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7 Occupational respiratory diseases in the rural environment

Florin-Dumitru Mihălțan, Agripina Rașcu, Alexandra Rașcu, , Andreea Vlădău, Vali Coșei

7.1 Occupational allergic rhinitis in the rural environment

The nose, functioning as a gate to the respiratory tract, is the interface between the outer and the inner environments, and it is permanently exposed to air contaminants and therefore has to react to all environmental changes and various stimuli. In the process of breathing, the air that comes in is warmed up, cleaned and kept moist in the nose.
Rhinitis is defined as irritation and inflammation of the mucous membrane inside the nose. Common symptoms include: rhinorrhea, sneezing, nasal obstruction, nasal pruritus.

Classification: depending on the onset of symptoms and the production mechanism, the following types of rhinitis are known:

1. Depending on the onset of symptoms:
   - Acute or chronic
   - Episodic rhinitis: episodic response to respiratory irritants, cold air;
2. Depending on the production mechanism:
   - Allergic: seasonal rhinitis (hay fever or pollinosis) and perennial allergic rhinitis;
   - Non-allergic: infectious rhinitis, perennial non-allergic rhinitis (accompanied or not by eosinophilia), atrophic rhinitis, vasomotor rhinitis;

From an epidemiological point of view, the prevalence of rhinitis has grown a lot in the past years, affecting 9-42% of the global population, as a consequence of pollution and modern civilization. (1)

Professional rhinitis is caused by constant exposure to substances at the workplace (pollens, powders, detergents, etc.). Clinical manifestations become apparent after months or even years since the start of exposure.
Etiology: it a disease induced by occupational risk factors, which usually also cause asthma (3) (Table 1-4.1)

Table 1-4.1*: Risk factors for occupation rhinitis in rural environments*

Occupational allergens	Occupations at risk
POLLEN: Usually causes seasonal (regular) allergic rhinitis The risk of developing rhinitis as an allergic response to pollen is higher in warm, dry and winding environments. Pollen of wild graminea (poaceae) • poaceae cover more than 20% of the dry land	 - farmers (11% of them) - horticulture workers - gardeners - zootechnicians - workers in agro-plant science Agricultural workers (11% of them)

Occupational allergens	Occupations at risk
• poaceae cause some 80% of the total number of cases of seasonal rhinitis; Ambrosia pollen (Artemisfolia major, minor)	
FUNGI (THEIR SPORES): Chladosporium sphaerospermium Alternaria- In Romania (rare) Aspergillius fumigatus, flavus oryzae Penicillium pallidum(rare) Fusarium Candida albicans	- tomato growers - hay handlers - oilseed rape and wheat growers - millers, bakers, pastry bakers (fungi in wheat flower) Tomato growers • shepherds- cheese makers • corn growers -animal technicians - farmers - horticulture workers
ACTINOMYCETES : thermophilic actinomycetes	- workers in silos - farmers
HAY, STRAWS, FODDER Allergens through: cereal crops, molds, thermophiles, actinomycetes, dust mites)	- farmers and animal breeders (the use of feeds and fodder) - gardeners (grass mowing) - silo workers
PLANT ALLERGENS (wheat, rye, oat, corn, soy, castor-oil plant) Cereal flowers (proteins with high molecular weight) gramininea	- farmers - animal breeders
ANIMAL PRODUCTS (lactoser, casein, egg protein)	- farmers
ARTHROPODES (dust mites in cereals, storage dust mites, dust mites in tree bark)	- farmers - silo workers - forestry workers
SERICIN: a component of natural silk	- silk worm growing
BEE ANTIGENES: from wax, honey, propolis, pollen, wings, needles and venom	- beekeepers -horticulture worker - gardeners
MICROBIAL ANTIGENS	- zootechnicians - farmers - silo workers

Occupational allergens	Occupations at risk
ANIMAL ALERGENS FROM: skin appendage, hair, feathers, down, squamae, body waste Sitophillus granarius (contaminates wheat)	- zootechnicians - farmers/poultry farmers - millers - silk worm farmers - bee keepers
CHEMICAL SUBSTANCES – most of them are haptens with low molecular weight (also irritating agents) - red cedar dust - formaldehyde (fungicides, biocides, germicides, insecticides) - organophosphorus compounds (insecticides) - chloramine (disinfectant)	-forestry workers - farmers - fish farmers - silk worm farmers - mollusk farmers

Modified and added to after (4)(2) (3)

The prevalence of occupational rhinitis is unknown, and most studies associate it with occupational asthma (2).
Physio-pathological mechanisms: there are not enough well-documented studies on the production mechanism of rhinitis as singular entity; it is believed that its production mechanism is similar to that of asthma, as a preceding step (5). Therefore, the most incriminated mechanisms are usually the immunological ones (IgE mediated, IgG mediated or cellular mediated) as well as irritating mechanisms with non-specific inflammation (2).

Positive diagnosis
The clinical picture is that of vasomotor rhinitis or rhino sinusitis with an inflammatory component: rhinorrhea, sneezing, mostly paroxysmal, nasal obstruction, nasal pruritus. Sometimes it is also accompanied by: epistaxis, smell disorders (hyposmia, anosmia), pharyngeal – palatal pruritus, eye pruritus, tearing and conjunctival hyperemia, cephalea.

In patients with occupational rhinitis, there is no rule as to when clinical manifestations start to show: they may appear within a few minutes or hours after the start of the occupational activity, at the work place or at home, after work. One important element is that symptoms get better (at least in the first years after the onset of the disease) at the weekend and during vacations.
The diagnosis is based on the following elements:

- anamnesis, which highlights the presence of typical symptoms;
- examination of the eyes, years and throat, accompanied by anterior and posterior rhynoscopy, which can reveal inflammations of the nose and sinuses, hypersecretion, erosive lesions, crusts, polyps, mucositis in cavum (2);
- dosage of eosinophils in blood and nasal secretions;
- immunological testing: skin testing and IgE specific testing; this kind of testing is hampered by difficulties and limitations, one the one hand because of the lack of complete skin testing kits and, on the other, because of the high costs of such testing. The value of immunological testing has been proven for allergens with high molecular weight, but not for those with low molecular weight. (6)

NB: The presence of an atopic field revealed by skin tests and the presence of IgE total in blood does not exclude the diagnosis of occupational disease (7).

To establish the diagnosis of occupational disease, the following are important:

- anamnesis with occupational elements;
- elements telling of an occupational nature of the disease:
    - no symptoms prior to getting employed;
    - onset of symptoms months or years after the date of employment;
    - improved condition at the weekends or during vacations;
    - symptoms present in coworkers:
- proper testing at the work place;
- immunological and nasal challenge tests;
- acknowledging the existence of and exposure to risk factors;
- pre-employment medical examination and later on a regular basis;

Occupational rhinitis is often associated with: asthma, skin diseases (dermatitis, eczema), sinusitis, polyposis, conjunctivitis (8). Occupational rhinitis usually precedes the development of occupational bronchial asthma, that is why its presence must be seen as an alarm signal as to the subsequent evolution of the patient.

Therapeutic principles

Occupational rhinitis, just like non-occupational rhinitis, shall be treated in keeping with the international recommendations in the field (ARIA Guide) (11).

Prevention

In order to ensure effective prevention, the risk must be acknowledged and reduced by:

- Improving working conditions (replacing the substances known as risk factors, providing proper ventilation, etc.);
- providing the necessary respiratory protective equipment and imposing the mandatory use of this equipment;
- medical examinations upon employment and subsequently on a regular basis and a clear observance of all counter-indications (identifying atopic subjects, informing them on the risk of getting ill and professional re-guidance);

NB: The positive predictive value of the atopic field for the occurrence of occupational respiratory diseases is low, that is why the counter indication of employing atopic suspects in work places where there is a risk of developing rhinitis is not justified, either scientifically or ethically (9).

The early diagnosis and changing the work place in the case of workers suffering from rhinitis is necessary in order to avoid the aggravation of the disease and the development of bronchial asthma (5)(10). The elimination of the risk factor as early as possible after the onset of the disease can help in getting it cured.

7.2 Occupational asthma

Occupational asthma is one of the most frequent occupational diseases in the world (incidence rate 9-15%), with significant morbidity and invalidity rates (1) and entailing high costs (2). (1,3).
It is likely that the reported incidence is underestimated by up to 50% (4). Still, the number of cases of occupational asthma in agriculture is double as compared to the national average (5).

Table 2 – 4.2 *Occupational asthma incidence in Europe (6)*
Incidence in various agricultural activities in America (7,8)

Newly diagnosed occupational asthma			**Occupation**	**Occupational asthma**
Northern Europe	6%		Farmer – pig farm (7)	20-30%
Central Europe	12%		Farmer – chicken farm (7)	5-10%
			Farmer – daily worker (7)	4-7%
Southern Europe	23%		Agriculture worker (8)	20-26.7%
			Fisherman (8)	17.8-26.7%

The economic impact of occupational asthma is rendered by both direct medical care costs and indirect costs, due to the drop in labor productivity and efficiency, rehabilitation and compensation costs and the costs relating to the drop in the quality of life (1).
Losing a job or the incapacity to carry out one's work lead to financial losses that cannot be compensated. Some one third of the workers who have developed occupational asthma stay unemployed up to 6 years after being diagnosed (4).

In the European countries, compensations do not include recovery, retraining or the relocation of the work force, probably because of the high percentage of workers (30%) who keep on being exposed to the agents that cause asthma (1). The recurrence of symptoms and exacerbations or the progression of the disease can lead to an ineffective completion of job duties and absenteeism. In the countries where incomes are low and medium, the rate of mortality caused by asthma is high, even if the global incidence is the equivalent of that in the developed countries (9).

An occupational disease disrupts the physical, mental and/or social balance of the affected individual (2). The psychological impact, adding to the individual economic impact, is significant with regard to the quality of life of a patient suffering from occupational asthma. The prevalence of depression and anxiety among this population is high (1).

In order to avoid the development of occupational asthma and the consequences associated with it (2), a thorough information is of utmost important. People must know about the risk of contracting the disease, symptoms and treatment methods, as well as the control of the disease among people who are already involved in or about to choose a job in agriculture.

Definition of asthma – a chronic respiratory condition marked by attacks of spasm in the bronchi of the lungs, causing wheezing, dyspnea (difficulty in breathing), cough, thoracic constriction (the sensation of thoracic pressure) (1). In asthma, the respiratory pathways (trachea, bronchi, bronchiole, alveoli) have a reactive, immune response (by thickening, narrowing and inflammation) to various sensitizers – allergens or irritants.

During an acute asthma crisis or exacerbation, the flow of air that gets into the lungs gets significantly smaller(9), which has a significant physiological impact on the individual, and this could be life-threatening.
Occupational asthma is the consequence of exposure to specific biological, chemical and physical factors in the work environment, within in a certain period of time. Occupational asthma is either caused or aggravated (pre-existing asthma) by the conditions in the work environment (1). One of the types of occupational asthma with high global incidence is asthma in agriculture.

Allergens are airborne; they enter the body and activate the body's defense mechanisms.

With every exposure, the lung of the affected person becomes even more sensitive to the allergen, so that eventually the allergen triggers a major allergic response, which leads to a narrowing of the airways, inflammation and difficult breathing (1). After a first allergic response, even the tiniest exposure can trigger that response again (1,10);

There are two types of agents that cause occupational asthma (1, 11);

- sensitizers – require a longer period of exposure in order to produce symptoms (allergic asthma);
- Irritants – in high concentrations, they typically trigger the onset of symptoms within a few hours (non-allergic asthma; ex. wood dust, cereal dust (12)). There are also cases of isolated exposure (one inhalation incident), which we call bronchial hyper-activity syndrome / respiratory dysfunction (1, 13);

Allergic or non-allergic occupational asthma can be revealed or exacerbated by certain conditions, which are not seen as occupational risk factors, such as viral respiratory infections, gastroesophageal reflux, physical effort or cold air (12).
The relative risk of developing occupational asthma is 3.4% higher in the case of workers that already have some pre-existing conditions: inherited genetic data (from parents), bronchial hyperactivity, dry skin (10).

The risk factors for asthma in agriculture can be varied and intricate. There are more than 250 agents involved in the complex immunological process of occupational asthma in the rural environment, classified in keeping with their molecular weight (1): agents with low molecular weight – difficult to test immunologically (ex. Isocyanides, metals, wood dust, cleaning substances); agents with high molecular weight – with specific immune response IgE mediated, frequently involved in agriculture (ex. animal proteins and enzymes, plant proteins – flour, cereal dust, rubber, leather, talc powder, bacteria, fungi, insects, pesticides).

1. *Aquaculture*
   - Crustaceans, crabs (1) – trigger individual occupational asthma, only in already atopic patients (14);
   - Algae produce toxins during the blooming period: Cyanobacteria (15) (sea water 2%, salty waters/lakes 1%, fresh water 96%) and Chlorophyta (16) (in particular algae in the temperate areas: Chlamydomonas spp., Stichococcus spp.) may cause exacerbations in those who already suffer from asthma (16);

2. *Apiculture*
   - Hymenoptera venom (17): bee, wasp, bumble bee
   - Hive dust – allergen for those who are allergic to bee venom/honey-based products) (14)
   - Pollen from flowers and vegetation growing around hives (seasonal): lime tree, acacia, lavender, etc.)

3. *Aviculture*
   - Bird feathers (12) and bird dust mites (18) rarely cause IgE mediated occupational asthma (14);
   - Gaseous ammonia – released from the birds' urine (19), in high concentrations – may trigger asthma or exacerbations and can help the disease progress in workers that already have it (14); *Frequently, the concentration of ammonia exceeds the admitted levels in poultry cages (14);*
   - Bacteria, fungi, endotoxins from bird dust – feathers, epithelia, straws, bars, nest (20);

4. *Mollusk farming*
   - Molluscs (21) – their contamination with toxins (22);
   - Snails – ground species (Helix species) – the dust collected along with shells (24);
   - Oysters, mussels, clams, shrimps (25) – shell dust can cause allergic asthma (26);
   - Octopuses (27), squid (28);

5. *Pisciculture*
   - Certain species of fish can have allergenic antigens that are easily inhaled (29);
   - Larvae of worms used as bait (Tenibro molitor) (18);
   - Beetles, locusts, grass-hoppers, flies, butterflies (fishing) (21).

6. *Sericulture*
   - Silk worm (30,31,32);
   - Silk worm larvae (18).

7. *Animal husbandry*

Table 2-4.2
Proteins, enzymes, endotoxins produced by farm animals that can be allergens (7,12,18)

Type of allergen	Animal product	Farm animals
Serum albumin	Hair/fur	Dogs, cats, horses (14)
Other serum proteins	Hair/fur	Dogs, cats, cows (19, 33), horses (14, 19), pigs (19,33), goats (33) (Bovidae fam.), deer (Caproleus caproleus) (33)
saliva		Cats, dogs (14)
Gaseous ammonia	Released from urine (14,19) and feces (14)	pigs (7,14,19), cows, horses, cats (14)
endotoxins	From feces	Farm animals (19)
endotoxins	From urine	Male rabbits, small mammals (14)

Table 3-4.2 *dust mites, bacteria and fungi colonizing animals or farm facilities*

Type of allergen	Localization
Cellular components: endotoxins, glucans from air-borne microorganisms (bacteria and fungi)	Farm facilities (14)
Interior mold spores	Houses, shelters (14)
Some species of dust mites (Dermatophagoides spp.)	Colonize fleece (14,12)
parasites (Dermestidae spp.)	Fleece (18)
Dust mites, fungi, bacteria	Colonize horse hair (14)
Various allergens	Contaminate mice/rats spread in granaries, barns, etc. – the bite can be anaphylactic (14);

- *Pollens* – seasonal allergens (herbs: Bromus, Phleum pratens, Holcus, Cynodon dactylon, Ambrisia retroflexus)(34);
- Allergens in *cereal dust* used to feed animals;
- *Latex allergy*

8. *Plant technology*
   - *Cereal dust* – can be found in barns, mills, silos, warehouses (12);
     - Produced by cereals, hay or straws (14). It is hardly visible (only in bright light). (7)
     - Wheat, rye, oat, corn, sesame, soy, sun flower seeds (14);

- *Bacteria and fungi* : airborne, from agricultural construction, mold in barns/silos, depending on the type of crop stored there and the storing conditions (high level of humidity) (14);

   - *Dust mites*: are tiny insects that feed on organic matter; they can be found anywhere there is dust. There are many types of dust mites (14).
     - Storage mites – where organic products are stored (14);
     - Red spider mites – in some greenhouse crops; (12)
       - *oriental cockroach (Lepidoptera antigens (14))* : dust on cockroaches, eggs, saliva, waste and carcasses (35) especially in the poor rural areas (14); the areas preferred by the roaches should be cleaned at least every 2-3 days (12);
       - *crop pollens* or other types of allergens can be borne in the air by beetles, locusts, grasshoppers, butterflies (21);

Table 4-4.2 *Allergens on crops (specific to south-eastern Romania) 36*
- *personal archive Prof. Maria Vladau*

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Potential allergen	Particularities	Affected crop
Arthropods: Eurygaster, Pyrale18	Parasite	Cereals
Arthropods: Bronchus lentis(18)	Parasite	Other crops
Alternaria(14)	Saprophyte	Cereals, tomatoes, potatoes, hay, rape
Aspergillus (>3000 de specii)(14)		Cereals, hay, mushrooms (37)
Cladosporium(21)		Various crops
Fusarium(14)	Soil fungus	Tomatoes, cotton, melon, celery, cabbage, beans, peas
Epicoccum(14)		Corn
Stemphylium(14)		Tomatoes, vegetables
Trichoderma(14)	The most spread fungus on soil	Tulip bulbs (on paper or stamps that fell on the ground)
Ascomycetes: Chaetomium (14)		Textiles, mushrooms (14,37)
Agaricus bisporus (18)		White mushrooms (18,30)
Hyphomycete: Botrytis (14)	Parasite on plants and soft fruits when humidity is high	Beans, lettuce, tomatoes, onion, strawberries
Hyphomycete: Paecilomyces (14)		Greenhouse crops; wet wood

Potential allergen	Particularities	Affected crop
Hyphomycete: Penicillinum (14)	Saprophyte (the most spread fungus)	Fallen vegetation or cereal and lemon decomposing agent
Phycomycetes: Rhizopus (14)	Storage, transportation, handling	Corn, strawberries, sweet potatoes
Basidiomycectes: Ustilago (14)		Cereal/grass 'cinder'
Aspic (18)	„beet sugar worker"	
Lathyrus odoratus (18)		Sweet peas (greenhouse)
Făina (18)	Animal feed	White peas, marigolds
Crop pollens	Vegetable storage facilities	Cereals: wheat, rye, oat, barley, corn (34).
		Sunflower, soy (14)
		Cauliflower, broccoli, vetch (18)
		Courgette, chicory (18)

9. *Silviculture/forestry*
   - *Domestic wood* (most species) is 4 times more irritating-allergic than plastic dust in the same concentrations (12, 43). In wood processing, hard wood dust (40 species may cause allergic asthma) (35) and soft wood dust (coniferous) (35).

Table 5-4.2 *allergens in silviculture (specific to Romania's territory) (36,38)*
Personal archive Biology Professor Maria Vlădău

Pollens	Fungi	Other allergens
High allergenic potential (38,39,40,41): - maple (Acer genus) - spruce (Picea Abies) - oak – (Quercus genus, Q. robur(38); Betula(34)) – Pine (Pinus genus) – Poplar (Populus tremula, Populus alba) – Thuja (Thuja plicata)(35) – Wild lime (38)	On wood or plants (42) : – *Alternaria*, *Chaetomium*, *Cladosporium*, *Bipolaris*, *Fusarium*, *Ulocladium* – *Trichoderma koningii* (timber) – *Chrysonilia sitophila* (logs) – *Mucor species* (contain sedge fibres from house construction) (18) – *Penicillinum* – saprophyte from fallen vegetation(14)	Indirectly, through dermatitis (42) : – Certain lichens – Plants from the Asteraceae family (chamomile, daisies, dahlia) – Plants from the Primulas family (tulips)
With crossed reactivity*: – Beech – Alder – Birch – Hornbeam – Chestnut – Hazel **crossed allergies with: peanuts, strawberries, apples, apricots, cherries, peaches, wild strawberries; vegetables – celery, carrot, tomatoes, wild nuts, soy*		Various insects in the area(42): – Pine caterpillar (*Thaumetopoea pityocampa*) – Bee, wasp, wild beetle sting

Pollens	Fungi	Other allergens
With low allergenic potential: – Ash, cypress, elm, juniper, mulberry, willow		– Resin (21)
Seasonal herbs – Artemisia(34) – Sedge (18) – (*Stipa tenacissima, Lygeum spartum*)		– skin, epithelial desquamations, proteins in animal urine (eg. Rodents) (42)

10. Horticulture

Table 6-4.2 *Allergens in orchards and vineyards*

Allergen type	Affected crop
Dust mites – Red dust mites (Panonychus ulmi) – McDaniel spider mite (Tetranychus macdanieli)	– Orchards, apples (12,14,18) – Vine (18)
Moulds – Downy mildew (Plasmopara viticola)	– Vine (18)
Fungi – Hyphomycete: Botrytis – Epicoccum, Stemphylium – Phycomycete: Rhizopus – Phycomycete: Mucor (fungul "de zahăr")	– Vine (14) – fruits(14) – cherries, peaches (storing, carrying, handling) (14) – preserved food: juice, fruit, jam (14)
Pollens – apricot tree leaves (18) – lavender, hair grass, timothy grass, vitellary, (34,38) – Dactylis (34)	– Apricot trees – Orchard plants – Orchard grass

The duration of exposure is the main factor in the development of occupational asthma. (1). Allergic asthma usually occurs after a long period of exposure (from 18 months to 5 years)(1,21). The affected worker can fully recover if exposure is not prolonged (1). *Short-term exposure* (under 6 months) can accidentally cause an exacerbation of asthma, especially in workers with atopy or pre-existing allergic or non-allergic asthma. Isolated exposure can lead to the development of bronchial hyper-activity syndrome. (1, 10, 13).

Long-term exposure (more than 2 years) may trigger allergic asthma in workers with inherited genetic predisposition (atopy). In such cases, the incidence of newly diagnosed asthma caused by allergens with high molecular value is clearly higher than those with low molecular value and with incidence in workers with no genetic predisposition respectively (44).

Prolonged, quasi-continuous exposure leads to a progression of the disease through frequent exacerbations, with difficult response to treatment, and significant morbidity and invalidity (1). 25% of the workers suffering from occupational asthma experience exacerbations caused by the working conditions (45).

Diagnostic criteria in occupational asthma:

1. Professional exposure proven by documents, site visits, lab test report, etc.

2. The clinical history of the worker is essential in diagnosing occupational asthma.
3. Investigations

A diagnosis of occupational asthma *must not be excluded* even in the absence of symptoms during years of work in the same work environment (21). The occurrence of any symptom or the lack of control in case of already established asthma raises suspicion of an occupational component (45,46).

Symptoms: paroxysmal dyspnea, wheezing, cough, thoracic constriction, diminishing of the capacity to carry out daily activities at the work place (47).
Symptoms can become worse when entering the work environment or after leaving it – at home, during the night, at the weekend or holidays (late symptoms). What is important is the association between asymptomatic periods and the absence of exposure and of symptomatic periods with exposure (21). The recurrence of symptoms causes somnolence during the day, a drop in the daily regular physical capacity, absenteeism (9).
Rhino – conjunctival symptoms can precede or coincide with the occurrence of occupational asthma. (21,48). The risk of developing occupational asthma in the year after receiving the diagnosis of allergic rhino-conjunctivitis, especially when high molecular weight agents are involved (21)
Clinical signs (47) are non-specific in the stable period of the disease and characteristic in cases of moderate-severe asthma or exacerbations:
- auscultation: wheezing (sometimes only in forced expiration), cough, sibilant ronchi and sonorous rales
- percussion: diminished diaphragmatic excursions, the use of the accessory muscles of respiration (signs of acute hyperinflation);

"Silentium" can be interpreted as an acute exacerbation or progressive ventilatory dysfunction, revealed by other signs such as cyanosis, drowsiness, speech impairment, tachycardia, chest wall hyperinflation, the use of accessory muscles, intercostal retractions.

Key investigations in occupational asthma:

1) spirometry and bronchodilator test (1, 47) – pre and post –dilation changes are not recommended to validate or exclude the diagnosis of occupational asthma (4).
2) Methacoline challenge testing (1,50) in selected cases; it's easy, sensitive but non-specific for occupational asthma;
3) peak expiratory flow measurements at the work place and outside for a minimum of 2 weeks (1, 47). Serial measurements (minimum 4 times per day, for 3 weeks in a row) is highly specific and sensitive for the diagnosis of occupational asthma (48). This depends on patient's cooperation (57);
4) work place challenge test with serial measurements of the forced expiratory volume; if negative in regular working conditions, this excludes the diagnosis of occupational disease (570;
5) skin or serological tests and enzyme-linked immunosorbent assay (ELISA) to detect allergen specific IgE antibodies (57);

Differential diagnosis with: chronic obstructive bronchopneumopathy (COPD) – which is often associated with – hypersensitivity pneumonia (extrinsic allergic alveolitis – farmer's lung), foreign body aspiration, malign or benign obstruction of the respiratory airways, laryngeal dysfunction, vocal chord dysfunction. (49)
Besides that, without taking it as occupational asthma, we can add effort asthma (especially in young adults), which can be associated with or mistaken for allergic asthma (49).

Monitoring occupational asthma entails measurements of the Peak Expiratory Flow (PEF), repeated spirometries and clinical evaluation based on questionnaires every 3 months in the first year, then every 6 months.
Workers with occupational asthma who have left the work environment or are no longer exposed to allergens should be monitored by a specialist for a period of minimum 3 years. (48). Sometimes, symptoms and the deterioration of the respiratory function may persist indefinitely (49) (years) after removing the agent that caused it (4).

Exposure criteria in occupational allergic asthma:
The minimum intensity of exposure varies depending on the type of allergen involved and the individual reaction of the worker exposed to that allergen.
The minimum duration of exposure under 24 hours (immediate response) – just one exposure to the incriminated agent would be enough.
The period of maximum latency is undetermined – may require repeated exposure over the years to trigger the disease (slow or atypical dual response, sometimes indeterminate) (1,51)

The etiological treatment ideal in occupational asthma consist in removing the causing agent at the workplace – an option that is difficult to put into practice (1). The best second option is to remove the worker from the area/sector where they are exposed to that agent (relocation of the work force) (1). Usually, when this is possible, if the duration of exposure is minimum or the worker used the available protection measures (technical – mask, protective equipment and/or medical equipment), improvement or even recovery are significant (1). Sometimes, asthma persists indefinitely after exposure ceases (49).

Many times, however, avoiding the agent (52) is difficult to do, and here is where the third option comes in: monitoring the level of exposure and using protection measures. Medical evaluation every 6-12 months by means of specific questionnaires, respiratory functional test, prick tests for allergens known in the area where the workers carry out their professional activities (1).

Immunotherapy may also be considered in certain situation as 'pathogenic treatment', with a variable rate of success: in case of just one triggering allergen, maximum two similar allergens, for which there are standardized extracts, provided the respiratory function has been maintained and the triggering agent removed (47).
Symptomatic treatment (controlling symptoms and exacerbations) is the main goal of pharmacological therapy according to a standardized algorithm (1,47,53,54). It entails two types of medicines: rescue medicines – for short term treatment, in exacerbations or light symptoms and control medicines – for long term treatment, to control symptoms and the development of the disease.

Table 7-4.2 *Classes of medicines used in asthma (47,53,54)*

Rescue medicines	Control medicines
Short-acting beta2-agonists (inhalers)	Long acting beta2 agonists (inhalers)
Costicosteroizii inahalatori (pe termen scurt)	Inhaled corticosteroids
	Antileukotrienes
Corticosteroizii sistemici	Systemic corticosteroids (severe asthma, hardly responding to inhaler therapy, difficult to treat)

	IgE monoclonal antibodies (in selected cases)

Adding to these are antihistamines, often before the already known period of exposure or depending on the action period of certain allergens.
Also, in case of asthma aggravated by work by means of non-specific stimuli, such as cold, physical effort, stress or discontinuity in treatment, controlling these factors and rendering the therapy optimum might be enough for the worker to be able to carry out their activities at the work place (45).

A worker who has *exercise induced asthma* can dose the effort and control the symptoms by using an inhaler (Beta-2 short term agonists) or oral medication (antileukotrienes) before starting the physical activity (49).
Asthmatics who are *smokers*, on the other hand, are resistant to therapy, and may develop COPD characteristics; they must be counselled and treated for smoking addiction first (47).

Medical prophylaxis might consist in successfully completed immunological therapy (apparently with minimum risk at exposure in case it is necessary), anti-smoking counselling, avoiding exposure for those who have been tested positive (before the symptoms start), using anti-allergic medication, inhalers or oral rescue medication for those with isolated or light symptoms, owning an EpiPen especially in bee-keeping (55), compliance with control treatment, the treatment of allergic rhinitis in order to lower the risk of developing asthma. (57).

7.3 Extrinsic allergic broncho-alveolitis

Extrinsic allergic broncho-alveolitis (EAA), known as Hypersensitivity Pneumonitis represents a large group of immunologically induced respiratory diseases, which develop as a result to repeated exposure to fine organic dust, dispersed both in the occupational environment and outside the work environment.
The disease was described for the first time by Ramazzini in 1710 in cereal farmers and animal breeders, showing the connection between exposure to organic dust and respiratory ailment (1).

In 1932, Chambell acknowledged the occurrence of the disease in farmers exposed to moldy hay, and in 1964 Pepys spoke for the first time about the immune mechanism involved in the production of EAA along with the discovery of precipitating antibodies in patients' serum (1).

Etiology
The factors that cause the disease, in various degrees, are exogenous (allergens) and body factors such as the host's immunological reactivity, age, smoking history. (1)
The agents most incriminated are microorganisms, animal and vegetal proteins, chemical substances (2).
Since 1932, when "the farmer's lung" was described for the first time, the list of etiological forms has been constantly added to. The main types of occupational allergic alveolitis in agriculture and the antigens involved can be seen in table 8-4.3 (1,2,3,4).

Table 8-4.3 *Occupational allergic alveolitis in agriculture*

Etiological type	Antigen reservoir	Antigen involved
1. **"Farmer's Lung"** The first form of EAA described; the most frequent type	Hay; fodder; straws; cereals; manure; moldy vegetation; Ventilation/climate control systems Animal feeds that contain soy	*Thermophilic Actinomycetes* – Micropolispora faeni (Faenia rectivirgula); Thermoactinomyces vulgaris; Thermoactinomyces sacchari *Fungi:* – Aspergillus sp.; Aspergillus umbrones; Candida albicans; Streptomyces sp.; Penicillium brevicompactum; Penicillium olivicolor; Rhizopus sp. *Bacteria*: Erwinia herbicola *Antigenes:* soy shells
2. **"Bird breeder's disease "** Described for the first time by Plessner in goose and duck breeders, then by Pearsall in a parrot breeder	Feathers, barbs, down, waste from parrots, pigeons, ducks, geese, turkeys, owls, etc.	Bird proteins (IgA) Intestinal mucins Undetected bird substances
3. **"Miller's lung"**	Contaminated wheat	Sitophilus granarius; Tyroglyphus farina
4. **"cheese washer's lung"** Affecting the lungs of workers in the cheese industry	Blue/white mold cheeses	Penicillium (casei; roqueforti)
5. **"gardener's lung "**	Fertilizers and contaminated vegetal leftovers; wood compost, used by orchid growers;	Streptomyces albus; Aspergillus sp.; Cryptostroma corticale
6. **"mushroom grower's lung"**	Compost for mushrooms mushrooms	*Thermophilic Actinomycetes* : Micropolispora faeni; Thermoactinomyces vulgaris; Actinobifida dichotomica; Exellospera flexurosa; Thermomonospera alba *Micromycetes:*Aspergillus glaucus; Lycoperdon; Pholiottes; Pleurottes
7. **"woodworker's lung":** – Maple bark peeler's disease – Sequiosis – Wood cutter's disease – "chainsawer's" disease	Molds in maple bark Sequoia dust (red sawdust)	Coniosporium corticale; Cryptostroma corticale; Aureobasidium sp.; Penicillium sp.; Rhizopus sp.; Alternaria sp.; Pellularia sp.

Etiological type	Antigen reservoir	Antigen involved
8. **"potato grower's lung"**	Molds on potatoes	*Thermophilic Actinomycetes* ; Aspergillus sp.
9. **"vine-grower's lung"**	Molds on grapes	Botrytis cinerea
10. **"malt grower and processor's lung"**	Moldy hop and barley	Aspergillus fumigatus Aspergillus clavatus
11. **Bagassosis** – EAA caused by exposure to bagasse	Moldy residues of bagasse, bagasse resulting from sugar cane processing	Actinomicete termofile: -Thermoactinomyces vulgaris -Thermoactinomyces sacchari
12. **"tea grower's lung"**	Tea dust	Candida albicans
13. **The disease of the coffee bean grower and roaster**	Green coffee dust	unknown
14. **suberosis** developed by: - cork workers - cork handlers (wine bottling)	Moldy cork	Penicillium frequentas
15. **"sericulture worker's lung"**	Animal proteins	unknown

Pathogeny, physio - pathological mechanisms

The production mechanisms of this disease are not entirely clear. Still, extrinsic allergic alveolitis is considered an immune disease. Apparently, two of the traditional hypersensitivity mechanisms Gell and Coombs seem to be involved: type III (mediated by the production of IgA, IgG and IgM antibodies) and type IV (cellular mediation).

From a physio pathological point of view, EAA is characterized (2) by an inflammation of the interstice, terminal bronchioles and alveoli, affecting therefore the units that take part in the lung's gaseous exchanges.

Positive diagnosis

There are no pathognomonic elements of this type of diagnosis, therefore an association between clinical, imagistic, functional, immunological and histopathological elements is necessary. (4)

Clinical picture:

From a clinical point of view, the disease may develop in three forms:

- Acute: onset 4-6 hours after exposure to high concentrations of antigens and the symptoms include: sickness, shivering, fever, dry cough, dyspnea. Symptoms disappear spontaneously within a few hours or days. A physical examination can reveal: cyanosis, tachypnea, tachycardia, crepitants in the bilateral thorax.
- Sub-acute: develops insidiously, usually after an acute episode. Manifestations are those typical of bronchitis: productive cough, effort dyspnea, anorexia, weight loss;
- Chronic: is the result of continuous or repeated exposure to allergens and the symptoms are associated with pulmonary fibrosis: effort dyspnea, dry or productive cough, anorexia, weight loss. The clinical examination reveals: cyanosis, drummer's fingers, weight loss, tachypnea, basal lateral crepitants.

Functional respiratory picture

In the acute form of the disease, the alveolar-capillary transfer is altered (a drop in the transfer coefficient), secondary to alveolitis.
In the chronic form, changes are of the restrictive type (with dropping pulmonary volumes), with alveolar-capillary diffusion altering (a diminishing of the transfer coefficient and factor) and a reduction of pulmonary compliances. Also, obstructive modifications may occur.
Measuring blood gas can show changes such as effort or rest hypoxemia.
The pulmonary function suffers a progressive decline in time. Therefore, there are chances respiratory failure might occur (1).
Specific challenging tests have a limited value for diagnosis (5)

Imagery
Standard lung X-ray: cannot ensure a certain diagnosis; it shows nodular microopacities distributed equally in both pulmonary fields, except for tops and bases. An X-ray can be normal, even in the presence of obvious clinical manifestations (2).
HRCT is much more useful in establishing a diagnosis. The following elements can be found: (2,6)

- In the acute and sub-acute forms: ground glass opacity and/or nodular micro-opacities in the center of the lobe;
- In the chronic form: fibrosis, traction bronchiectasis, emphysema lesions;

Immunological changes

- *the presence of precipitant antibodies IgG in the serum is a marker of exposure, not a diagnosis element (1);*
- *bronchoalveolar lavage (1,2,7) is the most sensitive diagnostic method.*

The cytology of the lavage liquid has different configurations depending on the stage of the disease:

- in the first week of exposure, neutrophils, mastocytes and plasmocytes are predominant;
- in the chronical forms of the disease (after repeated exposure), lymphocytes are predominant, most of them of the suppressor / cytotoxic type (CD8) (1.2,7)

Histopathological examination of bioptic material can provide elements of diagnostic certainty (2).

EAA is not exclusively an occupational disease, as it can also be conditioned by extraprofessional activities and even the household environment (1). That is why, to establish the diagnosis of occupational disease, the correlation between the moment of exposure and the occurrence of acute symptoms, followed by chronical episodes of repeated exposure must be established.

In order to differentiate between the occupational and non-occupational character of the disease, the following elements are important:

a) acknowledging the presence of risk factors at the work place;
b) acknowledging exposure at the work place and/or outside the work place;
c) information provided by pre-employment and post-employment regular examinations:

- the results of the pre-employment examination (the existence/non-existence of symptoms before employment)
- the results of the regular medical check-ups (anamnesis, clinical examination, spirometry, immunological investigations if necessary)

Prevention
Most authors admit that the treatment of EAA is prophylactic by excellence (1).
In order to ensure proper prevention, the following are important:

- acknowledging the existence of the risk and measures to control the occupational and extra-occupational environment, in order to eliminate or drastically reduce the source of antigen;

- providing the necessary respiratory protective equipment and imposing the use of the equipment as a mandatory measure;
- avoiding or curbing activities that are associated with a massive antigenic load (2);
- medical examinations before and during employment properly carried out and a clear observance of counter-indications; identifying symptomatic subjects and changing their workplace;
- informing the employees about the risk, the seriousness of the disease and the need to observe prevention measures;

7.4 Organic dust toxic syndrome (ODTS)

Known since as early as 1950 as the farmer's lung or lung mycotoxicosis was described for the first time as ODTS in 1985 (1).
It is defined as a self-limiting respiratory disease with a systemic component, characterized by an acute respiratory syndrome, triggered by the inhalation of bio-aerosols or organic dust contaminated with microorganisms (2).

Etiology

The main incriminated agents are: mycotoxins and endotoxins, constituents of the Gram negative bacteria's cell walls, *peptidoglycans* that form the cell wall of Gram positive and negative bacteria and *beta-glucans*, insoluble compounds that enter the cell walls of molds, actinomycetes, bacteria, which contaminate organic dusts. They enter the body through the respiratory tract.

It is believed that the duration and intensity of exposure are the main risk factors for ODTS.
This syndrome occurs exclusively in the agricultural environment (2.4.5), in workers in (table 9-4.4):

Table 9 -4.4: work places at risk

Work places at risk
Cereal silos
Animal/poultry farms
Pig farms
Waste management facilities
forestry (lumberjacks)
Potato farms
Mushroom farms

The pathogenic mechanisms involved in the production of ODTS are not clear yet. It is seen as a disease that does not have just one allergic mechanism, as there are several systemic immune-inflammatory mechanisms involved, mediated by pro-inflammatory cytokines (IL1, IL8, IL17, IL23, TNFα) or mediated along the lymphocyte path (involving CD14 lymphocytes). (7,7)

A positive diagnosis is based on the correlation between clinical data and the existence of exposure circumstances.

Clinical picture
Symptoms can start 6-10 hours after the first exposure (2). ODTS is characterized by systemic manifestations (fever, shivers, nausea) and respiratory manifestations (coughing and dyspnea, accentuated by effort). Normally, ODTS's evolution is towards spontaneous cure, within 34-48 hours

after exposure stops (2), but it might develop into obstructive bronchopneumopathy if exposure is repeated.
Clinical examination can reveal normal values, and only in rare situations disseminated bronchial sounds.
Respiratory functional picture: spirographic values are normal, with rare drops in the ventilation flow rate: a drop in the maximum expiratory volume in the first second of a maximum forced expiration and the instant maximum flow at 50% of the vital capacity.

Therapeutic principles
Drug therapy is symptomatic.
Prevention entails:

- acknowledging the risk by employers, employees, physicians, all those involved in occupational health and safety;
- informing/educating the workers on the existence of such risks;
  - the need to wear protective equipment;
  - recognizing the signs of the disease;
- reducing the level of exposure (improving working conditions) by means of:
  - properly storing cereals and ensuring proper ventilation;
  - providing protective equipment (it is very important to provide respiratory protection by means of anti-particle and anti-gas filters);
- medical examination upon employment and then regularly, acknowledging the risk factors and by observing counter-indications;

It has been noticed that workers who have a history of atopic field present clinical manifestations that are more severe (2).

7.5 Byssinosis

Byssinosis is a respiratory disease, recognized and described for the first time in 1831 by Kay as the "cotton spinners phthisis". The first clear clinical description was made in 1845 by Mareska and Heyman (1)(2). It was first acknowledged as an occupational disease in 1941.

It is defined as an acute respiratory disease with the following symptoms: dry cough, feeling of thoracic constriction, dyspnea, which appear after a variable time of exposure to natural textile dust (of more than 10 years for cotton and a few months for flax and hemp), upon resumption of work, usually on the first day after an interruption of activity (weekend or holiday), which evolves towards chronicity (2,3).

Etiology
Types of exposure that cause byssinosis: Table I: (2,4,5)

Table 10-4.5 Etiological factors and work places/occupations at risk

Etiological factors	Work places/occupations
Cotton dust (from leaves, stems, seeds), cotton bracts	– harvesting, ginning, sorting, mineral oils mills (from cotton bracts), storing, processing (mills), fabric manufacturing, textile waste processing – for cotton

Hemp dust (stem)	– harvesting, retting, processing (mills), fabric manufacturing, textile waste processing, dockers
Flax dust	– harvesting, retting, processing (mills), fabric manufacturing, textile waste processing, dockers
Jute dust (stem)	– harvesting, retting, processing (mills), fabric manufacturing, textile waste processing, dockers
Other types of dust: - kapoka (fruit) - sisal (stem, leaves) - coconut	– harvesting, shelling, sorting, processing

Pathogeny, physio-pathologic mechanisms: changes at intra-bronchial level: inflammation, hyper-production of mucus and spasm; the incriminated production mechanisms: immunological, non-immunological release of mediators and the direct effect of contaminants in the dusts (5).

Positive diagnosis

Clinical picture. Respiratory symptoms: chest pain, dyspnea, dry cough, which occur after a variable time of exposure (months, years) on the first day of the week, or on the first day after a gap in activity of at least 48 hours, which puts it in the "Monday syndrome" category. Symptoms usually occur at the end of the day, but in time they develop and become permanent and chronic, characterizing the symptomatic picture of chronic obstructive bronchitis, considered by many a stage in the evolution of byssinosis (5). Depending on the occurrence and disappearance of symptoms, in 1956, Schiling proposed a stage classification of byssinosis, which has been adapted in time. The classification used today was proposed by the WHO in 1983 (table 11-4.5)

Table 11-4.5 *Clinical stages of byssinosis (OMS 1983)(5)*

Classification	Symptoms
Stage 0	No symptoms
Byssinosis	
Stage B_1	Thoracic constriction and/or suffocation – frequent on the first day of resumption of work
Stage B_2	Thoracic constriction and/or sensation of suffocation – on the first day and on other days of the working week
Irritation of the respiratory tract (IR)	
Stage IR_1	Cough associated with exposure to dusts
Stage IR_2	Persistent expectoration (more than 3 months per year) caused or exacerbated by dust exposure
Stage IR_3	Persistent expectoration caused or worsened by dust exposure, associated with pain for a period of 2 years or longer

Stages B1 and B2 correspond to the acute form of the disease (classic byssinosis); symptoms in the IR stages are related to a chronic development, of the bronchitis type

Functional respiratory picture
Clinical manifestations are associated with alterations of the air flow. The spirogram shows a drop in the pulmonary function during a day of work. Usually, the decrease in the maximum respiratory volume in the first second of a forced maximum expiration is higher on the first day of the working week (5). In severe chronic cases, the forced vital capacity (FVC) also diminishes (6).
There is a link between clinical manifestations and the drop in the FEV, that is why a classification of functional respiratory changes was required, in order to be used in surveillance programs (table 12.4.5)

Table 12-4.5 *Changes in the forced expiratory volume in byssinosis (WHO)(5)*

Acute modifications	
No effect	Drop in FEV – by less than 5% or growth during work shifts
Light effect	Drop in FEV by 5-10% - during work
Moderate effect	Drop in FEV by 10-20% - during work
Severe effect	Drop by 20% or more in FEV – during work
Chronic modifications	
No effect	FEV > 80% of the theoretical values
Light-moderate effect	FEV = 79-60% of the theoretical values
Severe effect	FEV < 60% of the theoretical values

In order to establish the diagnosis of occupational disease, the following are important:

- *history of the disease, including occupational elements*

The following elements are indicative of an occupational character of the disease:

- *the lack of symptoms before starting working in conditions entailing exposure to 'byssnogenous' dusts*
- *the onset of symptoms within months, years after the start of the activity*
- *improved symptoms at first at the weekend and then symptoms becoming permanent*
- *acknowledging the existence of risk factors in the work environment and the exposure to risk factors*
- *information provided by pre-employment medical examination and then regular check-ups*
- *the results of the pre-employment medical examination (the absence of previous exposure and symptoms, the absence of bronchial hyper-activity) 97)*
- *the results of the regular medical consult (history, clinical examination, spirometry)*
- *a properly conducted assessment at the workplace (monitoring changes in the FEV during the day/week)*

Prevention
In order to ensure an effective prophylaxis, the risk must be acknowledged and curbed by:

- Improving working conditions (reducing the concentration of dusts incriminated as risk factors, proper ventilation, etc.)
- Providing the necessary protective equipment and making the wearing of such equipment mandatory;
- Pre-employment medical examination and regular check-ups carried out properly and a clear observance of counter indications (people with obstructive lung diseases, tuberculosis,

asthma or any other disease that may cause respiratory failure). Discovering atopic subjects and smokers and informing them about the high risk of getting sick and, if necessary, guiding them towards a different job (5,8)

- informing the employees about the risk and the need to observe prevention measures;
- early diagnosis and stopping exposure/changing the work place of those who have been diagnosed with byssinosis, in order to prevent the disease from getting worse. Eliminating, as much as possible, the risk factors in the early stages of exposure can ensure the curing of the disease.

7.6 Chronic laryngitis, laryngeal cancer, lung cancer and mexothelioma, pulmonary fibrosis

Chronic laryngitis

It's a chronic inflammation of the mucosa of the larynx. The symptoms include hoarseness, odynophagia, dry cough. The most frequent cause is gastroesophageal reflux. Other, less frequent causes are fungal, parasitic or micro bacterial infections (tuberculosis). As regards the connection with agriculture, it may appear as a result to exposure to smoke (produced by burning fossil fuels), organic and inorganic dust, or exposure to volatile or aerosolized substances. The diagnosis is established with the help of indirect or direct laryngoscopy. The treatment consists in avoiding contact with irritating substances, nicotine withdrawal, treatment for gastroesophageal reflux.

Laryngeal cancer

When it comes to cancers of the respiratory system, laryngeal cancer comes second in terms of frequency of occurrence, after lung cancer. Squamous carcinoma is the most frequent type of head and neck cancer. The incidence of this type of cancer varies depending on the geographic region, gender (more frequent in men). It develops mostly in people with a history of drinking and smoking. Some studies have also revealed causes relating to occupational and environmental exposure. There are studies that have shown that laryngeal cancer occurs more frequently in certain occupational groups, such as workers in the textile industry, mechanics and machine operators (1).

Workers in agriculture are exposed to a number of factors, including pesticides (insecticides, herbicides, fungicides), which, in vitro, have tested as carcinogens. In vivo, it seems that they can be blamed for a higher incidence of lung, kidney, stomach, rectum cancer. As regards laryngeal neoplasm, studies are rather contradictory. Some studies show a higher incidence among workers in agriculture. Another study, (2) conducted in Poland in 2006 shows that tumors are more frequently localized at the level of the glottis and that there are less determinations of lateral – cervical ganglions (favorable prognosis factors). Otherwise, no differences have been revealed between people working in agriculture and other types of workers as regards the diagnosis age, TNM staging, recurrence or metastases with localizations other than at ganglion level. In a study carried out in Puerto Rico and published in 2003, the incidence of oral cancer was higher among workers in the sugar processing industry, except for laryngeal cancer (3).

The signs and symptoms of laryngeal cancer are: dysphonia (or even aphonia), dysphagia, dyspnea (predominantly inspiratory, accompanied by cornaj or stridor), aspiration, sanquinolent sputum, weight loss, physical asthenia, halitosis, the presence of lateral-cervical tumorous formations, otalgia. Diagnosis can be established with the help of laryngoscopy, tumor biopsy and histopathological examination. The extension of the tumor is established by means of CAT scan or MRI of the neck. The treatment is a combination of surgery, radiotherapy and/or poli-chemotherapy. In case of metastases, the therapeutic intervention may b palliative (for instance permanent tracheostomy).

Chronic obstructive pulmonary disease (COPD)

COPD is an association of symptoms (eg. cough and sputum production), pathological changes (e.g. emphysema) and functional modifications typical of the irreversible obstructive syndrome (GOLD 2015).
The most frequently involved etiological factor is smoking, and COPD is extremely rare in non-smokers. When a non-smoker develops the disease, then most likely the cause is occupational or environmental. Most of the times, the connection between exposure and COPD is difficult to establish, especially in the context in which is predominantly associated with smoking. Exposure to organic or inorganic dust, gases and fumes can trigger an inflammation and irritation of the air paths.

As regards the population, apparently up to 15% of the cases of COPD are caused by occupational exposure to irritants. Theoretically, long term exposure can lead to a chronic limitation of the air flow, because of obstruction, or to a drop in the elastic recoiled of the affected parenchyma. Rates of mortality caused by COPD are not high in agriculture compared to other occupations, which can be explained by the lower number of smokers among those who work in agriculture. (10).

A study conducted in Denmark (4) on 4742 patients speaks of a relative risk of COPD in agriculture of 1.59 in workers exposed to organic dust, without speaking though of an increase in the risk of COPD as a result of exposure to inorganic dust, gases or vapors. In another study, conducted in Poland in 2014 (5), the risk of COPD was associated with a low social-economic status. A study on greenhouse workers in China, in the province of Liaoning, correlates the risk of COPD with smoking, age and work in mushroom farms; the number of years in other types of greenhouses was identified as a protective factor (6).

A study on 1108 subjects, assessing the symptoms specific to chronic bronchitis (cough and expectoration) and the obstruction of airways (evaluated through spirometry) in case of various activities (animal care taking, hay harvesting, mixt farms, milling, fertilization, silo work, the use of pesticides) has revealed a higher prevalence in those with a history of smoking and in older people, with no differences with regard to the typ of activity or size of the farm. (13)

Specific symptoms include productive chronic cough, at least 3 months per year throughout at least 2 consecutive years, accompanied by persistent, progressive effort dyspnea, which characterize a smoker. Clinical examination and lung radiography are non-specific. Signs of emphysema (flattened diaphragms, hypersounding thorax upon percussion, globally diminished murmur) may be identified. The presence of digital hypocratism must raise suspicions of other pathologies, such as bronchiectasis, lung cancer or asbestosis.

A COPD diagnosis is established when spirometry describes an irreversible limitation of the air flow (PEF/FVC<0.7, normal or lower FVC, with no significant response to the bronchodilation test); the seriousness of the disease is classified depending on the degree of FVC drop, the way in which the quality of life is affected (CAT questionnaire), the severity of dyspnea (mMRC) questionnaire and the number of acute episodes per year. Studies (12) have not identified a significant diminishing of the pulmonary function in agricultural workers, compared to the reference population, despite an elevated rate of occurrence of chronic bronchitis symptoms.
A differential diagnosis must be established in relation to bronchial asthma, congestive heart failure, bronchiectasis and tuberculosis.

The treatment is aimed at preventing a further development of the disease and the occurrence of complications, improving symptoms, increasing tolerance to effort, improving the quality of life,

treating exacerbations and improving chances of survival. The most important stage of the treatment is nicotine withdrawal, as the only one that can influence the natural history of COPD and the accelerated drop in the PEF. Exposure to irritating factors should be avoided, both at work and at home. Anti-pneumococci and anti-flu vaccination are recommended, as they can prevent exacerbations. There are several types of medicines that can be used to treat COPD, including (according to GOLD 2015):
Bronchodilators:

- Beta agonists: short acting, effective for a period of 4-6 hours (ex. Fenoterol, Salbutamol) and long acting, effective for 12 hours or longer (eg. Formoterol, Salmeterol, Indacaterol);
- Anticholinergics: short acting (ipratropium bromide) and long acting (tiotropium); they block the effect of acetylcholine at the level of muscarinic receptors. Tiotropium seems to be able to reduce the number of hospitalizations, improves symptoms and the quality of life.
- Methyl xanthine (e.g. Theophylline) has a weak bronchodilation effect; its advantage is oral administration, which enhances compliance.

Corticosteroids:
Inhaled corticosteroids (e.g. beclometasone, budesonide, fluticasone) improve the symptoms, the pulmonary function and the quality of life, reduce the number of frequent exacerbations (in patients with PEF <60%).
Systemic corticosteroids (oral or injectable) are only indicated in case of severe exacerbations, in short doses.
A combined inhalation therapy makes administration of medication easier, thus raising the level of compliance. There are studies showing that the use of combinations is more effective than the separate use of each drug.
Other types of drugs: mucolytic, antitussive, immunomodulatory, antibiotics;

Lung cancer and pleural mesothelioma

Lung cancer is usually found quite late in its development, that is why the rate of mortality is quite high. Most cases are reported in big smokers (10% of them are diagnosed with lung cancer). In 10% of those suffering from lung caner elements of occupational or recreational exposure to potential pathogens can be identified.
There are studies showing a high risk of developing lung cancer in those who spread pesticides (particularly Diazinon), with a relative risk of 1.60 (IC 95% 1.11-2.31) (7). Another study carried out in Italy between 2002-2005 describes a relatively high risk of lung cancer among farmers of 1.59 (IC 95% 1,12-2,38) (8). However, most studies link the risk of lung cancer with smoking. A study published in 2015, carried out in France, on the death rates in agricultural workers, enrolling 180,000 patients, did not identify a death rate higher than in the general population (9). The author explained the finding by the low incidence of smoking among these workers.

The most frequent symptoms are persisting cough, loss of appetite and weight loss, hemoptysis, repeated pneumonia, pleural flooding or abnormal results of the X ray.
Diagnosis is usually confirmed by a combination of procedures, including a CT scan, bronchoscopy and bronchial biopsy (or lavage, etc.), lung biopsy (trans-bronchial through bronchoscopy, trans-thoracic under CT guidance or thoracotomy). The severity of the disease is established depending on the stage of TNM, histological type, the degree of cellular differentiation. Treatment consist of a combination of surgical interventions, radio therapy and poli-chemotherapy. In case of an advanced stage of a disease or metastases, therapeutic interventions can have a palliative purpose.

Pleural mesothelioma

It is a malign tumor that affects the pleura, usually as a side effect of exposure to asbestos (especially the following types: crocidolite). Latency can be of up to 40 years. In most countries in Europe, the use of asbestos was banned in the early 1990s. However, people are still exposed to asbestos in the rural environment, as asbestos is present in roofs, or pipes. Clinically, mesothelioma signals its presence with thoracic pain, dyspnea, and dry cough. A lung X-ray examination usually reveals the presence of massive unilateral pleural flooding. A histopathological diagnosis can be established by means of thoracentesis, trans-thoracic pleural biopsy, video-assisted thorascopy or open thoracotomy. Bronchoscopy can be useful in differentiating mesothelioma from metastatic lung adenocarcinoma (endo-bronchial lesions are rare in mesothelioma).

Pulmonary fibrosis

Pulmonary fibrosis is a group of diseases characterized by scars formed in the lung tissues, which in time affect the gaseous exchange. Etiology is represented by exposure to pollutants, some medicines, diseases of the conjunctive tissue or it can be idiopathic. Clinical manifestations include dyspnea, dry chronic cough, physical asthenia, involuntary weight loss, joint or muscle pain, digital hypocratism. The diagnosis is established through imagery testing (high resolution CT), respiratory tests (especially by establishing the CO transfer capacity, which is low) or broncho alveolar lavage (assesses inflammation). Sometimes, for confirmation, lung biopsy may be necessary.

One of the diseases that can lead to the development of pulmonary fibrosis is extrinsic allergic alveolitis. It appears secondary to exposure to dust and organic and inorganic dusts. One example is that of people who come in contact with hay (farmer's lung disease), who handle wood contaminated with Graphium spp. or Pellularia spp, who work in greenhouses (probably due to exposure to Aspergilus spp., Penicillim spp.) or who work on tobacco plantations (Aspergillus spp.)(15)

Treatment is limited. When the potential ethological agent is identified, what is important is to avoid contact with that agent. Some forms of fibrosis may respond to systemic corticosteroids. Other therapeutic options include immunosuppressants (especially in idiopathic form). When proper oxygenation cannot be ensured, oxygen therapy may be necessary, and even non-invasive ventilation. In severe forms, resistant to treatment, lung transplant can be an alternative.

Prevention of respiratory tract diseases

In agriculture, exposure to air pollutants which act at the level of the respiratory tract can occur during specific activities:

- Preparing the farming land and harvesting; the machines used for that generate dust (exposure to organic and inorganic dust);
- Maintaining farming equipment/machines can lead to exposure to oil substances or substances resulting from their burning;
- Spreading pesticides and fertilizers;
- Storing and handling seeds;
- Taking care of animals and cleaning the animal shelters;
- Noxious substances that farmers may be exposed to while carrying out their regular activities include:
- pollen and other seasonal allergens
- organic dust, from cereals or other crops or of bacterial origin (spores, bacteria, endotoxins);
- dust mites
- animals (hair, urine, feces)

- gas and fumes: from mud/manure and fertilizers (carbon dioxide, ammonia, methane, hydrogen sulphide), from silos (carbon dioxide, nitric dioxide), exhaust fumes, welding fumes;
- chemical substances: pesticides (insecticides, herbicides, fungicides), disinfectants, paints;
- infectious agents (zoonoses) ;

Prevention methods cover primary and secondary prevention. Primary prevention consists in informing workers about potential substances they may be exposed to and educating them on the existing protective measures, including substitution through automation.

As regards secondary prevention, it consists in establishing a detailed history of exposure and conducting an annual clinical examination, carried out by the occupational physician to detect early signs of the disease (14). Also, additional tests may be recommended (such as spirometry, lung X-ray, etc.), depending on the type of exposure.