The Common Cold

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Abstract
One of the prize-winning essays for the Lewis Cameron Undergraduate Prize 1962.

The common cold is ubiquitous. It affects all races and occurs in all climates. It is not a killing disease, but figures suggest that colds cause a loss of several million man working hours each year. One estimate put the figure at forty million,¹ another at eighty million: in either case the figure is large. Lindwell and Williams report in an investigation carried out on four groups of office workers, three in London and one in Newcastle, that 10.3% of all colds lead to an absence from work, on an average, of 2.6 days duration. It has been suggested that the common cold should be treated as a quarantable disease but it is obvious that if everybody spent an extra of 2.6 days, or longer, away from work twice a year the economic results would be devastating.

¹
THE COMMON COLD

by N. Wright, B.Sc.

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“A family unit is composed not only of children but also of men, women, an occasional animal and the common cold” (Ogden Nash).

The common cold is ubiquitous. It affects all races and occurs in all climates. It is not a killing disease, but figures suggest that colds cause a loss of several million man working hours each year. One estimate put the figure at forty million, another at eighty million: in either case the figure is large. Lindwell and Williams report in an investigation carried out on four groups of office workers, three in London and one in Newcastle, that 10.3% of all colds lead to an absence from work, on an average, of 2.6 days duration. It has been suggested that the common cold should be treated as a quarantable disease but it is obvious that if everybody spent an extra of 2.6 days, or longer, away from work twice a year the economic results would be devastating.

HISTORY

Many suggestions have been made as to the aetiology of the disease. In particular various bacteria such as H. Influenzae, and Strep. haemolyticus have been suggested. But it was not until Kruse who had been sceptical of the bacterial hypothesis following his failure to isolate any such organisms from the initial nasal discharge of the common cold, showed that the infecting agent was filter passing and therefore a virus. Efforts have been made to cultivate the virus but until recently practically all these failed.

DEFINITION OF THE COMMON COLD

In popular parlance the term “common cold” refers to any minor infection of the respiratory tract. Bacteriologists and virologists have found it difficult to be any more precise, and just where to draw the line between a severe cold and a mild attack of influenza is not very clear. In fact it is well known that a mild attack of influenza A virus can give a clinical picture very similar to that of the common cold.

The common cold is now defined according to the clinical picture of what is thought to be its commonest form. The clinical course lasts eight or nine days and has been carefully defined by Rodens. The first phase, or prodromal phase, starts within twenty four hours, usually around eighteen hours of inoculation with infected nasal droppings. A slight soreness of the throat together with a sense of dryness develops; thirty-six hours after inoculation there is an increase in nasal discharge and a feeling of malaise. Slight nasal obstruction and a slight cough becomes apparent but usually the patient remains afebrile though a number get headaches. The second phase usually starts three or four days after inoculation with secondary bacterial invasion, probably from the saprophytic naso-pharyngeal flora, leading to a greater sensation of discomfort, a mucopurulent discharge and obstruction of the passages. These latter changes take a variable time to clear up but if the prodromal symptoms occur alone the condition lasts eight or nine days.

Pathologically the condition is characterised by thickened oedematous nasal mucosa. The mucosa is red or grey depending on the degree of hyperaemia, and is covered by a thin watery discharge. The nasal cavities are narrowed and the turbinates enlarged. Histologically there is extreme oedema of the subepithelial connective tissue and sparse acute inflammatory cell infiltration. Secondary bacterial invasion leads to mucopurulent discharge, hyperplasia of the mucous secreting cells, and in severe infection ulceration of the ciliated cells occurs.
OCCURRENCE AND CULTIVATION

The common cold affects all races and occurs in all climates. Early research was directed towards finding suitable laboratory animals that could be infected. Docherty reported that chimpanzees could be infected with the common cold virus. He also showed that chimpanzees could be infected with bacteria free nasal washings from people suffering from mild respiratory symptoms. However this was not a step forward as chimpanzees are particularly expensive and difficult animals to deal with. Since then other animals such as rabbits, guinea pigs, rats, mice, cotton rats, voles, grey squirrels etc. have been tried with inoculations given intramuscularly, intranasally and intravenously. All these failed.

Efforts, especially after the progress made by Embers next turned to cultivation in tissue cultures and we will now consider each virus for which claims have been made as a causative organism of the common cold.

ECHO 28

Two viruses were isolated from the nasal secretions of children aged between five and fifteen, student nurses and medical students suffering from minor respiratory conditions. These viruses, which were provisionally called J.H. and 2060, were cultivated in monkey kidney tissue cells maintained in Parkers mixture 199 with 2% horse serum added. The cultures were maintained at 37°C. Cytopathic changes, which consisted of enlargement, rounding and pyknotic changes of the nuclei together with loosening of a few cells from the glass container, were observed in the tissue culture cells. These viruses are similar in their antigenic constitution and general behaviour but are distinguishable. Further tests, in view of their possible relationship to the common cold, were carried out. The virus was inoculated into 58 volunteers. Eleven became infected as judged by the recovery of the virus from nasal washings and six colds occurred, four in volunteers infected with J.H. virus and two in volunteers who failed to give a culturable virus. Attempts to isolate a similar entity in England have failed but serological evidence suggests that it may occur, though uncommonly, in this country. More recently the J.H. virus has been included in the ECHO group as it shows their characteristics e.g. ether resistant, complement fixing antigens and approximately 25 m\textmu in size.

COE VIRUS

The Coe virus was originally described by Lennett and identified with an organism isolated by Pereira. It was found to be resistant to 20% ether but not culturable on monkey tissue cells, it could be grown on Hela cells which showed cytopathic changes. It was finally placed in the Coxsackie group number 28.

Of 11 volunteers inoculated with the virus all 11 gave common cold symptoms though fever occurred more often than in the typical infection. Immunological tests do not show it to be very common in Britain.

RESPIRATORY SYNCITIAL VIRUS

This virus was originally isolated by Morris from a group of chimpanzees suffering from coryza. At the same time it was noticed that a person dealing with the animals, suffered from a minor respiratory complaint. Later it was shown that this virus, which could be cultivated on monkey kidney cells could infect man. Sixteen per cent of a population of infants suffering from mild respiratory complaints and 32 per cent suffering from lower respiratory complaints such as bronchiolitis were infected with the R.S. virus. The condition that this virus gives rise to is more severe than the normal "common cold".

ECHO 11

A virus was isolated by Phillips and Wessler from a person suffering from a mild respiratory complaint. It has been shown to grow on monkey kidney tissue cells, to appear in faeces of infected persons and to be approximately 27 m\textmu in size. It is, therefore, included in the ECHO sub group of enteroviruses.

Experiments at Salisbury have shown that this virus gives rise to atypical common colds accompanied by abdominal symptoms.

ECHO 20

Rosen et al. reported the isolation and cultivation on monkey tissue cells of a virus obtained from children living in a residential home in U.S.A. The virus was originally called junior village virus but, fortunately, it was designated to the ECHO group after its isolation from faeces and the cytopathic changes in the tissue culture cells as well as other properties were observed and renamed ECHO 20.

Again the Salisbury Common Cold research unit found that it gave rise to atypical symp-
toms such as aching limbs and fever when experimentally inoculated into volunteers\textsuperscript{16}.

\textbf{PARA INFLUENZA 1 AND 3}

This virus was first isolated by Chanock\textsuperscript{18} and was grown on monkey kidney cells. Its presence could be detected by cytopathic changes and also agglutination of guinea pig erythrocytes. These viruses are serologically distinct, and larger than influenza viruses. Similar organisms have been found in Britain, France and Denmark and they cause typical common colds. However it was found that only 54 out of 1738 infants suffering from the common cold were infected with these organisms and hence it is a relatively uncommon causative agent\textsuperscript{19}.

\textbf{RHINO VIRUSES}

One of the original aims of the Common Cold Research Unit at Salisbury was to find some means of culturing the causative virus other than in man or the chimpanzee. We have seen that efforts to infect laboratory animals were unsuccessful so tissue cultures were tried. In 1949 it was shown that the virus remained in human embryonic lung tissue cultures but propagation was not demonstrated\textsuperscript{20}. In 1953 successful cultivation using this type of culture cells seemed to have been attained\textsuperscript{21}. The tenth subculture showed infectivity. Unfortunately these results have never been reproduced even though variations in the tissue culture technique have been tried, and what the transmitted agent was still remains a mystery.

While varying the tissue culture technique it became apparent that transmission probably took place through one subculture if incubation took place at 33°C using human embryonic kidney cells rather than embryonic lung. Immediately a search was made for a means whereby an infected tissue culture could be recognised without using human volunteers\textsuperscript{22}. No cytological abnormalities were observed but it was noticed that cells supposedly infected with common cold virus could not support the growth of parainfluenza 1 virus. The presence of this virus could be tested for by haemagglutination. The agent causing inhibition was, itself, inhibited by heating to 56°C and by a pH2, thus ruling out the activity of interferon. This inhibition of the challenge virus was used to test the sensitivity of cultures to the common cold virus. Finally optimum conditions for growth were found to be incubation at 33°C in 199 medium enriched with glucose and bovine plasma albumin.

Then one of those “fortunate” disasters occurred. A new batch of medium 199 was found to be toxic for the cultures and, at first, a repeat of the 1953 set back seemed imminent. In desperation various different batches of medium 199 were obtained from different centres. It was noticed that the cells grown in one of the new batches of medium showed definite cytopathic effects after common cold inoculation. An analysis it was shown that the medium contained less sodium bicarbonate than usual (.05% instead of .16%).

Following these successes it was possible to determine some of the properties of the virus. It was not destroyed by 20% ether but is by heating to 56°C for thirty minutes, and by a pH2. The size of the virus was found to be approximately 40 m\textsuperscript{u} and was not neutralised by Coe or ECHO 28 antisera. It was soon found that the cultural strains could be subdivided into two groups: those that would grow on human embryonic kidney culture cells alone (H strains) and those that would grow on monkey kidney cells as well (M strains)\textsuperscript{23}. Preliminary serological studies have already differentiated six different strains.

These viruses present a problem as far as classification is concerned. In that they are small and ether resistant they resemble the entero-viruses, but they have not been cultivated from faeces and their cultivating characteristics are atypical. For the time being they have been assigned to a new group: the rhino-viruses\textsuperscript{24}.

From studies made on viruses obtained from nasal swabs throughout the country it has been estimated that the new rhino-viruses are responsible for between 25 and 50% of common colds in this country. Studies in Chicago give a rather lower figure (16%)\textsuperscript{26}.

\textbf{CORYZAVIRUS}

Just lately an organism has been isolated from 15% of a population of 110 cases of mild respiratory infection in both adults and children. This, together with a rise in antibodies during convalescence suggests an aetiological role. It has been cultivated on foetal lung tissue but not monkey kidney cells and gives rise to cytopathic changes. Serologically it is distinct from at least 2 rhino-viruses, ECHO 11 and 28, the Coe and Respiratory syncitial viruses. It is ether resistant, contains R.N.A. and has been estimated to be 17 - 18 m\textsuperscript{u} in size\textsuperscript{27}. Its importance as an aetiological agent of the common cold is not yet certain.
FACTORS PREDISPONING TO INFECTION

It is an everyday assumption that cold weather, the winter, and damp conditions predispose to infection. Experiments have shown that one means of spread of the common cold is contact between the sufferer and a person of low resistance though the rate of cross-infection is low. Jackson puts the figure at 10% \(^{28}\). Heusman\(^{19}\) suggests that infection becomes higher with the number of people infected in the household. Children seem to be considerably more effective transmitters of infection than adults.

Experimental colds are most easily produced by intranasal inoculation. Inoculation on the conjunctiva produces no conjunctivitis and similarly no cold was produced by inoculation on the throat. In a number of experiments it has been noticed that in a few cases the virus exist in volunteers without clinical symptoms appearing. Certain epidemiological findings support the hypothesis of carriers but their importance has not been carefully assessed.

Efforts were made, under laboratory conditions to increase the proportion inoculated with live virus strains to develop clinical symptoms. Nasal washings were at their greatest infectivity if they were taken 36 hours after inoculation. Chilling the volunteer by giving a hot bath and then making him stand in a draughty corridor did not increase the proportion of clinical colds. Also the workers at Salisbury did not find that either smoking or tonsilectomy increased the incidence of colds \(^{30}\). On the other hand Brown\(^{31}\) found the opposite.

People with a history of allergy appear to be more susceptible to colds than the normal. Similarly women in the third week of their period\(^{32}\) and also emotionally disturbed people\(^{33}\) seem to be more susceptible. It has been suggested that the common factor in all these conditions is that the nasal mucosa is more congested than in the normal person and this is an aid to infection. Hope-Simpson\(^{34}\) reported that in studies made on 350 people in Cirencester he was able to correlate the number of colds with the difference between the indoor and outdoor humidity. This suggests that the change in humidity when passing from indoors to outdoors gives rise to circulatory changes in the nasal epithelium.

Apparently the cold virus is very susceptible to drying and this, probably, is the most effective way of stopping spread.

IMMUNITY

A few people appear to be completely immune to colds. The reason for this is uncertain but it is known that the conditions in the nose varies from person to person. Perhaps these people have an unfavourable nasal environment for invasion by cold viruses.

Initially it was thought that immunity to colds following infection fell quickly. However when it became possible to isolate single strains, Jackson and Dowling\(^{35}\) were able to show that immunity to that particular strain lasted over a year. A neutralising factor in the gamma globulin fraction was found and the level of this factor was found to correlate significantly with the degree of immunity.

EPIDEMIOLOGY

A number of small isolated communities have been studied. For example in Longyear city Spitzbergen the distribution of colds throughout the year was studied. Each year an epidemic of colds starts on the 25th May rising to a peak by the 31st and then gradually tailing off. The start coincides with the arrival of the supply boat\(^{36}\). Heirbecken reports that when isolated communities mix an epidemic of colds occur\(^{37}\). These findings suggest that a greater degree of immunity is acquired by the population and it is only when it is confronted with a new strain that epidemics occur. J. J. Van Loghem\(^{38}\) collected records in Holland and then analysed them for seven different regions. In each region the separate curves of morbidity were similar in shape and time. These findings certainly do not resemble the normal epidemic or endemic picture and suggests that other factors come into play in large communities.

PROPHYLAXIS

Numerous efforts of a very variable nature have been tried to prevent common cold infection. For example treatment with ascorbic acid has been suggested but evidence of improvement is inconclusive. Another suggestion has been the use of antihistamines\(^{39}\). This treatment probably arose from confusion between hay fever and a cold.

Vaccines have been prepared from the cultured bacterial flora of the volunteers nose. This has apparently given quite good results\(^{40}\). Another approach to the problem was the eradication of the unpleasant effects of secondary infection by antibiotics. However it is now
considered malpractice to give antibiotics for the prevention of such a minor condition as the common cold.

In neither of these two attempts was there any attempt to get at the root cause of the condition. Attempts, in particular by Price, to produce an antiviral vaccine were made, but as would be expected from the multiplicity of causative agents this attempt failed.

It has not yet been possible to produce interferon in quantity so it is not known whether this substance would be effective in the control of the common cold.

SUMMARY

We have seen that the common cold causes great economic loss to the country. Some, though not all, of the causative viruses have been isolated and cultured. In particular the rhino and Coe viruses have been shown to cause typical common colds. ECHO 28 and parainfluenza 1 and 3 have been shown to be uncommon aetiological agents and ECHO 20, 11 and R.S. virus cause atypical colds. Immunity develops but the multiplicity of infecting agents precludes the possibility of developing a vaccine. Two epidemiological patterns are found, in isolated communities the typical picture of an organism entering a community of low resistance, in large communities the pattern of incidence does not resemble that of an infective agent and quite what determines the incidence is unknown. No satisfactory prophylactic measures have yet been found though autogenous vaccines against secondary bacterial invasion gives protection against these secondary symptoms. It is hoped that an antiviral substance may provide the answer.

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READERS' VIEWS

Before making the changes in this journal, we were able to obtain the views of many members, fellows, and others. Most people we talked to shared our opinion that the journal could be improved. We welcome readers' letters, to find if there is a general opinion that such an improvement has indeed taken place.