CRITICAL REVIEW

ACUTE CATARRHAL RHINITIS

A review with especial reference to the importance and causation of "the common cold"

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MANY irritants of the nasal mucosa, physical, chemical or bacterial, evoke a catarrhal inflammatory response, but the "common cold" is by far the commonest example. The ancient Greek physicians called it "coryza"; it is also described by Celsus, but an account of the common cold begins most conveniently at about the time of the origin of the virus theory, because few writings prior to 1914 are noteworthy.

The common cold is usually a mild illness and, therefore, few patients seek medical advice. It is little more than a nuisance to many people, and not a few continue to attempt their usual duties during its course, regardless of the infection they spread around them. Yet this mild, and apparently insignificant, illness has serious aspects. Its economic importance has been studied in America, and an early investigation was that of Honeij (1911), undertaken for the Boston Board of Commerce. A questionnaire was prepared, and the lay indifference to this disease is well indicated by the fact that of 15,000 cards despatched, 10,000 were never returned, and another 1,181 were returned without answers to the questions. There remained but 3,013 replies, a few others being incomplete, from which to prepare statistics. The investigation covered the period between December 1909 and June 1910, during which 1,633 of the 3,013 who replied had had colds, i.e. approximately 54 per cent., most of whom were between 30-40 years old. A smaller group of 568 persons, of known occupation, was also examined and this showed that those who worked in departmental stores were especially prone to colds. Colds were the cause of absence from work, on the average, for six days per patient during this six months; also, following a cold, there was probably an additional loss of three days work through loss of energy.

Reilly (1917) mentioned this investigation, but no further statistics were published until 1923, when the incidence of colds amongst some 6,700 employees of the Metropolitan Insurance Company of the U.S.A. was briefly described. Acute respiratory illness amongst this group, during the year ending July 1923, occurred in 420·7 per thousand employees; 2,824 persons had been

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absent on this account, on the average, for 2·2 days, representing a loss of 0·9 day per employee on the pay roll. There was a total loss of 6,233 days' work, on account of colds, bronchitis and tracheitis.

Blanton (1927) examined the records of 800 persons and found that the incidence of colds amongst them averaged 1·7 days annually. Since a cold usually lasted four days, the loss to the community, on the basis of this sample, was tremendous.

The health records, over a period of ten years, of persons employed by the Edison Company of Boston, U.S.A., were examined by Brundage (1928). Respiratory illness had been responsible for 54 per cent. of all absenteeism due to sickness. Furthermore, considering illness lasting one day or longer, the common cold was responsible for nearly three-fourths, 71 per cent. of respiratory disease, but not, as is sometimes quoted, of all diseases. The latter were the cause of absence, on the average, for only 6·92 days, whereas respiratory disease occasioned an average absence of 3·23 days. It was also shown that the common cold disabled four of every ten men for 3·4 days, and seven of every ten women for 3·1 days annually.

The economic loss caused by the common cold was estimated by Holmes, Piggott, Sawyer and Comstock (1936) as a loss of some 108,000,000 hours of work, which they valued at about 5,000,000 dollars. Ross Smith (1937) is justified in her comment that the effect of the common cold on industry is "staggering". This has been recognized at the present time by the British Government, and an official campaign against the common cold was launched in 1941.

Although the manifestations of the common cold are usually trivial, it must not be forgotten that this condition sometimes has serious effects. Extension of the inflammation to the sinuses of the nose and to the middle ear is by no means uncommon. Pneumonia and meningitis are not infrequently preceded by a cold, and it is possible that a predisposition to grave disease is thus brought about, if by nothing more than a lowering of bodily resistance. Colds also tend to exacerbate chronic disease in those who have asthma, rheumatic heart trouble, or diabetes. Dochez (1936) inclined to the view that colds, complicated by sinusitis, might be the origin of chronic arthritis, neuritis, and myositis. As Dochez then said, the common cold "may be the key-stone of a complex series of diseases".

The Ætiology of Acute Catarrhal Rhinitis.

There is general acceptance that the common cold is infectious, but the agent is still to be identified precisely. In 1914 Kruse, unable to accept the bacterial origin of colds, suggested that it was a virus infection. An assistant, at the time suffering from a cold

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provided nasal secretion, which was diluted, and filtered through a Berkefeld candle ; the filtrate was then introduced into the noses of twelve healthy men. Four of them contracted colds in from one to four days after inoculation. Kruse repeated his experiment on thirty-six students, 42 per cent. of whom contracted colds. The filtrates appeared to be sterile on culture. It is an unexplained fact that subsequent workers, including Dochez, Mills and Kneeland (1931), and Andrews and Oakley (1933) also obtained about 44 per cent. of positive results with primary filtrates.

Foster (1916 and 1917) confirmed Kruse's experiments and obtained positive results with nine of ten inoculations in one experiment and in all of eleven others in another. He cultured " a peculiar minute micro-organism " from his filtrates and, although he did not claim to have obtained conclusive proof, he believed that this organism " bears a definite relation to the true infective agent ".

Schmidt (1920) carried out 196 inoculations with filtered nasal secretion from sixteen patients and there resulted twenty-five colds (Schnupfer bzw. Grippe), an incidence of 12 per cent. Control inoculations with physiological saline, of which there were forty-three, were followed by eight or 19 per cent. of colds.

Branham and Hall (1921), closely reproducing Foster's methods, failed to obtain a virus on culture. They reported that "no bodies were found in the 'cultures' which could not be found also in those from normal persons, in controls in all simple mediums examined, and on blank slides ".

Olitsky and McCartney (1923) demonstrated a small Gram-negative anaerobic bacillus in Berkefeld filtrates of the nasal secretion from coryza patients. They failed to confirm the culture findings of Foster.

Robertson and Groves (1924) observed " coccoid bodies ", resembling those of Foster, in their cultures but concluded they were not pathogenic and doubted if they were organisms. They also made 100 inoculations with filtrates of nasal secretion derived from eleven patients ; 95 per cent. were negative, since no symptoms appeared in the volunteers by the end of twelve days after inoculation. The five positive results, which included two cases of laryngitis and one case each of bronchitis, coryza and influenza, might equally well have been accounted for by causes external to the experiment.

The virus theory received its principal support from the well-known experiments of Dochez and his colleagues. With Shibley and Mills, Dochez (1929) studied the nasal flora of healthy chimpanzees kept under carefully controlled conditions. These apes were then inoculated with the filtered nasal secretions from patients in the early stages of a common cold. Four of seven apes contracted colds,

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indistinguishable from the human lesion, about thirty-six hours after inoculation. The filtrates, however, yielded a Gram-negative, anaerobic bacillus, similar to that described by Olitsky and McCartney.

A change to Seitz filters was then made, and, with these, Dochez, Mills and Kneeland (1930-31 and 1931) obtained filtrates which were sterile on anaerobic as well as aerobic culture. Colds were produced in chimpanzees, but with primary filtrates alone; secondary filtrates yielded consistently negative results. Experiments were also carried out on human volunteers with an incidence of about 44 per cent. of positive results with primary filtrates. The next step was an attempt to culture the virus by the methods of the Maitlands (1928) and Li and Rivers (1930). In Dochez's hands the virus remained active for at least thirteen days, when kept at room temperature or on ice, under anaerobic conditions. It was claimed that in culture the virus was kept active up to the fifteenth sub-culture, by which time the virus had survived a matter of seventy-four days after its collection from the original sources. It would seem, moreover, that this sub-culture, representing a dilution of the primary filtrate by a matter of about one part in one or two quadrillion, contained none of the original virus. The pathogenicity of the respective sub-cultures varied but good results appear to have been obtained with the fifteenth. Two in this group of three volunteers contracted colds, which were particularly severe. These researches earned the *Lancet's* editorial tribute (1931) to "a brilliant piece of work". An important omission, however, which Hoyle (1932) was prompt to comment upon, was the absence of adequate control experiments.

Similar results with primary filtrates were obtained co-incidentally by Long and Doull (1930-31) and Long, Doull, Bourn and McComb (1931). Eleven of twenty volunteers, inoculated with filtered nasal secretion, from patients with colds, contracted colds in from 20-70 hours after inoculation.

Andrews and Oakley instituted a repetition of the experiments of Dochez, Mills and Kneeland in November 1931, by an appeal for volunteers as experimental subjects. The results, published in 1933, differed materially from those of Dochez. Ten primary filtrates were prepared, of which five were active, and produced colds in about 44 per cent. of the students inoculated. In all, there were fifteen positive results from thirty-six inoculations. Three of the more likely primary filtrates were then selected for culture and further inoculations were made with the secondary and subsequent filtrates. All of the twenty-four students who received the cultured material remained "in exasperatingly blooming health". When this was reported to Dochez, he made a personal visit to England and brought with him three strains, which were potent in America.

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Seven healthy students were inoculated by him with one of these strains, and six others received first sub-cultures of the other two. All these inoculations were negative. When Dochez returned home he found that the cultures kept in America had died out but, Dr. Andrews informed me, Dochez carried on with those which had undergone the double Atlantic crossing and believed that the virus had survived this. With regard to these investigations, Andrews (1941) said, " I must confess that I am wholly sceptical as to these results, being much impressed with the difficulty of deciding exactly when a person has or has not got a cold. So much depends on the subjective element and it is noteworthy that where this is eliminated, as in experiments on chimpanzees, Dochez got chiefly negative results."

When Hoyle criticized Dochez's work in 1932, he stressed the absence of any mention of, and presumably, therefore, any attempt to make, adequate control by way of tests with the nasal secretion from healthy persons. In 1941 Hoyle commented on the fact that with the passing of time adequate methods for the identification of a virus had become available. Yet the virus of the common cold remains unidentified, although that of influenza, discovered in 1933, is now well established. " A virus is a perfectly definite thing with measurable particulate size and determinable antigenic structure; it can be cultivated on egg membranes in which it produces recognizable anti-bodies, both neutralizing and complement fixing, in the serum. Men and animals can be vaccinated with it and vaccination can be shown to result in the appearance of serum anti-body " (Hoyle, 1941).

These doubts about the virus theory have renewed the study of the nasal flora in the search for a cause of the common cold. Hoyle's experiments of 1932 are an example. He showed that although no specific organism was associated with the onset of a cold, a sharp rise occurred in the incidence of B. Influenzae or pneumococci in the nose and throat. This immediately preceded, or was coincident with, the attack ; it seemed to him, therefore, that these organisms were responsible for some of the colds. Dochez and his colleagues, on the other hand, although noting an increase in the incidence of S. Hæmolyticus and B. Pfeifferi, coincident with the onset of colds in apes, ascribed this to the action of the virus which " plays a most important rôle in promoting respiratory infection ". Such a conflict of opinion is apparently general, and Topley and Wilson (1936), after weighing the evidence, concluded that the results " had failed to establish consistent significant changes in association with the onset of the common cold ".

The term " the common cold " is, perhaps, not a little responsible for difficulty in elucidating its ætiology, because it tends to

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the impression that this is a disease entity, which it is not. With Hoyle (1941), it may be said that there has never been "any reason to suppose that coryza is a specific disease, always due to the same agent; the symptoms are simply those of an inflamed naso-pharyngeal mucosa and have no specific features". It may prove, as he suggests, that "when the epidemiology of the pneumococcus is clearer, there will not be much left unexplained in the story of coryza". There is point, also, in the observation of Hilding (1930) that "the most striking fact brought out by these studies is that the predominating organism varies between years, epidemics and individuals. It is not constant, as would be expected in a disease entity. . . . A cold is simply the non-specific reaction on the part of the nasal mucous membrane, to any infection". At any given time one or more of the flora of the human naso-pharynx may be the cause, and the onset of a cold is furthered by one of more secondary factors, for example, abrupt chilling of the body. The evidence in favour of virus infection is distinctly unsatisfactory, and it seems unlikely that this theory will be proved.

The source of infection in colds may be the naso-pharynx of the patient or that of another person. This is widely accepted and the latter receives support from the observations of Winholt and Jordan (1923). The mothers of 500 infants who had colds were, themselves, twice as often subject to colds as the mothers of 500 infants who were well.

Contributory Factors in the Causation of Colds.

Exposure to cold has long been mooted as a cause of colds, and at one time these were deemed distinct from the infectious kind. The evidence now accumulated indicates that it is an important contributory factor. Two observations, on a large scale, are described by Schade (1919). One concerned 8,000 soldiers of whom 2,700 spent three days and nights in cold wet trenches at 0°-3° C., while the other 5,300 remained in barracks. The incidence of colds was about four times greater amongst those who went to the trenches than in those who remained under cover. On a second occasion, 4,500 soldiers were exposed to a sharp wind from −9° to −12° C.; during three days, the control group of 3,500 being in barracks. Again, colds were about four times more numerous amongst those who were exposed to the wind.

The effect of cold has also been studied experimentally by Mudd and Grant (1919), and Grant, Mudd and Goldman (1920). They prevailed upon volunteers to submit, while bare, to draughts caused by electric fans; additional discomfort included wet cold towels for the feet. During these experiments temperature changes in the nose, throat and blood were determined by an electrit thermophile. The blood temperature remained steady, but thac

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of the naso-pharynx fell by from 1° to 2° C. and in the nose there was a fall by as much as 6° C., accompanied by distinct ischæmia of the mucosa. Some of the volunteers subsequently complained of sore throats or colds. Parallel investigations of doubtful value on animals by Lipari (1889), Fischl (1897) and Lode ? , suggested that the chilling of animals rendered them unduly susceptible to infection.

Polar explorers are notoriously free from colds when in the Arctic or Antarctic regions, yet they have no peculiar resistance to colds on their return home. Nansen (1898) confirmed this. Particularly severe cold was experienced during " The Worst Journey in the World " to the Antarctic, and Cherry-Garrard (1937) stated that the usual range of temperature was from −10° to −30° F. in the hills ; on one occasion during this expedition −73° F. was recorded. He has much to say of frostbite and septic hands following injury, but nothing about colds ; presumably, therefore, there were none.

The members of the Observatory staff on Ben Nevis formed a similar group ; according to Gardner (1897), they remained free from colds while on duty, but contracted colds on their return to sea level. (Unfortunately it has not been possible to check this, in respect of recent years, since the Observatory is at present closed.) Gardner also mentioned that the inhabitants of the island of St. Kilda remained free from colds until they visited the mainland. They then tended to contract cold almost as soon as they reached the harbour.

Exposure alone, therefore, is unlikely to cause colds, and the explanation of the freedom from colds in these three instances is doubtless because the people concerned are far removed from sources of infection. Moreover, in respect of Polar explorers, and presumably those who worked on Ben Nevis, a careful selection was made beforehand, in order to include only persons of strong physique, and they were equipped with suitable clothing. As Garrard said, " these temperatures . . . are not very terrible to men who are fresh and whose clothing is new ". That they contracted colds on their return is understandable, for they were then no longer fresh, their clothing was worn and, they returned to sources of infection.

Abrupt change of temperature is much more important than persisting cold. When people are slow to adapt their clothing to the external temperature colds increase appreciably. It is this omission at the end of summer which leads to the early autumnal peak in the incidence of colds. Even on a relatively warm day it is easy to contract cold if, when resting while warm after physical exercise, addition to one's clothing is neglected. The Metropolitan Insurance Company's report showed that colds increased by eighteen a week when the temperature fell by 10° F.

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The colder seasons of the year are associated with an increase in the incidence of colds. There is a peak period in January to February, as shown both by Brundage and the Metropolitan Insurance Company's records. A second, though lesser peak in the early autumn was observed by Gover, Reed and Collins (1934). Differences in climate, however, did not appear important. Six American cities, differing appreciably in climate, were selected by Gover, Reed and Collins, who arranged for a group of students in each to record their colds. No appreciable difference between the six groups was observed. Decrease in atmospheric temperature in each city, on the other hand, was associated with a common increase in the incidence of colds. This investigation also showed that increase in atmospheric humidity predisposed to colds, although it was less important than decrease in atmospheric temperature.

The influence of ventilation was studied by Dutton (1916), who found a distinct increase in colds amongst school children when they worked in overheated rooms, and in which the air was stagnant. Room temperature should at all times be below 69° F. These observations were confirmed by Koirianski (1934).

It was suggested by Paton (1931 and 1933) that dietetic error, notably excess of carbohydrates, was responsible for an increase in catarrhal illness. Although he was careful not to claim proof, he succeeded in presenting a prima facie case, based upon the health records over the period 1904-1928, which included that of the 1914-18 war, of a girls' school in Scotland. Contrary to expectation the war period was one in which a distinct decrease occurred in the incidence of acute catarrhal illness. During the Spring term the incidence of 4·15 per cent. in 1904-14 fell to 0·6 per cent. in 1914-18, and rose to 10·5 per cent. in 1919-28, and this was reflected in the annual incidence, for which the corresponding figures were: 2·6, 0·8, and 7·25 per cent., with an especially high incidence of 12·8 per cent. in 1918. Searching for an explanation, Paton suggested that a possible factor was the severe food rationing, notably of sugar, during the war. He instanced clinical evidence in further support. Paton was well aware, however, that there were other possible factors, for example, the restriction upon travelling and thereby lessened opportunities for infection.

The possible relationship between nasal catarrh and the sexual apparatus was discussed by J. N. MacKenzie (1898). It was his experience that nasal trouble in patients was aggravated at the menstrual period or by sexual excess. He instanced the spontaneous cure of intractable nasal trouble following measures which rectified co-existent gynæcological disease. Many women are particularly sensitive to cold at the menstrual period, and doubtless this is a state of lowered bodily resistance during which they may more readily contract a cold.

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Personal idiosyncrasy is yet another contributory factor, for some people are distinctly prone to colds. Smith (1937) classes those who contract four or more colds each year as "susceptible persons", and urges that they should be controlled. Were this done, the incidence of epidemics and their extent would be appreciably reduced. Unfortunately, she does not go further and outline a scheme of control. Nor is this surprising, for Topley and Wilson (1936) have said that the common cold forms a major problem of preventative medicine. Employers might be urged to adopt measures, whereby those, who appear at work, while infectious, are fined, whereas those who wisely stay at home, if not awarded a bonus, at least suffer no loss of pay. But it is not imagined that the solution of the problem is quite so simple!

THE PATHOLOGY OF ACUTE CATARRHAL RHINITIS.

The naked eye appearances are familiar. Nasal obstruction commences soon after the onset, and is caused by hyperæmic, œdematous swelling of the mucous membrane of the nose. There is a short initial dry period when the interior of the nose and throat is sore, and then follows a rapidly increasing stream of nasal secretion, at first watery and irritant, and, later, it is turbid and more viscous. Reddening and excoriation of the alae nasi and of the upper lip are usual. The initial secretion is usually described as mucinous and, when the inflammatory reaction is established, the fluid is muco-purulent or purulent.

Microscopical evidence, on the other hand, is scanty for the obvious reasons that patients do not die of coryza and clinicians will not readily risk the "profuse and stubborn bleeding", observed by Hilding, in order to obtain biopsy material; nor is the technique easy.

Suchannek (1893) described the naked eye and histological appearances of two cases of nasal catarrh due to influenza and of two diphtheritic lesions. In the mildest form, acute rhinitis was characterized by pale rose coloured œdema of the mucosa; the œdema was not pronounced and was accompanied by slight secretion, at first mucinous and later muco-purulent. The principal histological changes related to the epithelium of the mucous secreting glands; there was some leucocytic infiltration of the submucosa.

Seifert (1894) described briefly the histological changes in biopsy material from a patient at about the second day of a cold. The cilia were missing but there was no mucous degeneration of the cells; the principal change was intense leucocytic infiltration of the submucosa.

Hilding's (1930) investigation is unique because he examined 100 scrapings and 25 biopsy specimens from patients with colds;

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the histological changes as from two hours to two weeks, were represented by this material.

The initial, and an early, change was œdema of the submucosa. Inflammatory reaction was established by the end of three days, when œdema was accompanied by cellular infiltration. These cells were polyblasts and scanty polymorphonuclear leucocytes. There were also degenerative changes in the epithelium. At the outset the epithelial cells were separated as if by the accumulation of fluid between them, and later the superficial and deeper cells were detached until none remained. In due course superficial and deep zones of necrosis were observed. Regeneration was advanced in ten days, and almost complete at the end of the fourteenth day.

These findings are difficult to correlate with the generally accepted changes of acute catarrhal inflammation, of which coryza affords a good example. It is difficult to exclude that the factor of operative trauma was responsible for the changes in Hilding's material; the technique was admittedly difficult. Some doubt is raised by the specimen taken at two hours after the onset of a cold for, in man, this interval must surely be no more than relative. The paper is generously illustrated, but some of the figures do not convince.

In view of the discrepancy between Hilding's findings, and the general belief, it is desirable that the matter be re-investigated. No opportunity has occurred to repeat his observations on man but, as an inadequate substitute, cavies were used. Six cavies were exposed to bromine vapour until a free flow of nasal and lachrymal secretion occurred. They were then killed, by air embolism, in from four hours to three days later. Coronal sections of the nose were then prepared. The object in view was to discover whether œdema and epithelial destruction were outstanding changes. The initial change was hyperæmia of the submucosal vessels, œdema being negligible. Some of the epithelium lost its cilia and a few of the superficial cells were detached, but even in the animals most severely effected, epithelial destruction was not a feature. Polymorphonuclear leucocytic reaction, which in the cavy is mainly eosinophilic, began by the end of twenty-four hours and was established at the second day. Excessive secretion of mucin, while not outstanding, was demonstrated. This phase is probably of short duration, and evidence of excessive storage of mucin granules in the cells seems likely to be seen only in from 12-24 hours after the onset of rhinitis.

Non-infective Acute Rhinitis.

Non-infective acute rhinitis is uncommon, probably because the noxious agents are well recognized and steps to avoid injury are taken by those who use them. Physical agents are represented by

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tobacco, wood and cement dust, which may act coincidentally by virtue of chemical properties. Some people suffer from nasal catarrh if exposed to fog, probably because of its dust content.

One of many chemical agents may be responsible, but these, apart from ammonia, which, in these days, is less commonly used for household cleansing purposes, are found, ordinarily, only in laboratories or factories. Those in contact with them are well aware of their dangers. Bromine, chlorine, iodine, formaldehyde, fuming nitric acid, osmic acid and mercury are examples. Potassium dichromate has special dangers, leading to septal perforation, and its use in industry is subject to supervision by the Home Office.

Arsenic and iodides, even in therapeutic doses, may provoke nasal catarrh. Dan McKenzie (1926) based an homœopathic cure for colds on this fact. The idea, however, was not new. Tanner (1869) said, " In coryza an immediate cure is said to result from the inhalation of iodine vapour, every three or four minutes, for an hour, each inhalation lasting a minute, and being accomplished by merely holding, in the warm hands, a bottle of the tincture under the nose." Stirnimann (1908) suggested the use of formaldehyde vapour as a remedy for colds ; it was his practice to pour a few drops of " lysoform " on his hands and inhale the vapour, four or five times, whenever he had a cold.

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