

# Use of Nasal Cytology in Diagnosis of Sinonasal Disorders

*Marco Capelli*

## Abstract

Nasal cytology is an important diagnostic tool in nasal disorders, especially those regarding nasal mucosa. This technique allows clinicians to observe the morphology and the structure of nasal epithelium cells—such as ciliated, mucous-secreting, striated, and basal cells—and to detect the presence of degenerative or phlogistic phenomena in the respiratory epithelium. Moreover, it makes it easy to identify the presence of inflammatory cells, such as neutrophils, eosinophils, and mast cell. Over the past few years, nasal cytology allowed researchers to discover new clinical issues that were still unexplored: the nonallergic rhinitis with eosinophils, the nonallergic rhinitis with mast cells, the nonallergic rhinitis with neutrophils, and the nonallergic rhinitis with eosinophils and mast cells. Nasal cytology is easy to perform and barely invasive; therefore, it can easily be repeated. Since it makes it possible to evaluate the patient's response to a therapy, the technique is a very useful tool in follow-up checks of nasal disorders. We have reported in the following chapter our working experience, and we observed the results of cytological exams performed in our Center from 2013 to 2018. We therefore developed an easy and intuitive classification of sinonasal chronic inflammatory diseases.

**Keywords:** nasal cytology, rhinosinusitis, neutrophils, eosinophils, classification

## 1. Introduction

The nose is composed of two nasal cavities separated by an osteocartilaginous structure called nasal septum. The initial portion is called nasal vestibule, while the next part is called nasal cavity. The nasal cavity borders on the nasopharynx, from which it is separated by the choanae. In the most cranial portion of the nasal fossa, we find the olfactory fissure. This region is responsible for the perception of odorous stimuli. The nasal cavities are occupied by osseous structures with mucous lining called turbinates. These are divided as follows: the inferior turbinate that through its cavernous vascular tissue contributes to humidify and heat the inspired air, the middle turbinate that anatomically defines a sort of pre-sinus space, and at last the superior turbinate. In some cases we also recognize a fourth turbinate called supreme [1].

We observe four different nasal epithelia. A layered keratinized floor epithelium covers the region of the nasal vestibule, and an epithelium called transitional is located at the level of the valve. On the other hand, the nasal cavities are covered by a mucosa with pseudostratified ciliated epithelium (enriched with olfactory cells at the level of the olfactory fissure). The ciliated pseudostratified epithelium is composed of four types of cells: ciliated cells, muciparous cells, columnar cells, and basal cells, anchored by desmosomes and hemidesmosomes. This epithelium is separated from

the underlying tunica propria by a basal membrane. In the context of the tunica propria, we can find three layers. At the beginning, just below the basement membrane, we can find the lymphoid layer, which is characterized by the richness of lymphocytes (nasal-associated lymphoid tissue (NALT)). Then we have the glandular layer, characterized by glands that have a significant immune function producing secretions rich in lysozyme and IgA. Last, we can find the vascular layer, characterized by important vascular representation, especially in the mucosa of the inferior turbinate [2].

This brief description of microscopic anatomy of the nasal mucosa allows us to highlight the many important physiological functions it performs.

First of all, in the respiratory epithelium, the mucociliary clearing action is carried out thanks to the cooperation of ciliated and muciparous cells. This process is fundamental in determining the circulation of mucus, and therefore it performs a nasal cleaning with immuno-protective tasks [3]. At the level of the superficial mucous layer (thanks to the presence of lymphatic tissue) and at the level of the intermediate glandular layer (thanks to the secretion of lysozyme and IgA), immunocompetence functions are also performed. At last, the vascular layer, thanks to the presence of cavernous tissue, allows to change the physical-chemical characteristics of the air inhaled before its passage in the middle and lower respiratory tract [2]. With the passage of air through the nasal cavities, water vapor is transferred through the mucosa of the inferior turbinates with consequent lowering of oxygen partial pressures [4]. Furthermore, due to the contact between the mucosal surface of the turbinate and the air, the heating of the same is ensured [5].

The pathology of the rhinosinusal district appears to be varied and diversified [2], and it is characterized by many different types of clinical entities that sometimes are present individually, sometimes they overlap: this creates, in our opinion, classification difficulties. Another critical aspect for clinicians is to understand the real extent of rhinosinus disease, that is, if we are dealing with an exclusively nasal or sinus involvement or an involvement of both districts.

Our experience has led us to use in diagnosis of a rhinosinusopathy both a cytological examination of the nasal mucosa that will allow us to identify the problem and a radiological study (better if using cone beam CT) to define the real extent of the problem.

In this discussion we will explain how to perform a cytological examination and how to interpret it, and we will try to define a systematic classification of rhinopathies relying on the analysis of cytological compartments of patients affected by rhinopathy from our Center in the last 5 years.

## **2. Cytological Examination**

For about 10 years, we have been analyzing cytological samples from the lower turbinate mucosa in patients with chronic rhinopathies. This type of evaluation allowed us to study the microscopic characteristics of the healthy nasal mucosa and to identify the characteristic aspects of the different forms of rhinopathy. Performing a cytological examination is simple, rapid, and minimally invasive. It is also a cost-effective investigation.

From October 2013 to September 2018, we performed cytological sampling and subsequent microscopic analysis on the sample obtained from 300 patients with chronic rhinopathy. These patients reported suffering from several months or even years of nasal respiratory obstruction, rhinorrhea, in some cases complaining of recurrent headache or hyposmia or sneezing and nasal itching.

The cytological examination of each patient was performed according to the Italian Academy of Nasal Cytology (AICNA) procedures. We briefly summarized the modalities in the following paragraph.

## 2.1 How to perform a cytological sampling

### 2.1.1 Sampling

Through a small spoon called Rhino-Probe<sup>®</sup>, we collect mucous material joined to cells of the nasal mucosa, exerting a slight pressure on the body of the inferior turbinate. This technique is called nasal scraping (there are other sampling techniques such as brushing, nasal swab, and the washing that we report but of which we have no experience).

### 2.1.2 Processing

The material taken is distributed on a special slide, while avoiding to touch the surface of the slide with your fingers while always using gloves.

### 2.1.3 Fixation and coloring

We proceed to fix the material taken on the slide, then we apply the May-Grunwald-Giemsa (MGG) coloration. In our experience, we have been using a fast-acting MGG staining method (MGG Quick Stain<sup>®</sup>) for some years now. Cytological staining method is very numerous and each of them has its own specificity and application. In nasal cytology the most widely used is the MGG method which is able to easily differentiate the various cells found in the nasal mucosa.

### 2.1.4 Assembly of the slide

Through a specific synthetic product (Bio Mount HM<sup>®</sup>) the cover slip is applied above the slide. This way, the sample is ready to be observed.

## 2.2 Microscopic observation

The analysis of the sample of cytology material mounted on the slide is done with an optical microscope equipped with multiple objectives, each with different magnification power.

Phenotype	Cellularity	Subclasses	
Cellular	Neutrophil		
	Eosinofil		
	Mast cell		
	Miscellaneous		Neutrophil-eosinophil
			Neutrophil-mast cellular
		Neutro-eosino-masto cellular	
		Eosinophil-mast cellular	
Non cellular	Medicamentosa		
	Hormonal		
	From decubitus		
	Atrophic		
	Mechanical		

**Table 1.**  
 Classification of rhinosinusitis.

Initially, a general inspection of the material is carried out with a lower magnification objective (4×/0.10). Once the most significant part of the sample has been identified, the evaluation will be carried out with increasingly powerful objectives to exploit the maximum possible magnification (100×/1.25) with the help of oil for immersion.

In accordance with the guidelines of the Italian Academy of Nasal Cytology (AICNA), for each sample taken, we analyze at least 50 fields at maximum magnification (100×/25) by counting the different types of cells found. The observed data are then shown in a **Table 1**.

### 3. Results

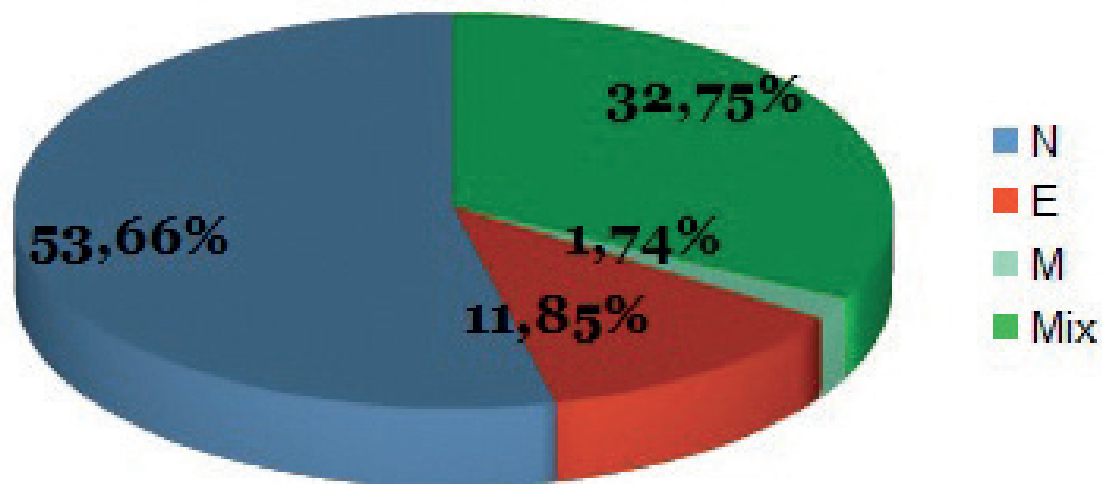
We have collected in **Figure 1** the results of the cytological tests performed from October 2013 to September 2018 (**Figure 1**).

Of the 300 patients studied, 154 (equal to 53.66%) were affected by a pathology of the nasal mucosa of neutrophilic type that is characterized by the presence of more or less numerous neutrophil granulocytes. The majority of them, 136 patients (88.31%), had chronic nonpolyposis pathology, while only 18 (11.69%) of them presented a polyposis pathology (**Figure 2**). The patients with nonpolyposis pathology were subjected to cone beam computed tomography (CBCT). Ninety-seven patients (71.32%) showed a pathological thickening of the paranasal sinuses mucosa. This situation indicates an involvement of the paranasal sinuses by the pathology and suggests a diagnosis of chronic rhinosinusitis (**Figure 3**).

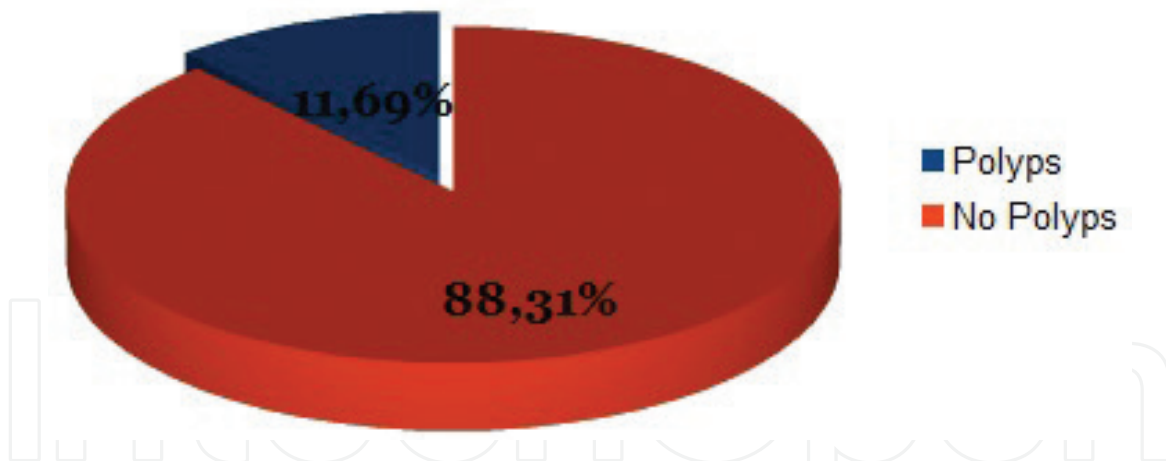
Thirty-four patients, equal to 11.85% of the total, showed a significant presence in the nasal mucosa of eosinophilic granulocytes. Of these, 29.41% of patients (10) had polyposis, while 70.59% of patients (24) had nonpolyposis (**Figure 4**).

Only five patients (1.74% of the total) showed instead a significant presence of mast cells in the nasal mucosa, and in no case we observed a form of polyposis. Finally, 32.75% of patients (94) had a mixed cell infiltration in the samples of nasal mucosa (**Figure 1**). Of these, 23.40% (22 patients) presented a polyposis pathology (**Figure 5**).

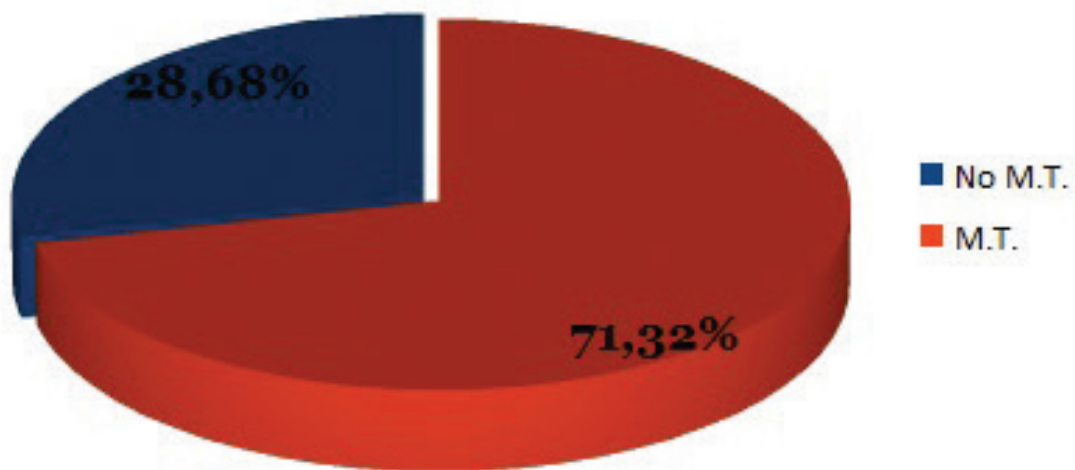
We analyzed the cytotypes of the “mixed cellularity rhinosinusopathy” category, distinguishing four subclasses: neutrophil-eosinophil forms (50 patients, equal to 53.19%), neutrophil-mast cell forms (8 patients equal to 8.51%),



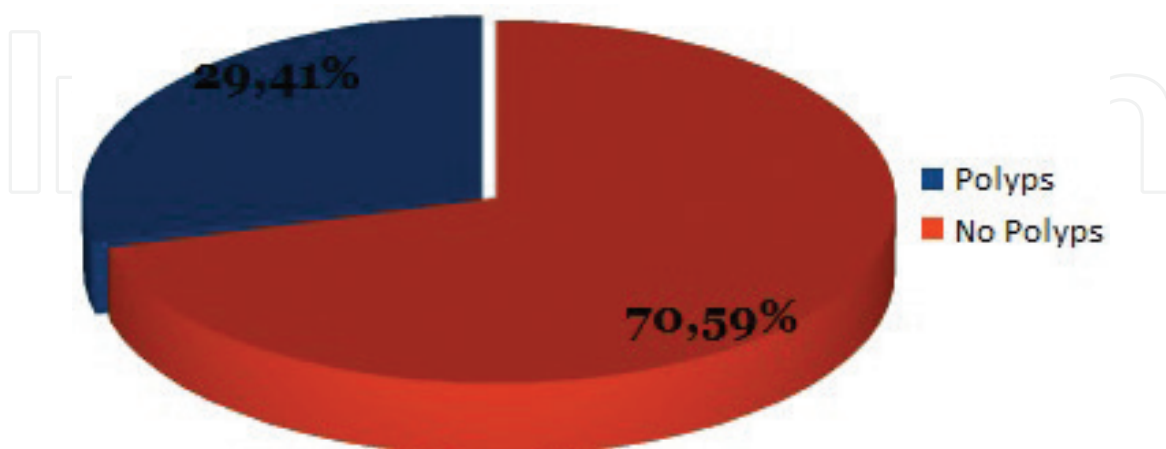
**Figure 1.**  
*Type of cells in nasal pathology.*



**Figure 2.**  
*Neutrophil pathology: presence of polyps.*



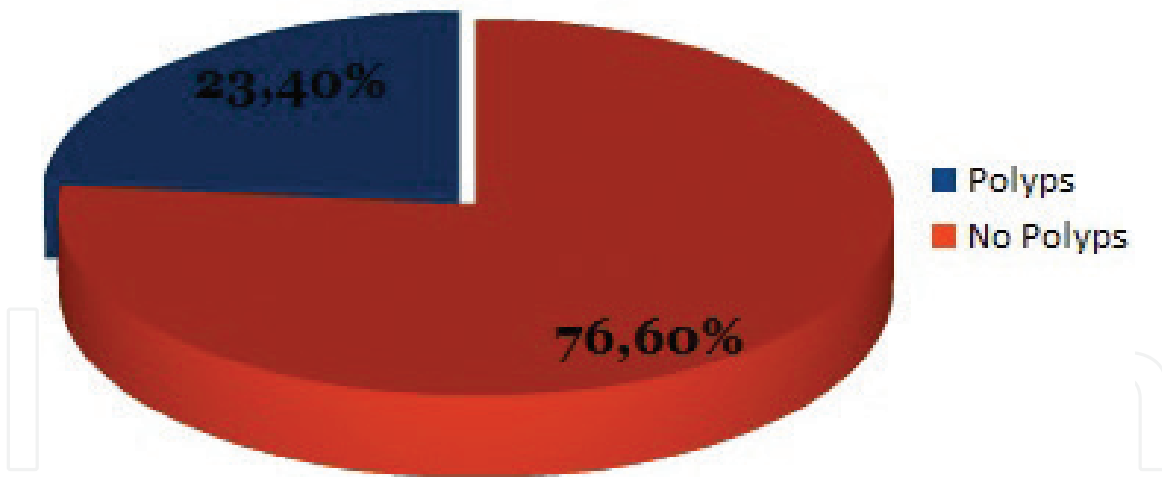
**Figure 3.**  
*Neutrophil nonpolypoid pathology: mucosal thickening.*



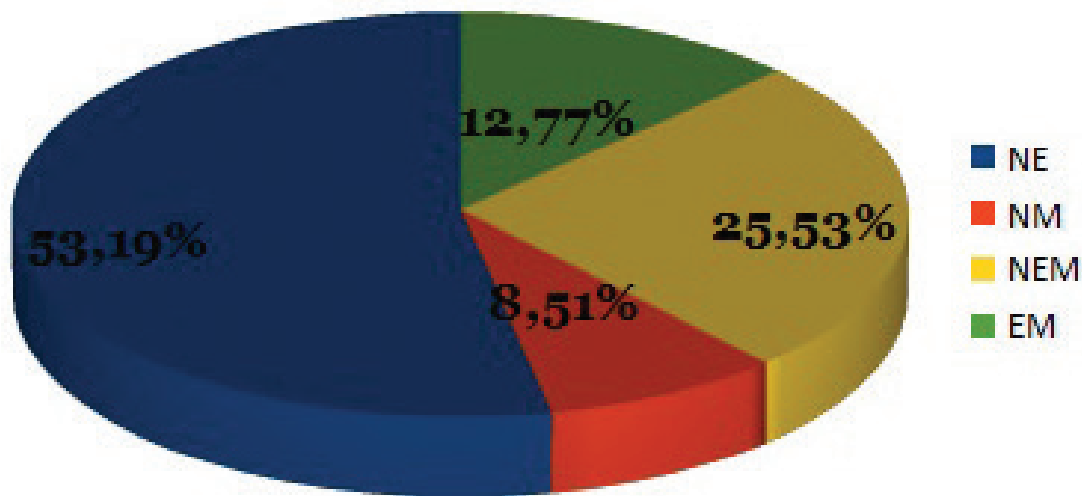
**Figure 4.**  
*Eosinophil pathology: presence of polyps.*

neutrophil-eosinophil-mastocyte forms (24 patients equal to 25.53%), and eosinophil-mast cell forms (12 patients equal to 12.77%) as indicated in **Figure 6**.

In 33 patients (equal to 11% of the total patients studied), we did not find any pathological changes in the nasal mucosa.



**Figure 5.**  
*Mixed pathology: presence of polyps.*



**Figure 6.**  
*Types of cells in mixed rhinosinusitis.*

The picture that emerged from this evaluation allowed us to distinguish nasal pathologies in a practical and clear way on the basis of cytological aspects and therefore, in our opinion, to simplify their classification. Furthermore, the cytological characterization allows us to address the therapy in a very personal way and, in addition, to periodically evaluate the results in a more rigorous way.

We therefore distinguished the nasosinusal pathologies in groups based on the inflammatory cytotype most significantly represented in the analyzed sample:

- Neutrophilic rhinosinusitis
- Eosinophilic rhinosinusitis
- Mast cell rhinosinusitis

However, in some patients we found that it was not possible to define a dominant cytotype as the nasal mucosa was quantitatively similarly affected by more than one cell type. In these cases we use the term rhinosinusitis with mixed cellularity.

We then divided the mixed cellular rhinosinusitis into four subclasses:

- Neutrophilic-eosinophilic form
- Neutrophilic-mast cell form
- Neutrophil-eosinophil-mastocitary form
- Eosinophilic-mast cell form

### 3.1 Neutrophil rhinosinusitis

In our experience, it represents the most frequently encountered pathology. This condition is characterized by the more or less significant presence of inflammatory cells called neutrophils granulocytes.

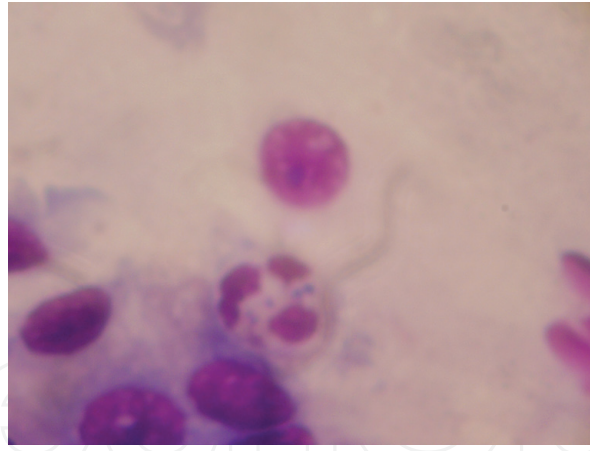
The neutrophil granulocyte has a roundish shape and presents a clear (“neutral”) cytoplasm with a purplish-red polylobate nucleus after MGG staining. The neutrophil granulocytes are distinguished in six different types based on the shape of the nucleus [2]. It is possible that the number of lobes is related to the age of the cell. In fact, in young granulocytes the nucleus often appears to be reniform, while in the older ones, it has different lobes.

The neutrophilic granulocyte plays an important immune function defending us from pathogenic microorganisms [6] and other irritating substances toward which it has an effective phagocytic activity. Once the phagocytosis process has been performed, a “killing” function is performed against pathogens thanks to the intracytoplasmic release of substances with a lithic action including hydrogen peroxide, superoxide ion, and some enzymes as elastase, lysozyme, collagenase, phosphatase, and lactoferrin.

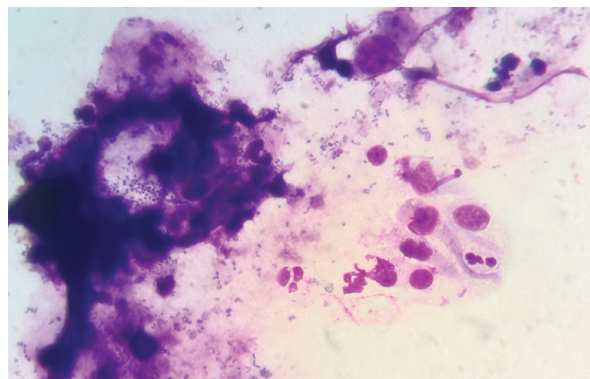
According to Gelardi et al., the presence of sporadic neutrophils in the nasal mucosa would not represent an index of pathology. Instead, we have to make a diagnosis in case of high number of neutrophils. With infectious rhinosinusitis, the number of neutrophil granulocytes increases significantly. They are called back in the nasal mucosa in order to engulf the pathogenic microorganisms and eliminate them [7]. We observe in **Figure 7** some granulocytes with intracytoplasmic bacteria. In this image the moment immediately following the phagocytosis is shown, before the lithic enzymes are activated for digestive purposes. In the proposed image, we observe a bacterial infectious pathology. Microscopic observation can help us to differentiate the various types of germs involved in infection. We can in fact recognize the round shape of the bacteria as *Staphylococcus*, *Streptococcus*, and *Moraxella* or the elongated shape of the haemophilus and diphtheroids. Neutrophilic rhinosinusopathy with an infectious etiology may also present a viral or fungal etiology. In the latter case, we will observe the presence of fungal spores that present themselves with a particular “bulb” shape.

In infectious neutrophil rhinosinusitis, in addition to the increase in neutrophils and the presence of microbial agents (**Figure 8**), we will also be able to see an increase in lymphocytes, macrophages, and plasma cells and an increase in mucipar cells associated with decreased ciliated cells.

We found very interesting the observation of bluish areas that we define “infectious spots” [2]. Those represent the expression of bacterial biofilm or an exopolysaccharide matrix within which fungal bacteria and spores live. The structure of the biofilm would correspond to a sort of shell that guarantees pathogens a greater resistance to drugs.



**Figure 7.**  
*Phagocytosis (neutrophil granulocyte with intracytoplasmic bacteria).*



**Figure 8.**  
*Infectious neutrophil rhinosinusitis.*

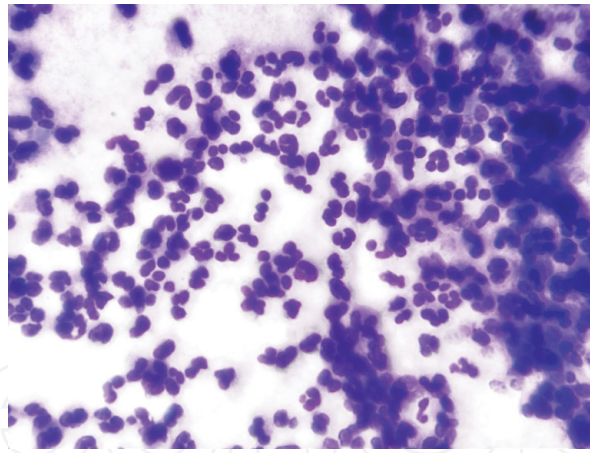
In the forms of viral etiology, we will not be able to find pathogenic microorganisms due to the insufficient magnification power of the optical microscope. However, we can observe some indirect signs of ciliated cells strongly suggestive of viral infection. In fact, they can present both alterations of the nuclear structure (polynucleation) and of the cytoplasmic component (inclusions and separations). Also usually in the viral infection, we observe an important increase of the lymphocytes. The finding of neutrophils in the nasal mucosa, however, also occurs in cases of noninfectious diseases. In these cases we can observe a variable number of neutrophil granulocytes without the cytological aspects described above. In this case, we are talking about a form of irritating rhinosinusitis in which often the etiologic agent is represented by a substance with an irritating action, which can be exogenous (powders, environmental pollutants, tobacco smoke, and toxic substances present in the professional field) or endogenous (gastroesophageal reflux disease) (**Figure 9**) [8].

In addition to the already described presence of neutrophils we can observe an alteration of the normal relationship between ciliate cells and muciparous cells. In fact, we often observe a reduction of the former and an increase in the latter. In other cases we can observe areas of squamous epithelium. According to some authors the severity of these rhinopathies would be associated with the number of neutrophils present.

In fact, by releasing their lithic enzymes and their toxic substances, they would cause damage to the respiratory mucosa proportional to the quantity of substances released.

Furthermore, in these patients, chronic mucosal damage and consequent alteration of mucociliary clearness would favor greater nasal fragility and a greater risk of contracting respiratory infections.





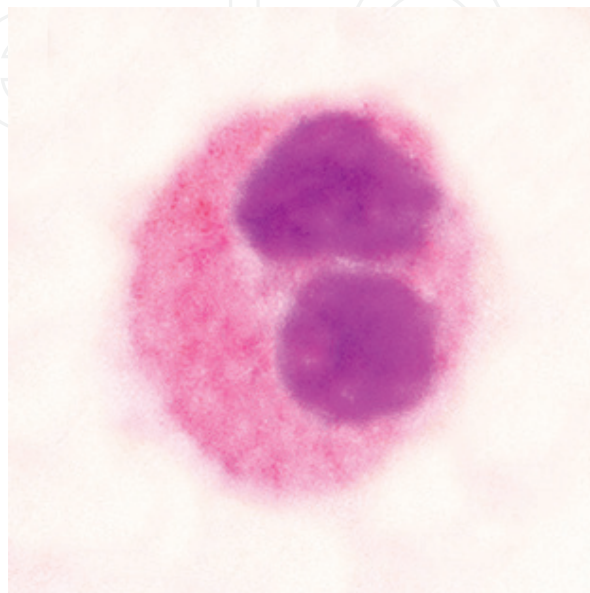
**Figure 9.**  
*Noninfectious neutrophil rhinosinusitis.*

### 3.2 Eosinophilic rhinosinusitis

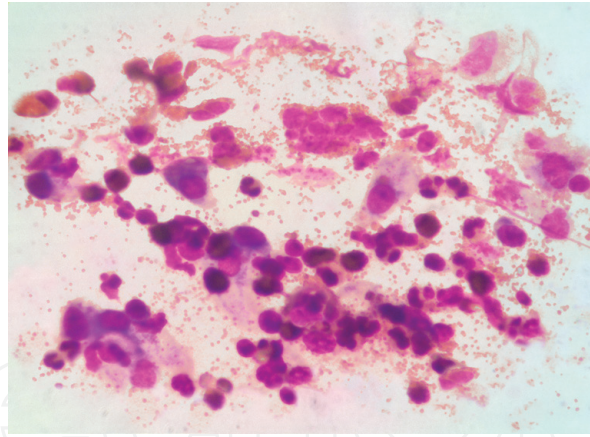
This condition is represented by the presence in the nasal mucosa of eosinophilic granulocytes. The eosinophilic granulocyte belongs, as well as neutrophil, to the group of leukocytes and also presents a roundish form, although of slightly greater dimensions. Frequently the nucleus appears bilobed (**Figure 10**).

The cytoplasm is of variable color from orange to intense pink, very distinctive and unmistakable. Inside, small granules are observed that contain substances such as the major basic protein (MBP), the eosinophilic cationic protein, and the eosinophilic peroxidase [9]. These substances have a cytotoxic and antibacterial function. In the cytoplasm of eosinophils, we also find enzymes (collagenase, phosphatase, and phospholipase) and substances derived from the metabolism of arachidonic acid as leukotrienes and prostaglandins (LTC<sub>4</sub>, PGD<sub>2</sub>, PGE<sub>1</sub>). These substances play a fundamental role in the mechanisms of inflammation, especially in the delayed phase of the allergic reaction (**Figure 11**).

The LTC<sub>4</sub> leukotriene in particular has a bronchoconstriction action as well as prostaglandin PGD<sub>2</sub>, while prostaglandin E<sub>1</sub> has a vasodilatory action. Other substances present in nongranular form in the cytoplasm of eosinophils are released



**Figure 10.**  
*Eosinophilous (frequently the nucleus appears bilobed).*



**Figure 11.**  
*Eosinophil rhinosinusitis (we observed an important degranulation reaction).*

for chemotactic and amplification of the inflammatory processes. We recall among these IL2, which performs chemotactic action toward mast cells, IL3 with chemotactic action toward eosinophils, and IL5 with chemotactic action toward neutrophils [10].

Frequently we have found eosinophilic rhinosinusitis. Of 34 patients with this type of pathology, 38.24% (or 13 patients) had allergic rhinitis, the remainder suffered from other forms of rhinitis.

We have found in the 32.35% of subjects (11 patients) a vasomotor rhinitis and in the 29.41% (10 patients) a nasal polyposis.

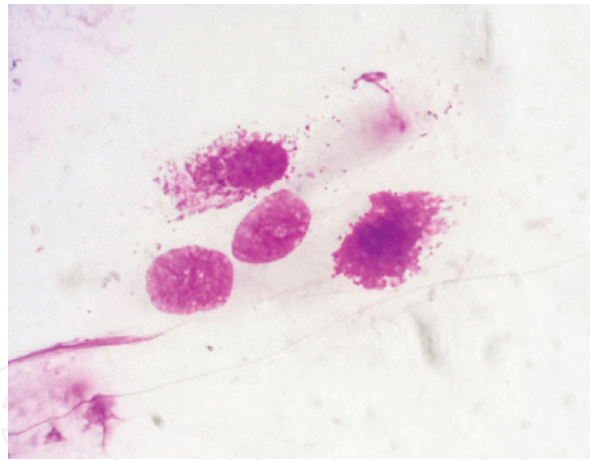
Eosinophilic rhinosinusitis has very specific clinical features. Affected patients complain of a very troublesome symptomatology, often characterized by sneezing and rhinorrhea, nasal itching, and nasal congestion. Symptoms can be triggered suddenly by the contact of the nasal mucosa with a known allergen, but also by the occurrence of some particular stimuli (such as sudden changes in temperature or humidity, contact with intense perfumes, tobacco smoke).

Patients with eosinophilic rhinosinusitis are often affected by other eosinophilic phenotype disorders such as bronchial asthma. For a long time, we have known that the course of the nasal pathology has a singular influence on the prognosis of the associated bronchial pathology. For this reason, a correct treatment and a good control of the nasal pathology are to be considered necessary.

We know that some granular components of eosinophils, such as major basic protein (MBP), have the ability to attack the desmosomal junctions by weakening the barrier action of the respiratory mucosa and exposing it to the action harmful to infectious chemical or physical agents [11]. Therefore patients suffering from eosinophilic rhinosinusitis not only suffer from symptoms that we could define direct and that are related to the action of components such as prostaglandins and leukotrienes but also indirect symptoms (purulent rhinorrhea, headache, pharyngodynia, cough, recurrent fever, episodes of dyspnea) derived from the overlap of other diseases favored by the weakening of the mucosal barrier and by the inefficiency of mucociliary clearance.

### 3.3 Mast cell rhinosinusitis

This condition is characterized by the presence of mast cells in the nasal mucosa. The mast cell is presented to the observation with a variable optical microscope: it can be vaguely roundish or lozenge shaped. It is characterized by a marked basophilia and has a coarsely oval nucleus generally covered by numerous granules (**Figure 12**). They are generally larger in size than eosinophilic granules.



**Figure 12.**  
*Mast cell with degranulation.*

The surface of mast cells is characterized by the presence of IgE receptors. When they bind to these receptors, the mast cell releases by exocytosis its granules with the substances contained therein including histamine, a preformed substance with multiple actions [12].

In fact, it acts on the vascular receptors favoring vasodilation and edema of the surrounding tissues. It also acts on the nasal glands, feeding the rhinorrhea, and stimulates the nerve endings favoring itching and sneezing. The mast cell through its granules also eliminates some preformed chemotactic factors such as IL4, IL5, and IL13. Arachidonic acid is also synthesized by newly formed metabolites such as PGD2 and LTC4, whose actions on smooth muscles and vessels have already been described previously.

The mast cell, once stimulated, determines immediate symptoms. This rapidity of action can be observed in the early phase of the allergic reaction [13]. However, this cell is able, through the release of chemotactic factors, to influence also late phlogistic reactions.

As we can show in **Figure 1**, mast cells are rarely the only cells involved in the pathogenesis of a rhinopathy. In fact, we found only 5 cases of mastocytic rhinosinusitis in 300 patients studied (1.67%). Of these patients two presented an allergic disease, while three patients had a nonallergic disease.

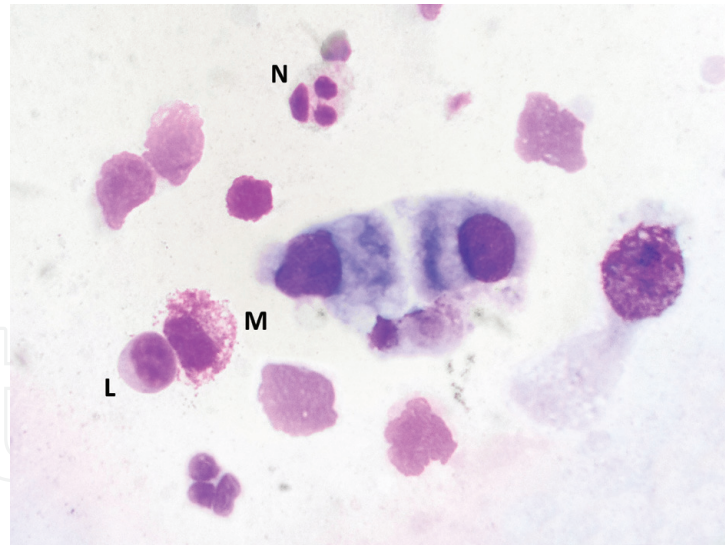
On the other hand, cases of mixed cellular pathologies with the presence of mast cells are very frequent.

Mast cell rhinosinusitis are characterized by very intense symptoms, characterized by marked nasal obstruction, serous rhinorrhoea, nasal pruritus, and sneezing. Also in this case as in eosinophilous cellularity diseases, we have reestablished an association with other pathologies with a similar phenotype such as bronchial asthma.

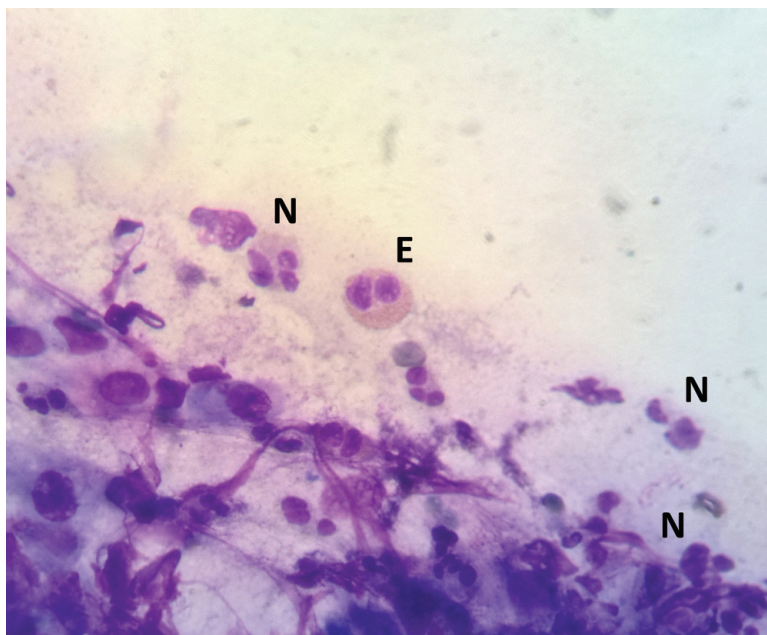
### 3.4 Mixed rhinosinusitis

We found a mixed rhinosinusitis in 94 patients corresponding to 32.75% of patients with rhinosinusitis and inflammatory phenotype (**Figure 1**). As we can see from the graph below, mixed rhinosinusitis is characterized by the presence in the nasal mucosa of several inflammatory cytotypes (**Figures 13** and **14**).

In 53.19% of the cases (50 patients), we found a pathology characterized by neutrophil and eosinophilic infiltration; in 25.53% of cases (24 patients), a type with neutrophilia-eosinophilia-mast cell; in 12.77% of cases (12 patients), eosinophilic and mast cell type and in 8; and 51% of the cases (8 patients), we found neutrophils and mast cells in the nasal mucosa. In many cases, mixed rhinosinusitis is found in



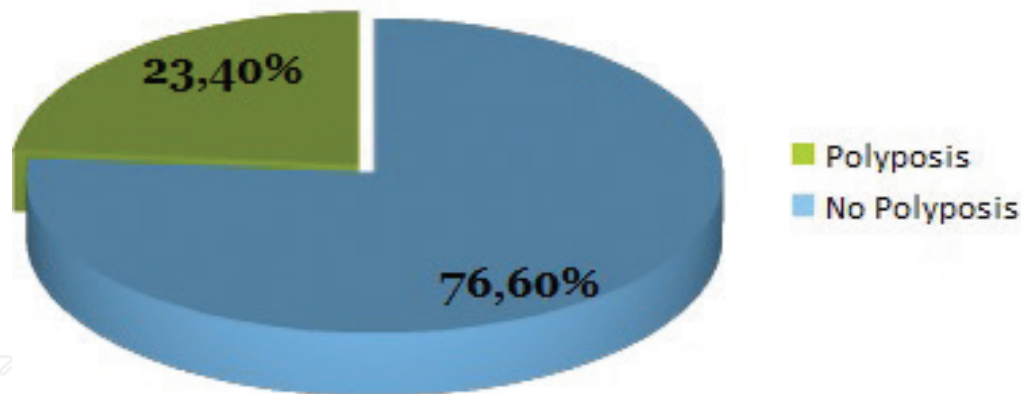
**Figure 13.**  
*Mixed rhinosinusitis with neutrophil (N), mast cell (M), and lymphocyte (L).*



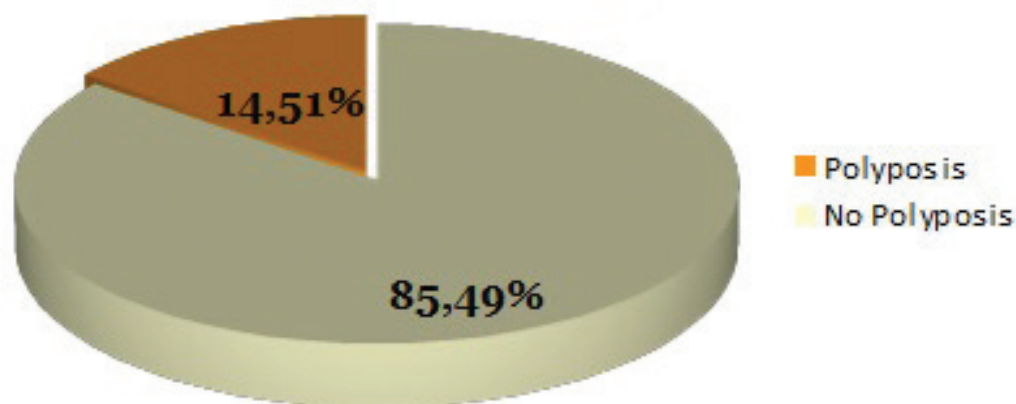
**Figure 14.**  
*Mixed rhinosinusitis with neutrophil (N) and eosinophil (E).*

allergic patients. We have observed that a low intensity but stable and protracted allergenic stimulation, as in the case of allergies to Dermatophagoides, produces at a cytological level a framework defined by Gelardi et al. “Minimal persistent inflammation” is characterized by the presence of numerous neutrophil granulocytes and a small number of eosinophils or mast cells. Another interesting aspect is the greater association of the mixed forms with nasal polyposis compared to the other forms of rhinosinusitis as shown in the graph below (**Figures 15 and 16**).

We have indeed observed that in the category of rhinosinusitis with mixed cellularity, 23.40% of patients had developed a nasal polyposis, while in the other forms of rhinosinusitis, the percentage of patients who developed a nasal polyposis is lower (14.51%). The symptoms of this kind of disease varies according to the most characterizing cytotype. In any case we must remember how these forms are particularly harmful for the nasal mucosa and for mucociliary function, as they, according to our clinical experience, contribute in favoring an increased risk of respiratory inflammation in those affected.



**Figure 15.**  
*Prevalence of polyposis in mixed rhinosinusitis.*



**Figure 16.**  
*Prevalence of polyposis in other types of rhinosinusitis.*

#### 4. Discussion

Our experience has allowed us to consider the nasal cytological examination as indispensable diagnostic tools for a better understanding of chronic inflammatory diseases of the rhinosinusal district.

Thanks to the information provided by the cytological examination, we can define the etiopathogenetic characteristics of the disease. Obviously the collection of the anamnesis represents a complementary and indispensable diagnostic element.

By carrying out these three diagnostic aspects, we are able to trace the identification of the pathology very precisely.

Daily experience has led us to acknowledge the necessity of a simplification regarding the classification of rhinosinusal diseases.

Once there was a clear demarcation between pathological processes at nasal localization, the rhinitis, from those with sinus localization, the sinusitis.

In agreement with the European guidelines present in the EPOS12 [14], we argue that very often the two pathologies are closely related, so that a clear border between the two is impossible. We therefore think it is practical as well as appropriate to use in clinical practice a single term that includes the two old forms of nasosinusal pathology. For these reasons, we will talk about chronic rhinosinusitis about any chronic inflammatory process that affects the rhinosinusal district.

The teaching of the pulmonologists, as explained in the GINA guidelines, led us to consider the nasal pathology narrow related to the bronchial situation. This is

the reason why the phenotypic classification adopted for asthma is, in our opinion, extremely suitable also for the rhinosinusal pathology.

We have therefore redesigned the pneumological experience in order to use in our daily practice a simple and immediate distinction for the various forms of chronic rhinosinusitis. We have distinguished 2 large groups of pathologies based on the phenotype:

- Cellular rhinosinusites
- Noncellular rhinosinusitis

This first distinction in the 2 phenotypic classes arises from the firm belief that the clinical characteristics of the sinonasal pathology are closely related to the type of cell involved in the inflammatory process.

As shown in **Table 1**, in the cellular rhinosinusitis group, we contemplate the neutrophilic, eosinophilous, mast cell, and mixed cell forms. In the second group, (noncellular rhinosinusitis) we contemplate pathologies characterized by a normal cytological expression but equally characterized by sinonasal symptoms. Among these we include the iatrogenic forms, the hormonal forms, the atrophic forms, the mechanical forms (associated with septal dysmorphism), and the decubitus forms (characterized by significant nasal respiratory obstruction when the patient lies supine). In our case series, the number of patients affected by this type of pathology was much lower than patients affected by cellular rhinosinusitis. Precisely the individuals affected was 13 (equal to about 4.5%).

Indeed, the number of negative rhinocytograms was superior, almost three times as high. However, we have also included in the cellular group patients with negative cytological examination; in those cases we knew that the negative result originated from temporal circumstances. This applies, for example, to certain diseases with seasonal or recurring cellular characterizations. We have therefore attributed to the group of eosinophilic rhinosinusitis also those patients with clearly allergic symptoms and in which sensitization to seasonal allergens was ascertained despite having found in them a normal rhinocytogram. This situation occurs when we performed the sampling outside the allergy period.

We are sure of the central role of the cytotype in the sinonasal pathology manifestation, and we have also distinguished the mixed rhinosinusitis in four subclasses: the neutrophil-eosinophilic cellular form, the neutrophil-mast cell form, the neutrophil-eosinophil-mast cell form, and the eosinophilic-mast cell form.

This classification, with the support of an adequate imaging and with a correct anamnestic study, allows clinicians to diagnose all types of rhinosinusitis by means of an easy and intuitive classification.

The diagnostic classification performed by cytological examination allows a targeted therapeutic planning. In fact, the knowledge of the etiopathogenetic and cytological principles of a pathology allows a “tailor made” therapeutic planning and also allows to achieve a precise monitoring of the pathology. This leads to optimal control of symptoms and an inevitable prognostic improvement of chronic inflammatory diseases.

## 5. Conclusion

The classification of rhinosinusitis is still very complex and diversified today. Thanks to the information we can obtain from the nasal cytology and the anamnesis, we are able to easily frame the majority of rhinosinus pathologies in order to obtain a targeted therapeutic planning and adequate monitoring.

We have listed the pathologies observed and classified from the cytological point of view in 5 years of experience, and we have come to propose a simple and versatile classification that takes into account the different clinical and etiopathogenetic characteristics of the pathologies observed.

Based on the phenotype, we distinguished cellular rhinosinusitis from noncellular rhinosinusitis. The former are divided into four classes (the neutrophil form, the eosinophilic form, the mast cell form, and the mixed form). These types of rhinosinusitis are characterized by a specific cytological framework. We then grouped rhinosinusitis with a negative rhinocytogram in the noncellular phenotype. Among these we remember the iatrogenic forms, the forms on a hormonal base, the positional and decubitus, the atrophic, and the mechanical forms.

According to us, the distinction we have proposed is simple and immediate.

## **Acknowledgements**

The author would like to thank Mauro Corinti for his contribution in photographic materials.

## **Conflict of interest**

The author declares that there is no conflict of interest regarding the publication of this paper.

## **Notes/thanks/other declarations**

Thanks to Giorgia Bottani for general support and assistance.

## **Author details**

Marco Capelli  
Columbus Clinic Center, Milan, Italy

\*Address all correspondence to: [info@otorinocremona.it](mailto:info@otorinocremona.it)

## **IntechOpen**

© 2019 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

## References

- [1] Galarza-Paez L, Anatomy DBW. Treasure Island. FL: StatPearls Publishing; 2018. p. 22
- [2] Gelardi M. Atlante di citologia nasale—per la diagnosi differenziale delle rinopatie. 2nd ed. Milano: Ermes SRL; 2012
- [3] Piqué N, De Servi B. Rhinosectan<sup>®</sup> spray (containing xyloglucan) on the ciliary function of the nasal respiratory epithelium; results of an in vitro study. *Allergy, Asthma and Clinical Immunology*. 2018;**14**:41. DOI: 10.1186/s13223-018-0268-3
- [4] Rouadi P, Baroody FM, Abbott D, Naureckas E, Solway J, Naclerio RM. A technique to measure the ability of the human nose to warm and humidify air. *Journal of Applied Physiology*. 1999;**87**(1):400-406
- [5] Freeman SC, Kahwaji CI. Treasure Island. FL: StatPearls Publishing; 2018. p. 27
- [6] Hergott CB, Roche AM, Naidu NA, Mesaros C, Blair IA. Weiser bacterial exploitation of phosphorylcholine mimicry suppresses inflammation to promote airway infection. *The Journal of Clinical Investigation*. 2015;**125**(10):3878-3890. DOI: 10.1172/JCI81888
- [7] Kolaczowska E, Kubes P. Neutrophil recruitment and function in health and inflammation. *Nature Reviews Immunology*. 2013;**13**(3):159-175. DOI: 10.1038/nri3399
- [8] Caruso AA, Del Prete S, Ferrara L, Serra R, Telesca DA, Ruggiero S, et al. Relationship between gastroesophageal reflux disease and Ph nose and salivary: Proposal of a simple method outpatient in patients adults. *Open Medicine*. 2016;**11**(1):381-386. DOI: 10.1515/med-2016-0069
- [9] Zhu X, Liu K, Wang J, Peng H, Pan Q, Wu S, et al. C-C chemokine receptor type 3 gene knockout alleviates inflammatory responses in allergic rhinitis model mice by regulating the expression of eosinophil granule proteins and immune factors. *Molecular Medicine Reports*. 2018;**18**(4):3780-3790. DOI: 10.3892/mmr.2018.9380
- [10] Varricchi G, Bagnasco D, Borriello F, Heffler E, Canonica GW. Interleukin-5 pathway inhibition in the treatment of eosinophilic respiratory disorders: Evidence and unmet needs. *Current Opinion in Allergy and Clinical Immunology*. 2016;**16**(2):186-200
- [11] Acharya KR, Hogan SP. Eosinophil granule proteins: Form and function. *The Journal of Biological Chemistry*. 2014;**289**(25):17406-17415
- [12] Vukman KV, Försönits A, Oszvald Á, Tóth E, Buzás E. Mast cell secretome: Soluble and vesicular components. *Seminars in Cell & Developmental Biology*. 2017;**67**:65-73
- [13] Korošec P, Gibbs BF, Rijavec M, Custovic A, Turner PJ. Important and specific role for basophils in acute allergic reactions. *Clinical and Experimental Allergy*. 2018;**48**(5):502-512
- [14] Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. *Rhinology*. 2012;**50**(1):1-12