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# STUDIES UPON THE NASAL SECRETIONS. I. THE CELLULAR CONTENT OF THE NASAL SECRETIONS IN ACUTE DISEASE OF THE RESPIRATORY TRACT

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Although common colds are probably the most frequent ailments from which we suffer, very few studies have been made upon the changes that take place in the nasal mucous membranes during acute upper respiratory infections. In 1885 MacKenzie (1) first described the histological appearance of the nasal mucous membranes during acute coryza. He found an intense engorgement of the cavernous tissue which was especially well marked over the lower halves of the middle and posterior portions of the inferior turbinates with rupture of the vessels. Along the inner walls of the dilated spaces were congregations of lymphoid cells and in some of them collections of fibrinous exudate. A moderate cellular infiltration was present below the basement membrane.

Forty-five years after this report, Hilding (2) published his observations upon the histopathology of the nasal mucous membranes in "colds." He found that "the pathologic process is that of a mucous membrane inflammation showing rather marked tissue changes, including the loss of many of the surface cells and a proliferative reaction in the submucosa. The epithelium is regenerated and repaired by the growth and multiplication of the stellate cells normally found deep in the epithelium."

While studying the nasal secretions, Hilding noted that the cellular content changed rapidly. Early in colds the secretion was watery and contained few cells. Ciliated epithelial cells appeared during the first twenty-four hours and became more numerous by the second day. The deeper epithelial cells, polyblasts and polymorphonuclear cells appeared in the secretions on the second day and rapidly became numerous. Within a few days the polymorphonuclears made up most of the cellular content of the secretions.

Hilding did not believe that the cellular content of the secretions or the pathological picture in the nasal mucous membranes was related to any one causal agent in colds, but interpreted the observed changes as a response to any one of or a combination of etiological factors.

D. and R. Thomson (3) have briefly described nasal secretions from cases of acute watery catarrh. Their observations are of interest chiefly

because of their description of certain round bodies which they saw in the cytoplasm of squamous epithelial cells. Attention is called to the resemblances of these bodies to the guarnieri bodies found within the epithelial cells in vaccinia and variola.

During the past two years we have been studying the cellular content of the nasal secretions in the course of common colds in an attempt to determine the types of cellular response, the nature of the cells, and if possible, the underlying factors which govern the appearance of the various cellular constituents of the nasal secretions in acute upper respiratory tract disease. This communication describes our observations upon the types of cellular response found in the nasal secretions in disease of the upper respiratory tract.

#### MATERIAL AND METHODS

The subjects utilized in this study were medical students and laboratory workers in the Johns Hopkins University Medical School. A definite attempt was made to obtain the nasal secretions at the beginning and at frequent intervals during the course of the colds. The secretions were gained by having the subject blow his nose upon a clean piece of non-absorbent brown paper and from the nasal discharge preparations were made upon glass slides covered with dried neutral red and Janus green for "supra vital" studies. Permanent preparations were made by evenly smearing the discharge upon clean glass slides and permitting it to dry in the air. The secretions were also observed as to color, consistency and amount.

The "supra vital" preparations were examined immediately in a warm box at 37° C. and the percentage of the different types of cells was determined. The air dried smears were subsequently stained with thionin blue and were studied for the presence of bacteria and bacterial phagocytosis. Other air dried slide preparations were stained with either Wright's stain or Mallory's eosin-methylene blue stain and were studied for cell types and for the possible presence of intracellular inclusion bodies. No attempt was made to determine the total number of cells in the specimens of nasal secretions.

We have had the opportunity of examining 302 specimens of nasal secretions in the various stages of 98 colds. The majority of the examinations were made in the first week of the infection. We have been unable to obtain what we considered to be normal nasal secretions for control studies, so we have therefore used the nasal discharge from individuals suffering from acute hay fever to control our observations upon the secretions obtained from persons ill with "colds."

#### EXPERIMENTAL OBSERVATIONS

In the early stages of colds one commonly finds polymorphonuclear leukocytes, macrophages (monocytes and clasmatocytes), squamous and

columnar epithelial cells, eosinophilic leukocytes, lymphocytes and red blood corpuscles present in the nasal secretions. The cellular response (in the nasal discharge) during the first forty-eight hours of a cold may be of three types. In the first type the majority of the cells are macrophages and epithelial cells, in the second type polymorphonuclear leukocytes, and in the third eosinophilic leukocytes. Striking examples of these three types are not commonly encountered as most of the samples of early nasal secretions showed cellular contents which were gradations between the extremes. The three types of response together with the average are shown in Charts 1, 2, 3 and 4.

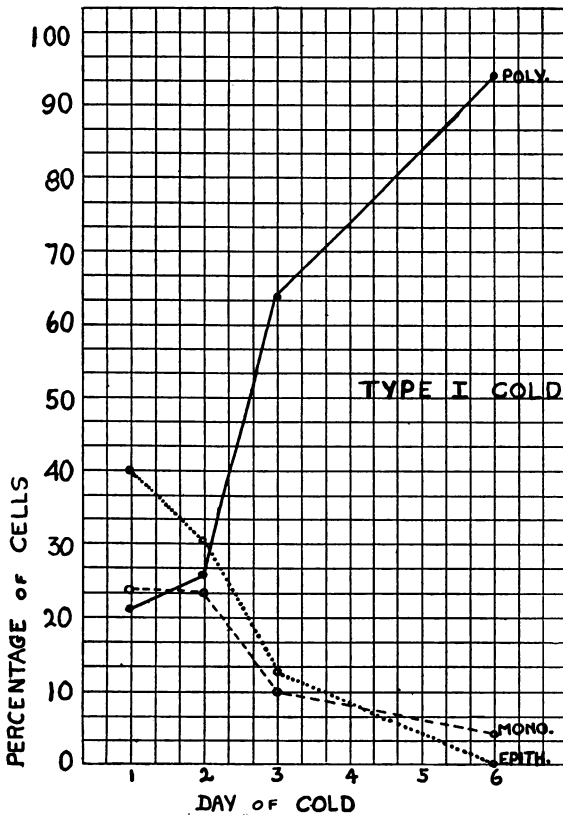


CHART I. A COMMON COLD SHOWING A PRIMARY MACROPHAGE-EPITHELIAL CELL RESPONSE IN THE NASAL SECRETIONS.

When the macrophage-epithelial cell type of response is present the secretions contain many macrophages and epithelial cells. The macrophages are easily distinguished in the "supra vital" preparations, but at times the classification of the epithelial cells is difficult because of the bizarre forms which are seen. It is common to find the upper half of the

cells pinched off and then one sees curious globular ciliated cells which resemble bursting grenades. Again one may observe elongated, rounded end, finely granular cells with no visible nuclear structure which may or may not contain vacuoles holding the neutral red and which may or may not have cilia. We think that these cells represent degenerated ciliated columnar epithelial cells. The amount of neutral red taken in by the columnar cells varies from none to 7 or 8 vacuoles filled with this

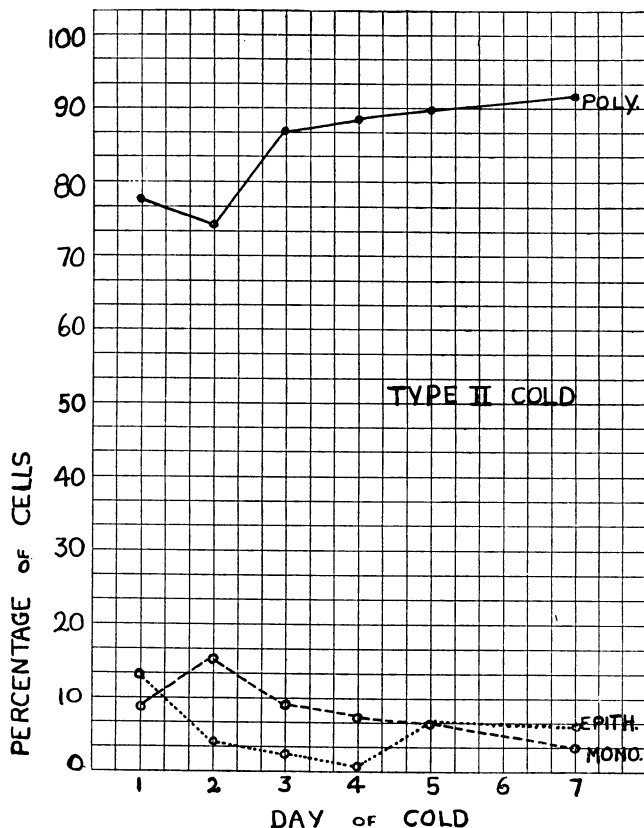


CHART II. A COMMON COLD SHOWING A PREDOMINANT POLYMPHONUCLEAR LEUKOCYTE RESPONSE IN THE NASAL SECRETIONS.

dye. The recognition of the squamous epithelial cells from the posterior rhinopharynx and vestibule offers no difficulties.

An evaluation of the viability of the ciliated columnar epithelial cells upon the basis of motility of the cilia and staining of the nucleus has been attempted without much success. In many preparations the cilia were highly motile, in others non-motile. We suspect that in most instances these cells are alive in the secretions, but that due to unavoid-

able crushing during the preparation of the supra vital slide the cilia are so injured that their lack of motility loses its value as a criterion of viability.

The macrophages generally appeared to be alive and always showed various amounts of phagocytosed material. We were unable to determine the exact mechanism which regulated the degree of phagocytosis, but we believe that it depended upon the amount of cellular debris present

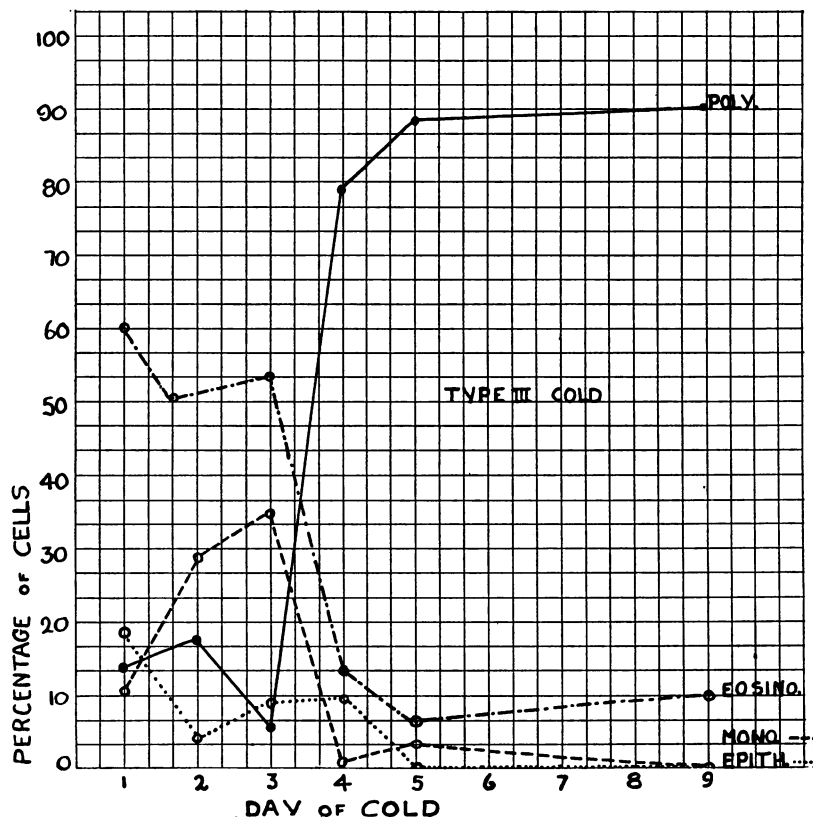


CHART III. A COMMON COLD SHOWING A PRIMARY EOSINOPHILE LEUKOCYTE RESPONSE IN THE NASAL SECRETIONS.

and not upon the bacterial content of the secretions. Generally, in the macrophage-epithelial cell type of response occasional lymphocytes and eosinophiles were present. Red blood cells were encountered in the majority of specimens but a grossly bloody specimen was rarely encountered.

This type of response seldom lasted more than forty-eight hours. By the beginning of the third day of the cold the polymorphonuclear leukocytes were abundant and by the fourth day their percentage out-

numbered that of all of the other types of cells. Twenty-three of the ninety-eight specimens of nasal secretions showed this type of response at the first examination.

In the second type of response the percentage of polymorphonuclear leukocytes was always elevated from the first and earliest possible examination. These cells remained predominant throughout the entire course of the cold. Thirty-three of the ninety-eight specimens of nasal

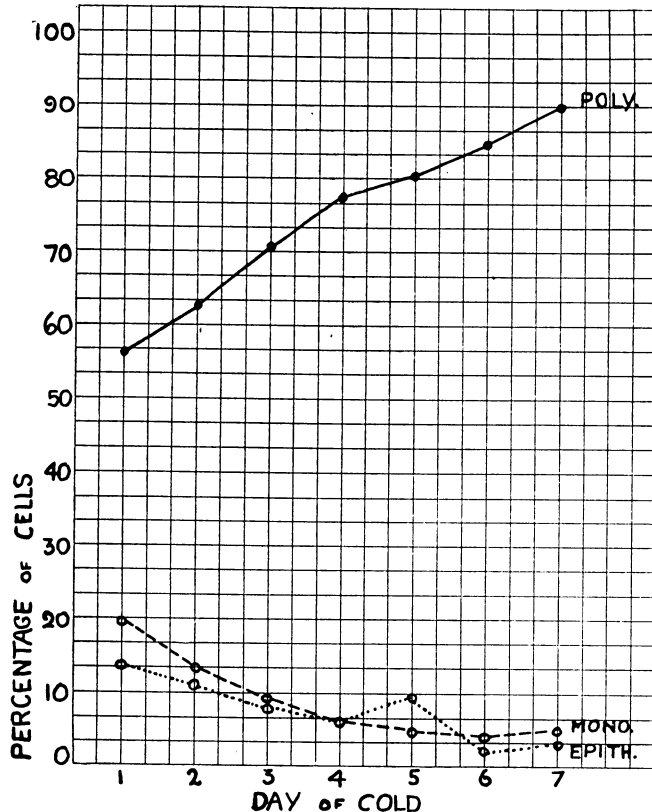


CHART IV. THE AVERAGE PREDOMINANT CELLULAR RESPONSE AS DETERMINED IN A STUDY OF THE NASAL SECRETIONS IN 98 COLDS.

secretions showed 70 per cent or more polymorphonuclear leukocytes at the first examination. Thirty-nine specimens fell in between these two types of response in that the percentage of polymorphonuclears ranged between 49 and 70 in the initial specimens.

There were three interesting examples of a variation from the general types of cellular responses seen in the nasal secretions in colds. This variation occurred in individuals who gave definite histories of having repeated attacks of pollen hay fever during the past years. In these

individuals there was a marked outpouring of eosinophilic leukocytes into the nasal secretions, which persisted throughout the early stages of the cold. The eosinophiles replaced the polymorphonuclear leukocytes to a large extent without disturbing the macrophage-epithelial cell formula. In each instance in which this was encountered the differential white blood cell count was well within normal limits.

It has long been known that in individuals who suffer from hay fever, the nasal submucosal tissues are heavily infiltrated with eosinophiles and that this infiltration persists during the intervals when the acute allergic process has abated. Hence it is not surprising that these individuals should react to an acute infection of the nasal mucous membranes with an eosinophilic response in their nasal secretions.

In our control group of individuals suffering from acute hay fever we invariably found a high percentage of eosinophile leukocytes in the nasal secretions. However, it was interesting to note that macrophages and epithelial cells were present in these secretions in a percentage that is commonly found in colds.

Many of the air dried smears of the nasal secretions were stained with eosin-methylene blue and the cells were searched for the presence of intranuclear inclusion bodies. In several instances homogeneous acidophilic bodies were seen in the cytoplasm of columnar epithelial cells in the secretions from early colds. These closely resembled inclusion bodies, but due to the lack of control studies upon normal epithelial cells, we feel that the assumption that these acidophilic bodies are inclusion bodies would be unwarranted at the present time.

#### DISCUSSION

It is our opinion that in general our findings confirm the observations of Hilding (2). Undoubtedly the first changes taking place in the nasal mucous membranes during a cold must be an intercellular edema with congestion and an infiltration of macrophages or polymorphonuclear leukocytes. The epithelial cells become swollen and soon detach themselves from the submucosa and are found free in the nasal secretions. The infiltrating macrophages and polymorphonuclear leukocytes either actively wander into the secretion or are passively swept out of the tissue spaces by the edema fluid.

Within forty-eight to seventy-two hours the polymorphonuclear cells become the predominant cell in the nasal secretion and the secretion tends to change from a watery type to a mucopurulent type of discharge, and remains so throughout the remainder of the infection until the stage of crusting is over and the nasal mucous membrane has regenerated. It is well known that a monocytic tissue response is characteristic in certain virus diseases and we feel that the outpouring of monocytes seen in the nasal secretions in early colds may represent a response to the filterable agent of "common colds."



We realize that it is dangerous to argue by analogy, but nevertheless, we would like to call attention to the similarity of the changes taking place in the nasal mucous membranes in colds, to those taking place in the skin during vaccinia. There is first, the stage of engorgement of the nasal mucous membranes which resembles the formation of the vaccine papule. Then comes the tissue edema and destruction of the nasal mucous membrane with an outpouring of fluid containing monocytes which corresponds to the formation of the vesicle filled with fluid in which the mononuclear elements predominate. In the third stage of the cold the secretions have a high polymorphonuclear leukocyte content as does the fluid in the pustule of vaccinia, and finally in both diseases the last stage is characterized by crusting. Here the analogy ends because in colds the mucous membrane is restored while in vaccinia a scar generally results.

#### CONCLUSIONS

There are two main types of cellular response found in the nasal secretions early in the course of colds. In the first type the macrophages and epithelial cells predominate and in the second the polymorphonuclear leukocytes predominate. Variations between these two types are commonly seen. By the third day of a cold the polymorphonuclear leukocytes become the chief cellular constituent of the nasal secretions. A third type of cellular response in colds in which eosinophiles predominate has been described. It is thought that these observations upon the cellular content of the nasal secretions in colds lend further evidence to the belief that a filterable agent is the cause of acute common colds.

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