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GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF CYSTIC FIBROSIS

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(MUCOVISCIDOSIS) ASSOCIATION

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GUIDELINES FOR THE

DIAGNOSIS AND MANAGEMENT

OF

CYSTIC FIBROSIS

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P R E F A C E

This publication is intended primarily for paediatricians, physicians and other health professionals involved in the diagnosis and care of patients with cystic fibrosis. Few diseases illustrate more vividly the inequalities in knowledge, practice and resources which exist between the health services of affluent, 'developed' countries and those at an earlier stage of 'development'. It is therefore intentionally written in a style and at a level which should be relevant and accessible to clinicians working in all countries. Mention of high-technology, expensive and experimental treatments which are likely to be restricted in availability is brief and superficial, while the principles of care applicable in all countries are given greater attention.

Nonetheless, it is impossible to deal adequately with the complexities of cystic fibrosis in such a booklet, and we have attempted to merely provide an introduction to the disease for those who are beginning to deal with a few patients. More detailed information can be obtained by consulting books recommended under Further Reading. As a companion to this volume, a second book of guidelines intended for allied health professionals is in preparation. It will include practical technical details of physiotherapy, dietary management and laboratory methods.

Fernando A. de Abreu e Silva ♦ John A. Dodge

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INDEX

Page

/...

INDEX continued

Page

INTRODUCTION

Cystic Fibrosis (CF) is a genetic disease affecting the respiratory and gastrointestinal tracts and the sweat gland. It is the most the most common cause of suppurative lung disease in children and young adults.

Formerly it was considered to affect predominantly white children but now it is known to occur in all races in all parts of the world, although with varying incidence.

When it was first identified many years ago, CF was called a "fatal" or "lethal" disease because the life expectancy then was below five years of age. Today however with a more thorough understanding of the disease and a positive therapeutic approach, it is recognized and treated earlier and more effectively and as a consequence mean life expectancy in developed countries is about 30 years. This improvement is not evenly distributed and it has been calculated that up to 95% of cases in Latin America are never diagnosed, while life expectancy in the few who are identified is reduced by two thirds compared with that in the best world centres.

The incidence varies according to the population considered but it ranges between 1:2000 to l:4000 live births in most European populations although it is less common in blacks and rarely reported in orientals.

GENETICS

Cystic Fibrosis is inherited in an autosomal recessive way. When both parents are heterozygotes and are thus only carriers of the abnormal gene their offspring have the l:4 chance of being born with Cystic Fibrosis. It is important to emphasize to parents that each pregnancy carries the same risk and is a separate event: "chance has no memory". Please see Figure 1 below.

Fig. 1 Inheritance Pattern of Cystic Fibrosis

Gene carriers usually have no clinical symptoms as only the homozygote state is associated with symptomatic disease. To date more than 500 mutations in the large gene responsible for CF have been identified. Some are associated with more severe forms of the disease and some are present more often in certain population groups. It is estimated that the carrier rate is about 1:25 in most of Europe and North America.

The mutation causes the faulty production of a protein which forms a channel for the passive movement of chloride through epithelial cell membranes and which is called Cystic Fibrosis Transmembrane Conductance Regulator (CFTR). In the respiratory mucosa under normal conditions sodium is secreted, followed by chloride and then by water, and that is how the mucosa remains moist. In CF sodium is secreted but the chloride channel "blocked", so sodium and water return to the interstitium to maintain electroneutrality. The respiratory secretions in common with those in the gastrointestinal tract and pancreas have a low sodium, low chloride and low water content. In contrast abnormal CFTR function in the sweat duct inhibits chloride absorption, resulting in salty, concentrated sweat.

PATHOGENESIS

Cystic fibrosis is sometimes known as "mucoviscidosis". This name implies that mucous secretions are particularly viscous, and although the concept is limited it explains much of the pathogenesis of this disease.

Respiratory System

The mucous glands produce large quantities of a thick secretion which sticks to the airways and blocks the small bronchioles. As infection of this stagnant mucus by various microorganisms takes place (see below), inflammation follows and sputum production increases. The secretions change from mucoid to purulent. The upward movement of mucus by ciliated epithelium (the "mucus escalator") is impaired, leading to further obstruction and infection and creating a vicious circle.

The walls of the airways show varying degrees of inflammation and progressively thicken; supporting structures of the airway walls are progressively destroyed leading to bronchiolectasis and bronchiectasis. As the smaller airways (due to their narrower calibre) tend to be blocked, air trapping can occur very early in the course of the disease. Persistent mucous obstruction of the airways may lead to atelectasis.

With the progression of the disease, widespread bronchiectatic changes take place, with destruction of lung parenchyma. In later stages, due to sustained hypoxemia, pulmonary hypertension appears and finally cor pulmonale. It is important to keep in mind that it is the status of the lungs that will usually determine the survival of the CF patient.

Infection

At some time during the first year of life or later, frequently after a viral infection which might lower the local defences, the lower respiratory tract is invaded by a number of different microorganisms.

Staphylococcus aureus, and *Pseudomonas aeruginosa* (mucoid and non-mucoid strains) are by far the most common infecting organisms, followed by *Haemophilus influenzae*, *Escherichia coli* and *Klebsiella pneumoniae*, and by others of much less prevalence. In recent years *Burkholderia cepacia*, formerly called *Pseudomonas cepacia*, has appeared as a major pathogen in many centres. *S. aureus* may be the first pathogen to invade and is often followed by *P. aeruginosa*. Once *P. aeruginosa* is regularly isolated from the respiratory tract of a CF patient it can only rarely be eradicated.

Pancreas

Inspissated secretions often block the pancreatic ducts even before birth, and the pancreatic enzymes normally produced by the pancreatic acini are prevented from reaching the duodenum. Autodigestion of the pancreas then occurs. When this process is advanced, often in the first months of life, the pancreas appears to be composed of cysts and fibrosis -hence the name of the disease. Maldigestion and malabsorption are then an inevitable consequence, and unless treated result in severe failure to thrive. Some CF mutations are associated with relative sparing of the pancreas, and the process of chronic

pancreatitis described above may then be postponed, with retention of adequate pancreatic function, sometimes for many years.

Intestines

Impaired chloride secretion and increased mucus secretion also occurs in the intestinal tract. In up to 20% of affected infants, this produces meconium ileus: an obstruction to the distal small bowel at birth caused by inspissated sticky meconium. Small intestinal atresias also occur. The distended bowel sometimes perforates before birth, producing meconium peritonitis. Meconium ileus nearly always indicates that the infant has CF although it can very rarely occur in isolation.

Distal intestinal obstruction syndrome (DIOS, also called meconium ileus equivalent), is a term used to describe acute, subacute or chronic obstruction to the proximal colon produced by an adherent mass of mucus and faeces, and it is a feature of CF in older children and adults. Intussusception may also be a cause of intestinal obstruction in CF children.

Liver

In a small number of infants, prolonged neonatal jaundice due to "inspissated bile syndrome" may be a presenting feature of CF. Nearly all CF patients have some degree of hepatic fibrosis, but in 5-10% this progresses to overt liver disease with biliary cirrhosis and portal hypertension.

Skin

Sweat from cystic fibrosis patients has a higher concentration of sodium and chloride, up to approximately five times the normal salt content. This abnormality is present from birth and persists throughout life. It is the basis for the diagnostic sweat test. In hot climates excessive salt loss in the sweat leads to metabolic alkalosis and heat prostration.

Reproductive System

With very few exceptions men with CF have obstructive azoospermia due to congenital absence, atrophy or obstruction of the vas deferens and are therefore sterile. This anatomical abnormality also affects a proportion of male carriers.

Females with CF have decreased fertility due to increased viscosity of the cervical mucus making sperm migration difficult, but many have borne children.

CLINICAL FEATURES

CF symptoms appear in the first year of life in the great majority of patients but may appear later, even in adulthood. The presentation depends in part upon the specific mutation(s) present, and the most common (ΔF508) is nearly always associated with pancreatic insufficiency and early presentation. However, cystic fibrosis is a multi-organ disease and as the mean age of survival has increased so has the incidence of late complications formerly thought to be uncommon, such as diabetes or serious liver disease.

Some patients despite an early diagnosis and appropriate treatment experience rapid progression of their lung disease, while others will have a much more favourable course and reach adulthood. It is impossible to predict the outcome of a patient with cystic fibrosis, even when the precise mutation is known. Other genetic and non-genetic factors have important, perhaps decisive roles in determining prognosis. They include treatment, nutrition, lifestyle and compliance, and chance events such as exposure to specific viral, bacterial and fungal infections.

Presenting Features

At birth

Cystic fibrosis may present in the neonatal period with intestinal obstruction (meconium ileus) sometimes associated with peritonitis secondary to perforation. Abnormal x-rays show a characteristic "ground glass" or bubbly appearance, with distended bowel loops but no air fluid levels and contrast enema reveals a microcolon. Treatment may be medical, using a high osmolarity contrast enema such as "Gastrografin", in which case it should be performed by a skilled radiologist and accompanied by large amounts of IV fluid. Otherwise, surgical treatment is needed, the operation of choice being a temporary ileostomy with irrigation of the proximal and distal bowel. Every neonate who presents with meconium ileus should have a sweat test and be considered to have cystic fibrosis until proven otherwise.

Prolonged jaundice in the neonatal period may also be an isolated first sign and it is present in 50% of the cases of meconium ileus.

In the first year

The typical infant with CF has a repetitive dry cough, bulky offensive motions, and fails to thrive, but in some either respiratory or gastrointestinal symptoms predominate. The classic picture is of an infant who fails to thrive, with frequent, pale, bulky, foul smelling and sometimes oily stools, containing foodstuffs, and which float in water and are difficult to wash away. There is a poor growth pattern with decreased subcutaneous tissue and muscle mass in spite of a normal or even voracious appetite.

Some infants do not present such a typical picture of malabsorption and steatorrhoea, and failure to thrive can be the sole manifestation. Pancreatic insufficiency may develop at any time in the life of the CF patient. In the great majority (90%) it is demonstrable in the first year of life, it is progressive and it may take a long time for

typical malabsorption signs to appear. Secondary deficiencies of fat soluble vitamins, particularly A and E, are common in untreated patients.

Infants often present with cough which in the beginning is dry and occasional but may progress to chronic, harsh, frequent and productive and may provoke vomiting during a bout. Cough sometimes mimics whooping cough and can be initiated by a viral upper respiratory infection. At first, chest auscultatory signs may be absent but on close inspection the infant with CF may show an increase in respiratory rate, increase in antero-posterior diameter and a slight but persistent lower rib retraction. Some infants present a history of respiratory symptoms, resembling recurrent respiratory infections that take longer than normal to clear up. These symptoms become continuous with time and are accompanied by positive findings on chest auscultation: wheeze, rales and rhonchi. At this stage chest x-ray already shows some degree of abnormality such as peribronchial thickening, areas of consolidation as well as hyperinflation of a variable degree. Segmental or lobar atelectasis can also be present and when it involves the upper right lobe it is highly suggestive of CF.

The majority of infants present with a combination of respiratory symptoms, failure to thrive and abnormal stools; however any of the three may be the major feature or only one or two may be noted or mentioned by the parents, but CF should be suspected in the differential diagnosis of each symptom (Table 1).

Excessive salt loss from sweating, which happens more often in hot countries, may be important as it leads to depletion of sodium and chloride and chronic hypoelectrolytemia (Pseudo-Bartter syndrome). Sometimes parents spontaneously comment that their child's sweat is salty or that salt crystals can be seen on the skin.

Rectal prolapse may be the presenting manifestation in 5% of the CF patients. It is a strong indication for a sweat test, but it may also occur in the absence of CF.

Table 1:When to think of CF in an infant

•Chronic or recurrent respiratory symptoms such as cough and wheeze
•Recurrent or chronic pneumonia
•Failure to thrive
•Malformed, bulky, offensive stools with an oily appearance
•Chronic diarrhoea
•Rectal prolapse
•Prolonged neonatal jaundice
•Salty taste
•Heat prostration or dehydration in hot weather
•Chronic hypoelectrolytemia
•Family history of deaths in infancy, or of living children with similar features
•Hypoproteinemia/oedema

In the pre-school age child

Although most CF children will present with symptoms in their first year of life some will present later in the pre-school age.

In some centres where the diagnosis of CF is not yet regularly thought of, the diagnosis may be delayed until the signs and symptoms are too obvious for CF to be missed and extensive permanent lung damage has occurred. Delay not only postpones treatment for the child but also deprives the family of time to become accustomed to a chronic disorder.

A few children however may present more obvious symptoms at this stage, such as malnutrition, progressive changes in the stool appearance and rectal prolapse, probably reflecting the late onset of pancreatic insufficiency.

Rectal prolapse is a not uncommon form of presentation and it should raise serious suspicion as to the diagnosis of CF. Rectal prolapse occurs in 25% of untreated patients most commonly between the ages of 1 and 2 years and it is less frequent after the age of 5 years. It can be precipitated by bouts of coughing in a child who has bulky stools, malnutrition, poor muscle tone, abdominal distention and occasionally constipation, and is usually managed successfully by increasing the intake of pancreatic supplements.

Table 2:When to think of CF in the pre-school age child

•Persistent cough with or without purulent sputum
•Unexplained chronic or recurrent wheezing
•Slow weight and height gain
•Rectal prolapse
•Intussusception
•Chronic diarrhoea
•Clubbing of the fingers
•Salt crystal formation on the skin
•Hypotonic dehydration
•Hypoelectrolytemia and metabolic alkalosis
•Hepatomegaly or unexplained liver disease

In the school age child

By this time very few patients should have escaped diagnosis. Those who have, may have a "mild" mutation and pancreatic "sufficiency". These children are very likely to show signs of malnutrition, may have abnormal stools, with continuous respiratory symptoms, x-ray changes and moist rales on auscultation of the chest. Any child with "asthma" associated with suggestive x-ray changes and evidence of infection should have a sweat test.

However CF occasionally presents at this stage with a severe respiratory infection which may resemble bronchopneumonia and which heralds the onset of the respiratory symptoms.

Recurrent colicky abdominal pain may be among the first symptoms and may start at this age group. A palpable mass can be found in the right lower quadrant of the abdomen and it can be tender. Abdominal distension, vomiting and constipation may follow and fluid levels may be shown on plain x-ray. Faecal masses mixed with stiff, tenacious mucus collect in lumps within the intestinal lumen, most often in the region of the caecum and terminal ileum, and are the cause for the pain and obstruction. This condition has been

termed meconium ileus equivalent or more appropriately distal intestine obstruction syndrome (DIOS). Abdominal pain can more rarely be secondary to recurrent attacks of pancreatitis. In this age group other signs and symptoms may become prevalent.

Table 3:When to think of CF in the school age child

•Chronic unexplained respiratory symptoms •*Pseudomonas aeruginosa* in the sputum •Chronic sinusitis •Nasal polyposis •Bronchiectasis •Finger clubbing •Chronic diarrhoea •Distal intestinal obstruction syndrome •Pancreatitis •Rectal prolapse •Diabetes mellitus with respiratory symptoms •Hepatomegaly •Unexplained liver disease

In adolescence and adult life

It is rare for CF to present in adolescence or adulthood without any previous symptoms, but this may eventually happen and these patients may show the less common characteristics.

Table 4:When to think of CF in adolescence and adult life

•Chronic and unexplained suppurative pulmonary disease •Finger clubbing •Pancreatitis •Distal intestinal obstruction syndrome •Diabetes mellitus with respiratory symptoms •Signs of liver cirrhosis and portal hypertension •Growth retardation •Delay in sexual development •Male sterility with azoospermia •Reduced fertility in females

It is important to remember that the signs and symptoms in the preceding four tables show the approximate age groups in which they often appear. However any item (symptom or sign) from a table may be delayed or appear prematurely for a specific patient; for instance, although it is uncommon, finger clubbing can appear in the first year of life, and liver disease can also already be present in the first years of life.

DIAGNOSIS

An early diagnosis is very important because:

1.If CF diagnosis is delayed irreversible pulmonary disease may occur.

2. An earlier therapeutic intervention may have a better outcome.

3.Gastrointestinal problems may cause failure to thrive and malnutrition.

4.Unnecessary, uncomfortable, expensive and inadequate diagnostic and therapeutic interventions may take place.

5.It resolves uncertainty and enables parents to begin the process of adjustment to the implications of a serious disease in their child.

6.It allows reproductive options to be considered before a further pregnancy begins.

The diagnosis of CF is usually considered on the basis of clinical findings and then confirmed by demonstration of elevated levels of sodium and chloride in the sweat. On the other hand CF is a serious diagnosis and should not be diagnosed unless the evidence is conclusive.

The majority of healthy young children have sweat sodium and chloride concentrations below 40mEq/L and may be as low as 20 mEq/L or less. If the values are between 40 and 60 Meq/L the test should be repeated and if it remains in the same range, should be considered carefully together with the other evidence before a decision is made about the diagnosis. Values of chloride over 60 mEq/L in children should be considered abnormal but in the majority of children with CF it exceeds 80 mEq/L. In adolescents and adults the situation is different and in normal individuals sweat sodium may occasionally reach 60 to 90 mEq/L, but the chloride level is more reliable and usually lower.

The diagnosis in adults with relatively mild disease is made on the basis of repeated high sweat electrolyte values in conjunction with clinical features such as nasal polyposis, recurrent pancreatitis, azoospermia, decreased fertility in the female, salt depletion and cirrhosis. Gene mutation analysis is becoming increasingly available and may resolve difficult problems of diagnosis.

The Sweat Test

The standard technique involves using quantitative pilocarpine iontophoresis, which consists of driving the drug into the skin with a small electric current, where it stimulates the sweat glands. The sweat is then collected, weighed and the concentrations of chloride and sodium determined. The detailed procedures are presented in the Guidelines for the Allied Health Professionals Manual (in preparation).

When performed correctly the quantitative pilocarpine iontophoresis sweat test is extremely accurate. Most errors are due to technical mistakes such as inadequate sweat collection, skin not cleaned well enough, evaporation and concentration of sweat samples

during collection, transfer and transport, errors in sample weighing and electrolyte analysis. Laboratories performing small numbers of sweat tests often produce unreliable results, and whenever possible patients should be referred to a large, experienced centre before the diagnosis is confirmed.

A minimum of 100 milligrams of sweat should be collected; a trained and experienced laboratory technician should do the test; if positive, the test should be repeated, so there should be at least two positive tests and supportive clinical evidence, for the diagnosis to be made. Borderline tests should also be repeated. If there is a high clinical suspicion and the test is negative, it should also be repeated. When a formerly negative test is called for repetition, it is essential to get as much sweat as possible because the concentrations of chloride and sodium in the sweat increase proportionally to the sweating rate.

Consistently borderline tests in a patient with high clinical suspicion and other evidence of CF such as steatorrhoea should incline the doctor to treat the patient as having CF. The diagnosis in such patients should be reviewed from time to time. If available, genetic tests may confirm the diagnosis.

*When samples are difficult to obtain, one should consider to stimulate the collection site with heat, the patient may be encouraged to feed when sweat is being collected, physical exercise may also induce sweating. We must also not forget to repair dehydration in case it is present before the test is done. Areas of oedema can produce reduced sweat levels. Repeated stimulation over the same area can cause exhaustion of glands, with an increase in electrolyte concentrations.

*Chloride and sodium reach approximately the same levels in sweat, however if there is a difference between both of over 10 mEq/litre, it should alert the clinician for the possibility of technical error.

*Sweat electrolytes may be elevated in some normal infants on the first few days of life, and as there is considerable difficulty in obtaining sufficient sweat at this time,newborns should only be tested after a week of life and some even prefer to test them when one month old.

*Although the concentration of sweat electrolytes remains quite stable throughout childhood, above 15 years of age, sodium and chloride concentration in the sweat increase in normal individuals but they can still be used as discriminants for the diagnosis of CF in older patients.

*Other forms of sweat testing represent variations of the above method, are generally more costly and increase the possibility of unreliable results. Sweat testing kits using modified methods are useful for screening in small clinics or remote locations, but if they give positive results the patient should always be referred to a recognized centre for confirmation of the diagnosis.

*Nasal potential difference is increased in patients with CF, and has been used to help confirm the diagnosis in borderline cases. This test is rarely available outside specialist centres.

These conditions listed in Table 5 overleaf are either rare or have distinctive clinical

features and are not likely to be confused with CF, exception perhaps for AIDS which can present with protean non-specific symptoms.

Table 5:Other conditions in which elevated sweat tests have been found

Acquired immuno deficiency syndrome (AIDS)
Adrenal insufficiency
Down syndrome
Ectodermal dysplasia
Familial cholestasis syndrome
Familial hypoparathyroidism
Fucosidosis
Glycogen storage disease Type I
Glucose-6-phosphatase deficiency
Hypothyroidism
Hypoparathyroidism
Malnutrition
Mauriac syndrome
Mucopolysaccharidosis
Nephrogenic diabetes insipidus
Nephrosis

False negative results: The most likely causes are: technical error,newborns tested in the first few days of life, infants that present with oedema and hypoproteinemia.

Genetic Testing

As there are over 500 mutations related to cystic fibrosis it would be expensive and impractical to test all mutations for diagnostic purposes, but genetic analysis may be used, if available, to clarify doubtful diagnostic results. The incidence of particular mutations varies widely between and sometimes within different countries, but if none of the 10 locally most frequent mutations is present on either chromosome, and the parents are unrelated, the probability of a patient having CF is greatly reduced.

Neonatal Screening

Immunoreactive trypsin (IRT) levels in the blood are about five to ten times higher in CF neonates than in normal neonates. IRT can be measured by a radioimmune assay or an enzyme-linked assay (ELISA) from dried blood spots collected from neonates. There is a small margin of false positive and false negative results (<10%). When a programme of neonatal screening involving IRT is planned, it is important to have in mind the cost-benefit of the programme. Where the objective is to identify CF infants in a country where the diagnosis is regularly missed, a much cheaper alternative involves the measurement of protein in meconium using an indicator stick (BM sticks, Hoechst). Up to 15% of affected infants may be missed using this technique, and pre-term infants often give false-positive results, but its low cost and relative simplicity makes it an attractive option for countries where awareness of the existence of CF needs to be increased.

Neonatal screening offers the possibility to:

*Define the incidence of CF in countries where it is believed to be under-diagnosed.
*Identify children with CF so that treatment can be started as early as possible.
*Identify couples for genetic counselling.

Tests for Pancreatic Insufficiency

Full pancreatic function assessment is not usually necessary for the diagnosis of CF, which depends on clinical suspicion and sweat testing but it is important to confirm steatorrhoea before instituting pancreatic replacement therapy. In doubtful or borderline cases it may also help support a tentative diagnosis.

Microscopic examination of the stools of a CF patient with pancreatic insufficiency will reveal oil droplets. It is a simple, indirect test and when positive it is very helpful. Measurement of faecal chymotrypsin, which is low or absent in CF, will also confirm pancreatic insufficiency. Analysis of the total fat content of the stools, after a three day collection during a period of a diet with known fat content, is relatively unpleasant and not normally needed for diagnosis. A very low or unmeasurable blood IRT level is an indication that exocrine pancreatic function is inadequate, and in most patients this develops within the first year of life. Indirect tests of pancreatic function include the PABA and pancreolauryl tests.

MANAGEMENT

The Newly-Diagnosed Patient

Once the diagnosis is made, the doctor who will give clinical care is the one that preferably should break the news. At this time it is important that both parents should be together if possible. In this first interview it is likely that very little will be understood or retained by the parents because of the shock of the diagnosis and also because sometimes the use of medical jargon is very difficult for the parents to understand. It is important that the doctor should use a very simple vocabulary, that may allow lay people to understand. A new meeting should be planned for the next day or two, when the same information will be conveyed again, allowing time for questions from the parents. A grandmother, a godparent or another member of the family may wish to attend and this may be very helpful for the parents because relatives may lend a lot of support.

Other members of the team should also talk to the parents,so the nurse, the social worker, physiotherapist or dietitian who is familiar with CF may be very helpful and may clarify or emphasize some points, using their own language and approach.

It is not uncommon for the doctor to learn later that some very important and basic facts have not been apprehended by either parent. Suitable literature plays an important part in providing authoritative information and it should always be made available to CF families.

Surveillance

Frequent and regular surveillance is essential if patients are to have their infections and other complications diagnosed and treated before they produce permanent damage.

Routine Management

Patients tend to get worse with time due to progressive lung damage. What has caused the remarkable change in prognosis is no doubt the increasing and widespread knowledge of the disorder by doctors, leading to earlier diagnosis, and the introduction of more effective antibiotics, plus improved physiotherapy techniques. The increasing recognition of the importance of good nutritional management has also played a significant role. Treatment of CF is not curative and must be continued throughout life.

CF patients whenever possible should attend a centre with an experienced team of professionals and a range of expertise among the caregivers. The care of CF patients involves much more than merely the medical measures: the patient should be treated as a whole, and the team - nurse, dietitian, physiotherapist, social worker and doctors -should attempt to be involved with as many aspects of treatment as possible.

The patient's family should also be considered. Both parents will be involved in the treatment of their child and for this they should be trained. Genetic counselling should be offered routinely to parents and should be made available for other family members.

When treating a CF patient our aims should be:

*To maintain a lifestyle as close to normal as possible.
*To control respiratory infections.
*To ensure adequate nutrition.

Treatment of the Pulmonary Manifestations

The pulmonary manifestations are secondary to the vicious circle of obstruction, infection and mucus production (Figure 2).

Fig. 2 Circle of Obstruction, Infection and Mucus Production

Treatment of respiratory obstruction involves the use of chest physiotherapy, exercise, bronchodilators and possibly substances that alter the viscosity of mucus such as amiloride and DNase.

Since there is accumulation of thick, viscous mucus in the lungs with blocking of the airways, a logical step is to try to remove this mucus through physical means.

Physiotherapy

Physiotherapy is very important in helping to clear the tenacious secretions which block the airways and predispose to respiratory infection. There are several techniques described; some CF centres favour one set of techniques other centres prefer others. The same is true for patients, some feel better and are able to clear their chests with one technique, but others can cough up more sputum and better tolerate another method. Techniques described include postural drainage, chest percussion and vibration, coughing exercises, the Active Cycle of Breathing (ACB), previously Forced Expiratory Technique (FET), and Autogenic Drainage (AD). Some mechanical aids have been introduced such as the "Flutter" and the "PEP Mask". These techniques and their correct use are described in the Guidelines for Allied Health Professionals. In the beginning, the younger the child is, the more passive physiotherapy will be. With an infant, only chest percussion and compression is possible; as the child grows, however, one should attempt to have more active participation which will make physiotherapy more effective with the gradual training and introduction of controlled coughing.

Exercise

Patients should be encouraged from an early age to participate in physical activities and to engage in any exercise they like: football, volleyball, cycling, dancing, gymnastics, basketball, swimming etc. It is of no use to choose a sport which the patient will not agree to do or which he/she will not enjoy. The patient should choose the sport he/she wants to play; if they do it willingly the longer and better they will do it.

Exercise training increases the airway clearance of the sticky mucus and will strengthen the respiratory muscles. Some forms of exercise will also mobilize the thorax and improve posture. Exercise will give a general sense of well being and will help patients to integrate in their peer group. Very few patients are too ill to be able to perform any exercise at all, but if they are sick exercise can be started slowly and cautiously and gradually increased. Some patients do not enjoy taking part in sports with others. One way around this is to encourage them to practice skipping at home, in the morning and late afternoon, which can be done as soon as they wake up and before their first session of physiotherapy, or when they come home from school.

Treatment of respiratory infection

Survival and quality of life have remarkably improved with the introduction of newer anti-*Pseudomonas* antibiotics, mainly Aminoglycosides, Penicillins and third generation Cephalosporins.

There are considerable differences of opinion as to when, for how long and how often antibiotics should be given; however in recent years the use of antibiotics has undergone a major change, with earlier introduction at the onset of symptoms and more prolonged courses to adequately control the infection. Regular surveillance should identify signs of an exacerbation of infection (Table 6, overleaf).

One must aim at identifying the specific pathogen in the respiratory secretions preferably by culture of sputum or if this is not obtainable at least by cough swab.

Table 6:Warning signs of clinical exacerbation

1Increased cough
2Change in the characteristics of the sputum: quantity and colour
3Decreased tolerance to exercise
4Increased dyspnoea
5Fever
6Loss of appetite
7Loss of weight
8Malaise
9X-ray changes
10Auscultatory changes
11Deteriorating lung function tests

Staphylococcus aureus

In the first few years of life *Staphylococcus aureus* is the predominant pathogen, and is thought to be the primary invader, later substituted by *Pseudomonas aeruginosa*. Both, however can co-exist for some time and care should be taken when analysing sputum cultures because the growth of one microorganism may camouflage the growth of the other. There is some evidence that continuous prophylactic treatment with oral anti-staphylococcal antibiotics for long periods may delay colonization of the lungs with *Pseudomonas*, but other centres use anti-staphylococcal drugs intermittently when *Staphylococcus aureus* can be isolated from the sputum.

Each patient is considered individually for antibiotic treatment of exacerbations of *Staphylococcus aureus* infection: some require treatment once or twice a year and remain symptom-free in the interval between treatments, while others require very frequent courses of antibiotics and have very short symptom-free intervals between their exacerbations.

Table 7:Antibiotics used for the treatment of Staphylococcus aureus infection

DRUG	**AMOUNT IN mg PER kg PER DAY**	**ROUTE**	**NUMBER OF DAILY DOSAGES**
Dicloxacillin	25-50	oral	4
Flucloxacillin	50	oral	4
Chloramphenicol	70-100	oral	4
Cephalexin	50-100	oral	4
Clindamycin	20-30	oral	4
Rifampicin	20	oral	2
Erythromycin	30-50	oral	4
Vancomycin	40	IV	2-4
Lincomycin	30	oral	3-4
Teicoplanin	6-10	IV	1-2

Haemophilus influenzae

Haemophilus influenzae is associated with chronic colonization and with significant pulmonary function deterioration. It is more difficult to grow *Haemophilus* because of its nutritional requirements but it should be suspected when Gram-negative organisms are seen in sputum smears but do not grow in routine culture media, in which case a special medium for *Haemophilus* should be used.

Table 8:Drugs used for the treatment of Haemophilus influenzae infection

DRUG	AMOUNT IN mg PER kg PER DAY	ROUTE	NUMBER OF DAILY DOSAGES
Amoxycillin	25-50	oral	3
Amoxycillin + Clavulanic acid	25-50	oral	3
Ampicillin	50-100 (-200)	oral	4
Chloramphenicol	70-100	oral	4
Cotrimoxazole	40 for Sulphamethoxazole 8 for Trimethoprim	oral	2
Erythromycin	30-50	oral	4
Rifampicin	20	oral	2
Ceftriaxone	50-100	IV	1-2
Cefaclor	40	oral	3
Cefotaxime	100-200	IV	4
Cefuroxime	100	IV	3-4
Cefoperazone	50-100	IV	2
Doxycycline	1st day: 4 afterwards: 2	oral	1

Pseudomonas aeruginosa

Once infection by *Pseudomonas aeruginosa* is established it is almost impossible to eradicate, but there is evidence that a course of intravenous antibiotics or first culture of *Pseudomonas* followed by regular inhaled colistin may postpone chronic colonisation. Established infection of the lower respiratory tract is generally related to a worsening of respiratory symptoms due to the damage caused to lung tissues, with inflammatory mediators such as cytokines playing an important part.

Pseudomonas aeruginosa may produce a mucoid strain in which the *Pseudomonas* loses its O-antigen and is surrounded by a mucoid layer (alginate) which protects it against the effects of antibiotics, antibodies and other host defenses.

Since *Pseudomonas* infection is associated with a quicker deterioration of lung function, it is of maximum importance that it is treated aggressively when *Pseudomonas* is first isolated, in order to slow down further deterioration. There is improvement of symptoms with appropriate treatment even though the organism may still be present.

Table 9:Antibiotics used for the treatment of Pseudomonas aeruginosa infection

DRUG	AMOUNT IN mg PER kg PER DAY	ROUTE	NUMBER OF DAILY DOSAGES
Amikacin	15-30	IV	2
Tobramycin	10-20	IV	3
Ciprofloxacin	20-40	oral	2-3
Ceftazidime	150-300	IV	3-4
Cefsulodin	100-150	IV	3-4
Piperacillin	300	IV	4
Ticarcillin	200-400	IV	4
Azlocillin	300	IV	4
Carbenicillin	500	IV	4
Aztreonam	150-250	IV	4
Imipenen	50-75	IV	3-4
Thienamycin	50-75	IV	4

*Treatment is usually started with two drugs in the hope of a better remission of symptoms and with the possibility of synergistic action and a reduced risk of emergence of resistance

*For instance, an aminoglycoside should be used associated either with a third generation cephalosporin: either Amikacin plus Ceftazidime or Tobramycin plus Ceftazidime or Cefsulodin.

*Other combinations depending on in vitro sensitivity or clinical response can also be made, e.g., Tobramycin + Piperacillin; Amikacin + Thienamycin; Ceftazidime + Aztreonam.

*It is important not to combine Ceftazidime and Thienamycin, because of drug incompatibility.

*High doses of antibiotics should be used because antibiotics do not reach good levels in the sputum; patients with CF have changed pharmacokinetics and a higher antibiotic clearance than normals.

*Higher doses of antibiotics are also required because the mucoid strains of Pseudomonas aeruginosa are encased in alginate and it forms a difficult barrier for the antibiotics to cross.

*Treatment should last at least fourteen days and as long as necessary for the patient to return to the previous clinical baseline level as measured by symptoms, weight, lung function and sputum production. This may take more than just two weeks or until

symptoms subside. It may take more than just two weeks for the patient to return to his baseline.

*Since the drugs are used intravenously, treatment will be hospital based, unless there are facilities for it to be done at home, when there should exist a hospital visiting system and the parents or patient are well aware of all the procedures to be used.

*When using aminoglycosides whenever possible and after their first 48 hours of use, to check the trough levels, mainly when high doses are being used, this should be repeated 1 - 2 times per week.

*When using aminoglycosides one has to be aware of their cumulative effects; renal and ototoxic effects should be monitored closely.

*It is important that as far as possible sensitivity tests be carried out and that any decision-taking as regards to antibiotics should be as closely matched as possible to the microbiology laboratory results. However in vitro sensitivity tests do not always reflect the in vivo response of the patient.

*Aminoglycosides and penicillins should not be mixed together in the same vial or syringe, neither should cephalosporins; to avoid inactivation each drug should be infused separately whether in a bolus shot or by diluted infusion.

*Antibiotics have helped the patients with CF to survive but their role is limited if not associated with vigorous physiotherapy. For an antibiotic treatment to work, one should attempt to achieve better results with the removal of mucus or purulent sputum from the lungs.

Some centres, notably Copenhagen, have achieved good results in treating *Pseudomonas aeruginosa* in chronically infected CF patients every three to four months, irrespective of worsening of symptoms or exacerbation. They claim improved survival and have not seen a significant increase in bacterial resistance. It is however important to note that the cost of such treatment may be beyond the financial possibilities of some communities.

Aerosol antibiotics

Antibiotics by the aerosol route can be used as an adjunct to systemic therapy, to increase the concentration of the drug in the sputum. Nebulization can also be used for delivery of aminoglycosides as an alternative to the intravenous route. Since aminoglycosides are not absorbed from the mucous membranes, this avoids the problem of overdose and unwanted side effects. Tobramicin, Amikacin or other aminoglycosides can be offered as courses of anti-*Pseudomonas* therapy without intravenous treatment. The frequency and dosage depend in part on the patient's tolerance, as high concentration of the drug on the pharynx may produce a sore throat.

Colistin (Polymyxin E) may also be used as regular maintenance therapy via nebulization, and *Pseudomonas aeruginosa* does not seem to become resistant to it.

Table 10:Aerosol antibiotics for the treatment of Pseudomonas aeruginosa infection

DRUG	mg/DOSE	NUMBER OF DAILY INHALATIONS
Colistin *	33 - 66	2 - 3
Gentamicin	80	2 - 3
Tobramycin	80 - 200	2 - 3
Ticarcillin	1000	2 - 3
Ceftazidime	1000 - 2000	2 - 3

* One milligram of Colistin = 30,000 units

Burkholderia cepacia

Burkholderia cepacia (formerly *Pseudomonas cepacia*) infection in some patients has a rapid, fulminating course but others seem to deal with it as with *Pseudomonas aeruginosa*. Unfortunately, *Burkholderia cepacia* tends to rapidly become resistant to all antibiotics. There is evidence that the continuous use of doxycycline reduces some of its deleterious effects. Since there is no way to know beforehand which patients will suffer a rapidly progressive course, strict isolation measures between patients having and not having *Burkholderia* in their sputum are recommended. *Burkholderia cepacia* is detected by using special selective media which suppress *Pseudomonas aeruginosa* growth.

Occasionally and less commonly other microorganisms such as *Klebsiella pneumoniae*, *Escherichia coli*, *Serratia marcescens*, *Xanthomonas maltophilia* and *Proteus* species are isolated as well. Treatment should then be dictated by the sensitivity tests or by antibiotics to which these microorganisms are usually sensitive.

Aspergillus

Aspergillus fumigatus if often found in CF and should be suspected in patients with persistent wheezing associated with the production of sputum containing small dark plugs. These patients may need oral steroids for 4 to 6 weeks and sometimes even longer.

Other Respiratory Therapy

*Amiloride: this is a diuretic which when nebulized can prevent the absorption of sodium across normal and CF airway epithelia, thus preventing dehydration of mucus, which becomes less sticky and easier to be coughed up. Amiloride works well for some patients but others do not seem to respond and it also has the disadvantage of short duration of effect. It should be used a minimum of three times a day, continuously.

*DNase: nebulized human recombinant DNase will reduce sputum viscosity by cleaving DNA which is an important viscous component of sputum, derived from

disintegrated neutrophils in purulent lung secretions. As with amiloride, some patients may respond well to it and some seem unaffected by its use. The biggest limitation to its use is its high price.

*Bronchodilators: reversible bronchial constriction is often present in CF patients and makes an important contribution to their airways obstruction. This is frequently seen in younger children. Standard bronchodilators such as salbutamol are used as for asthma, and are particularly useful before physiotherapy.

*Oxygen: in the late stages of CF some patients find great relief from continuous low-flow oxygen therapy, particularly at night.

*Lung transplantation: programmes of lung or heart-lung transplantation for end-stage respiratory failure have been developed in some countries. Apart from the major problem of insufficient donors, and those resulting from transplant rejection and immunosuppression, the very high cost involved means that this approach is restricted to relatively wealthy states. However, many fortunate recipients with CF have literally enjoyed a new lease of life.

Gene Therapy

Although it would seem a logical form of treatment, early clinical trials have shown no convincing benefit to date. Gene therapy is directed towards the pulmonary disease in CF, and either viruses such as adeno-associated virus, or artificial liposomes, have been used as the vector for conveying a modified gene coding for normal CFTR into the respiratory epithelium. It is too early to predict the long-term place of this approach to therapy. Other vectors would be needed if gene therapy were applied to the prevention or treatment of other organs affected by CF, and for the pancreas and male genital tract treatment would be needed during fetal life.

Pulmonary Function Tests

Pulmonary function tests are difficult to perform in young children and may therefore not identify lung disease which develops early. When they are altered the disease has already progressed. They are however useful in patients over 7 or 8 years, who are able to perform the required manoeuvres and they are helpful in assessing the progress and response to treatment.

Airways obstruction occurs first in the small airways and later the large airways also show signs of involvement.

Simple tests of airways obstruction will always depend on patients' cooperation and training.

Peak Expiratory Flow Rate (PEFR) is the maximum rate at which air can be expired through the mouth after a maximal inspiration. It is measured using a small portable Peak Flow Meter, and normal individuals perform at a level above 80% of predicted values for height and sex.

Forced Vital Capacity is the total volume of air expelled through the mouth during forced

maximal expiration following maximal inspiration. It is assessed with an spirometer which is larger than the Peak Flow Meter, but nowadays smaller portable ones are also being produced. With the progression of the pulmonary disease there is a fall in the Forced Expiratory Volume in one second of the Vital Capacity curve (FEV1) and also of the Forced Vital Capacity (FVC). The pulmonary disease which is at first obstructive, later shows also a restrictive pattern due to the progressive destruction of lung parenchyma.

Children with CF may present with increased bronchial lability. Pulmonary function tests will indicate the degree of response to a bronchodilator and whether a specific patient will benefit from its use.

Treatment of Pancreatic Insufficiency

Good nutrition is one of the main goals when treating CF patients. Patients with a good nutritional status have a better prognosis. It may improve immunological status and will also help the child to be more active, willing to perform more physical exercise and as a consequence have a better appetite.

Table 11: Nutritional problems are secondary to:

*Maldigestion and malabsorption due to pancreatic insufficiency *Poor nutritional intake in patients who feel ill *Increased requirement for calories as the work of breathing increases *Chronic respiratory infection

The great majority of CF patients have pancreatic insufficiency which results in very little or no pancreatic enzymes (lipase, amylase and trypsin) reaching the duodenum and a simple stool examination may show that the patient has gross steatorrhoea.

Pancreatic malabsorption can be successfully treated by the use of pancreatic supplements, which may be provided as powder, enteric coated tablets or enteric coated granules. The enteric coated preparations are designed to dissolve at a higher pH, that is, upon reaching the duodenum, in order not to be destroyed by the acid gastric juice. The enteric coated granules or microtablets within gelatin capsules are by far the most efficient preparation and they are probably the most widely used.

Pancreatic supplements should be given with each meal, either just before or half before and half in the middle of the meal. Pancreatic supplements should <u>not</u> be given <u>after</u> meals.

The dosage should be tailored to the individual needs of each patient. It is important to discover how many capsules are needed for the larger meals, for small meals and for snacks, except where the snack consists of fruit and soft drinks. It will always be a matter of trial. There is no standard dosage. The satisfactory dosage will be the one which will reduce the symptoms of malabsorption: the size, frequency and consistency of the stools and that will ensure that the patient is gaining weight. It is usually started with one capsule of low strength preparation and gradually increased. Ideally, dosage is monitored by the results of faecal fat estimation in a 3-day stool collection but this is not widely

available. There is not much extra benefit in increasing dosages to very high levels and it is important to remember that the pancreatic insufficiency of cystic fibrosis is never entirely corrected; there will always be a degree of steatorrhoea which the supplements will fail to control.

Very high dosages, in excess of 2,000 lipase units per kg per meal or 15,000 per kg per day, have been associated with the formation of strictures in the colon, and with colitis, presumably caused by active enzymes attacking the bowel wall.

Pancreatic supplements in powder form should not be sprinkled over the food or mixed with milk. When capsules which contain small enteric coated microtablets or pellets are used, the capsule can be opened and the contents taken with a small amount of food, or taken whole, without opening, when the child is old enough and able to swallow.

If a child does not appear to respond as well as expected, it may be because the pancreatic enzymes have not been released from their enteric coat or have been inactivated by elevated gastric and duodenal acidity. The use of antacids and/or H_2 receptor antagonists should then be considered, such as sodium bicarbonate, aluminium hydroxide, cimetidine, ranitidine or perhaps misoprostrol.

Nutritional Management

The diet should be as normal as possible, without fat restriction, using the available foodstuffs present in each household, provided it is rich in protein and calories.

The caloric intake varies from child to child but it has been suggested that CF patients need 120% or more of the calories that the normal child would need. The pancreatic supplement should be adjusted to the child's regular diet.

Vitamins: Fat soluble vitamins (A,D,E and K) should be provided daily. Clinical vitamin A deficiency was formerly common in untreated infants. Vitamin E deficiency causes haemolytic anaemia in the infant and neurological changes in the older patient. Although the serum level may be low, it only rarely gives rise to clinical symptoms. It is important to supplement vitamin K in patients with liver disease and sometimes during prolonged antibiotic usage. The daily allowance of fat-soluble vitamins in CF is about twice the normal recommended allowance for age, whenever possible in water soluble form, or if not, associated with pancreatic supplement treatment.

Nutritional supplementation using ready made commercial elemental formulas should not be used unnecessarily because besides being expensive these may have an unpleasant taste and depress the patient's appetite for the available foodstuffs his family has access to. In very few and chosen cases, ready made nutritional supplements may be prescribed. Otherwise, good "home made" supplements can be designed by a dietitian or nutritionist. Detailed guidelines for nutritional intervention are available in the Guidelines for Allied Health Professionals Manual.

Nutritional management is one of the mainstays in the treatment of Cystic Fibrosis; in certain instances when the child does not gain weight in spite of all the measures taken, tube feeding can be considered for a few days or weeks and in some centres, chosen patients are given a gastrostomy. Neither of those two methods is devoid of problems

and they should only be considered when all other measures have been tried. Supplementary feeding can only too often become substitute feeding.

Treatment of Meconium Ileus

Cases of meconium ileus uncomplicated by perforation can be treated medically by contrast enemas with a high osmolarity such as meglumine diatrizoate ("Gastrografin"). More than one enema may be needed and it is important that the fluid should run well back into the ileum, where it induces secretion of water into the lumen and thus mobilizes the retained meconium. Large amounts of intravenous fluid are needed. The procedure is hazardous and should only be undertaken by an experienced radiologist in centres where surgery is readily available if needed.

Most infants with meconium ileus require surgery, and it is often exploratory because the precise diagnosis may be in doubt. The usual finding is of a dilated ileum filled with sticky dark meconium. Distal to the site of obstruction, the bowel is small and contracted ("microcolon"), and may contain a few small hard faecoliths. Surgical management is to irrigate the bowel both proximally and distally, washing out as much of the meconium as will come away easily. Gangrenous or compromised sections of gut may need resection. A Miculicz-type double enterostomy or a Bishop-Koop entero-enterostomy is constructed to give access to both proximal and distal bowel for post-operative irrigations, and this is closed at a later date (usually a few weeks) when continuity of transit is assured. Post-operative nutritional and respiratory problems are frequent and the child should be managed jointly by the surgeon and the CF paediatrician. Whereas meconium ileus was formerly usually fatal, with modern management mortality is now under 5%.

Treatment of Distal Intestinal Obstruction Syndrome (DIOS)

If symptoms are not severe, treatment is by carefully introducing oral laxatives such as lactulose until faecal masses are eliminated and abdominal pain subsides. If faecal masses are very large at palpation, enemas can also be used. N-Acetyl-Cysteine can be used orally two to three times a day because of its mucolytic properties.

If the obstructive element is severe, pain may be important, there may be abdominal distension, vomiting, constipation and fluid levels on plain abdominal x-rays. These patients should be admitted to hospital, their hydration status monitored and their management should include attempts at bowel evacuation through enemas with a high osmolarity or with large volumes of a balanced electrolyte solution such as "Golytely", more commonly used for preoperative or pre-x-ray bowel lavage. It may take a few days to accomplish the removal of all the faecal masses and surgery should never be attempted unless the obstruction is irreversible.

Afterwards it is important to adjust the pancreatic supplement, usually by increasing. The patient should be followed closely to see if this complication is going to recur, and if necessary to prescribe oral laxatives.

CF patients are prone to intussusception. They are also subject to co-existing diseases such as appendicitis or Crohn's disease. These conditions may cause major problems of differential diagnosis from DIOS.

Management of Late and Less Common Complications

Nasal polyps:These are a common finding in CF. They are often asymptomatic, but when nasal obstruction is present they usually respond well to nasal sprays of a topical steroid. Surgery is generally contraindicated because the polyps recur.

Pneumothorax:Emphysematous bullae may rupture and the resulting pneumothorax can precipitate acute respiratory failure. Management is by pleural aspiration and intercostal drainage as for other forms of pneumothorax. Pleurodesis, if necessary, virtually rules out any prospect of a future lung transplant.

Haemoptysis:Small haemoptyses are very common in patients with bronchiectasis, and while they may alarm the patient they are rarely serious. Occasionally a massive haemoptysis indicates rupture of a varicose bronchial collateral blood vessel and presents a life-threatening emergency. The source of the bleeding may not be easy to locate, except by contrast radiography, and when this is available in specialist centres the vessel may be embolise and occluded. If this is unsuccessful or not possible, surgical ligation or excision of the affected segment or lobe is needed.

Gastro-oesophageal reflux:This is a frequent occurrence in CF and not only causes discomfort but may also contribute to pulmonary infections. When troublesome, postural therapy and treatment with a pro-kinetic drug, such as cisapride, may help.

Oesophageal varices:In patients with significant liver disease oesophageal varices are often demonstrable by endoscopy or radiology. They may remain asymptomatic for the lifetime of the patient but if bleeding occurs the treatment of choice is endoscopic sclerosis. Once started, further treatments will usually be needed as an elective procedure.

Gallstones:Many patients with CF have gallstones. They are usually asymptomatic, in which case they should be left alone. If surgery is needed, a laparoscopic technique may minimize the respiratory complications which frequently follow abdominal surgery in these patients.

Diabetes:Diabetes mellitus is a late consequence of the extensive pancreatic destruction in CF and affects about 20% of adult patients. It may be precipitated by the use of steroids or by supplementary nutrition. It presents in the usual way, with thirst, polyuria, polydipsia and weight loss, but differs from classical diabetes in that ketosis is rare. Although the diabetes of CF may initially respond to oral hypoglycaemic drugs, insulin therapy is usually needed. Management then follows conventional lines fordiabetes, but the insulin dose must be adjusted to the high caloric intake required for managing cystic fibrosis, and the diet should not be restricted. Clearly, the specialist dietitian (nutritionist) plays a key role in management.

Corpulmonale Cardiomyopathy: A feature of advanced CF lung disease.

FURTHER READING

For parents and patients

Many National Cystic Fibrosis Associations publish a variety of information literature in their own languages, which they are pleased to send to enquirers.

Larger books include:

•Shapiro BL and Heussner RC Jr. 1990. A Parent's Guide to Cystic Fibrosis. University of Minnesota Press, Minneapolis, 124 pp.

•Orenstein DM. 1989. Cystic Fibrosis. A Guide for Patient and Family. Raven Press, New York, 239 pp.

•Harris, Ann and Super, Maurice. 1995. Cystic Fibrosis. The Facts (3rd Edition). Oxford University Press, Oxford, 138 pp.

For health care professionals

•Goodchild MC and Dodge JA. 1989. Cystic Fibrosis. Manual of Diagnosis and Management (2nd Edition). Baillière Tindall, London, 211 pp - a concise book containing practical instructions for management.

•Physiotherapy in the Treatment of Cystic Fibrosis (CF). Information pamphlet available from the International Physiotherapy Group for Cystic Fibrosis (IPG/CF) (appended).

Two recent **reference textbooks** are:

•Davis PB (ed). 1993. Cystic Fibrosis. Marcel Dekker, Inc., New York, 551 pp.

•Hodson ME and Geddes DM (eds). 1995. Cystic Fibrosis. Chapman and Hall, London, 439 pp.

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A N N E X

P H Y S I O T H E R A P Y

I N T H E T R E A T M E N T O F

C Y S T I C F I B R O S I S

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I P G / C F

International Physiotherapy Group for Cystic Fibrosis (IPG/CF)

The IPG/CF wishes to thank those who have contributed to the contents and layout of this booklet.

1st edition 1993
2nd edition 1995

This booklet is a collection of definitions and principles of current basic physiotherapy.

Table of Contents

1. Introduction

Despite the many advances in the understanding of the genetics and the basic defect in Cystic Fibrosis (CF), the problems of the lungs remain the major difficulty which has to be dealt with on a day-to-day basis. Ever since the discovery of the illness, physical treatment of the lungs has been the major part of management and there is no doubt that this has greatly improved both the extent and the quality of life for all CF patients for many years. Initially, treatment was carried out using standard physiotherapy techniques, but as knowledge has developed, a number of other methods have become available which are just as efficient and often more convenient than those previously practiced.

It is extremely important to make sure that the treatment advised for each individual patient is that which is most suitable to them for their age, cultural background and disease severity. One other major aspect is the compliance with daily treatment on a regular basis. If the patient and the parents understand and accept the techniques used, then daily treatment is more likely to be carried out regularly.

A number of new techniques for clearance of the lungs in CF have recently been developed and evaluated through careful research and assessment of their efficiency. These techniques now offer a much wider choice for the individual patient in the type of physical treatment which he/she can undertake. This has greatly facilitated the physical management of chest disease in CF and further improved the quality of life for these patients.

It is the role of the IPG/CF to review and develop these techniques further, and the purpose of this booklet is to illustrate them in a straightforward way which is easy to understand for all of those who are concerned in the management and care of patients with this difficult and demanding illness. The rewards for the professional involved in the care of these patients are well worth the effort put into discovering the most suitable treatment regimen for each individual.

Dr R. Dinwiddie
Medical Adviser IPG/CF
June 1995

2. Airway Clearance Techniques

i. Active Cycle of Breathing Techniques

The active cycle of breathing techniques (ACBT) is used to mobilize and clear excess bronchial secretions (Pryor et al 1979). The components of the ACBT are breathing control, thoracic expansion exercises and the forced expiration technique. The regimen is flexible, adapted to suit the individual and can be used in the elderly, the young, the sick and the fit. It was first documented by Thompson and Thompson in 1968. The ACBT can be used either independent of an assistant or with an assistant.

Breathing control (Webber, Pryor 1993) is normal gentle breathing at tidal volume, using the lower chest with relaxation of the upper chest and shoulders. It is an essential part of the cycle to allow pauses for rest and to prevent any increase in airflow obstruction. The length of the pause is dependent on the individual patient's signs of airflow obstruction.

Thoracic expansion exercises are deep breathing exercises emphasizing inspiration and with a quiet, unforced expiration. With an increase in lung volume the resistance to airflow via the collateral channels is reduced. Mobilization of secretions can be facilitated by air passing along these channels and behind secretions. In some patients a three second hold at the end of inspiration will augment this effect. Three to four thoracic expansion exercises may be combined with chest shaking or chest clapping, and are followed by breathing control. Chest clapping and shaking appear to be helpful in some patients, but are unnecessary in others.

The forced expiration technique is one or two huffs combined with breathing control. Huffing continued down to a low lung volume will help to mobilize and clear the more peripherally situated secretions. When secretions reach the larger, more proximal airways they are cleared by a huff or cough at a high lung volume. The length of the huff and force of contraction of the muscles of expiration should be altered to maximize clearance of secretions.

The concept of the equal pressure point (West 1992), with collapse and compression downstream (towards the mouth) of the equal pressure point, explains the mechanism of the effectiveness of the forced expiratory manoeuvre of a huff or cough in airway clearance.

The ACBT can be introduced as huffing games from the age of about two years, and from the age of about eight or nine years the child can begin to take some responsibility for his/her own treatment, gradually becoming independent.

The ACBT should never be uncomfortable or exhausting and the huff should never be violent. It can be used in any position according to the requirements of the individual. The sitting position may be indicated if secretions are minimal or when it is inconvenient, unnecessary or contraindicated to use gravity assisted positions.

Active Cycle of Breathing Techniques

Key: BC - breathing control
TEE - thoracic expansion exercise

FET - forced expiration technique

The flexibility of the regimen is demonstrated in the figure. It may vary from day-to-day for an individual and will vary between individuals. The ACBT is repeated until the huff becomes dry sounding and non-productive or it is time for a rest. A minimum of ten minutes in a productive position is often required. If gravity assisted positions are used, two positions are possibly enough for one treatment session. The total treatment time is usually between fifteen and thirty minutes. By assessment the physiotherapist and/or the patient determine the most suitable regimen, the positions required for treatment, the length of time and the number of treatments in a day.

Studies using the ACBT have shown it to be an effective and efficient technique for the mobilization and clearance of secretions (Pryor et al 1979). It is not further improved by the adjuncts of positive expiratory pressure - PEP (Hofmeyr et al 1986), the Flutter (Pryor et al, 1994) or mechanical percussion (Pryor et al 1981). An improvement in lung function following the instigation of the ACBT (Webber et al 1986) has also been shown, and hypoxemia is neither caused nor increased (Pryor et al 1990).

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ii. Autogenic Drainage (AD)

Autogenic drainage is a technique based on recently evoked principles of the physiology of breathing. The expiratory flow is the active force that is utilized to mobilize the mucus.

In chronic obstructive pulmonary diseases (COPD) higher flows are achieved in the medium and small airways by monitored and controlled expiration in the various levels of the vital capacity.

Autogenic drainage is a collection of individual important principles enabling the patients to develop the best possible technique of drainage that is individually adapted to their pathology and lung function.

Breathing in Autogenic Drainage

Autogenic Drainage (AD)

Pulmonary function tests have demonstrated that correctly dosed expiratory movements improve the flow and volumes, in contrast with forcefully executed expirations. These improved flow rates last longer, thus moving the mucus over a greater distance during each expiration. By adjusting the tidal breath at low- mid- or high-lung volume level, depending on the peripheral, middle high or central localization of the mucus, one gets even better flow rates in the concerned generations of airways without causing appreciable increase of the airway resistance in the other airways. Correct dosage of the expiratory force only increases the bronchial resistance a very small amount, keeps the alveolar gas compression very low and does not collapse the airways in an early stage. It also lightens the expiratory efforts and decreases the appearance of paradoxical breathing movements. For some reason the stimulation to coughing is less strong so that the cough can be inhibited more easily.

The AD Technique in Practice

1. Choose a breath-stimulating position like sitting upright or lying down.

2. Clear the upper airways (nose and throat).

3. Breathing ***IN.***

   .Slowly breathe IN the necessary volume of air through the nose, keep the upper airways ***OPEN*** to avoid severe ventilation asynchronism.

   Use the diaphragm and/or the lower chest if possible.

   .Hold the breath for approximately 3 to 4 seconds during which ***ALL*** the upper airways are kept open, thus improving the even filling of all lung parts. During this particular phase, enough air gets ***BEHIND*** THE OBSTRUCTIONS.

   .Depending on where the mucus is, in peripheral, middle-large or large airways, the tidal volume needed is ventilated at low-, mid- or high-lung volume level.

4. Breathing ***OUT***.

.Preferably breathe ***OUT*** through the nose if the flow is not slowed down by it. If a drop in velocity does occur or if one wants to hear the bronchial noises in a better way, breathe ***OUT*** through the mouth. In this case always keep the upper airways (glottis, throat, mouth) ***OPEN.***

.The expiratory force is so ***BALANCED*** that the expiratory flow reaches the highest rate possible ***WITHOUT*** causing airway compressions.

.Breathing ***OUT*** in the proper way, the mucus can be heard distinctively. Putting a hand on the upper chest, one can also feel the mucus vibrating. The frequency of these vibrations give an idea where the mucus is.

This ***FEEDBACK*** makes it possible and easy to adjust the technique.

5.Repeat the cycle by breathing ***IN.*** Inhale ***SLOWLY*** to avoid the mucus going back. Continue to breathe until the mucus starts to collect by moving upwards. If this occurs the level of the ventilated tidal volume is gradually raised. Thus, the breathing evolves from a lower to a higher lung volume breathing level. Finally, the collected mucus plug arrives in the trachea from where it can be evacuated by a strong expiration or a high-lung volume ***HUFF.*** Coughing must be avoided as much as possible.

Frequency

The duration and number of the AD sessions depends on the total amount and the viscosity of the secretions. Experienced patients drain their lungs quicker than others. Drainage should always be done thoroughly.

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iii. Modified AD (M AD)

AD is a self-care technique designed to remove mucus from the airways. Autogenic Drainage (AD) was developed by a Belgium work-group. It was adapted by the German work-group in 1984 and further developed and modified to M. AD, in co-operation with Professor Lindemann of the Children's Hospital, University of Giessen.

Method

inspiration through the nose -

pause -

expiration through the nose or mouth

1) ***passive***: initial rapid airflow without use of the respiratory muscles.
2) ***active***:slower end expiratory airflow with careful support of the respiratory muscles.

The length of the expiration is determined by the amount and position of the mucus in the airways, i.e., the less mucus in the larger airways the longer the expiration, the more mucus in the larger airways the shorter the expiration.

Breathing out against a resistance avoids bronchial collapse or spasm in cases where the bronchial system is unstable and/or hyperactive.

Effectiveness

Deepened breathing causes a varying bronchial diameter in the airways thereby moving the mucus. The recoil effect of the lungs and bronchi during passive expiration transports the mucus upwards to the mouth against the force of gravity. Careful active expiration pushes the mucus out of the smaller airways into the larger ones.

Procedure

The breathing manoeuvres are performed in either a sitting or a lying position, breathing with controlled chest and diaphragm movement - hands are laid on the chest and epigastric region to monitor the breathing and the progress of the mucus as indicated by a rattling in the large airways and trachea.

As soon as the mucus reaches the larynx. It can be effortlessly coughed out. When indicated, the mucus should be coughed out against a resistance.

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iv. Positive Expiratory Pressure (PEP)

The rationale for positive expiratory pressure (PEP) treatment in Cystic Fibrosis is described in Andersen JB & Falk M. Chest Physiotherapy in the Pediatric Age Group. Respir Care 36:546-522, 1991.

At the Danish Cystic Fibrosis Centre, Copenhagen, PEP treatment is administered as outlined below:

The PEP system (Astra Tech, Denmark) consists of a mask and a one-way valve to which expiratory orifice resistors can be attached. A manometer determining the correct PEP level can be inserted between the valve and the resistor. The diameter of the resistor used for treatment is determined for each individual patient to give a steady PEP of 10 - 20 cm H_2O during the middle part of expiration. This pressure should be maintained during tidal volume breathing with only slightly active expirations.

Treatment is carried out sitting in the upright position (babies are carried on the arm during treatment). A treatment session consists of periods of breathing with PEP followed by the forced expiration technique or cough.

The frequency and duration of each treatment is adapted to the needs of the individual patient. About 10 - 15 minutes twice a day is recommended during stable pulmonary disease.

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v. High Pressure PEP

Technique

The High-Pressure Technique of PEP mask's physiotherapy employs forced expiratory manoeuvres against the PEP mask's expiratory resistor for mobilizing and transporting intrabronchial secretions. The instrument used for this technique is the same as the one described in the previous chapter, albeit equipped with another manometer for monitoring higher pressures. Therapy is performed with the patient seated, elbows resting on a table, and shoulders moved close to the neck to cover and support the lung apices. PEP breathing for eight to ten cycles is done using moderately increased tidal breathing, then the patient inhales to total lung capacity and performs a forced expiratory manoeuvre against the stenosis. Thereby effected mobilization of secretions usually results in coughing at low lung volume. After expectorating sputum, the same sequence of breathing manoeuvres is repeated until no more sputum is produced. Care must be taken not to terminate these forceful expirations before reaching residual volume; sustained expiratory pressures achieved usually range between 40 and 100 cms of H_2O. The dimension of the expiratory resistor and the pressure developed against it is determined individually by a spirometer- assisted method. For this purpose the outlet of the PEP mask is connected to a spirometer, and the patient performs forced expiratory vital capacity manoeuvres through a series of resistors with different internal diameters. The resistance for daily therapy is chosen on the basis of maximal homogenization in the expiratory behaviour of different lung units, as determined by the shape of the flow-volume curve.

Physiologic background

(a) ***Mobilization phase***

The effects of High PEP mask therapy are explained by increased collateral airflow to under ventilated regions; air expired from there will mobilize obstructing secretions. In addition, a forced expiration against a marked resistive load will squeeze Pendelluft from hyper-inflated into unobstructed and atelectatic lung units. Mobilization of mucus plugs is supported by back-pressure-effected dilation of airways.

(b) ***Transportation phase***

As in the FET, upstream movement of the equal pressure points with ongoing forced expiration and a progressive incorporation of the peripheral airways into the compressed downstream segment is a prerequisite for efficacy. Incomplete manoeuvres, either caused by the choice of an inappropriate resistor or by incorrectly performed technique should be avoided.

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vi. Oscillating PEP - Flutter Therapy

The ***Flutter VRP1 (VRP1 Desitin/Scandipharm Flutter VarioRaw SA)*** is a pocket device which generates a controlled oscillating positive pressure and interruptions of the expiratory flow when breathing out through it.

Its aim is to improve pulmonary ventilation and to ease expectoration. The device is made of a mouthpiece (1a), a plastic cone (1b), a steel ball (1e) and a perforated cover (1d).

During exhalation through the device, the patient's respiratory system undergoes internal vibrations which are triggered by repeated variations of the exhaled airflow and by oscillations of the endobronchial pressure.

The Flutter VRP1 has two main characteristics:

1.it generates an automatically controlled oscillating positive pressure. The patient is thus protected against a collapse of the airways, as well as against any prolonged hyper pressure which could occur should the instructions for use not be followed and exhalations be repeatedly forced.

2.it enables a modulation of the pressure and airflow oscillation frequency. By tuning this frequency to his/her own lung resonance frequency (usually between 6 and 26 Hz) the patient induces maximal vibrations of the bronchial walls which promote clearance of the small airways where CF infections and airway damage occur.

Modulation of the flow and pressure oscillations is obtained as follows, applying the same approach as for the Autogenic Drainage:

The patient should sit comfortably (2), hold the Flutter VRP1 horizontally (4), then take as deep a breath as possible, put the mouthpiece of the device into his/her mouth, hold his/her breath for 2 to 3 seconds (permitting the inhaled air to be more evenly distributed in the lungs and behind the mucus in the very small airways), close his/her lips tightly around the mouthpiece (5) and breathe out normally and deeply, keeping his/her cheeks flat and hard, using the method of unforced abdominal exhalation while relaxing the muscles of his/her upper chest. Repeat breathing in through the nose and out again into the Flutter.

On successive attempts, the patient may find it necessary to move the Flutter VRP1 (6) slightly upwards (higher pressure and frequency) or downwards (lower pressure and frequency) by a few degrees until he/she can feel the full effects of the vibrations at the abdominal level during the first stage of the exhalation process (tuned to the resonance frequency of the lungs). It is not necessary to complete a full exhalation each time when breathing out through the Flutter VRP1.

The following treatment session could, after a few exercises in the sitting position (3a), also be done in a lying down position (3b), provided the angle of the cone to the horizontal is always respected (30 degrees).

A Flutter VRP1 usual session consists of up to 10 to 15 breaths followed by mucus expectoration, which is repeated until the patient feels that he/she has expectorated all mucus (about 10 to 15 minutes). During each 10 to 15 breaths cycle the coughing should be suppressed until the last exhalation, which should be done at about twice the speed of a normal exhalation. This should automatically bring up a cough followed by mucus expectoration. The frequency and duration of each session should be adapted to the needs of each patient.

Oscillating PEP - Flutter Therapy

The flutter VRP1 is a hand-held pocket device which can be used at all times by the patient.

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vii. Postural Drainage and Percussion

Postural drainage and percussion was first introduced for the treatment of Cystic Fibrosis in the 1950's and remained the cornerstone of therapy until the 1980's.

Postural drainage consists of placing the patient in a position which allows gravity to assist in draining mucus from the periphery of the lungs centrally. Usually, between six and twelve postural drainage positions are used, depending upon which lobes or segments of the lungs are to be drained (Fig 1). Babies are placed in postural drainage positions over the caregiver's lap. As the child gets older, pillows or a postural drainage board may be substituted.

Percussion is used an adjunct to postural drainage. While in each postural drainage position, the patient usually has his/her chest percussed for between three to ten minutes. This is followed with deep breathing exercises, vibration on expiration and huffing.

Treatment is divided into two or three daily treatment sessions.

Effectiveness

Studies have shown postural drainage and percussion to be an effective means of clearing excessive bronchial secretions in patients with Cystic Fibrosis. However, patients may experience some adverse effects. Studies have shown that patients with moderate or severe lung disease often experience oxygen de-saturation when receiving postural drainage and percussion. In addition, it has been demonstrated that in Cystic Fibrosis patients who have Gastroesophageal Reflux, by placing them in a head down postural drainage position, the reflux is aggravated and patients may aspirate into their lungs.

Drawbacks

Postural drainage is time consuming, often requiring the assistance of a second person, and is uncomfortable for the patient. As a result, there is only a 40% compliance rate with this treatment regimen.

Due to the adverse effects and drawbacks with postural drainage and percussion it has largely been replaced in many countries by the other modalities of Physiotherapy outlined in this booklet. Today, it is mainly used in the treatment of babies with Cystic Fibrosis who are unable to cooperate fully enough to perform other types of physiotherapy. Often, the child is changed over to one of these other modalities as she/he has learned how to huff effectively.

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3. Physical Exercise

Aims

To stay physically fit is of great importance for many reasons in patients with CF. Having good endurance, good muscle strength, good mobility and good body awareness influence the quality of life, infection sensitivity, infection coping, looking like others and spare time activity level. Staying physically fit also helps to make mucus mobilizing more efficient.

Physical exercises of different kinds should be included in the chest physiotherapy from the very beginning in order to ***maintain*** good function, rather than rehabilitating function that has been lost. Rehabilitation takes time, can be hard and is sometimes painful. Maintaining good physical fitness is often fun or at least enjoyable and it does not hurt.

Physical exercise could be performed either:

- as one part of the mucus mobilizing therapy or
- as an addition to the mucus mobilizing therapy.

Additional Therapy

Malnourished patients will not benefit from either endurance training nor muscle strengthening exercises since they lack the material needed to build up muscles. A nutritional support programme should proceed or at least be commenced parallel to the exercise programme. Mobility exercises are not as dependent on nutritional status.

Some patients will develop exercise induced bronchospasm. This can vary from time to time since it to a certain extent is dependent on the general condition. Those benefitting from inhaled bronchodilators or Sodium Chromo Glycate should use this prior to mucus mobilizing therapy and physical exercise.

Patients de-saturating during exercise should exercise with supplemental oxygen. Their endurance training is based on function training adapted to their ability and their home oxygen equipment, so that the physical exercises do not bring them below 90% in saturation.

i. *Physical exercises as a part of the mucus mobilizing therapy*

Physical exercises used in order to loosen mucus should be a mixture of endurance training, muscle strengthening exercises and mobilizing exercises for chest, spine, neck and shoulders. The intensity and content of the exercise programme must be individually adapted.

Endurance training increases ventilation and opens up clogged or collapsed airways. If the chosen strengthening and mobilizing exercises are performed in as many different positions as possible such as standing upright or sitting, sidelong bilaterally, lying supine or on the stomach, different parts of the lungs are ventilated. When mucus has been loosened it has to be transported and evacuated. Physical exercises used for this purpose must therefore be interspersed with AD-manoeuvres or huffing and coughing. Whether AD or huffing and coughing is used depends on each individual's airway stability, tendency to develop bronchospasm and ability to learn.

Physical exercises as a part of the mucus mobilizing therapy could be used either at each chest physiotherapy session, at one of the sessions every day or at least at 3 - 4 sessions each week. Other sessions consist of other methods.

Less efficient in some individuals

In some cases (those severely ill) obstruction increases in connection to physical exercise, even though properly pharmaceutically treated. In these cases physical exercises as part of the mucus mobilizing therapy are usually not efficient since long pauses are needed before secretions can be efficiently transported by the help of huffing or AD. An alternative method or combination of methods should be tried to make the mucus mobilizing therapy as efficient as possible during the time allocated for it. Physical exercise should then be added, afterwards.

The advantage

The advantage of using physical exercises to loosen mucus and not as an addition to other methods is to save time for the patient. Also it offers patients another alternative way to clear their lungs assisting them in finding the optimal method for each different situation.

ii.***Physical exercises performed in addition to the mucus mobilizing therapy***

When performed in addition to the mucus mobilizing therapy they should contain both training of endurance, muscle strength and mobility according to the aims. Physical exercises should be performed at least 3 - 4 times a week. The content of each session could vary from time to time, or be the same, depending on what suits the individual best. If needed, the intensity of each session is adapted to the individual. Additional therapy as mentioned above comes along with the exercise programme.

Endurance training should of course not be performed during exacerbations, especially not if fever is present.

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4. Inhalation Therapy

Inhalation therapy is now considered an important component of the treatment in CF with the physiotherapist often administering the inhalations in conjunction with the airway clearance techniques. When considering the use of inhalations there are three things to consider:

i.Purpose of inhalation
ii.Mode of administration
iii.Positioning and breathing pattern

i. *Purpose of Inhalation*

a.***Bronchodilator*:** Various beta 2 agonists are used prior to physiotherapy to open up the airways and thus promote easier clearance of secretions.

b.***Inhaled steroids*:** These are used to decrease mucosal swelling and inflammation and often takes a couple of weeks of treatment before full effect is noted. Usually they are given post physiotherapy with the belief that once secretions are cleared, the steroid will be more effectively delivered within the respiratory tract.

c.***Antibiotics*:** Given aerosolized rather than systemically to directly attack the bacteria attached to the mucin. Usually they are given post physiotherapy, to increase peripheral distribution to the mucus obstructed parts of the lung which were not readily cleared with airway clearance techniques.

d.***Agents to decrease mucus viscosity*:** Include hypertonic and isotonic saline, DNase, amiloride and UTP. Hypertonic saline has been shown to increase airway clearance but can induce bronchoconstriction in patients with reactive airways. These responses are not elicited when isotonic solution is used. The delivery of DNase is recommended only with certain nebulizers to control for particle size. There is no consensus as to whether DNase should be given prior or post physiotherapy.

ii. ***Mode of Administration***

It is important that the particle size be less than 5um for deposition into the lungs. Particle size of 10um lomicron is delivered to the upper airways only.

a.***Inhalers: Powder and Metered Dose (M DI).*** There are several different forms of inhalers. Some are loaded with a capsule before each dose is administered and some are loaded with several capsules with one being punctured before inhalation. Others are preloaded with up to 200 doses, where each dose is prepared beforehand. With the powder inhalers an optimal inspiratory flow is needed to lift the powder from the inhaler and allow it to be deposited into the lungs.

***Metered Dose Inhalers (MDI)*:** Have a velocity of 70m/hr with the majority of aerosol being deposited into the pharynx. To use inhalers effectively, they require good coordination and breathing technique. Thus, the physiotherapist needs to spend time in educating the patient on correct technique. Their effectiveness is significantly increased when combined with a spacer. The spacer increases the deposition of aerosol and acts as a reservoir. A mask can be attached to the spacer for younger children.

b.***Nebulizers*:** The two groups of nebulizers are jet and ultrasonic. The jet nebulizers are very popular, but need to be used with the appropriate compressor as the particle size is dependent on the driving gas flow rate and volume of solution. Often the systems are found to be malfunctioning and require regular maintenance. In ultrasonic nebulizers, the particle size is influenced by the frequency of crystal oscillation, thus correct usage is essential.

iii.***Positioning and Breathing Pattern***

When using inhalations, the patient should be sitting upright with a good posture and use relaxed abdominal breathing. MDI's require deep inspiration with a hold 5-10 seconds. Nebulizers may be used while performing relaxed abdominal breathing. Alternatively, the patient may

perform autogenic drainage manoeuvres while using the nebulizer. Where one part of the lung is a problem, the physiotherapist may choose an alternative position to promote increase ventilation to the affected portion of the lung.

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5. **The International Physiotherapy Group for Cystic Fibrosis, IPG/CF**

The International Physiotherapy Group for Cystic Fibrosis is an international working committee founded in 1986. IPG/CF consists of a national contact person in each member country and a committee. All countries are welcome to become a member.

The IPG/CF is a member of the Scientific/Medical Advisory Council (S/MAC) of the International Cystic Fibrosis (Mucoviscidosis) Association (ICF(M)A).

The objectives of the IPG/CF are:

.To encourage high standards of physiotherapy practice in the treatment of patients with cystic fibrosis (CF).

.To promote rigorous research in physiotherapy for patients with CF.

.To disseminate information and knowledge of physiotherapy practice in the treatment of patients with CF.

.To promote communication with, and among, contact ersons and respiratory interest groups in countries throughout the world.

.To advance knowledge and understanding of CF among both medical and related professionals and lay people.

.To represent physiotherapists with the SMAC.

The duties of the national contact person are:

.To fulfil, as far as is possible, the objectives of the IPC/CF within their own country.

.To disseminate, as appropriate, information from the Committee to interested persons within their own country.

.To present, in writing, an annual report to the Committee for presentation at the Annual General Meeting of the IPG/CF.

.To submit annually the recommended subscription for contact persons, or a donation, to the Treasurer of the Committee by 31 March of each year.

.To receive correspondence from the Committee.

A list of national contact persons can be requested from the secretary or any member of the committee.

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