challenged with corona virus it was found that the nasal temperature and body temperature were increased in those volunteers who were infected compared to volunteers who were uninfected after viral challenge (33).

It is of interest that the temperature sensitivity of the replicative cycle of a virus is an important ele-

ment in the virulence of a virus (33). Some of the respiratory viruses, such as the rhinoviruses, have been shown to replicate best at temperatures well below normal body temperature, i.e. 33°C, equivalent to the temperature of the nasal epithelium in healthy persons (37). It was only when the temperature of the cell culture medium was lowered from 37°C to 33°C that rhinoviruses could be successfully cultured (37). It is therefore reasonable to assume that an increase in the temperature of the nasal epithelium above that found in healthy persons is likely to inhibit viral replication.

Nasal congestion is commonly associated with acute upper respiratory tract viral infection (38), and unilateral nasal obstruction is common (39). The decrease in nasal airflow, together with nasal vasodilation, associated with inflammation will cause an increase in the temperature of the nasal epithelium. Nasal airflow in healthy persons is normally asymmetrical and exhibits spontaneous and reciprocal changes termed the "nasal cycle" (40). The amplitude of the nasal cycle is increased with acute URTI so that one side of the nose is often completely obstructed whilst the other side is patent (39). Periodic unilateral nasal obstruction allows periodic increases in the temperature of the nasal epithelium. The so-called "nasal cycle" of obstruction may be part of the respiratory defence as it causes the nasal epithelium to be warmed to body temperature for several hours, without causing bilateral, complete nasal obstruction.

#### GENERAL DISCUSSION AND CONCLUSIONS

Body temperature is normally maintained within a range narrower than 1°C despite marked changes in air temperature. Extra clothing and bedding provide good insulation against the effects of seasonal changes in air temperature on body temperature, and any tendency for body temperature to fall below normal is resisted by various temperature-regulating mechanisms. However, the nasal airway has no such insulation or defence against cooling on exposure to cold air. Heat loss from the upper airway is obligatory as the cold inspired air is raised to body temperature. Some heat can be regained from the expired air but around two-thirds of the heat transferred to the inspired air is lost on expiration (19).

This review proposes a new hypothesis, namely that seasonal exposure to cold air causes an increase in the incidence of URTI due to cooling of the nasal airway. There is no doubt that the nasal airway is subject to seasonal cooling, but it is difficult to determine experimentally if the degree of nasal cool-

ing is sufficient to compromise nasal respiratory defence against infection. A case is made above to suggest that cooling of the nasal airway may compromise nasal respiratory defence against infection, and that by inference this will cause an increased susceptibility to URTI.

The seasonal increase in URTI in the winter months of the year does not preclude occasional epidemics of URTI during the summer. If a new and virulent virus is introduced into a susceptible population then infection will spread rapidly no matter what the season. If a new strain of influenza or another URTI virus is introduced into a population in the summer months it is likely to result in an epidemic of URTI. However, if viruses responsible for URTI are circulating throughout the year in a population then seasonal factors such as air temperature become more important in determining the incidence of URTI.

If nasal airway cooling is a major factor in the seasonality of URTI, is there anything that can be done to prevent or limit the effects of cold air? This is particularly important in the elderly and others at risk from serious and even life-threatening complications associated with URTI. In one of the first reports in the UK (1874) to discuss the causes of excess winter mortality it was proposed that seasonal mortality could be controlled: "But it must not therefore be assumed that the mortality (caused by this cold spell) is beyond control. The cold is most effectively combated by exercise, which excites the heating energy of the system, and warmth is sustained by nutritious food, by artificial heat, by warm woollen or fur clothing and by the respirator which returns heat exhaled by respiration! The aged poor in this cold season of pressure require all these helps and have claim not only upon their kindred but upon their wealthier Christian brethren." [Registrar General's annual report 1874; quoted by Curwen (9)].

Heating, clothing and food are obvious ways to promote winter health but it is surprising that the idea of some form of respirator to conserve respiratory heat loss has not been developed. A simple face mask has been shown to reduce the incidence of asthma induced by cold air (41). Even a simple woollen scarf has been shown to halve the bronchoconstrictor response to inhaling cold air (42). Perhaps the simple precaution of wearing a scarf over the nose and mouth could provide similar protection against nasal airway cooling and susceptibility to URTI in the elderly when they are obliged to be exposed to cold air.

In conclusion, the present review puts forward a new hypothesis to explain the seasonal increase in URTI, based on the idea that seasonal cooling of the nasal airway compromises local respiratory defence.

## REFERENCES

1. Johnston F. Seasonality and human biology. In: Ulijaszek S, Strickland S, eds. Society for the study of human biology. Symposium 35: Seasonality and human ecology. Cambridge: Cambridge University Press, 1993: 5–16.
2. Collier L, Oxford J. Human virology. Oxford: Oxford University Press, 2000: 231–2.
3. Wells M. The seasonal patterns of measles and chick-enpox. *Am J Hyg* 1944; 40: 279–317.
4. Duncan CJ, Duncan SR, Scott S. The dynamics of measles epidemics. *Theor Popul Biol* 1997; 52: 155–63.
5. Holmes S. Mumps. In: Evans AS, Kaslow RA, eds. Viral infections of humans. Epidemiology and control. New York: Plenum, 1997: 531–50.
6. Smillie WG, Caldwell EL. A study of pneumonia in a rural area in southern Alabama. *J Exp Med* 1929; 50: 233–44.
7. Lieberman D, Lieberman D, Friger MD. Seasonal variation in hospital admissions for community-acquired pneumonia: a 5-year study. *J Infect* 1999; 39: 134–40.
8. Alderson M. Season and mortality. *Health trends* 1985; 17: 87–96.
9. Curwen M. Excess winter mortality in England and Wales with special reference to the effects of temperature and influenza. In: Charlton J, Murphy M, eds. The health of adult Britain 1841–1994. London: The Stationery Office, 1997: 205–16.
10. Stout R, Crawford V. Seasonal variations in fibrinogen concentrations among elderly people. *Lancet* 1991; 338: 9–13.
11. Collins K. Seasonal mortality in the elderly. In: Ulijaszek S, Strickland S, eds. Society for the study of human biology. Symposium 35: Seasonality and human ecology. Cambridge: Cambridge University Press, 1993: 135–48.
12. Van Loghem JJ. An epidemiological contribution to the knowledge of the respiratory system. *J Hyg* 1928; 28: 33–54.
13. Crowcroft N, Cutts F, Zambon M. Respiratory syncytial virus: an underestimated cause of respiratory infection, with prospects for a vaccine. *Commun Dis Publ Health* 1999; 2: 234–41.
14. Mackenzie M. Diseases of the throat and nose, vol. 2. London: J. & A. Churchill, 1884: 1–573.
15. Hill L, Clemen M. Common colds, causes and preventive measures. London: William Heinemann, 1929: 126.
16. Andrewes C. The common cold. New York: Norton, 1965: 187.
17. Johnston S, Holgate S. Epidemiology of viral respiratory infections. In: Myint S, Taylor-Robinson D, eds. Viral and other infections of the human respiratory tract. London: Chapman & Hall, 1996: 1–38.
18. Lacy R. Climate and building in Britain. London: HMSO, 1977: 3.
19. Cole P. Modification of inspired air. In: Proctor DF, Andersen I, eds. The nose. Upper airways physiology and the atmospheric environment. Elsevier: Amsterdam, 1982: 351–76.
20. McFadden E, Pichurko B, Bowman H, et al. Thermal mapping of the airways in humans. *J Appl Physiol* 1985; 58: 564–70.
21. Webb P. Respiratory heat loss in cold. *J Appl Physiol* 1951; 4: 378–82.

22. Cole P. Respiratory mucosal vascular responses, air conditioning and thermo-regulation. *J Laryngol Otol* 1954; 68: 613–22.
23. Proctor DF. The mucociliary system. In: Proctor DF, Andersen I, eds. *The nose. Upper airways physiology and the atmospheric environment*. Elsevier: Amsterdam, 1982: 245–78.
24. Bang F. Mucociliary function as protective mechanism in upper respiratory tract. *Bacteriol Rev* 1961; 25: 228–36.
25. Baetjer A. Effect of ambient temperature and vapor pressure on cilia-mucus clearance rate. *J Appl Physiol* 1967; 23: 498–504.
26. Eliasson R, Mossberg B, Camner P, Afzelius BA. The immotile cilia syndrome: a congenital ciliary abnormality as an etiologic factor in chronic airway infections and male sterility. *N Engl J Med* 1977; 297: 1–6.
27. Proetz AW. *Essays on the applied physiology of the nose*, 2nd edn. St. Louis, MO: Annals Publishing Co, 1953: 284.
28. Diesel D, Lebel J, Tucker A. Pulmonary particle deposition and airway mucociliary clearance in cold-exposed calves. *Am J Vet Res* 1991; 52: 1665–71.
29. Roit I. *Essential immunology*. Oxford: Blackwell Scientific Publications, 1991.
30. Mims C, Nash A, Stephen J. *Mims' pathogenesis of infectious disease*, 5th edn. San Diego, CA: Academic Press, 2001.
31. Salman H, Bergman M, Bessler H, Alexandrova S, Beilin B, Djaldetti M. Hypothermia affects the phagocytic activity of rat peritoneal macrophages. *Acta Physiol Scand* 2000; 168: 431–6.
32. Kaslow RA, Evans AS. Epidemiologic concepts and methods. In: Evans AS, Kaslow RA, eds. *Viral infections of humans. Epidemiology and control*. New York: Plenum, 1997: 26.
33. Bende M, Barrow I, Heptonstall J, et al. Changes in human nasal mucosa during experimental coronavirus common colds. *Acta Otolaryngol (Stockh)* 1989; 107: 262–9.
34. Milam DF, Smillie WG. A bacteriological study of "colds" on an isolated tropical island (St John, United States Virgin Islands, West Indies). *J Exp Med* 1931; 53: 733–52.
35. Cabanac M. Phylogeny of fever. In: Bligh J, Voigt K, eds. *Thermoreception and temperature regulation*. Berlin: Springer-Verlag, 1990: 284–96.
36. Zeisberg E. From humoral fever to neuroimmunological control of fever. *J Therm Biol* 1999; 24: 287–326.
37. Couch RB. Rhinoviruses. In: Fields BN, Knipe DM, eds. *Fields' virology*. New York: Raven Press, 1990: 607–29.
38. Tyrrell DA, Cohen S, Schlarb JE. Signs and symptoms in common colds. *Epidemiology Infect* 1993; 111: 143–56.
39. Eccles R, Reilly M, Eccles KSJ. Changes in the amplitude of the nasal cycle associated with symptoms of acute upper respiratory tract infection. *Acta Otolaryngol (Stockh)* 1996; 116: 77–81.
40. Eccles R. Nasal airways. In: Busse WW, Holgate ST, eds. *Asthma and rhinitis*. Oxford: Blackwell Science, 2000: 157–63.
41. Millqvist E, Bake B, Bengtsson U, Lowhagen O. A breathing filter exchanging heat and moisture prevents asthma induced by cold-air. *Allergy* 1995; 50: 225–8.
42. Millqvist E, Bake B, Bengtsson U, Lowhagen O. Prevention of asthma induced by cold-air by cellulose-fabric face mask. *Allergy* 1995; 50: 221–4.

## Address for correspondence:

R. Eccles  
Common Cold Centre  
Cardiff School of Biosciences  
Cardiff University  
Cardiff CF10 3US  
UK  
Tel.: + 44 29 2087 4099  
Fax: + 44 29 2087 4093  
E-mail: eccles@cardiff.ac.uk