Substances acting on respiratory system
Required recollections

In respiratory diseases therapy there are several directions that require integration of nervous, circulatory and pulmonary aspects which finally result in establishment of homeostasis by:

- appeasement of secretory or excretory motor functions;
- emphasizing these functions
- desired result = improvement of respiratory function.
Lung or airways associated inflammation is often the main cause of intervention.

<table>
<thead>
<tr>
<th>inflammation includes:</th>
<th>caused by:</th>
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<td>bronchitis, tracheitis, laryngitis, pneumonia.</td>
<td>bacterial attack, parasitic attack, fungus, irritants, allergy, viruses etc..</td>
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Interference with the amplitude and rate of breathing is related to:
- depressing or
- stimulation of the respiratory center
Chronic respiratory disease is usually the most frequent form encountered in veterinary medicine.

Status of the animal is generally little changed, dependent on the etiology and severity of the inflammatory process, usually the primary cause remaining occult.

The situation will determine the practitioner to establish symptomatic treatments that remove in the first instance cough, permanent, irritative to the lung.

The next steps of treatment are:
- reducing the viscosity of bronchial mucus, or the mucopurulent secretion,
- control of the inflammatory process and
- dilation of bronchioles.
Expectorant substances
In pathological situations tracheobronchial secretions may be:
Increased or diminished.

Consistency in the first case is lower because they are diluted in the second case are more viscous.

Remediation can be ensured by:
fluidifiants
Excretomotor medication and antisecretory.
inhalational expectorants

The active substances used are:
- either heated
- or dissolved in water warmed up to vaporization and administered by inhalation in confined spaces.

Small animals can be exposed repeatedly to water vapors through a mask or cages where animals will be closed.

These methods are effective in chronic respiratory diseases and may be supplemented by appropriate physiotherapy, intended for drainage and expulsion of liquid exudates.
benzoin
aromatic resin (in the Friar's Balm)

Eucalyptus oil (Eucaliptol)
volatile oil obtained by distillation from the leaves of eucalyptus,
fumigation in: treatment of aerophore tract catarrh or administered internally, even s.c. at dog.
similar uses has tincture, which is officinal.

Gomenolul (Niaouli oil)
volatile oil obtained by distillation of Mirtaceae plants.
is used 1% mint oil
in: nasal instillation in coryza or fumigation.

Although it is considered that these substances have direct action on bronchial secretory cells, there seems little reason to be able to say that they have other effects.
Oral expectorants
Some of them are substances that can act with vomit, but are administered at sub-emetic dosage, some are intestinal absorbed and are excreted at least partially through bronchial mucosa. Administered p.o. they are eliminated at the bronchial glands level and in small doses are fluidifiant.

Tolu balm
soft mass oleoresin that hardens with time, after absorption is eliminated in part pulmonary, favoring expectoration and reducing bronchial gland secretions. It is antiseptic. In animals can be used as a syrup.
Primula root
-in root is: emetine.
-officinal drug: 10% saponins.
-dog: decoctions 5%
-officinal: 10% tincture.
-apart from vomiting action is a valuable expectorant.
-lasting effect: principles are absorbed and eliminated slowly.

Soapwort root
-are used: rhizomes and roots.
-drug containing 8% saponins.
-officinal tincture 20%.

Senega root
-from Poligala Senega
-contains saponins, senegine: 2% ac. poligalic salicylate Antil
-drug: irritant, therefore: infusions or decoctions 3-10%
-in dogs: in bronchitis.
Fluidifiant adjuvants

Candle Flower (Flores verbasci)
- are used: corollas and stamens.
- contains saponins, mucilage, carbohydrates, etheric ol.

Licorice root (Radix Liquiritiae)
contains: glicerizină resembling saponins.
drug: good fluidifiant.
Mucolytic expectorants

Mucolytic substances are intended to facilitate the elimination of bronchial secretions by:
- movement of cilia or
- cough,
thereby reducing its frequency.

Action mechanism
- not only fluid iflant but excretory motor due to:
contraction of bronchial smooth muscle activation
cilia vibration stimulation of the respiratory mucosa
emetine
- lyzes the spasm of bronchial smooth m. that will prevent mucus elimination, especially if is adherent.
- included in the composition of Dover powder (with opium and lactose) and is Venena stored.

emetic
- irritates the digestive muscosa
- produces reflex increase in bronchial secretions quantity.
- excites the respiratory center and acts excretory-motor.

Antimony sulfides
Orange sulphide of antimony.
Black sulphide of antimony.
Red sulphide of antimony (kermes mineral)

Used as an expectorant in large and medium-sized animals.
Ammonium salts after absorption are eliminated by bronchial glands fluidifies secretions. stimulates respiratory center and vibratile cilia, diminishes bronchial spasms normalizing tonus. also acts reflex.


Liquor ammonia Anis. contains ammonia, anise, alcohol. in the stomach under the influence of HCl pass into ammonia chloride. is used: in dogs.
Acetylcysteine sodium

- 20% inhalation solution in the form of sprays or aerosols.
- Causes: respiratory tract irritation, but except for these cases is fairly safe and effective in rapid liquefaction of mucopurulent secretions.
- Acetyl cysteine sulfhydryl group cleaves the disulfide bonds from glycoprotein exudates, thus modifying its physical properties.
- DMSO-like, sodium acetyl cysteine has the property to eliminate the hydroxyl radicals.
- Repeated exposure, a few minutes 2-3 times / day = best results
Bromhexine (Bisolvon)

- is administered p.o. 1% powder.
- 1% in injections.
- favorable results: liquefies mucus, increases its volume, decreases its viscosity, favors elimination.
- improves lysosomal function,
- hydrolyzes mucopolysaccharides mucus fibers.
- powders or solutions,
- alone or in combination with antibacterial substances.
- doses: 1mg/kg/c., 2 x / day and 0.1-0.25 mg l / kg., horses, either po or parenteral for 7 days.
Dembrexina

-to be administered to horses;
-on the secretory activity of the secretory glands from the respiratory mucosa.
-following administration = mucus composition modified and low viscosity = reduction of cough and mucus production ceases in treated animals.
-i.v or p.o.: 0.3-0.5 mg / kg., 2x / day, 10 days.
-in prevention / elimination of mucus from lower branches of the airway.

apomorphine
= expectorant in small doses for all animal species.
Antisecretory substances (conditioned)

- substances that in small doses = fluidifiant, can become in large doses = antisecretory by reducing secretions that determine cough, dyspnea and pulmonary congestion
- volatile oils, p.o. or fumigation,
- Small doses are eliminated by bronchial gl. = hypertension,
- high doses = vasoconstriction = hyposecretion.
- bronchial antisecretory include:
  - salts of calcium,
  - parasympatholytic
Sodium benzoate.
-crystalline, granular, sweetish, odorless, soluble in water.
is officinal.
-after absorption, it removes by kidney and in large quantities by bronchial gl. = expectorant and even antiseptic activity.
It is also known:
cholagogue,
choleretic,
antipyretic activity.
in: dog bronchitis and pneumonia.
Terpinhidratul officinal from: turpentine oil, alcohol, nitric acid. as: fluidifiant in dog.

Trecid (Guaiafenezin, Miocanin) - Officinal, powder, white microcrystals, characteristic odor, bitter taste, soluble in alcohol and chloroform. - in 2% syrup form and tablets. qualities: expectorant, behic, slightly sedative, hemostatic and muscle relaxant.
Antitussive substances (Behic)
These substances act on exhausting, painful and with no physiological role cough

Antitussives:
- inhibit cough center,
- decrease sensitivity of mucosa stimulus,
- decrease / eliminate the causes that produce it (foreign matter, pathological secretions)

Act by:
- interfering cough reflex, sensory nerve terminals in the pharynx, larynx, upper respiratory tract,
- on nerve centers of the CNS are responsible for initiating and coordinating the cough reflex.
Direct acting antitussive

Local action: through edulcorants where active substances are dissolved.
Edulcorants (eg honey or syrups) form a coating that protects and soothes the inflamed mucosa for short periods.

Benzonaftat (Exangit, Tessalon, Ventusin) depresses affected sensory terminations of the cough reflex and pulmonary baroreceptors.
In emergency cases, to control severe cough, can be administered conventional local anesthetic.
Central acting antitussive

narcotic antitussive
a centrally mediated decrease in cough reflex was obtained by administering the derivative of opium alkaloids, and their semi-synthetic derivatives.
To this group were added substances with strong inhibitory effects, which do not present the risk of addiction and are unrestricted.
cough center = medullar located.
specific neurons involved in coordinating cough can be suppressed by antitussives, on conventional routes and at therapeutic doses or by direct injection into three pairs of medullary nucleus.
Codeine (Codicept)
Are known several codeine salts:
- acetate, hydrobromide, hydrochloride, salicylate, etc.,
antitussives effects have only:
- phosphate,
- methyl bromide and
- sulfate.
- natural alkaloid many years being used as an antitussive.
- numerous similar actions with morphine,
- lower level (eg, analgesic and constipating effect).
- effective doses: p.o 1-2 mg / kg.
Opium, heroin and morphine
- although active are not used in practice because they are drugs.
Dihydrocodeine and dihydrocodeinone
- essentially similar to codeine.
Non-narcotic antitussive

- intended to increase the safety of their use in humans, in an attempt to simulate the ability of codeine to suppress cough center but also devoid the CNS effects that other morphine derivatives have (eg respiratory depression, analgesia and tendency habituation).

- Pholcodin
  - (Codylin, Dia-Tuss, Ethnine, Glycodine, Memine, Pectolin)
  - two times stronger than: codeine, noscapine and dexomethorphan, have similar potencies,
  - dextromethorphan is less stronger than codeine, approx. 50% of its potency.
- Similar effects of codeine
- occasionally induce vomiting.
- levorotatory isomers of dextrophan and dextrometophan have analgesic properties but addictive.
Bromoform
-colorless, volatile liquid with characteristic odor, sweetish.
in: dog spasmodic cough.

Calmotusin (Clofenagol, Detigon)
-5% aromatized alcoholic solutions.
is administered p.o.
similar to morphine but do not cause adverse effects.
-moderate anesthetic, antihistaminic, parasympatholytic in dogs.

Pectoris species
-mix drugs with mucilaginous emollient principles
-eg. marshmallow, mullein, licorice, anise fruit
determine: soothe of congested and dry mucosa, thereby removing the cough reflex.
**Iceland Moss (Cetraria)**

- same effect as pectoris species.
- removes bronchial secretions, causing the cough.
- considered: antitussives and bronchial antisecretory (turpentine oil, eucalyptol oil, as fumigation), as well as fluidifiant substances of the adherent viscous bronchial secretions,
- facilitates restoration of excretory-motor mechanisms and expectoration, pathological secretions being removed without great efforts, decreasing cough.
- bronchoconstriction induction is part of a series of processes that initiate and include cough.
- In psychogenic asthma = consequence of chemical mediators release in hypersensitivity reactions and inflammatory reactions.
- Any change in airway diameter = effect on the effort in making respiratory movements through various mechanisms:
  - parasympathetic stimulation ►►► bronchoconstriction with parasympathetic modulation of the release of adrenaline.
  - sympathetic stimulation ►► relaxational as a result of direct action on β sites of the smooth bronchial muscles, the effect being visible particularly in the case of small airways.
Spasmolytics

Atropine
- bronchodilator in chronic pulmonary emphysema in horses.
Atropine may exceed muscarinic colinceptor-mediated bronchoconstriction.
- atropine derivatives (e.g., eucatropine) included in veterinary antitussive preparations
  effect: large bronchial dilator.
s.c.: 30-100 mg / kg.

Ipratropium
- bronchodilator blocking muscarinic,
- can be administered in the form of aerosol.
Sympathomimetic

Adrenaline, isoprenaline
-and other substances - stimulate β2-adrenoceptors - in asthma control.
-In small animal therapy are used some preparations for human use.
These include ephedrine 5mg/ml syrup, p.o, a sympathomimetic with mixed function;
Eg: stimulant effects α, β and CNS.
Also: α and β stimulant effects,
-effective s.c., i.m. or i.v. in conditions of severe anaphylaxis (epinephrine bitartrate sol 1 %)
-large animals 2 -4ml,
in dogs 0.1-0.3 ml i.v.
Clenbuterol

- is a β2 agonist, long duration of action, which has been used for improving bronchospasm in horses.
- In addition to the bronchodilator effect has the ability to enhance and improve bronchial secretions and the clearance of the bronchial content by the action of cilia.

Recommended management:
- chronic allergies,
- bronchitis,
- chronic obstructive pulmonary disease and equine influenza.
Methylxanthines

- include alkaloids of which the most important for M. V.
- are:
  - caffeine, theophylline and theobromine, drugs that have multiple uses already mentioned in part (such as CNS stimulant, diuretic, cardiostimulants and smooth muscle relaxants etc.).
  - last property is the one that is responsible for the bronchodilator effect of xanthines.
  - theophylline derivatives with superior pharmacokinetic properties represent the types of substances which are currently preferred therapy.
Aminophylline, diprophylline and etamphylline are administered slowly i.m, i.v and are effective in reducing the resistance from the aerofore ways in acute bronchoconstriction.

Aminophylline is more soluble than theophylline and is better absorbed.

In the form of an alkaline salt has a lower irritability (e.g. in the form of etamphylline camsylate).

This is another derivative that can be administered p.o or in the form of suppositories for sustained prophylactic effect.

The half-life is relatively short; in dog is approx. an hour for camsylate.
Surfactants

- Type II pneumocytes produce surfactants, responsible for maintaining open the alveoli.
- Production is amplified by pilocarpine or β2 agonists.
- Antepartum administration of corticosteroids to mothers will help prevent breathing problems caused by lack of alveolar expansion in newborn babies to which can be incriminated their own insufficient production of pulmonary surfactant (e.g., bowel syndrome in foals).
Decongestants
Corticosteroids

- for use in control of allergic chronic cough in dogs,
- by p.o administration at the lowest dose, or by using injectable preparations exists the risk of reducing the resistance to infections and the suppression of adrenocortical (in the case that the administration period is prolonged).

- Common effects on the inflammatory response include:
  - membrane stabilization,
  - reducing the synthesis of antibodies
  - reducing the release of mediators from antigen-antibody interactions and
  - reducing fibrosis.
NSAIDs (Non-steroidal antiinflammatory)

- does not suppress the immune response
- accompanies inflammatory actions of the corticosteroids,
- antipyretic effects
- ability to suppress the production of chemical mediators for inflammatory response emphasizes their ability to reduce structural and functional lesions of the lungs affected by pneumonia.
- ventilation, hemodynamic and gas exchange in the lung will be improved
- Commercial: Flunixin
Antihistamines

Properties:

-parasympathicolytics,
-local anesthetics, and
-CNS sedatives
-which is beneficial in controlling the coughing reflex

For these reasons, antihistamines (such as, for example, diphenhydramine, are often incorporated in the antitussives preparations)
Cromoglycates

Sodium cromoglycate
-available to treat horses with allergic respiratory diseases, protecting them against antigenic overburdening.
-with the help of nebulizers: 80 mg / once / day, 1-4 days, providing protection for approx. 3-20 days.

Action: stabilization of mast cell membranes, thus preventing their degranulation and release of chemical mediators (histamine and leukotrienes) in response to allergenic substances.

Recently it was shown that it can prevent the release of free radicals from platelets activated with IgE, which could damage the tissue.
Respiratory stimulants

Normal oxygenation of tissues depends on:
- the availability of air at the normal atmospheric pressure,
- extracting normal proportion of O\textsubscript{2} in the blood with normal pH and normal Hb concentration.

The normal use of the available oxygen may be altered in certain circumstances, such as, the cyanide poisoning of the respiratory enzymes.
Irritant and analeptics

- They are administered by inhalation.
- Ammonia determines reflex stimulation of the respiratory and vasomotor center, therefore having improved breathing and circulation (unless profound CNS depression).
- Analeptics are stimulating the medullary centers and have convulsive action.
- Are administered i.v. or i.m. = stimulation of the respiratory and vasomotor medullar centers and are more efficient as local irritants.
Physiological stimulants

Oxygen
- essential gas for life
- medical administration cylinders: 95% O2 and 5% CO2.
- in: respiratory depression, gas poisoning, in the case of drowning, severe pneumonia or decompensated heart failure with venous congestion and stagnation of blood, blood oxygen concentration decreases to the degree of hypoxia, which, if not countered quickly = irreversible neuronal damage and finally, death.
In simple respiratory depression, cyanosis indicates the existence of hypoxemia, which is accompanied by hypercapnia.

Hypercapnia is not accompanied by cyanosis, because the nervous center is depressed and respiratory rate does not increase.

The use of 50-80% O2 in extremely serious respiratory collapse, pulmonary edema, bronchopneumonia is not recommended in cases where administration is extended over 12 h.

For short periods, O2 can be administered to animals without any side effects.

In all cases it is advisable to include CO2, 5%, = ventilation capacity increases, by physiological stimulation of the respiratory center and receptors.
Pure carbon dioxide
- to supplement gas mixtures
- over or under dosing danger may be avoided by using prepared mixes.
- after use CO2 = prevention of respiratory alkalosis.
  oxygen dissociates from Hb faster under alkalosis, thus CO2 improves cerebral perfusion.

Hyperbaric oxygen therapy
- successfully in the treatment of ischemic ulcers, for the conservation of tissues that became ischemic after trauma,
- increases the radiosensitivity of malignant cells.
- administration of O2 to 2 atm. makes the animals to become independent of hemoglobin due to the amount of oxygen dissolved in the plasma.
Thanks for your attention!