## CHRONIC BRONCHOPULMONARY DISEASES

Department of pediatrics

## CHRONIC BRONCHITIS

**Definition:** chronic bronchitis is an irreversible inflammatory process of bronchial tree with chronic character and obstinate evolution, which is producing through 3 and more recurrences per year.

## Risk factors

- repeated respiratory infections
- chronic ORL pathology (sinusites, rhinites, nasal polyposis, tonsillitis)
- habitual, cosmetic inhalator irritants, passive or active tobacco smoking
- ecologic noxious factors (smoke, vapors, exhaust gases)
- familial antecedents of chronic respiratory diseases
- familial atopy (atopic dermatitis, allergic rhinitis, asthma)

## Pathogenesis

- hyperplasia and hypertrophy of bronchial tree mucosa cells, bronchial hypersecretion
- destruction and metaplasia of cilial epitheliocytes, degeneration of cilia, disturbance of mucocilial clearance
- · phenomena of bronchial wall fibrosis and sclerosis
- infiltration of mucosal and submucosal layer with inflammatory cells
- disorders of local microcirculation

## Clinical forms

- Simple chronic bronchitis
- Obstructive chronic bronchitis

# Clinical picture

## In exacerbation

- frequent, productive cough, more intense in morning period
- purulent expectorations, more expressed in morning
- thoracic pain, more intensive in night
- expiratory dyspnea, wheezing (in obstructive form)
- harsh respiration at auscultation
- polymorphous bubbly coarse crackles (in chronic obstructive bronchitis)
- febrile syndrome, toxico-infectious manifestations

## In remission

- Morning, with effort, at cold air cough (presence of bronchial hyperreactivity)
- Non-significant morning expectorations
- Dyspnoea on effort in obstructive form of bronchitis

## INVESTIGATIONS

## Spirography

- ventilator obstructive disorders by mixt and restrictive type (in advanced stages of chronic bronchopulmonary process)
- · disorders of small caliber bronchi permeability
- positive pharmacodynamic test with bronchodilators in chronic obstructive bronchitis

## Chest X-ray

- diffuse accentuation of pulmonary picture
- perihilar pronounced reactions
- · bronchial, especially basal, deformations
- pulmonary hyperinflation (in obstructive form)
   Bronchoscopy
- catarrhal-purulent endobronchitis
- focal hyperplasia of bronchial mucosa
- cylindric deformations of bronchi
   *CT scan*
- deformed peripheral bronchi
- thickening of bronchial wall

## Hemoleucogram

leucocytosis, neutrophilosis, increased ESR (in infectious episodes)

## Culture of sputum, tracheal aspirate, bronchial washing waters

- identifying of etiologic factor
- antibiogram of bacterial stems

## Immunology

- cellular, humoral immunocompromission
- phagocytary insufficiency
- non-specific humoral insufficiency

- Serologic tests
- identifying of specific antibodies to Chlamydia, Mycoplasma, respiratory viruses
- Blood gases
- hypoxemia, hypercapnia
- respiratory acidosis

## Differential diagnosis

- bronchopneumonia
- bronchiectasis
- pulmonary tuberculosis
- cystic fibrosis
- respiratory system malformations
- chronic sinusitis
- bronchial asthma
- congenital heart diseases

## Complications

- toxico-infectious syndrome
- cardio-respiratory insufficiency
- astenic syndrome
- pulmonary complications

## Treatment

### I. Treatment in exacerbation

- Restoring of bronchial permeability
- hydric regime corresponding to physiologic necessities and pathologic losses
- ✓ expectorant and mucolytic teas
- ✓inhalator procedures
- Mucolytics and expectorants for bronchial secrets fluidification
- ✓bromhexin, ambroxol
- ✓ acetylcystein, carbocystein
- ✓ phytotherapeutic remedies, teas from medicinal herbs, bronhipret

- *Inhalator broncholytics* in bronchoobstructive syndrome
- short action *b*ronchodilators: salbutamol, clenbuterol, bricanil, berotec, atrovent, berodual
- Long-term treatment with prolonged action bronchodilators (salmeterol, formoterol) in chronic obstructive bronchitis
- Corticotherapy in obstructive variant
- beclometazon, budesonid, fluticazon in inhalation (chronic treatment in remission)
- Prednison in perfusions or oral (in severe bronchoobstructive exacerbations, short cures a fev days)

- Etiologic treatment
- antibiotics (amoxicillin, protected amoxicillins, cefalosporins, aminoglycosides, macrolides)
- *antibioticotherapy* aimed conformable to identified germs antibiogram in sputum culture, bronchial washing waters
- antifungal drugs (fluconazol, ketoconazol): in fungal infections
- mode of administration: oral (soft exacerbations), parenteral (severe infectious episodes, purulent, toxico-infectious complications)

- Curative bronchoscopy with bronchial washing
- administration of antibiotics, antiseptics
- corticoids (hydrocortisone) local antiinflammatory action
- Symptomatic treatment
- antipyretics (febrile syndrome)
- antihistaminics (atopy, allergic dermatitis)
- anticonvulsivants (convulsive syndrome)
- Active and passive kinetotherapy, postural drainage, thoracic percussion, massage of thorax
- Physiotherapeutic programs
- microwaves, ultrashort waves, inductotherapy on thorax

# Prophylactic and recovering treatment

- *Curative respiratory gymnastics*, postural drainage, thoracic percussion, assisted respiration, respiratory kinetotherapy – systematically, every day, in morning (respiratory morning toilette)
- *Sanatory treatment* in pneumologic profile stations (saline mines, forest conditions, mountain stations)
- *Vitaminotherapy* (A,E,B5,B15,C)- consecutive cures by 2-3 weeks with different groups of vitamins, in period of clinical remission, in absence of purulent expectorations
- Antianemic remedies (iron, folic acid preparations)

- Immunomodulators
- Bacterial lysates with local naso-pharyngeal immunomodulatory effects (imudon, IRS-19)
- Bacterial extracts with systemic immunomodulatory action (Ribomunil, Bronchomunal, Bronchovaxon)
- Specific immunoprophylaxis
- annual antigrippal vaccines
- antibacterial vaccines (antipneumococcal, antihemophylus type B vaccine)
- Sanation of chronic infection foci (otorhinolaryngologic, dental, digestive, other localizations)

- *Hypoallergic alimentary regime* in chronic obstructive bronchitis
- Reducing of risk factors influences
- improving of sanitaro-hygienic conditions of child's habitual medium (optimal ventilation, elimination of dampness and mould, removing of negative influence of home chemical products, optimal termic regime)
- removing of active and passive tobacco smoking
- reducing of influence of noxious industrial atmospheric factors, unfavorable climatic factors (excessive humidity, negative temperatures, winds)
- avoidance of professional irritative noxious factors

- Evolution
- recurrent, persistent with minimal chances of healing in childhood period
- Continuous progressing in adult age with development of pulmonary and extrapulmonary complications, major risks of invalidity (in persistent noxious influences)

## **BRONCHIECTASIS**

Bronchiectasis is a chronic suppurative disease characterized by destruction of the bronchial and peribronchial tissues, dilatation of the bronchi and accumulation of infected material in the dependent bronchi.

## **Etiology**

Congenital bronchiectases:

- pulmonary sequestration, bronchogenic pulmonary cysts; Infections:
- tbc, convulsive cough, measles;
- Adenoviruses, herpesvoruses;
- Aspergillus, mycoplasma;

- Piogenic germs

- Congenital and hereditary diseases:
- Cystic fibrosis;
- $\alpha$ -1 antitripsin deficiency;
- Kartagener syndrome;
- Mounier-Kuhn syndrome;
- Marfan syndrome;
- Wiliams-Campbell syndrome;
- Congenital immunodeficiencies
- Foreign body aspiration;

### **Etiology**

Middle lobe syndrome;

Bronchial asthma;

Gastroesophageal reflux;

Fibrosant bronchopulmonary diseases;

Localized bronchial obstruction.

## **Clinical picture**

**Disease history:** frequent, chronic cough with expectorations (in medium 3 years), acute onset after acute viral bronchopneumopathies.

### Symptoms:

- Cough (97%): frequent, in morning, at position changing after sleeping (posterior or anterior bronchiectasis), during the day (apical localization), nocturnal (central localization)
- Expectorations: morning (bronchial toilette), at position changing, after effort, postural drainage, kinetotherapy, mucopurulent, purulent, with fetid smell
- Wheezing: bronchoobstructive syndrome in asthma, mycotic etiology, hyperimmunoglobulinemia E;

## Clinical picture

- Thoracic pain, bronchial secretion retentions, extension of affection on pleura;
- Hemoptisis, appears tardy on the background of infectious episodes;
- Dyspnea- in extended bronchiectases, in exacerbation phase;
- Intermittent fever in disease exacerbations;
- Failure to thrive, digital hyppocratism.

## Bronchopulmonary physical signs

- Normal or malformed thorax;
- Great transthoracic vibrations at palpation;
- Localized subcrepitant crackles, attenuating after cough, treatment, kinetotherapy;
- Localized pulmonary dullness;
- Diminishing of vesicular murmur, blowing respiration, bronchophonia;
- Signs of pulmonary condensation in pneumonia, fibrosis of peribronchiectatic parenchyma;
- Pleural syndrome;
- Cavity syndrome (amphoric breathing, bullous crackles)
- Recurrent wheezing.

## Extrarespiratory manifestations

- Pallor;
- Astenia;
- Intermittent fever;
- Failure to thrive;
- Headache, anxiety.

## Investigations

- **Hemogram:** leucocytosis, neutrophilia, lymphocytosis, shift to the left, increased ESR;
- **Sputum culture:** H. influenzae, St. pneumoniae, S. aureus, Gram-negative germs, Mycoplasma pneumoniae, Chlamidia pneumoniae, Candida and other fungi;
- Chest X-ray (suggestive changes):
- segmental accentuation and diminished pulmonary picture;
- Diminished pulmonary volume;
- Cystic bronchial dilatations, sometimes with hydro-aeric levels;
- Alveolar aspect "honey comb" of cystic dilatations (in severe forms);
- Compensatory hyperinflation.

### **Investigations**

### - Bronchography:

- Bronchial dilatations (cylindrical, ampullar, sacciform);
- Absence of distal bronchi opacity;
- Absence of bronchi wall parallelism;
- Anomalies of bronchial tree
- Bronchoscopy:
- Endobronchitis signs, bronchiectatic sectors, taking of probes for bacteriologic and histologic investigations
- CT-scan:
- Dilated peripheral bronchi;
- Thickened bronchial walls;
- Linear alveolar zone;
- Agglomerations of cysts

### **Investigations**

- Nuclear magnetic resonance:
- Bronchiectatic zones;
- Inflammatory pulmonary zones;
- Areas of fibrosis, pulmonary sclerosis;
- Tumoral tissues
- **Pulmonary scintigraphy** (screening-test for bronchiectasis):
- reducing or absence of pulmonary perfusion in affected zones
- Spirography:
- Obstructive modifications, associated with restrictive component, reduced vital capacity, increased residual volume
- Sanguine gases:
- Respiratory alkalosis, hypoxemia

## **Investigations**

### - ORL examination:

• X-ray of maxillary, ethmoidal sinuses, of nasopharynx, sinusitis, nasal polyposis

### Differential diagnosis

- Habitual (psychogenic) cough;
- Rhinopharyngeal, sinusal cough;
- Allergic cough;
- Atypical pulmonary infections
- Foreign body aspiration
- Gastroesophageal reflux;
- Bronchopulmonary supurations
- Pulmonary masses
- Mediastinal masses

### <u>Treatment</u>

- Hygieno-dietetic measures
- Sparing general regime with home treatment realizing (in soft exacerbations) or with hospital treatment (moderate, severe forms)
- Removal of irritant inhalator factors (tobacco smoke, industrial gases, etc)
- Optimized habitual conditions
- Hypercaloric, hyperproteic alimentary regime
- Sulfur containing mineral waters
- Sanation of infection foci
- Fluidification of bronchial secretions
- Bronchial permeability straightening
- Repeated curative bronchoscopies with bronchial lavage with antibiotics
- Postural drainage, kinetotherapy, respiratory gymnastics, assisted cough
- Thoracic physiotherapy: electrophoresis, microwaves, inductotherapy, thermotherapy

## Treatment

## - Measures of antiinfectious prevention:

- Vaccination;
- Systemic antibacterial lysates (Ribomunil, Bronchomunal)
- Local antibacterial lysates (IRS19, Imudon)
- **Balneary treatments** at stations with warm and dry atmosphere, in period of clinical remission
- Surgical treatment.

## PRIMARY CILIARY DYSKINESIA (IMMOTILE CILIA SYNDROME, KARTAGENER SYNDROME)

Immotile cilia syndrome – genetic autosomalrecessive disease characterized by ultrastructural and functional anomalies of ciliated cells characterized through chronic diseases of bronchopulmonary system, ORL organs and internal organs inversion.

## Pathogenesis

- Structural anomalies of ciliated cells cilia (transposition of microtubes, medial and radial dienine arms) from respiratory system (nasal cavity, paranasal, frontal sinuses, medium ear, bronchial tree);
- Disorder of mucociliary clearense, absence of ciliary oriented movements, installation of chronic bronchopulmonary phenomena;
- Functional affections of spermatozoids, uterine tubes with male, rarer female infertility
- Situs inversus is the result of visceral organs rotation process in intrauterine period conditioned by the absence of oriented movements of embryo ciliated cells cilia

## Clinical picture

## Onset

In the period of suckling baby with recurrent respiratory infections, long-term evolution, association of complications with chronic bronchopulmonary and ORL processes forming

## ORL organs affection

Rhinitis, sinusitis, chronic otitis, infectious perforations of tympanum, nasal polyposis, anosmia

## - Bronchopulmonary affection

- Productive recurrent daily, chronic cough
- Purulent expectorations
- Recurrent wheezing, bronchoobstructive syndrome
- Dyspnea, more expressed at physical effort
- At auscultation and percussion- signs of pulmonary condensation
- Digital hyppocratism in severe evolution
- Total situs inversus in 50% of cases
- Alteration of cilia movement at the level of embryonic tissue
- Absence of visceral organs rotation in embryonal period

## - Reproductive organs affection

- Spermatozoids motility decreasing, oligospermia
- Uterine tubes affection
- Male, rarer female infertility



ECG Kartagener's in syndrome showing features of dextrocardia: Negative P wave, QRS complex and T wave in lead I, right lower quadrant QRS axis and regression of QRS amplitude from V1 to V6 (as the heart is on the opposite side).

## Bronhoectasis



## Dextrocardia



## Chronic sinusitis



## Sterility in males



## Ectopic pregnancy



## Investigations

#### - X-ray:

- · ORL: sinuses opacity, mastoidian and medium ear sclerosis
- Pulmonary: situs inversus, chronic bronchitis, segmental atelectasies, middle lobe syndrome, images of bronchiectasis, sectors of pneumosclerosis

#### - Internal organs echography:

- Abdominal visceral organs (liver, spleen) and thorax organs (heart) inversion
- ECG: features of dextrocardia negative P wave, QRS complex and T wave in lead I, right lower quadrant QRS axis and regression of QRS amplitude from V1 to V6 (as the heart is on the opposite site)

#### - Spirography:

Bronchial obstruction (bronchial conductibility disorders), restrictive disorders (in extended bronchiectasies)

#### - Pulmonary scintigraphy:

- Severe reducing of pulmonary perfusion
- Sanguine gases: hypoxemia

## Investigations

### - Bronchoscopy:

- Anatomic inversion of bronchial tree, diminishing or absence of ciliary movements, purulent endobronchitis, bronchial deformations, bronchiectasies
- Bronchography:
- Cylindrical or sacciform bronchiectasies (more frequent affection of middle lobe)
- **Electronic microscopy** of nose, bronchi, spermatozoids cilia (cilia structural anomalies)
- **Bacteriologic examination:** identifying of etiologic germs in sputum, tracheal aspiration, aspiration of ORL secretions
- Audiogram: hearing modifications

## Differential diagnosis

Respiratory diseases with chronic cough (chronic bronchitis, cystic fibrosis, bronchial asthma, chronic interstitial pneumonias).

## Treatment

- Treatment of respiratory infections (antibioticotherapy)
- Broncholytic, expectorant medication
- Active and passive kinetotherapy, postural drainage
- Specific immunization (antigrippal, antipneumococcal vaccination)
- Avoiding of noxious inhalator factors (industrial, habitual, tobacco smoke)
- Balneary treatments in clinical remission periods

## Evolution

- Lent progressive with chronic evolution of respiratory system pathology
- Increased respiratory (ORL and bronchopulmonary) morbidity

## Prognosis

Favorable for long-term period

## Foreign body aspiration

**Definition.** Foreign body aspiration is an accidental getting of foreign body through pharynx and larynx in the inferior respiratory pathways which produces a state of asphyxia with life threatening.

#### Etiology. Organic foreign bodies

- sunflower, melon, water melon, pumpkin seeds
- beans, soya, pea, cereal seeds
- grains of different plants
- vegetal fragments, other alimentary products
- Mechanical foreign bodies
- fragments of bones
- little stones
- little plastic objects, little toys, beads, mosaic
- metal objects, nails, needles

### **Pathogenesis**

The aspiration of foreign body in respiratory pathways has the following evolutions:

- spontaneous expulsion through cough reflex immediately after aspiration
- good toleration without bronchopulmonary complications
- acute respiratory failure in acute laryngospasm, lobar athelectasis, localized emphysema (valve mechanism)
- secondary chronic bronchopulmonary processes with tolerance to classic therapy with antibiotics, bronchodilators, mucolytic drugs

## Clinical picture

Clinical signs in onset

- penetration syndrome
- sudden suffocation crisis conditioned by glottic spasm reflex
- inspiratory retraction of chest
- ≽ apnea
- asphyxia with cyanosis
- inspiratory stridor
- > wheezing
- rough voice, dysphonia
- > tormenting , quintal cough in expulsive accesses

Evolutive clinical signs ("stay" syndrome)

- chronic cough, cough in accesses, expulsive at position change, at clinical examination, physical effort
- pneumonia with long-term, recurrent evolution, refractory to classic treatments
- dullness at athelectatic areas percussion
- unilaterally attenuated respiration
- humid polymorphous hypersonorous crackles
- *symmetry of thorax* 
  - bulged hemithorax in valve mechanism
  - decreasing in volume in obstruction with athelectasis
- mediastinum shifting
  - in athelectasis to the athelectatic sector
  - in localized hyperinflation to the healthy lung

## Explorative picture

#### X-ray chest

- Athelectasis (triangular opacity) in obstruction
- Localized hyperinflation in valve mechanism
- Shifting of mediastinal organs
- Placed down diaphragm (in hyperinflation)
- Lifting of diaphragm dome (in athelectasis)
- Evidence of foreign body in respiratory system (radioopaque)

Bronchoscopy

- Identifying of foreign body in bronchial tree
- Traumatisms of bronchial mucosa
- Granulations of bronchial mucosa in the place of foreign body fixing
- Posttraumatic bronchial stenoses
- Catarrhal, purulent endobronchitis
- Pathologic bronchial secretions (sero-mucous, purulent, posttraumatic hemorrhagic)

## Differential diagnosis

- viral laryngotracheitis: acute onset with barking cough, dyspnea in children with fever, signs of acute respiratory infection
- *diphtheric croup:* inspiratory stridor, aphonia with progressive installation, anxious face, accesses of suffocation, diphtheric films in pharynx
- bronchial asthma: expiratory obstruction with diffuse pulmonary emphysema receptive to medication with bronchodilators
- *tuberculous lymphadenitis:* epidemiologic history of tuberculosis, positive tuberculinic tests
- retropharyngeal abscess, thymomegaly, laryngeal papillomas

### Treatment

Emergency measures

- Heimlici procedure
- urgent transport in specialized departments (ORL, pneumology) for diagnostic and curative bronchoscopy, extraction of foreign body from respiratory pathways

Etiopathogenetic treatment

- antibacterial protection treatment, therapy of bronchopulmonary infectious complications
- repeated curative bronchoscopies with endobronchial washing, administration of antibacterial preparations, antiinflammatory medication

### Symptomatic medication

- medication with bronchodilators (salbutamol, berotec, atrovent)
- antiinflammatory treatment for to reduce the posttraumatic and infectious inflammation – in infectious pulmonary complications (systemic corticoids, inhalator)
- mucolytic, expectorant drugs (ambroxol, etc.)
- kinetotherapy in the period after foreign body elimination

## **Evolution and prognosis**

- >decease in 4-6% cases of acute asphyxia
- chronic bronchopulmonary processes in the case of late diagnosis:
  - localized pulmonary fibrosis
  - fibroathelectasis
  - localized bronchiectases
  - chronic bronchitis

complete healing (in the case of timely addressing, correct diagnosis, elimination of foreign body from respiratory pathways)

## TRACHEOMALACIA

### Definition

Tracheomalacia is the absence of cartilaginous system development in trachea.

### Clinical picture

- Recurrent stridor
- Recurrent wheezing
- Recurrent bronchitis
- Chronic cough syndrome
- · Apnea with cyanosis in aliments swallowing phases
- Respiratory discomfort in rest with accentuation at physical effort
- Swallowing disorders

## Diagnosis

 Endoscopic (tracheoscopy) – absence of cartilage rings in trachea

## Treatment

- Symptomatic
- Kinetotherapy
- Antibiotherapy (in respiratory infections)

## Bronchomalacia

## Definition

• Bronchomalacia is the absence of cartilaginous structures in bronchial tree

## Clinical picture

- Is associating with tracheomalacia
- Dyspnea in neonatal period
- Recurrent respiratory infections in suckling period
- Congenital lobar emphysema

## Diagnosis

- Bronchoscopy absence of cartilage rings in bronchial tree
- Bronchography generalized bronchial dilatations

Evolution

• Progressive with grave chronic occurrence (severe bronchopulmonary infections, severe bronchoobstructive syndrome, respiratory insufficiency).

## **CYSTIC FIBROSIS**

• Cystic fibrosis (CF) is an inherited multisystem disorder of children and adults, characterized by obstruction and infection of airways and by maldigestion and its consequences. It is the most common life-limiting recessive genetic trait in children. A dysfunction of epithelialized surfaces is the predominant pathogenetic feature and is responsible for a broad, variable, and sometimes confusing array of presenting manifestations and complications.

## CYSTIC FIBROSIS

• CF is the major cause of severe chronic lung disease in children and is responsible for most exocrine pancreatic insufficiency in early life. It is also responsible for many cases of salt depletion, nasal polyposis, pansinusitis, rectal prolapse, pancreatitis, cholelithiasis, and insulin-dependent hyperglycemia. CF may present as failure to thrive and, occasionally, as cirrhosis or other forms of hepatic dysfunction. Therefore, this disorder enters into the differential diagnosis of many pediatric conditions.

## Etiology

- The most common severe inherited disease in the Caucasian population (autosomal recessive in inheritance).
- Cystic fibrosis transmembrane regulator (CFTR): functions as a cyclic AMP-activated chloride channel, which allows for the transport of chloride out of the cell. It is accompanied by the passive passage of water, which keeps secretions well hydrated.
- In cystic fibrosis, an abnormality in CFTR blocks chloride transport and inadequate hydration of the cell surface results in thick secretions and organ damage.
- The CFTR gene is 250.000 base pairs long and located on the long arm of chromosome 7. The most common deletion is three base pairs, which results in the absence of phenylalanine at codon 508.

## Epidemiology

Incidence of cystic fibrosis
1:2500 in Caucasian population
1:17.000 in African-American population (rarely seen in African blacks and Asians)

## **Symptoms**

- Chronic cough, recurrent pneumonia, bronchorrhea, nasal polyps, and chronic pansinusitis.
- Pancreatic insufficiency: occurs in 85% of patients. Fat malabsorption may lead to failure to thrive or pancreatitis.
- Rectal prolapse: occurs in 2% of of the patients.
- Meconium ileus: 15 20% of patients present with this symptom.
- Distal obstruction: of the large intestine may be seen in older children.
- Hypochloremic metabolic alkalosis.

## Signs

- Cough (frequently productive of mucopurulent sputum), rhonchi, rales, hyperresonance to percussion, barrel-chest deformity of thorax in severe cases, nasal polyps, and cyanosis (in later stages).
- Digital clubbing, hepatosplenomegaly in patients with cirrhosis, growth retardation, hypertrophic osteoarthropathy, and delayed puberty, amenorrhea, irregular menstrual periods (in teenage patients).

## Investigations

*Sweat test:* "gold standard" for the diagnosis of cystic fibrosis.

- Sweat chloride >60 mEq/L is considered abnormal. False positives are seen in severe malnutrition, ectodermal dysplasia, adrenal insufficiency, nephrogenic diabetes insipidus, hypothyroidism, hypoparathyroidism, mucopolysaccharidoses. False negatives are seen in patients with edema and hypoproteinemia.
- Genetic testing: over 600 identified genotypes, but only 20-70 of the most common are tested: thus, the lack of a positive genotype reduces (but does not eliminate) the possibility that a CF sample can be obtained from blood or buccal cell scraping.

## Investigations

- Sputum cultures: frequent pathogens include Staphylococcus aureus, Pseudomonas aeruginosa (mucoid and nonmucoid), Burkholderia cepaica.
- Pulmonary function tests: usually reveal obstructive lung disease.
- Pancreatic function tests: 72-hour fecal fat measurement, measurement of serum paraaminobenzoic acid (PABA) levels, stool trypsin levels, serum immunoreactive trypsin(IRT).
- Chest radiography: typical features include hyperinflation, peribronchial thickening, atelectasis, cystic lesions filled with mucus, and bronchiectasis.
- Sinus radiography: typically shows pansinusitis.

### Complications

- Respiratory: recurrent bronchitis and pneumonia, chronic sinusitis, pneumothorax, hemoptysis.
- Gastrointestinal: include pancreatic insufficiency; patients usually have steatorrhea; decreased levels of vitamins A, D, E andK; poor growth and failure th thrive; meconium ileus equivalent; rectal prolapsed; and clinically significant hepatobiliary disease (cirrhosis of the liver, esophageal varices and splenomegaly).
- Reproductive: include sterility in 98% males and 75% females.
- Endocrine: abnormal glucose tolerance; diabetes mellitus.

## Differential diagnosis

- Pulmonary: recurrent pneumonia, chronic bronchitis, immotile cilia syndrome, severe asthma, aspiration pneumonia.
- Gastrointestinal: gastroesophageal reflux, celiac sprue, protein-losing enteropathy.
- Other: failure to thrive (secondary to neglect, poor caloric intake or feeding problems), immune deficiency syndromes, nasal polyposis, male infertility, hyponatremic dehydration.

Treatment goals

- To maintain good nutritional status (good nutrition is associated with better prognosis).
- To slow pulmonary deterioration as much as possible.
- To maintain a normal lifestyle.

## Diet and lifestyle

- High caloric diet with nutritional supplements (given orally, via nasogastric tube feedings or through gastrostomy tube feeding).
- Vitamin supplements: multivitamins and fat soluble vitamin replacement (usually E and K).
- Pancreatic enzyme replacement therapy can be used in patients who are pancreatic insufficient. Dosage is adjusted for the frequency and character of the stools and for growth pattern.
- Stool softeners treat constipation or meconium ileus equivalent and include mineral oil, oral N-acetylcysteine, lactulose, enemas.

### Pharmacologic treatment

Antibiotic therapy (based on sputum culture results).

- Oral antibiotics: cephalexin, cefaclor, trimethoprimsulfamethoxazole, chloramphenicol, ciprofloxacin.
- Intravenous antibiotics (given for 2-3 week course)
- For Staphylococcus aureus: oxacillin, nafcillin;
- For *Pseudomonas aeruginosa or Burkholderia cepacica:* semisynthetic penicillin (ticarcillin, piperacillin) or a cephalosporin (ceftazidime) *plus* an aminoglycoside (gentamycin, tobramycin, or amikacin) to obtain synergic action.

For aid in clearing pulmonary secretions:

- Aerosolized bronchodilator therapy (to open airways): albuterol;
- Mucolytic agents (to help break up viscous pulmonary secretions): N-acetylcysteine, recombinant DNase.
- Chest physiotherapy with postural drainage.

## Prognosis

- Long-term prognosis is poor.
- The course of the illness is variable; it is impossible to predict the course of the disease in a specific person.
- The current mean life span is 29 years.
- Due to new antibiotics, enzyme-replacement therapy, and maintenance of good pulmonary toilet with chest physiotherapy and bronchodilators, the mean age of survival has been increasing for the past three decades.



- Routine care should be at Cystic Fibrosis Center.
- Frequency of visits is dependent on severity of illness: usually every 2-4 m.
- Usually lifelong nutritional support is required.
- Duration of antibioticotherapy is controversial. Chronic use is eventually required as the patient's pulmonary function deteriorates.
- All siblings should have a sweat test.