Chapter 2

Airborne Allergens

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Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/59300

1. Introduction

A huge number of substances of various origin forming atmospheric aerosols constantly circulates in the atmospheric air (Table 1). One of the most important components of such aerosols are airborne allergens. Airborne allergens are substances of biological origin, which getting into the human body promote the induction of the immune response with the subsequent development of an allergic disease. Allergic reaction is directly caused by proteins and glycoproteins forming the airborne allergen.

Type of particles	Diameter (mkm)
Smoke, smog	0, 001-0, 1
Dust	0, 1
Bacteria	0, 3-10
Fungi spores / conidia	1, 0-100, 0
Algae / seaweed	0, 5
Fragments of lichen	1, 0
Protozoa	2, 0
Spores of mosses	6, 0-30, 0
Pollen	10, 0-100, 0
Fragments of plants and animals, seeds, insects	>100

Table 1. The components of the atmospheric aerosols and their size [4].

More than 15 million people in Europe suffer from allergic rhinitis, conjunctivitis, bronchial asthma, atopic dermatitis and food allergy. Climatic and geographic features of the Russian Federation (its Northern and Southern parts, as well as European and Asian territories) contribute to a different sickness rate among the population [1, 2].

So far there are many questions concerning monitoring and a variety of the airborne allergens, and especially their influence on the human body. The study of the airborne allergens is of theoretical and practical interest for many specialists (allergists, laboratorians, ecologists, biologists). The biological study of the airborne allergens is connected with the problem of the origin, transport, protein structure and protein interaction with the macroorganism. Under the influence of the environment the airborne allergens may be a subject to significant changes and they may change their properties.

This chapter presents the main types of the airborne allergens: their origin, transport, properties, monitoring, etc.

2. Classification of the airborne allergens

The most common airborne allergens are pollen, fungal spores, house dust, house dust mites, animal allergens, insect allergens, industrial allergens, food and drug allergens.

Origin	Types of the allergens		
Noninfectious allergens			
Animals	Epidermal	Food-borne	Insect
	Hair/wool epithelium feather saliva excrements	Fish and cancroid protein Honey	Chitinous cover and products of insects vital activity
Plants	Pollen	foodstuffs	
Drugs	antibiotics, sulfanilamides, immunological drugs		
Industrial substances	polymers, pesticides, metalls		
Dust	house, library, archive dust		
Infectious allergens			
Phycomycetes	spores, products of fungi vital activity		

Table 2. Classification of the airborne allergens.

The scientific line-molecular allergology-intensively develops in modern allergology for the last 10-15 years. The modern allergen nomenclature adopted and approved in 2013 by WAO is now becoming routine in practice of the allergist [3].

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We will present the most well-known and popular airborne allergens in applied medicine which are used for the diagnosis and treatment of allergic diseases of reaginic type (IgE-dependent allergic reactions or type I of immune response). Such diseases include allergic rhinitis, allergic conjunctivitis, atopic dermatitis, bronchial asthma, urticaria, etc.

The knowledge of the airborne allergens types is very useful in routine practice of a medical specialist for the purpose of individual selection of methods of diagnosis and treatment of patients with respiratory allergosis, as well as for the prevention of allergic diseases in genetically predisposed to atopy or already sensitized patients.

3. Pollen allergens

3.1. Aeropalynology

Aeropalynology is a part of aerobiology studying pollen grains and spores of plants passively circulating in the atmosphere. Also, it is a branch of modern biology that studies the structure and laws of formation of the pollen rain. Aeropalynology is closely connected with allergology as pollen of plants and fungal spores belong to the most widespread airborne allergens causing diseases of the upper airways [4]. Aeropalynologists are the experts engaged in identification of qualitative and quantitative structure of a pollen rain. They study features of its daily rhythms and seasonal dynamics, compile a calendar of allergenic plants dusting and sporulation of mycelial fungi. These data are necessary for various experts (allergists, otorhinolaryngologists, general practitioners) and patients to predict exacerbations of allergic diseases and to take preventive measures.

Long-term observations over the years are the most informative for identifying patterns of plants dusting over large areas with different climate and landscapes.

Currently there is a single international aeropalynology service that possesses information about the dynamics of the pollen concentrations of the most common allergenic taxa in the air and the bank of these data. Since 1993, the database provides information on the dusting of different plants in Europe and forecasts the dusting based on the current and long-term aeropalynological observations [5, 6].

The program of aeropalynological research was launched in Russia in 2007. Several cities with installed pollen monitoring stations (volumetric Burkard SporeWatch sampler) had been included in this program (Fig. 1-3). These cities are Moscow, St. Petersburg, Saratov, Stavropol, Astrakhan, Rostov-on-Don, Krasnodar, Yaroslavl, Novosibirsk, Yekaterinburg, Ryazan, Smolensk, and others. The aeropalynological stations start working from 15 of April to 15 of September every year (the period of active flowering of wind-pollinated plants in Russia). The aeropalynological monitoring is carried out the year-round in Moscow and St. Petersburg. The studies of pollen are carried out by the Russian allergists and laboratory technicians, who were trained under the guidance of Severova E.A. at the Department of Palynology, Faculty of Biology of Moscow State University. The station in Moscow is the curator of a national Russian network of aeropalynological monitoring and represents Russia in the European and International association of aeropalinologists.

Figure 1. Burkard SporeWatch sampler

Figure 2. Burkard SporeWatch sampler Cylinder with 7-days or 24-hours periods of selection in Krasnodar

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Figure 3. Burkard-Hirst SporeWatch in Moscow, Saratov, Pyatigorsk, Rostov-on-Don, St. Petersburg, Stavropol

The measurement of the concentration of mycelial fungi spores in the atmospheric air is carried out by means of the automatic Burkard sampler on the Petri dish with Czapek agarized medium (Fig. 4).

Figure 4. Burkard SporeWatch sampler and sampler (St. Petersburg) PU-1B The determination of the spores concentration (colony forming units-CFU) in the atmospheric air of the premises, parks and industrial areas is also very informative for collecting the patient's medical history and selection of diagnostic tests in vivo and in vitro.

3.2. Pollen-grain morphology

For allergology the greatest interest is represented by pollen grains of wind-pollinated plants (angiosperms and gymnosperms) because pollen is spread by wind over hundreds of kilometers from the habitats of plants. Most of the entomogenous plants are not allergenic for human.

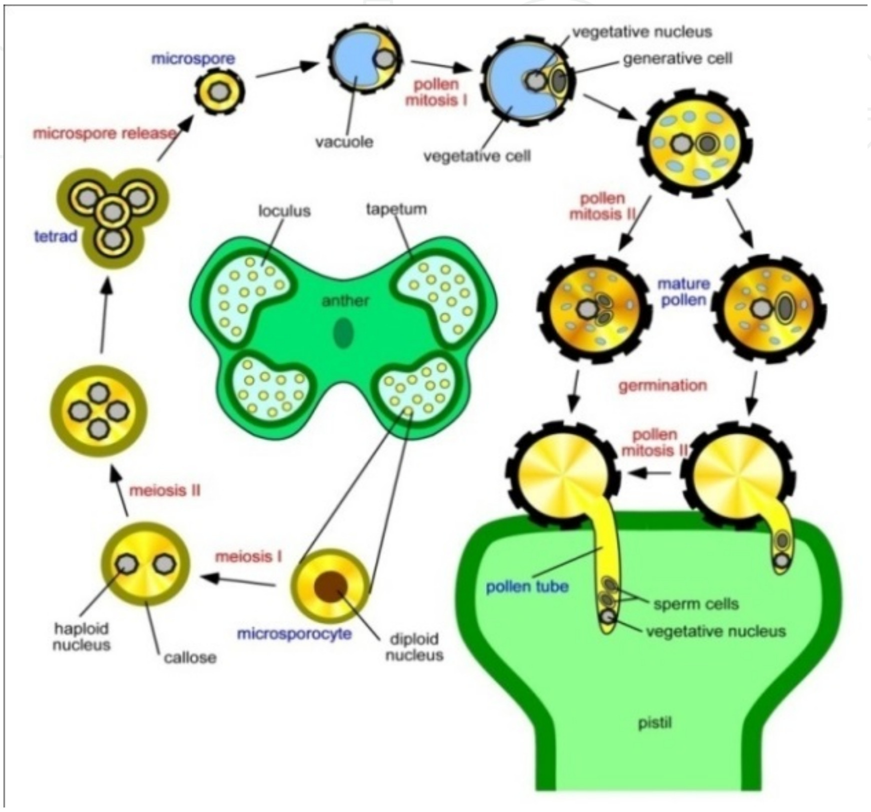

Figure 5. The pollen grain development and its participation in fertilization

Pollen grains are reduced male gametogophytes developing inside the microspore shell. Pollen grains of the angiosperms are formed from microspores (mother cells) in microsporangia which represent anther nests.

Each pollen grain consists of the vegetative cell, and the generative cell is immersed in the cytoplasm of the vegetative cell (Fig. 5). During the germination the vegetative cell forms a pollen tube, and the nucleus of the generative cell forms 2 sperm cells involved in fertilization [4].

3.3. Sporoderma

Sporoderma is a shell of pollen grains (Fig. 6).

Sporoderma is a set of morphologically different layers: perispory (Perina=trifina), exine (exosporium), and intine (endosporium) which protect the cytoplasm of the pollen grain from the external influence. The sporoderma layer structure is specific to orders, families, genera and species of higher plants.

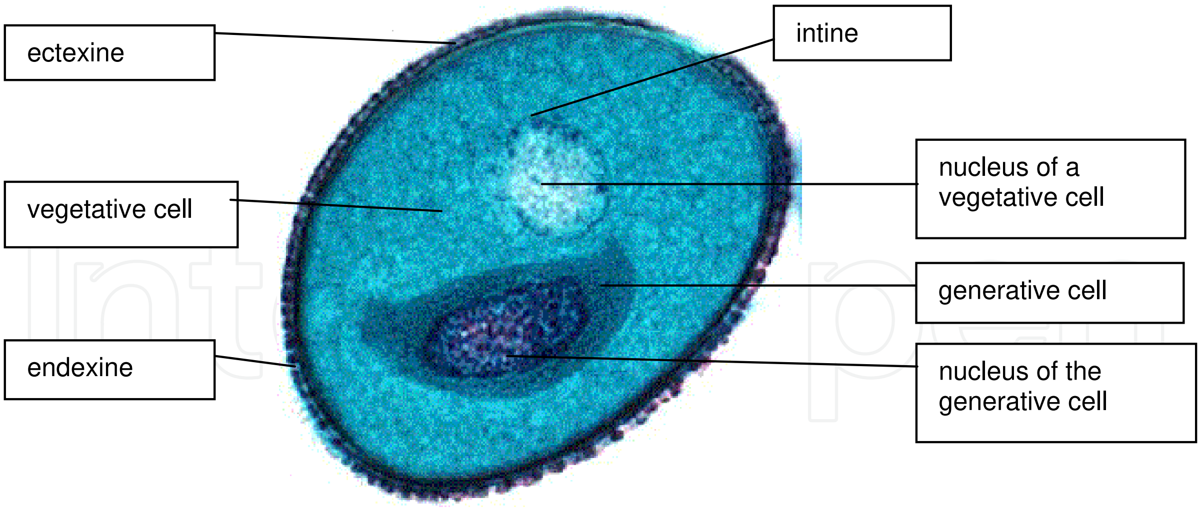

Figure 6. Pollen grain structure

The exine is the outer part of the pollen grain shell of most seed plants. The structure of the exine includes sporopollenin. It is a biopolymer that can withstand the high temperature, and is insoluble in alkalis and acids (Fig. 7).

The internal structure of the exine forms texture and sculpture. And that is a main point for the aeropalynologists in determining the morphological type of pollen grains.

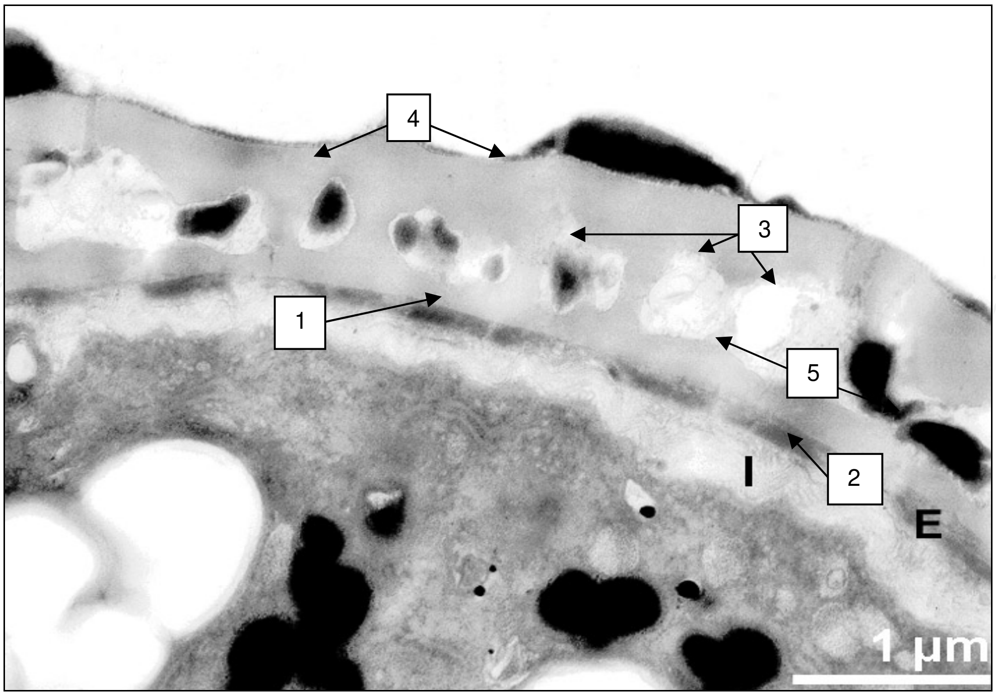

Figure 7. The structure of angiosperm sporoderma: 1-endexine, 2 – intine, 3-styles, 4-integument, 5-underlaying layer.

Intine is the inner layer of sporoderma bordering with cytoplasm and collapsing in acytolysis processing.

Trifina is a thin squamous layer of wind-pollinated plants. It is poorly visible in contrast to the pollen of the entomophilous plants.

The complex morphology and molecular composition of pollen helps to activate the immune system of a human for the purpose of elimination of airborne allergens from mucosa of the respiratory tract [4].

3.4. The main plants the pollen of which causes an allergy

In the central Europe, the most common cause of pollinosis is the pollen of wind-pollinated plants: trees, cereals and weeds. Their pollen is volatile, and during flowering of these plants the pollen accumulates in the air in quantity sufficient enough to create a relatively high concentration.

As a result of the aeropalynological researches the calendars of dusting are compiled annually. The calendars containing 15 taxa of plants are compiled for Europe.. However, in the North and the South of Russia (the European part of it) a range of airborne allergens is larger and depends on the trajectory of the distribution of pollen (Fig. 8) [4].

During the examination and management of patients with pollinosis, the seasonal and daily changes of the pollen content should also be taken into account.

The allergy to pollen of grasses and trees grows only in the period of their flowering. So each region has its own seasonal peaks of incidence. The maximum concentration of pollen in the air is in the early morning hours, from dawn until 12 p.m.

Among deciduous trees the allergic diseases are caused most often by pollen of birch, alder, hazel, maple, oak, and others. We present the main taxa of trees which are determined in the atmospheric air:

1. Alnus incana (Grey alder) (Fig.9)
2. Betula verrucosa (Common silver birch) (Fig.10)
3. Corylus avellana (Hazel) (Fig.11)
4. Quercus alba (Oak) (Fig.12)
5. Ulmus americana (Elm) (Fig.13)
6. Salix caprea (Willow) (Fig.14)
7. Populus deltoides (Cottonwood) (Fig.15)
8. Acer negundo (Fig.16)
9. Fraxinus americana (White ash) (Fig.17)

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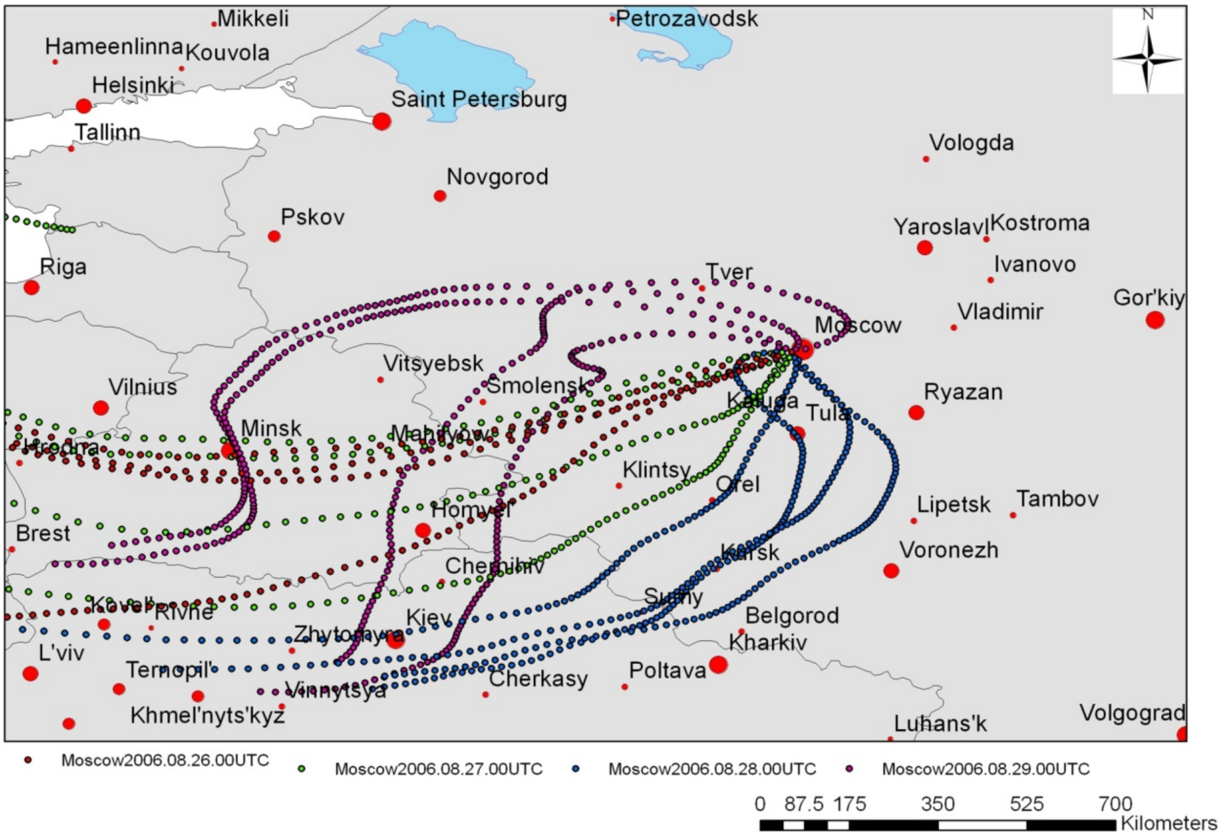

Figure 8. The trajectory of the distribution of pollen from Moscow.

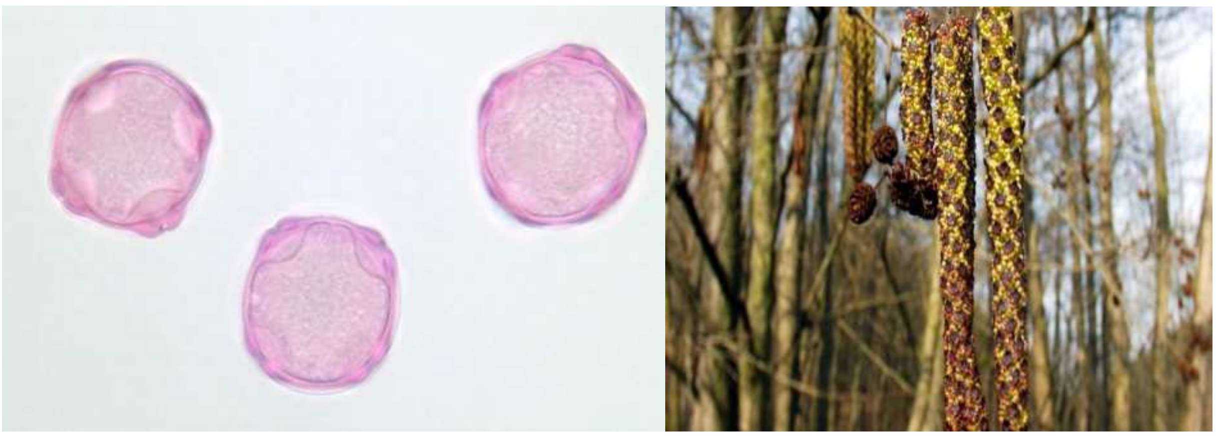

Figure 9. Alnus incana

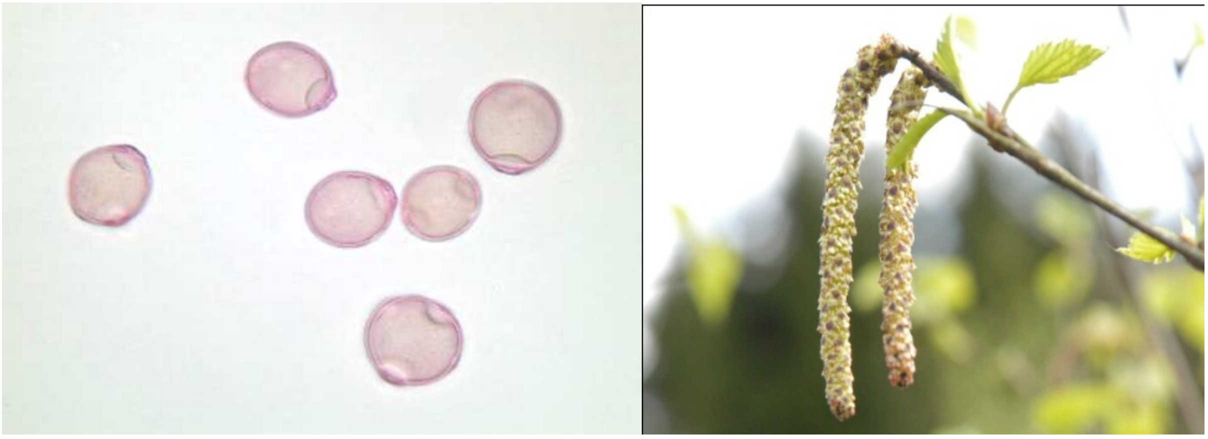

Figure 10. Betula verrucosa

Figure 11. Corylus avellana

Figure 12. Quercus alba

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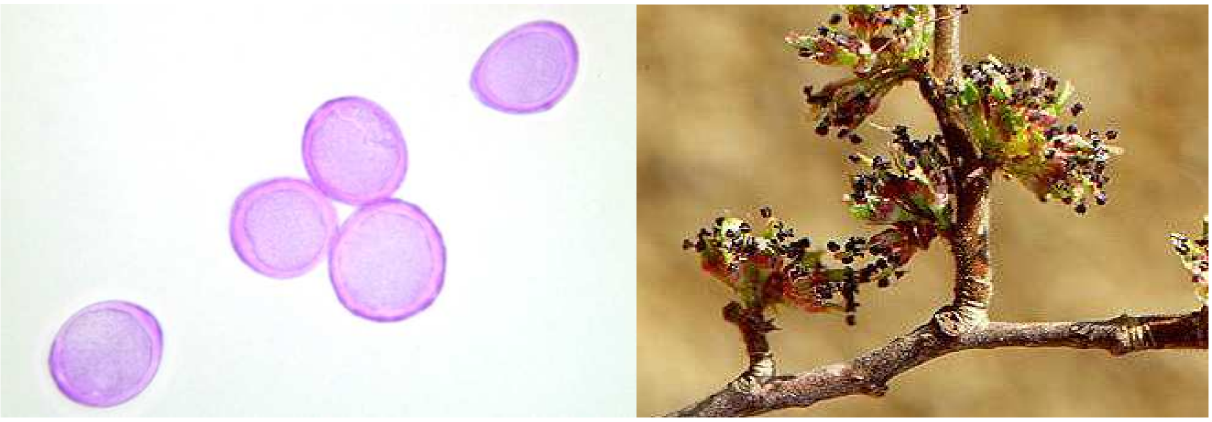

Figure 13. Ulmus Americana

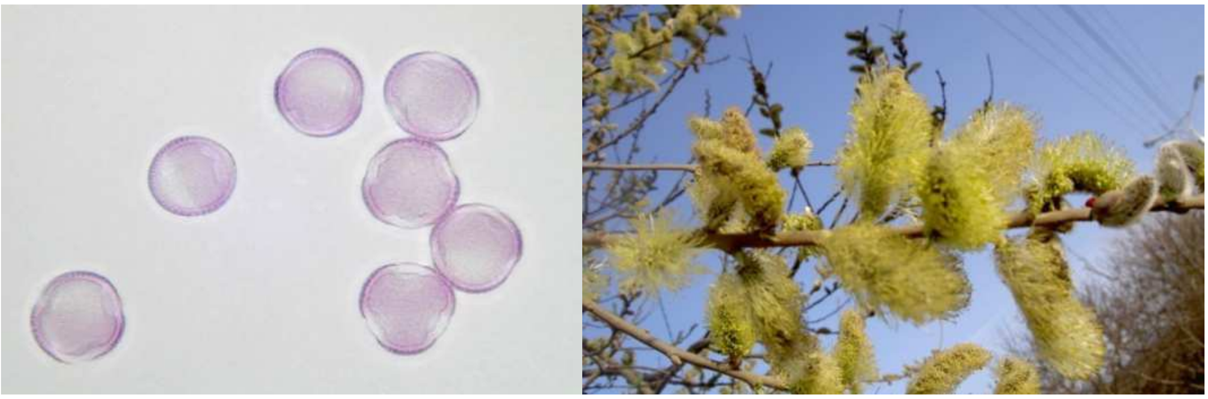

Figure 14. Salix caprea

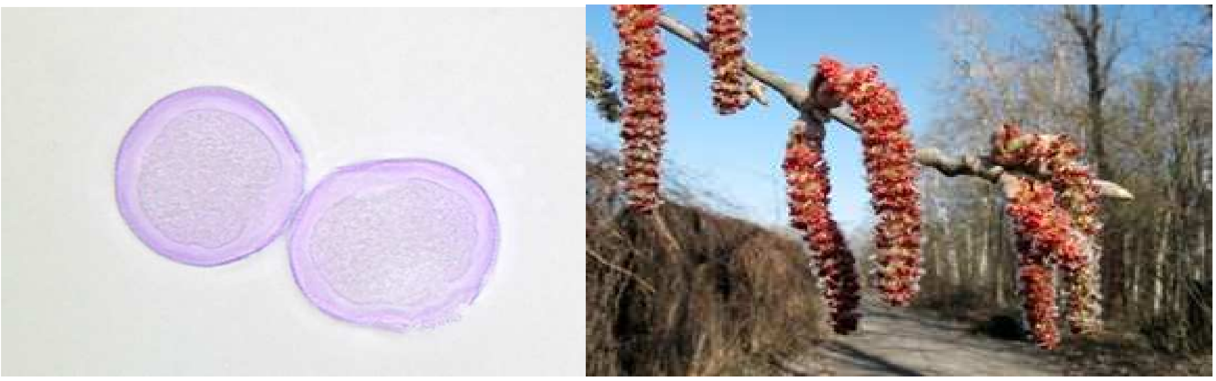

Figure 15. Populus deltoids

Figure 16. Acer negundo

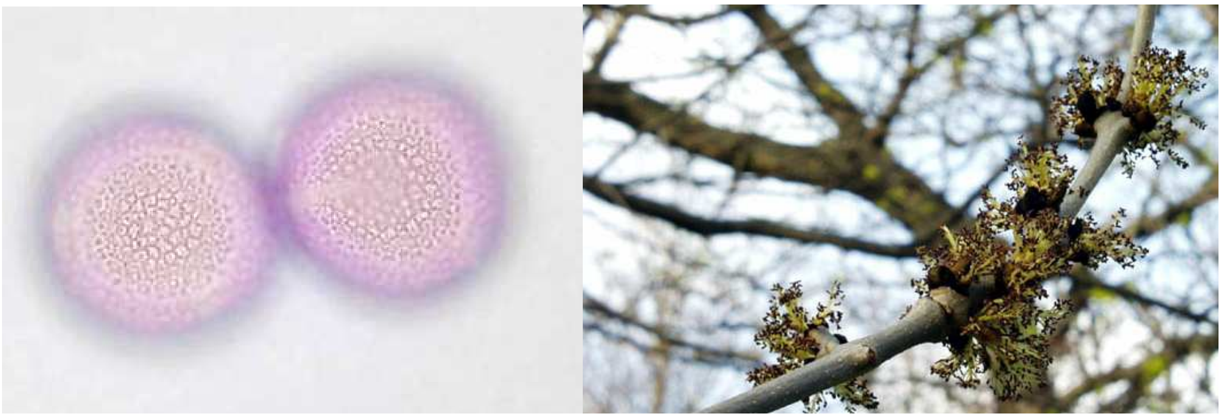

Figure 17. Fraxinus Americana

There is a structural homology between allergens of trees pollen, and it is expressed much more weakly, than the existing affinity of allergens of grass pollen. Therefore, the patients who have an increased sensitivity to the birch pollen react at the same time to the pollen of hazel and alder.

The coniferous plants produce the pollen in large quantities, but its allergenicity is lower because the diameter of pollen grains is 30 to 100 microns.

The birch pollen has the most evident allergenic activity among the analogs – the pollen of deciduous wind-pollinated plants-because it contains about 40 proteins, the 6 of which have the properties of allergens [11].

The development of technology of various recombinant allergens production has revealed that the common allergens of protein nature (e.g. "panallergens", Bet v 1 protein and Bet v 2 birch profilin) are responsible for cross-reacting of allergens of spring trees pollen [11].

The main taxa of cereals (Poaceae) (Fig.18):

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1. Dactylis glomerata (Cocksfoot)

2. Festuca elatior (Meadow fescue)

3. Phleum pratense (Timothy)

4. Poa pratensis (Meadow grass)

5. Agrostis stolonifera (Redtop, Bentgrass)

6. Bromus inermis (Brome grass)

7. Secale cereale (Cultivated rye)

8. Holcus lanatus (Velvet grass)

9. Alopecurus pratensis (Meadow foxtail)

10. Maize (Corn)

11. Arrhenatherum elatius

The main characteristic of the cereals pollen is its spherical, oval or elliptical shape. There are no many detailed species and genera definitions. But pollen grain has always one pore (Fig. 18) and a smooth surface. The size of the cultivated cereals pollen is usually larger than of wild one and ranges from 25 to 75 microns [4].

Eleven groups of major and minor allergens could be defined among the cereals [12, 13].

The allergens of the 1st group (Dac g 1, Poa p1, Phi p 1, Hol I 1) are glycoproteins with a molecular weight of 31-35 kD, and they represent major allergens with a high immunogenicity. They are homologous between different types of the cereal herbs in 90%. They bind with high affinity with asIgE (allergen-specific immunoglobulin E) and cause severe sensitization of the patient.

The allergens of the 5th group (Dac g 5, Poa p 5, Phi p 5, Hol I 5) have molecular weight of 27-33 kD. They are identical to the 1st group on a spatial configuration of amino acids (isoforms) and are major, because of their cross-stimulation of asIgE synthesis from 65% to 85%.

The allergens of the 2, 3, 4, 6, 7, 10, 11, 12 and 13 groups are the minor allergens of the cereals pollen. They are also homologous to each other. The sizes of the allergens of the 2 and 3 groups (Dac g 2, Dac g 3, Poa p 2, Phi p 2, Phi p 3, Hol I 2) to 1-12 kD are non-glycosylated proteins, which are homologous in 85-90% between species and have 15% of immunogenicity, causing the expression of asIgE in 40-60% of patients.

The 4th group of allergens (Poa p 4, Phi p 4) is represented by glycoproteins with α-helical and β-foliated structure having a molecular weight of up to 50-67 kD. Sensitization to them is detected in 80% of patients, but quantitatively the asIgE synthesis is less than to allergens of the 1st and 5th groups. The group Poa p 6 and Phi p 6 have cross-activity with Poa p 5 and Phi p 5 in 60-70% of patients, but they are not allergen-specific for the grass family.

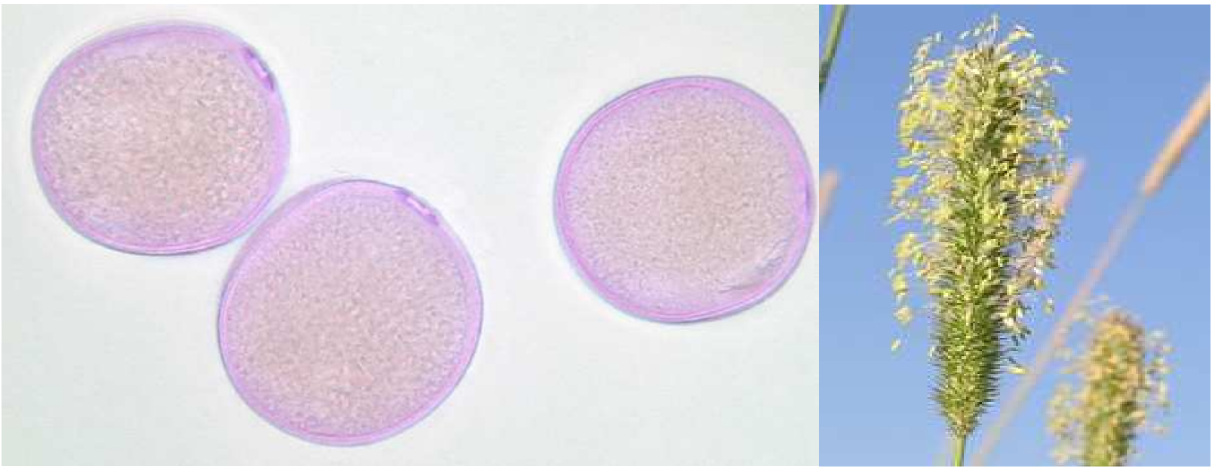

Figure 18. Poaceae. Phleum pratense.

The 7th group of allergens (Dac g CBP, Poa p CBP, Phi p 7) has a molecular weight of 8-12 kD, causes a sensitization in 10% of patients, and has a high immunogenicity. However, they are not very often recognized as minor allergens in the periodical literature. The minority of the allergens of the 10th group is associated with a low molecular weight of 12 kD. Less than 5% of patients are sensitive to them (Lol p 10, Poa p 10). The 11-13 groups of proteins (Dac g 11, Phi p 11, Poa p 12, Phi p 12, Phi p 13, Lol p 12, Fes p 13 et al.) The 12th group is represented by profillins. They have low allergenicity due to the molecular weight of 18 to 50 kD. From 15 to 55% of patients are sensitized to them [14, 15, 16].

The main taxa of weeds (Chemopodiaceae+Amaranthaceae):

1. Ambrosia elatior (Common ragweed)
2. Ambrósia artemisiifólia (Radweed) (Fig.18)
3. Ambrosia psilostachya (Western ragweed)
4. Ambrosia trifida (Gigant ragweed)
5. Artemisia absinthium (Wormwood) (Fig.20)
6. Artemisia vulgaris (Mugwort)
7. Atriplex canescens(Orach) (Fig.21)
8. Taraxacum vulgare (Dandelion)
9. Helianthus annuus (Sunflower)
10. Matricaria chamomilla (Camomille)
11. Urtica dioica (Nettle) (Fig.22)

The most aggressive allergen in the southern part of Europe and Russia is ragweed (Fig.19). It is also common in the North, South, Central America, Japan, Africa and the CIS countries. The population morbidity of the ragweed pollinosis in the Southern regions of Russia (Rostov region, Stavropol and Krasnodar territories)is from24% to38%. The spread of ragweed in the South of Russia began from the Stavropol territory. The Stavropol territory is located in the zone of boundaries favorable for the development of the quarantine weed of ragweed. 2.5 million hectares of land had been affected in the Stavropol territory since 1999 (according to the state inspection for plant quarantine of the Stavropol territory).

For the first time in the USSR the ragweed was found by the botanist S.G. Kolmakov in 1918 near Stavropol. Its seeds were brought in 1916-1917 by the railway builders among whom were the Americans. The ragweed spreads extremely quickly in the Krasnodar and Stavropol territories. Its advance on the North is limited by the duration of daylight hours and temperature factors.

In its homeland, this plant has more than 30 species. There are several varieties of ragweed: dwarf Ambrosia elatior, giant Ambrosia tritida and Ambrosia psilostachya. There are 2 common types on the Stavropol territory: Ambrósia artemisiifólia and three-separate and Ambrosia trifida. This annotinous spring weed, reproducing by seeds, is a light-, heat-loving, and wind-pollinated plant. This plant produces up to 1, 000 seedlings per 1 square meter. One bush can give 88.000 seeds which remain in the soil till 4-5 years. The windy weather, typical for Stavropol territory, contributes to the spread of pollen over distances of 20-30 km.

The ragweed pollen grains are round, of prickly sculpture, with the size of 23-24 microns and a molecular weight of 37 kD (Dalton), and they contain 5 major allergens (epitopes). For comparison, the orach pollen is 35 kD, the wormwood pollen is 19 kD, and the sunflower pollen is 14 kDa. The ragweed pollen contains two main antigens – the antigen E and the antigen K. The antigen E is 200 times more active than the antigen K [4].

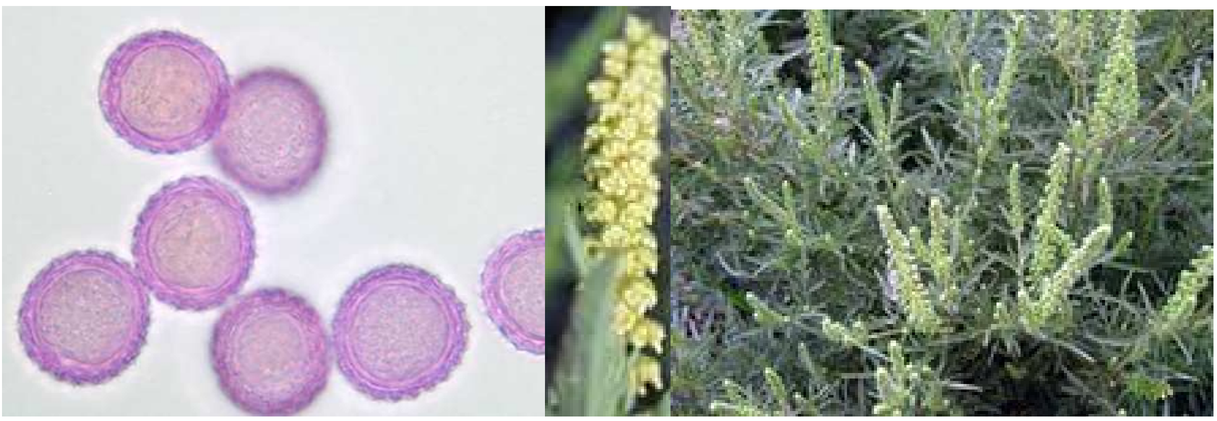

Figure 19. Ambrósia artemisiifólia

The weed pollen has also high homology and cross-allergenic properties. The co-sensitization between ragweed and wormwood among the patients is characteristic in 93% of cases. The major allergen of ragweed is Amb a 1 (E) and Amb a 2 (K) with a molecular weight of 38 kD. The minor allergen of ragweed is profilin with low Mm=11 kD. The major allergens of wormwood include Art v 1, Art v 2, Art v 4, Art v 5 and Art v 6 (Mm=35-67 kD). 62% of the patients with ragweed pollinosis are sensitized to them [17].

Figure 20. Artemisia absinthium

Figure 21. Atriplex canescens

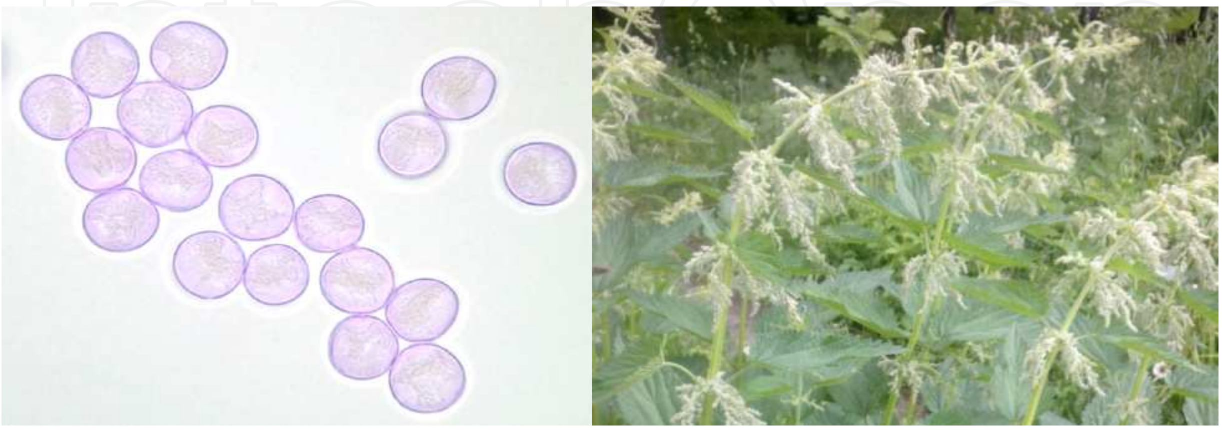

Figure 22. Urtica dioica

Depending on the climatic and geographic features of the region, it is appropriate to include in the calendar more information about plants flowering, the pollen of which is logged in the air in significant quantities. The calendars of plants flowering help the allergist to compare the clinical symptoms that develop in a patient depending on the season of the year and the place where he resides, rests or works.

4. The influence of ecology on morphopalinological properties of the airborne allergens

Due to the deteriorating environmental situation, there is a variability of allergenic properties of pollen. In recent years, there is evidence that the chemical compounds that pollute the environment, can change the allergenic properties of the plants pollen and, as a consequence, lead to the formation of new properties and combinations of the airborne allergens.

The major pollutants contained in the air are nitrogen oxides (32.3%) and hydrocarbons (24%). Harmful emissions from motor transport made 359 thousand tons or 85% of the total emissions in 2007-2008, and increased by 20% in comparison with 2006 [19]. In the structure of emissions from motor transport 75.4% accounts for carbon monoxide, 13.7% for hydrocarbons, 7.9% for nitrogen oxides, 1.2% for carbon black [19].

In 2011 we estimated the presence in the tests of spring atmospheric rain the changes in morphological features of pollen and technogenic particles. The changes were mainly observed in the pollen of Acer n. and Salix l, the trees growing along the motorway of the city of Stavropol (Fig. 23) [18].

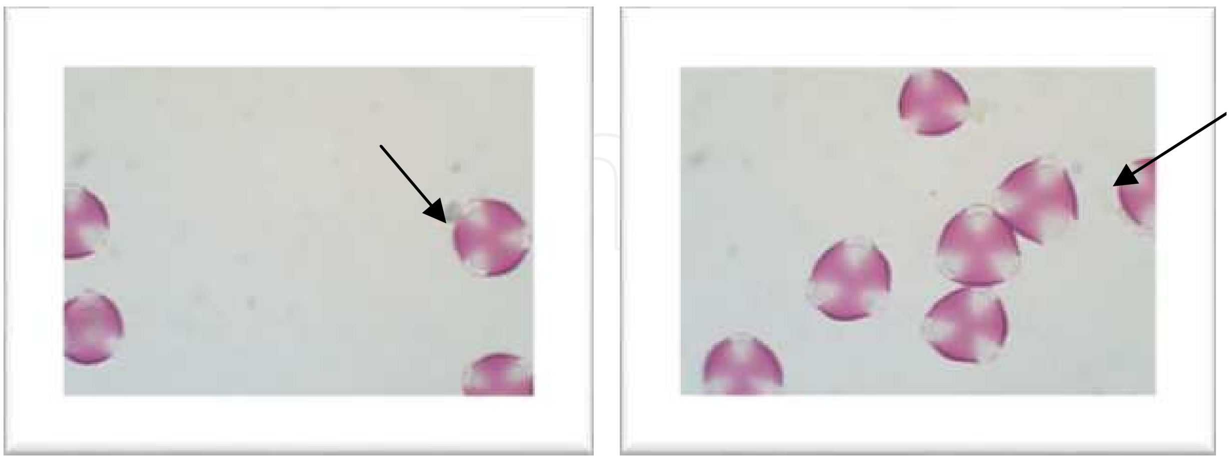

Figure 23. Salix sp. along the motorway. The arrow indicates the pollutants.

The same morphological changes of pollen are shown by Dr. Dzyba O. F. on the pollen of gymnosperms (Pinus sylvestris) growing in the city of St. Petersburg (Fig.24) [20].

Figure 24. The polymorphism of Pinus sylvestris.

In the conditions of the environmental pollution the plants pollen dominating during a pallination season, is capable to transfer microcells of a technogenic origin, forming the increased antigenic activity. The severity of clinical symptoms of respiratory allergies in patients, in addition to the weather conditions, is caused by the simultaneous effect of non-specific trigger and specific cause-significant factors on the upper airways mucosa. Thus, the safety of the living environment is an essential component of human ecology, as a key factor in reducing the risk of development of allergic diseases.

5. The insect allergens

5.1. House dust mites (Acarida)

Dust is the main multicomponent inhalation allergen. The allergen from house dust is distinguished by the complexity in antigenic composition. It consists of fungi, pollen particles, metabolic products of insects, epidermis particles of animals and humans. A powerful component of house dust allergen is also micromites Dermathophagoides pteronyssimus and Dermathophagoides farinae – the tiny arthropods like Arthropoda, invisible to the naked eye, the body diameter of which is about 0.3 mm. The number of micromites increases in autumn. These mites feed on flakes of desquamated corneal layer of human skin which is the largest part of the house dust components, and live in symbiosis with the microscopic mold fungi living in mattresses and other bedding. Mite excrements are also ideal allergens. Anti-genes of pincers rather large therefore allergic reactions to them arise not so quickly as on epidermis of cats. Mites antigens are large enough so allergic reactions to them do not occur as fast as to the cats epidermis. The allergy to house dust most often manifests itself in the form of bronchial asthma, rhinitis, and rarely-conjunctivitis. House dust and barns mites are microscopic arthropods invisible to the naked eye (). Their excrements, body parts are airborne allergens of the living premises, warehouses, barns, archives and libraries. The body diameter of an insect is about 0.3 mm. They have full-blown allergenic activity. The size of mites varies from 0.1 to 0.5 mm. They are widely spread around the globe. The normal cycle of their life is about

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65-80 days. The female mite oviposits about 60 eggs at once. The ideal habitat is an apartment with a temperature of 18-25 °C. In addition, they like increased humidity [21, 22].

House dust mite: Dermatophagoides pteronyssinus (Fig.25), Dermatophagoides farinae, Dermatophagoides microceras, Euroglyphus maynei, Blomia Tropicalis.

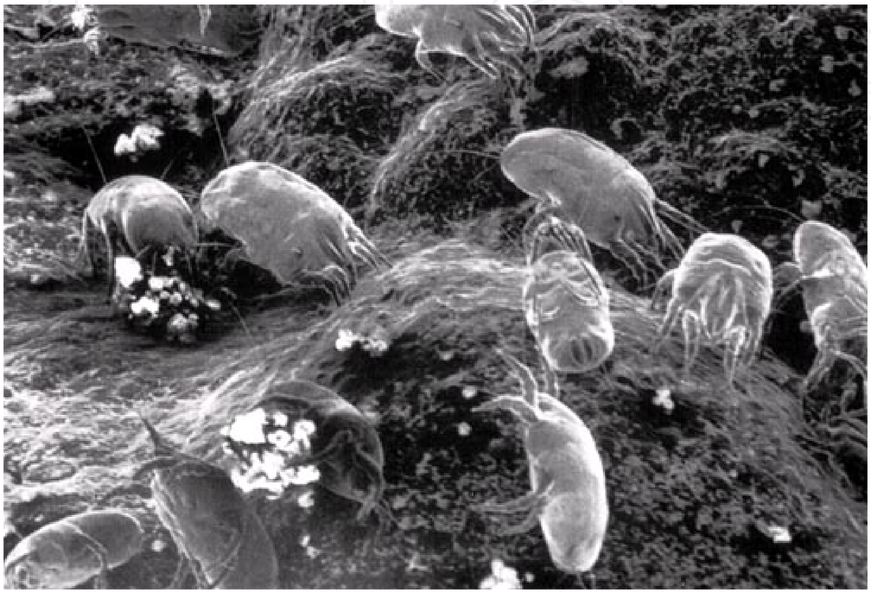

Figure 25. House dust mite. Dermatophagoides pteronyssinus

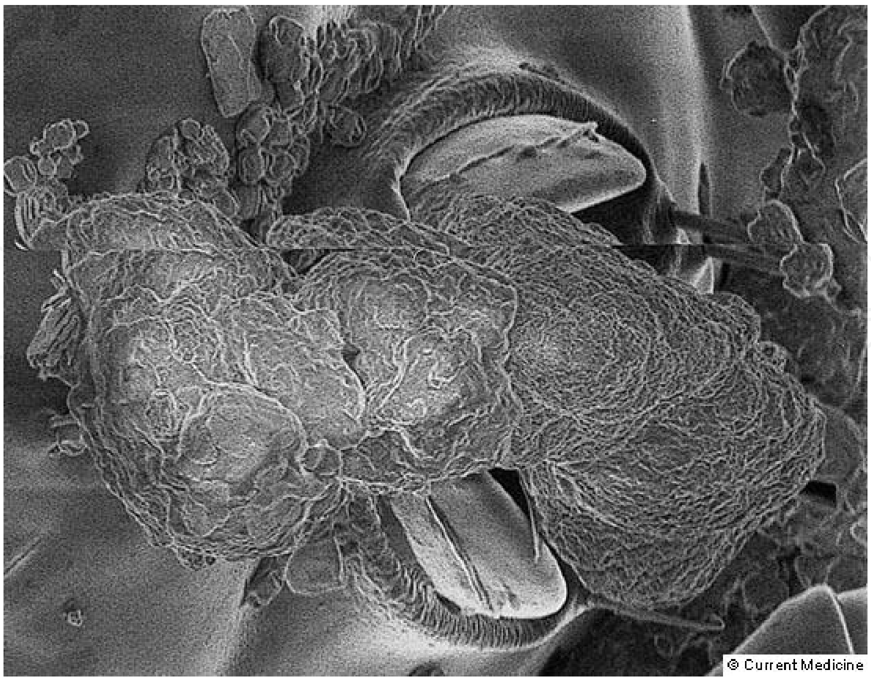

Figure 26. Mites excrements

Dermatophagoides pteronyssinus feed on flakes of desquamated epidermis of human skin which is the largest part of the house dust. Small fragments of mites (from 10 to 40 microns) and their metabolic products (especially fecal particles) have a remarkable ability to cause allergies: respiratory allergosis, bronchial asthma, allergic conjunctivitis and angioneuroticedema. The fecal balls of house dust mites contain about 13 different groups of major and minor allergens that come from the intestinal tract of insects. The most studied are the major allergens Dermatophagoides pteronyssinus-Der p 1 and Dermatophagoides farinae-Der f 1. The polypeptide chain of the main allergen consists of 216 amino-acid remains with a N-terminal threonine. The threshold concentration for the development of sensitization in genetically predisposed to atopy patients, is the content of 92 μg/g of dust of the major allergens of mites. Approximately 500 mites per 1 gram of dust provoke attacks of bronchial asthma in sensitized patients.

Storage mite: Acarus siro (Fig.27), Lepidoglyphus destructor, Tyrophagus putrescentiae, Glycyphagus domesticus.

Figure 27. Acarus siro

The flour mite damages grains of cereals, oil-bearing plants, legumes, preferring flour to cereals, fodder and dried vegetables, fruits, medical and tobacco raw materials, spices, leather, cheese, sausage, egg powder, fish and meat bone flour. Its body is oval and whitish, the body surface is shiny, legs and mouthparts are brownish-red. The body length of male mite is up to 0.5 mm, female mite is up to 0.7 mm [23]. The mite often penetrates into the embryo, forming a latent form of infection, and, first of all, dangerous for seed grain. In most cases, the patients sensitized to flour mites work in the agricultural industry and/or directly with the grain. A detailed medical history is very important to clarify the diagnosis, since a particular profession (a librarian, an archivist, an agronomist or a housewife) promotes sensitization to different kinds of mites and, therefore, the individual selection of immunotherapy.

Other representatives of Arthropoda are stinging and not stinging insects. As the airborne allergens, the insect allergens can be fragments and products of insects' vital activity. The patients, whose professional activity is connected with insects, are usually sensitized to them: the beekeepers, the persons living near apiaries, the workers of fish-farms, insectaries and granaries, entomologists and other. The known insects causing an allergy are cockroaches, gnats, caddis flies, moth, flies, mosquitoes, Daphnia. Very often the patients sensitized to mites can cross-react to the above-mentioned allergens.

The cross sensitization can be caused by Der p 10 (tropomyosine), the minor allergen for patients with the allergy to the house dust mites [22]. However it may point to risk of development of allergic reactions to Crustacea or snails. The cockroaches also have a major allergen Bla g 2 and cross-allergen tropomyosine Bla g 7 which indicates the risk of allergic reactions to Crustacea (most often to the shrimps) [24]. In their turn, shrimps and other Crustacea also contain other clinically relevant allergens: sarcoplasmatic calcium-binding protein and argininekinase [25]. The most important airborne allergens for such patients are parvalbumins (Gad c 1, Cyp c 1). These are major allergens of fish, stable to the action of temperatures and digestive enzymes. Parvalbumins have a high degree of cross-reactivity in which patients sensitized to one of parvalbumin may react to other fish parvalbumin. It may be a river, sea, ocean, white or red fish. There are cases of severe allergic reactions of patients on inhalation of vapours with fish parvalbumin through casual contact in everyday life (eating places, hotels, etc.) [26].

The special populations of patients with frequent and prolonged contact with hymenopterous insects are beekeepers, their families and their neighbors. The systemic allergic reactions may be developed not only after insects stinging, but also on inhalation of the body parts and the products of their activity [27]. As a rule, these reactions are caused in patients sensitized to the major allergens Api m 1 of a honey bee, Ves v 5 and/or Ves v 1 of a wasp. The allergic cross reaction between the bees and wasps allergen may be due to the carbohydrate part of glycoproteins (CCD)[28]. The poison and bodies allergens of the most Hymenoptera contain the CCD, which are responsible for the cross-IgE-reactivity between bees and wasps allergens [29].

6. The main fungal allergens

The role of fungal allergens in the structure of allergic diseases is very important. The mycogenic sensitization arising due to the long contact of a human body with allergens of microscopic fungi, plays an increasingly important role in people's lives, particularly the residents of megapolises [30]. Aeroallergens, which include fungal spores and fungal cell wall components, surround us everywhere in everyday life, at work places, in nature. By means of scratch test method, the frequency of sensitization to allergens of house dust mites, mycelial and yeast fungi was investigated among the patients of the allergic center. It was revealed that 12, 69% of patients showed hypersensitivity only to one of the allergens. 87, 31 % of patients had combined forms of sensitization to two or more allergens. It is noted that the sensitization to fungi allergens (82, 84%) in comparison with the occurrence of the sensitization to house dust mite allergens (67, 16%) is found more often [32, 33, 34, 35, 36].

All stages of micromycetes allergens intake into the organism have been studied up to the present day, and the mechanisms of their influence on the immune system have been proposed. There also have been conducted large-scale epidemiological researches; the role of fungal allergens in the pathogenesis of a number of allergic diseases was established.

Microscopic fungi are widespread in nature, they are capable to colonize all substrates and absorb almost any organic substance. The main reservoir for microscopic fungi is soil and plant remains, where the number of fungal propagules can be up to several hundreds of thousands of CFU per gram of substrate. Due to their small size, they easily enter the bioaerosols and can be transferred in the atmosphere over long distances. The concentration of fungal spores in the air may be 2-3 orders greater than the one of pollen [38]. In certain periods of the year (from spring to autumn) the total number of fungal propagules in the air bioaerosol can be 1-2 orders greater. However, not only quantitative but also qualitative composition of fungal allergens is of great importance for the development of mycogenic sensitization. There are new ecological niches for fungi habitat due to human activities in large cities. This is mainly organic waste in landfills and production as well as bioaffected objects of urban infrastructure (emergency buildings and facilities for various purposes).

The allergy to fungi is known for a long time. For example, hay fever had been described in detail in 1819, the role of micromycetes in its etiology was shown in 1873 [31]. Currently, numerous studies have proven the value of mycogenic sensitization in the pathogenesis of allergic rhinitis, bronchial asthma, allergic bronchopulmonary mycosis, exogenous allergic alveolitis, atopic dermatitis [32, 33, 34, 35, 36]. Epidemiological researches have shown that the level of mycogenic sensitization is very significant and varies depending on the genetic characteristics of the surveyed groups of population, climatic and geographical features of their habitats-from 5% (southern Europe) to 40% (Portland, USA) for patients with bronchial asthma [32]. And in the desert environment (Kuwait) there was the indicator of 46% among the surveyed patients with asthma [37].

In July 2014 the number of registered non-food fungi allergens, the list of which is available on the website www.allergen.org, reached 108, according to the Subcommittee on Nomenclature of allergens of International Union of Immunological Societies (IUIS).

Some strains of micromycetes can synthesize up to 40 macromolecules connecting IgE [39]. The vast number of the registered allergens belongs to 5 genera-Aspergillus, Alternaria, Cladosporium, Penicillium, Malassezia (Fig. 28-31), while the symptoms of respiratory allergies are connected with about 80 genera of fungi [40].

The sensitization of a macroorganism occurs, in particular, due to the action of proteases which can degrade proteins providing the impenetrability of the epithelial cell barrier. Partial proteolysis of these proteins causes a disturbance of the monolayer structure and the flow of allergenic material through it. The desquamation of epithelial cells was observed in the processing of cell cultures by means of proteases A. fumigatus. Using various inhibitors, the researchers defined a role of serine proteases in the process of destruction of the cell layer [41]. Also, the influence of fungi allergens on the immunological mechanisms operating on the principle of negative feedback is mentioned in a number of works.

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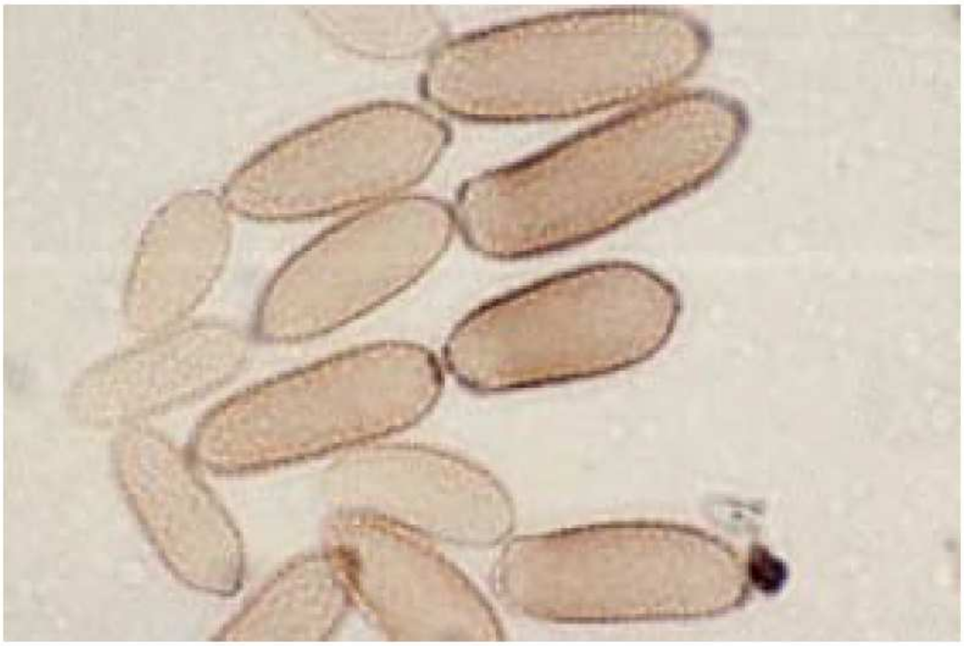

Figure 28. Cladosporium

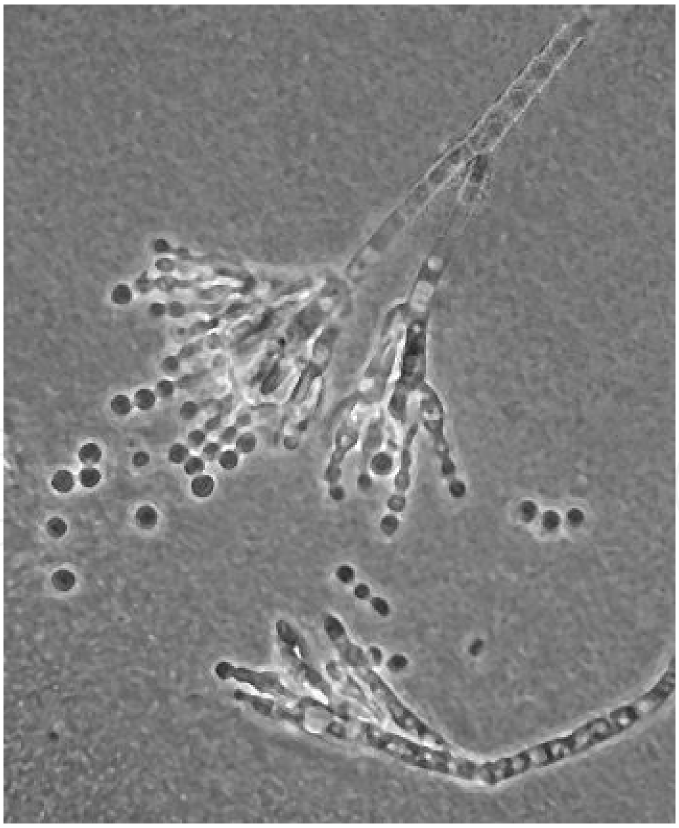

Figure 29. Penicillium

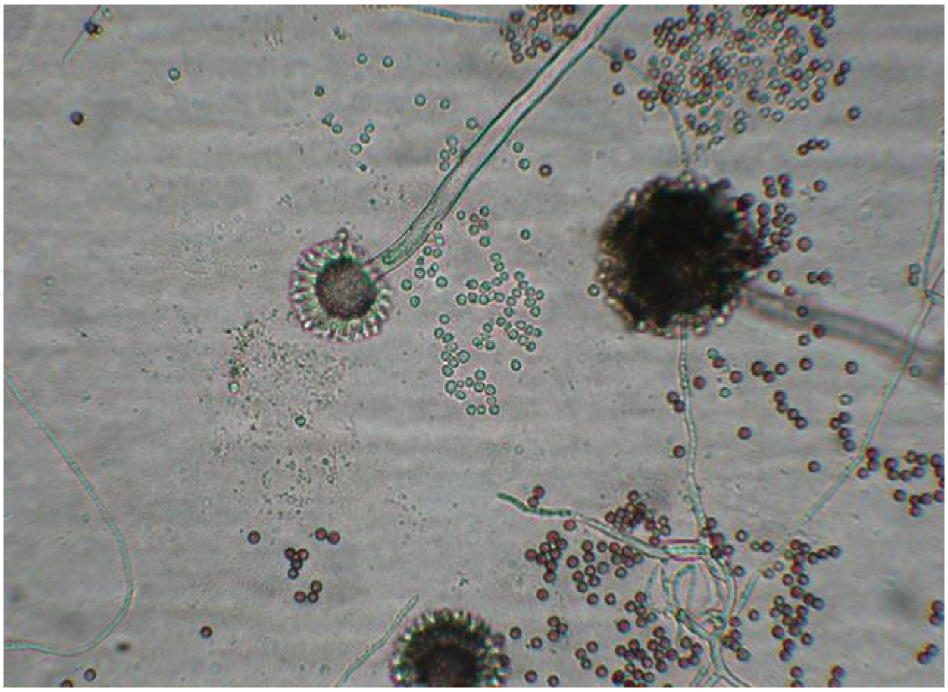

Figure 30. Aspergillus

Fungi allergens possessing the proteolytic activity, as well as proteases of dermatophagoidic mite allergens are capable to break protective barriers of an organism independently. They are able to overcome the immunological tolerance, and are recognized by immunocompetent cells, followed by the elaboration of specific reaginic antibodies and the induction of release of the allergic reaction mediators. In this regard, we should note the difference of fungal and plant allergens. It is known that there is an absence of proteases among known plant allergens. At the same time it is also known about high proteolytic activity of pollen plant extracts [42]. Obviously, there are unidentified proteases in the composition of these extracts and, presumably, they provide transportation and adjuvant functions, but they are not allergens.

To understand the features of a mycogenic sensitization we should into consideration theform in which allergens get into the respiratory tract. The inhaled allergens of plants and fungi, as opposed to domestic or epidermal ones, are present in the aerosol products primarily in encapsulated form. They are the pollen of grasses and trees, spores / conidia of fungi. Exceptions arise after the rain when there might be emission of contents of the swollen pollen grains in the form of submicroscopic particles [43] and in cases of technogenic emissions. Conidia, on the average, have much smaller size than pollen grains. The diameter of micromycete conidia of such widespread genera as Penicillium and Aspergillus doesn't exceed 2-5 microns. The exception is Alternaria with its large macroconidia, which, however, may be found in aerosols in segmented form (Fig. 30).

The antigen-presenting function is poorly expressed in pulmonary macrophage. To initiate an immune response, spores enclosed in hard envelope must have time to release a sufficient amount of sensitizing material into the environment before macrophages phagocytize them. This material containing the protease must penetrate the epithelial barrier and reach the

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Figure 31. Alternaria

dendritic cells and Langerhans cells in the airways or dendritic cells in the alveolar epithelium. It is necessary to take into account that the respiratory part of the lungs is the most tolerant due to the small number of antigen-presenting cells. At the massive inflow of antigenic material, the condition of tolerance can be overcome with the emergence of IgG-mediated exogenous allergic alveolitis. As for the speed of extraction of allergenic material from the spores, it was shown during the study of bazidiospores that it depends primarily on the thickness of the envelope [44].When studying the effect of conidia germination of several mitospore fungi on their excretion of detected immunochemical allergens into the environment, the Australian authors found that small and durable conidia of such fungi as A. fumigatus and P. chrysogenum, only slightly produce allergens without prolonged pre-incubation in a humid environment [45, 46].

In conclusion, it should be noted that, despite the pronounced "aggressiveness" of fungal allergens, there are constraints allowing a healthy organism to stand a natural background of mycoallergens with no harm. In case of the allergen load rise or in the development of atopic states the risk of a mycogenic sensitization significantly increases.

7. The airborne allergens of animals

The airborne allergens of animals are wool (hair), epidermis (Fig. 32), dried urine, saliva, and feces. The prevalence of an allergy to epidermis of pets is a worldwide growing problem of public health as a death rate in consequence of allergic diseases has disproportionate impact on socially and economically unprotected populations, in particular, on children [48].

Figure 32. Cat's hair

The allergy to cats epidermis is one of the most widespread forms of allergic diseases in the USA and Europe in 10-15% of patients suffering from allergic rhinitis and (or) bronchial asthma (WAO 2011). Cats are the major source of the allergen Fel d 1. Though there are few molecules of the allergens in the extract of cat dandruff. The most significant of them is the Fel d 1. At the same time, approximately 90% of people with allergies to cats have an increased level of IgE specific for the protein. The level of allergen (secretoglobin) Fel d 1 is significantly higher in houses where the cats live [47]. In houses where the cats have never lived, there is a direct relationship between the level of allergen in the house and the number of domestic cats in the immediate environment, in general. The allergen Fel d 1 is also present in many public places in a concentration that may cause the development or worsening of symptoms among the people with allergies. This is particularly relevant and problematic for school children (Morris 2010). The other allergen associated with asthma patients is lipocalin Fel d 4 [47, 48].

Typically, many patients are co-sensitized to several species of animals. The cross activity of pets is caused by the following main allergens: Mus m 1, Equ with 1, Can f 1, Can f 2 and Can f 5 [50]. However, the cross-reactivity between animals is poorly understood on the molecular level. The biological variability of a source of animal allergens does not always allow to identify the cause-significant allergen of the patient by means of a simple skin test. 38% of patients were revealed sensitivity to Can f 5-allergen from male dogs prostate (33) and approximately 60% of patients are sensitized to Can f 1, Can f 2-epidermal allergens of animals. As Can f 5 in low concentration may be found in the dog's hair, it is difficult to reveal the sensitivity of the patient to this allergen by means of skin tests [49]. That explains the doctor's recommendations to remove completely an animal and the products of its life activity from premises and the surrounding territory whenever possible, and the absence or existence of hair on an animal doesn't matter. The airborne allergens of animals are conservative (stable) and even after the elimination they are present in the premises for a long period of time, both independently and as a part of house dust.

The special place is given to the study of a professional allergy of persons employed with animals: veterinarians, laboratory and vivarium staff, factory workers, farmers, etc. The development of allergic reactions (allergic rhinitis, conjunctivitis, urticaria, bronchial asthma and atopic dermatitis) is observed in 10-30% of workers. All of them have contacts with animal allergens on production. In 2010 the Spanish scientists showed a high sensitization of workers to the hair of various animals (a rat, a mouse, a guinea pig, a rabbit, a hamster, a dog, a cat, cattle, a goat and a horse) by means of the skin test. 62% of them had at least one positive skin test to the hair of various animals. Thus, the statistically significant association with the age, the length of service, the allergic history, the clinical manifestations and the level of serumal IgE wasn't proved [51].

8. Toxicoallergic aerosols

One of the reasons for the growth of new cases of respiratory allergies among people of working age is the occupational exposure to toxic and allergenic aerosols. Toxic airborne allergens are able to penetrate into the respiratory system in the form of vapor and smoke in the pre-heating, grinding to dust or in combination with gas components and polymeric binders. These methods are applied on production and service for packaging food products, construction, welding, production of household chemicals and many other things.

For example, a special place is occupied by phthalates formed from polyvinyl chloride (PVC), the products of which are widely distributed in living and working environment. During the processing, packaging and stacking of various materials the high concentrations of mono-and diphthalates in combination with formaldehyde, formic acid, acetaldehyde, acetic acid and benzoic acid penetrate in the breathing zone of workers. These substances are known for their toxic and allergenic properties. Getting into the respiratory tract, they can cause irritation of the mucous membrane as well as the damage of the epithelium of the upper airways, the bronchial tree, the mucous membrane of the eye, development of edema, inflammation, and violation of the mucociliary clearance. This leads to the diseases of the upper airways, the formation of the syndrome of bronchial obstruction and bronchial asthma (BA).

The mechanism of development and the peculiarities of the clinical course of respiratory diseases caused by toxicoallergic aerosols are still not clear. This is due to the low molecular weight and the interaction with proteins of the skin and mucous membranes. The experimental data in animals demonstrate the ability of toxicoallergic aerosols to cause the development of airway inflammation of immune and non-immune nature (Larsen ST, 2004; Frederiksen H, 2007). The in-depth study in this area has not been conducted [51].

The most well-known toxico-allergic substances (low-molecular weight substances, haptens) which may contribute to the development of allergic respiratory diseases of humans are given below (Table 3).

Name of the group	Airborne allergens	Items containing this substance
Aldehydes	Formaldehyde, acetaldehyde, Formaldehyde resin, para-tert-butylbenzaldehyde	Means for processing of fabrics, preservatives, solutions for metal processing, adhesive substances/glue, plastic, detergents, construction materials, corrosion inhibitors; fillers used in industry; chemicals used in flooring; paints, varnishes, impregnating products; printing ink, polishing materials, binders, surfactants, deodorants
Dichromate	Potassium dichromate	Cement, chrome leather, petroleum products, textile paint, antiseptics, preservatives, cosmetics, mortar, printing industry, detergents, concrete, photoreactants
Aromatic substancec	Cinnamaldehyde (1%)Cinnamic alcohol (1%)Eugenol (1%)Geraniol (1%)Hydroxycitronellal (1%)Isoeugenol (1%)Evernia Prunastri (1%)	Perfumes, eau de toilettes, colognes, powder, soap, shampoos, shower gels. Essential oil. Detergents. Aromatic candles. Spices, seasonings
Rosin, turpentine		Perfumes and cosmetics, glue, spices, wood resin. Rosin containing dental materials. Glue, paints, varnishes
Metals:, cobalt, chromium, palladium and their connections, nickel	Nickel sulfate, Cobaltchloride, Palladium chloride	Nickel plated items used in shipbuilding, aerospace and automobile industries
Derivative thyuram	Tetramethylthiuram disulfide (0, 25%)Tetraethylthiuram disulfide (0, 25%)Tetramethylthiuram monosulfide (0, 25%)	Catalysts used in the vulcanization process in the production of rubber items. Pesticides, prints, tubes, glue. Emulsion for the treatment of scabies. Fungicides, adhesive substances, paints; pharmaceutical substance used in veterinary medicine
A mixture of mercaptans	N-cyclohexen-sotatila sulfenamid (0, 5%)Mercaptobenzothiazoles (0, 5%)Morpholinyl mercaptobenzothiazoles (0, 5%)	The catalysts used in the vulcanization process in the production of rubber items
Phenylendiamine	Paraphenylenediamine	Hair dye, textile paint, ink for printers, photoreactants, lubricants, oil, gasoline (petrol); antioxidants and catalysts used in the manufacture of resins and plastics
Quaternium-15	Quaternium-15	Cleaning and polishing substances. Cosmetics, skin care and hair care products, latex paint, the solutions used in the processing of metals
Ethylendiamine	Ethylenediamine dihydrochloride, hexa-methylenediamine	Corrosion-resistant materials

http://dx.doi.org/10.5772/59300

Name of the group	Airborne allergens	Items containing this substance
Epoxy resin	Epoxy resin	Materials of plastic, adhesive materials. Covering of household items, adhesive tape, paint, corrosion-resistant, water-resistant, insulating materials, sports goods. The materials used in shipbuilding, aerospace and automobile industries. It Can be used in the preparation of specimen for electron microscopy
Esters of phthalic acid	phthalics	Plastic, polyethylene
Antibiotic drugs	Penicillin, neomycin,	antibiotic production

Table 3. The list of toxico-allergic substances in aerosols

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