

A GUIDE TO:

# **CYSTIC FIBROSIS FOR HEALTH PROFESSIONALS**



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## 1. Introduction

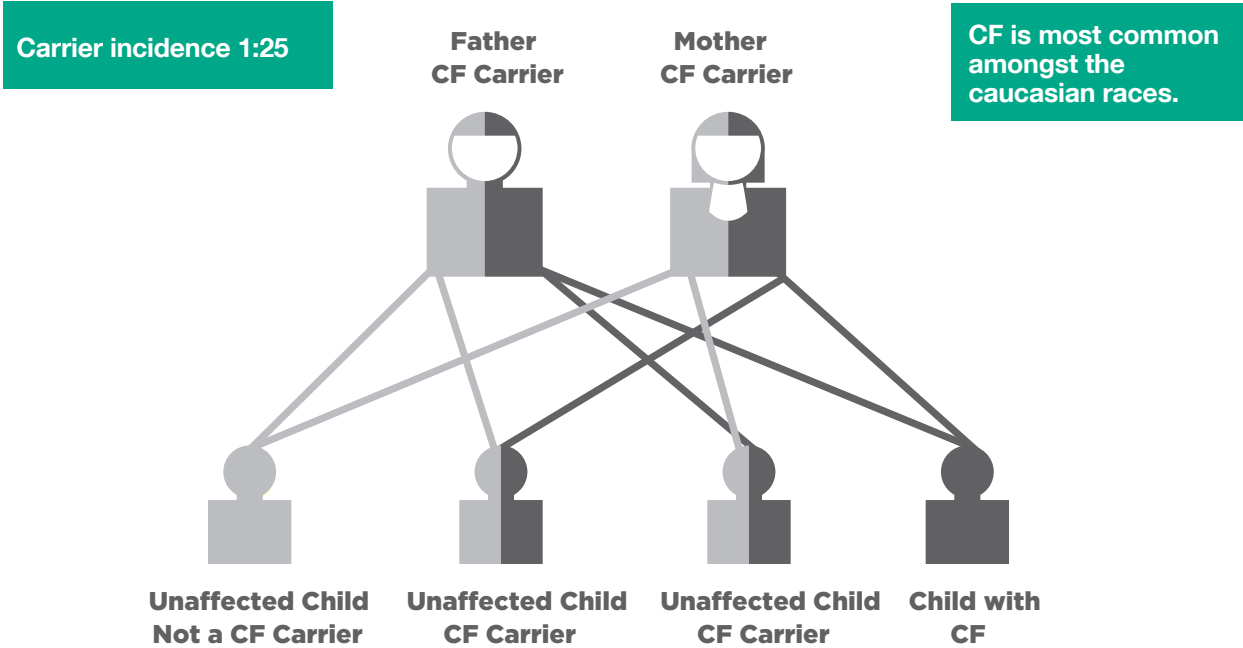
Cystic Fibrosis (CF) is the most common autosomal recessive condition in Australia, affecting approximately 1 in every 2,500 babies born in Western Australia (WA). Previously a disease of childhood, with advances in clinical care, most CF individuals now transition to adult care. In 2012 adults represented 49% of the CF population registered in WA (*Cystic Fibrosis Australia (CFA), 2013*).

CF is a multi-organ life shortening disease typified by chronic endobronchial infection and progressive obstructed lung disease and malnutrition, secondary to pancreatic insufficiency. Currently there is no cure, however present day treatment has increased life expectancy and it is projected children born in 2010 have an expected median survival rate in their 60s (*Lobo J, 2012*) thus can live full and productive lives. A proactive multidisciplinary approach to care, in combination with early antibiotic therapy has been a key to increased survival.

Treatment goals include:

- Protecting specific organ damage
- Reducing early bacterial colonisation
- Avoiding pulmonary exacerbations
- Slowing airway inflammation to preserve lung function
- Maintaining optimal nutrition and normal growth.

Peckham, 2013



2. The CF gene

The gene for CF results from a mutation in a single gene on chromosome 7 that encodes the CF transmembrane conductance regulator (CFTR) protein, a chloride channel. As there are over 1,800 mutations (Lobo J, 2012) that can affect the gene, the function of the CFTR protein varies from complete absence to partial function, resulting in a wide variation in disease severity. CF cells show decreased chloride secretion and increased sodium absorption in epithelial cells. The mutations of the CFTR gene are classified according to molecular features and functional consequences within the cell.

MUTATION CLASSIFICATION	DEFECT	MUTATION CLASSIFICATION	DEFECT
Class I	Interference with protein synthesis, resulting in no CFTR protein at cell membrane	Class IV	Altered channel conductance. CFTR protein trafficked to cell membrane but defect results in decreased chloride flow thus sodium retention
Class II	CFTR protein has a maturation defect and does not reach the epithelial cell wall (affects 80% of patients)	Class V	Reduced CFTR synthesis results in less CFTR protein at cell surface
Class III	Altered channel regulation. Protein reaches cell membrane but cannot be activated as a chloride channel	Class VI	Decreasing stability of CFTR resulting in accelerated breakdown and little functional CFTR at the cell membrane

(The CFTR mutations database, 2014)

3. CF diagnosis and screening

IN WESTERN AUSTRALIA,  
APPROXIMATELY 10-15 BABIES ARE  
BORN WITH CF EACH YEAR



- One person in 25 carries the gene for CF
- The WA Newborn Screening Program screens for CF along with phenylketonuria, galactosaemia, congenital hypothyroidism, and a range of disorders of amino, organic and fatty acid metabolism.

CF newborn screening (NBS) has been carried out in WA since 2000 and is mainly targeted at detecting elevated levels of immunoreactive trypsinogen (IRT) in the newborn’s blood. In this two stage IRT/DNA protocol, a positive IRT is followed by DNA testing to screen for the common CF mutations. Infants with one or two common mutations are usually recalled for a sweat test at 4 – 6 weeks of age.

The most common mutation in WA is a single mutation ΔF508. A sweat chloride > 60mmol/l in combination with CFTR genetic mutation is diagnostic of CF.

(Government of Western Australia Child and Adolescent Health Service Princess Margaret Hospital, 2009)

CARRIER SCREENING

It is important for people to make informed decisions associated with family planning. Carrier screening is available in WA. Information is available at:

[www.cysticfibrosis.org.au/vic/carrier-screening](http://www.cysticfibrosis.org.au/vic/carrier-screening)

Genetic Services of WA (08) 9340 1525



# 4. Clinical manifestations of CF

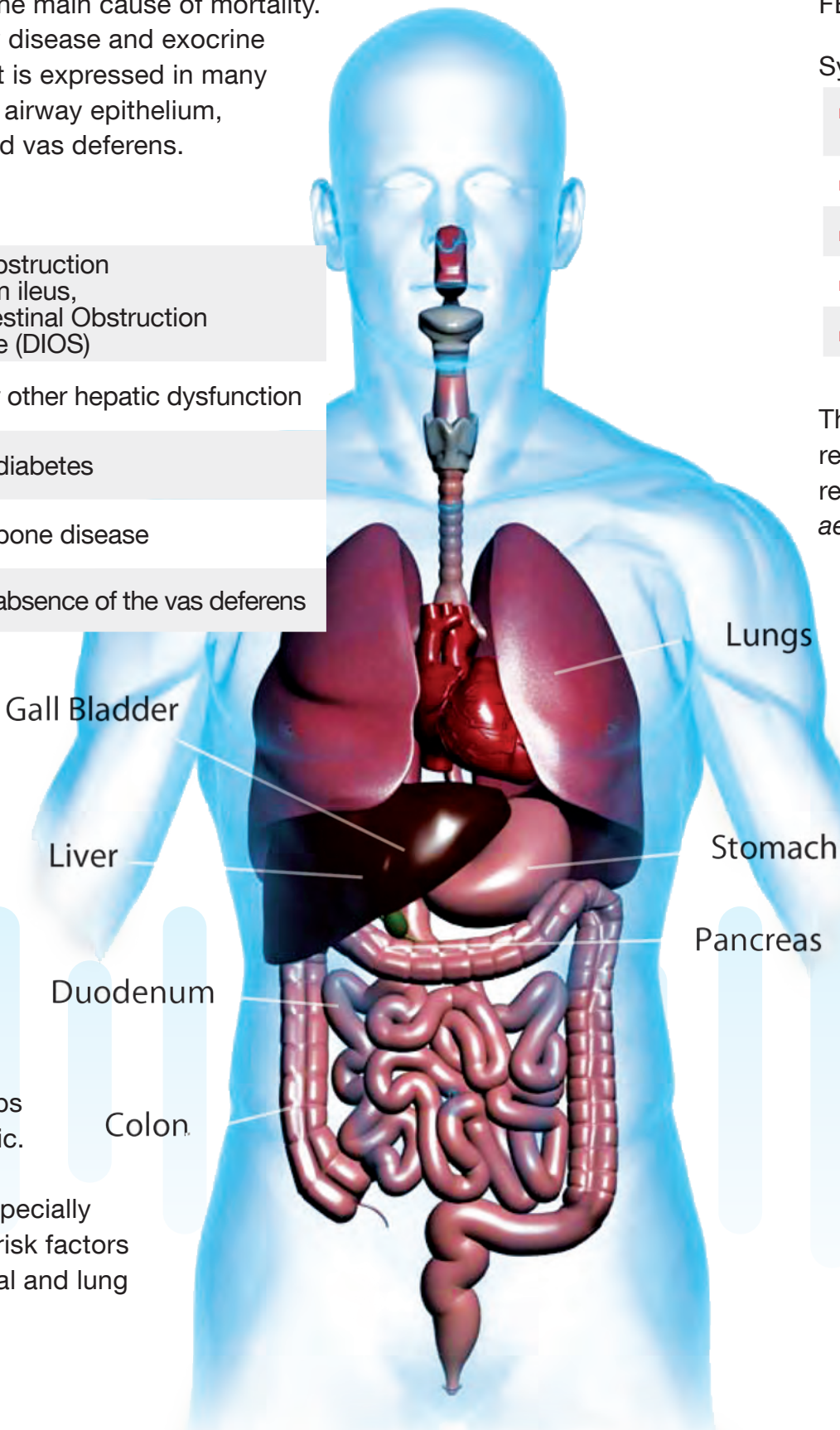
Although a multi-organ disease, it is the pulmonary disease that presents the most challenge and continues to be the main cause of mortality. Most individuals with CF have respiratory disease and exocrine pancreatic insufficiency. The CFTR defect is expressed in many epithelial cells including the sweat ducts, airway epithelium, pancreatic ducts, intestine, biliary tree and vas deferens.

Clinical manifestations include:

- |                     |  |
|---------------------|--|
| ■ Nasal polyps      | ■ Intestinal obstruction<br>- meconium ileus,<br>- Distal Intestinal Obstruction Syndrome (DIOS) |
| ■ Pansinusitis      | ■ Cirrhosis or other hepatic dysfunction   |
| ■ Rectal prolapse   | ■ CF related diabetes  |
| ■ Chronic diarrhoea | ■ CF related bone disease  |
| ■ Cholelithiasis    | ■ Congenital absence of the vas deferens   |

## RESPIRATORY DISEASE

The chloride and sodium channel defect results in thicker more viscous secretions from exocrine glands, particularly in the respiratory tract, and results in extensive chronic inflammation of the airways. The recurrent lower respiratory tract infections, and a chronic cough with sputum production, leads to structural airway changes including bronchiectasis, obstructive lung disease and finally respiratory failure. Bronchiectasis develops in infancy in CF and may be asymptomatic. Studies have shown neutrophilic inflammation and pulmonary infection, especially *Pseudomonas aeruginosa*, (*Pa*) are major risk factors for early disease in CF including nutritional and lung function decline (Sly et al., 2013).



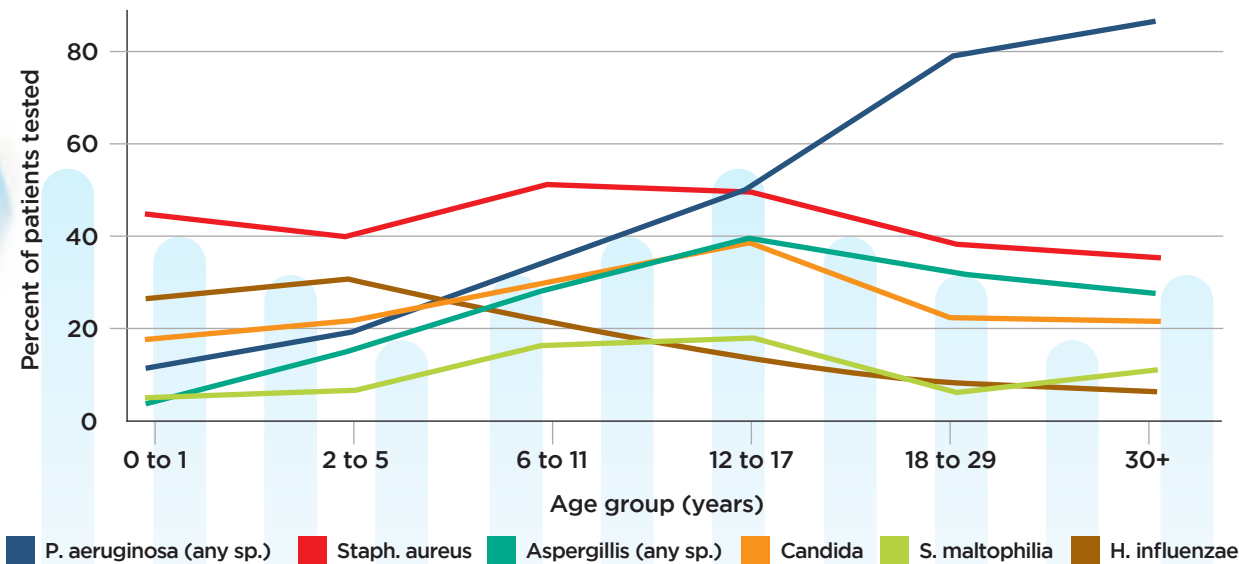
Acute pulmonary exacerbations are characteristic events in CF, and along with FEV<sub>1</sub>, are predictors of survival and quality of life.

Symptoms may include:

- |                                 |  |
|---------------------------------|--|
| ■ Dyspnoea, hypoxia, tachypnoea | ■ Increased cough and sputum, sputum may be purulent |
| ■ Chest pain                    | ■ Haemoptysis  |
| ■ Lethargy, fatigue             | ■ Loss of appetite, weightloss                       |
| ■ Fever                         | ■ Fall in FEV <sub>1</sub>                           |
| ■ Abdo pain                     |  |

The Australian CF Data Registry (CFA, 2013) describes the prevalence of respiratory infections and reports that in childhood these are predominantly related to *Staphylococcus aureus* and *Haemophilus influenza*, with *Pseudomonas aeruginosa* dominating adult years (Fig 1).

Figure 1. Prevalence of Organisms in Lungs of Adults and Children with CF (Cystic Fibrosis Australia, 2013)



## PANCREATIC INSUFFICIENCY

The overall proportion of Australian patients who are pancreatic insufficient is 83% (CFA, 2013).

In individuals with CF, the exocrine glands in the pancreas produce such thick secretions that the pancreatic ducts become blocked. Destruction of acinar pancreatic tissues occurs and lack of enzyme activity results in malabsorption, particularly of fatty foods and fat soluble vitamins. The resultant malnutrition and poor growth associated with fat malabsorption and pancreatic insufficiency is often accompanied by steatorrhoea, abdominal pain and failure to thrive.

Lack of functional CFTR in biliary epithelium results in increased viscosity of bile and may lead to liver complications.

## GASTROINTESTINAL COMPLICATIONS

The incidence of medical complications increases with age. The most commonly presenting gastrointestinal complications are: gastro-oesophageal reflux, liver cirrhosis, portal hypertension, pancreatitis, colelithiasis, constipation, DIOS and rectal prolapse.

## Chronic disease related co-morbidities

With advances in clinical care and improved survival rates, health professionals will be managing a range of co-morbidities outside the respiratory system. Treatment associated chronic kidney disease, bone disease (including osteopenia), osteoporosis, cystic fibrosis related diabetes and arthropathy, hypertrophic oseoarthropathy, depression and urinary incontinence are the common co-morbidities.

### CF Related Diabetes

The prevalence of CF related diabetes (CFRD) increases with age and is becoming one of the most common co-morbidities associated with CF. Acinar atrophy, fatty infiltration and pancreatic fibrosis occur with advancing age and result in decreases in insulin producing beta cells (Ornstein, Rosentstein, & Stern, 2000). CFRD is rare under 10 years of age and in Australia affects approximately 30% of adults by 30 years of age (CFA, 2013). All CF patients should be screened for diabetes annually from 10yrs of age. The onset of diabetes is linked with decreasing lung function, poor nutrition and decreased survival. The high energy diet remains unchanged in the presence of CFRD. Insulin is the treatment of choice.

## Anxiety and Depression

A chronic life limiting disease presents a burden to most individuals. Quon & Aitken (2012), reported a varying incidence of depression among adults with CF ranging from 11 – 30%. Living with CF can be emotionally and physically challenging for the patient and family. It is important to recognise and treat anxiety and depressive symptoms as this can impact on treatment adherence, family functioning and quality of life, and has been associated with reduced lung function.

## 6.

## Improved outcomes

### PREGNANCY

Women with CF are now surviving into their reproductive years and manage to have successful pregnancies. In WA there have been over 45 births to CF women. Lau, et al. (2011), concluded that most women had acceptable outcomes from their pregnancies, however, BMI and lung function were significant predictors of foetal complications. Pregnancy should be planned and involvement of genetic counselling for the couple should be part of the support team. The CF pregnancy is considered high risk and should be managed at a tertiary centre.

Most CF males are infertile due to a congenital absence of the vas deferens, a further complication of CF. However, they produce normal sperm and couples may conceive with IVF treatment.





## 7.

## Clinical management

CF care becomes more complex with increasing age and a multidisciplinary health care team is essential.

The focus for pulmonary management in CF relates to prevention of airway obstruction by improving mucociliary clearance and prevention and early treatment of respiratory tract infections. A comprehensive approach to maintaining lung health includes airway clearance, physical activity, drug therapy and optimal nutrition.

### RESPIRATORY CARE

(Australian Chapter International Physiotherapy Group for CF, 2008)

#### AIRWAY CLEARANCE

Airway clearance is an important part of CF management. The physiotherapist's role involves teaching effective clearance of secretions from the lungs and promoting optimal lung health and general physical fitness. Because CF affects each person differently, a treatment program is designed specifically for the individual, and needs to be reviewed regularly. Regular contact with the physiotherapist can help identify small changes, which may be hard for the individual to detect, thus allowing adjustments to the treatment program.

Physiotherapy treatment should be increased when a lung infection occurs and may be more effective when combined with inhaled medications and exercise.

#### Modified Postural Drainage (MPD)

For babies and young children, when active participation is not possible, the basic program usually involves daily or twice daily modified postural drainage (MPD) with percussion. As children grow, physio 'play', blowing games, coughing and deep breathing exercises are incorporated into the treatment.

#### Active Cycle Breathing Techniques (ACBT)

From about 3-5 years of age more emphasis is placed on breathing exercises. The active cycle of breathing techniques (ACBT) which incorporates deep breaths, breathing control and the forced expiration technique (FET), is taught as a method of clearing mucus more independently. Studies have shown it to be an effective method of mobilising and clearing secretions.

#### PEP (Positive Expiratory Pressure) devices

Devices such as PEP mask, mouthpiece PEP, Flutter or Acapella may be prescribed by the physiotherapist to enhance airway clearance. PEP therapy

is thought to promote collateral ventilation, increase functional residual capacity and recruit obstructed or collapsed airways. It is also used for airway clearance by increasing the volume of air behind an obstruction and creating pressure to force secretions centrally, towards the larger airways, where they can be more easily cleared. Bottle PEP can be used to help transition younger children to a device or used in hospital when there is no access to expensive devices. PEP can also be used in babies and toddlers where appropriate.

#### Autogenic Drainage

Autogenic drainage, or self drainage, is an airway clearance technique that is widely used throughout Europe. The technique is based on the principle of reaching the highest possible airflow in different generations of bronchi by controlled breathing. When performing autogenic drainage, individuals adjust the rate, depth and location of respiration in order to clear the chest of secretions independently.

#### PHYSICAL ACTIVITY

Another very important early recommendation for airway maintenance is regular exercise. Physical exercise that increases minute ventilation leads to the mobilisation of secretions and enhances airway clearance. Forced expirations and expectoration should be included with all physical activity to optimise airway clearance. It is recommended that all patients should be encouraged to exercise several times a week.

### DRUG THERAPY

#### Mucolytics

Inhaled mucolytic agents are used as an adjunct to airway clearance techniques (ACT). These include:

Dornase alfa (Pulmozyme) – an enzyme that reduces the viscosity of purulent lung secretions by targeting DNA in secretions

#### Hydrator Therapy

- Hypertonic Saline (nebulised) – increases airway surface liquid by osmotically drawing liquid into airway
- Mannitol (Bronchitol) – a dry powder inhaler that increases airway surface liquid and improves mucociliary and cough clearance (*Pharmaxis, 2012*)



Antibiotics

By adulthood, 80% of patients are colonised with *P. aeruginosa* (Schelstraete, Haerynck, Van Daele, Deseyne, & De Baets, 2013). Antibiotics will be administered orally, by inhalation and intravenously (usually in exacerbations).

Early eradication of *P. aeruginosa* is usually through inhaled antibiotics e.g. Tobramycin, Coliston, Aztreonam.

Anti-inflammatories

Azithromycin in maintenance doses is used as an anti-inflammatory.

CFTR modulation therapy

Current advances in molecular therapy relate to the development of specific drugs that correct the underlying CFTR protein defect. Kalydeco is used in those over 6 years of age with the G551D mutation.

NUTRITIONAL MANAGEMENT

Lung function and nutritional status are closely linked. Malnutrition related to inadequate energy intake is a common problem in CF patients.

Diet

The increased energy requirements associated with the work of breathing, chronic inflammation and infection result in recommendations of an energy intake 120%-150% greater than the general population. A diet unrestricted in fat and high in carbohydrates leads to better growth. Breast feeding is encouraged.

Enzyme Replacement

Pancreatic enzyme replacement therapy (PERT) along with vitamin supplementation is part of the management (DAA, 2006). Nutritional supplements may be required to optimise nutritional status. It is important pancreatic enzyme replacement capsules are taken with the first mouthful of foods that contain fat, carbohydrates and protein. The enzyme dosage is related to the fat content of food ingested and an additional dose may be needed if the meal lasts more than 30 minutes.

Sodium

Sodium reabsorption from sweat is abnormal in people with CF. The CFTR defect results in abolition of normal chloride conductance with consequently poor sodium reabsorption into the cells and a high concentration of salt in sweat. This increased sweat loss of sodium and chloride with exercise and in hot temperatures, predisposes the individual with CF to salt depletion and dehydration. Sodium supplementation is recommended in WA and additional salt will be required when exercising.

8.

Prevention of cross infection

It is recommended patients with CF are segregated from one another to minimise the risk of transmission of microorganisms. It is important to try to minimise exposure to common respiratory pathogens, therefore **admit patients to a single room when hospitalised**. Annual flu vaccination is recommended.

ON HOSPITAL ADMISSION:

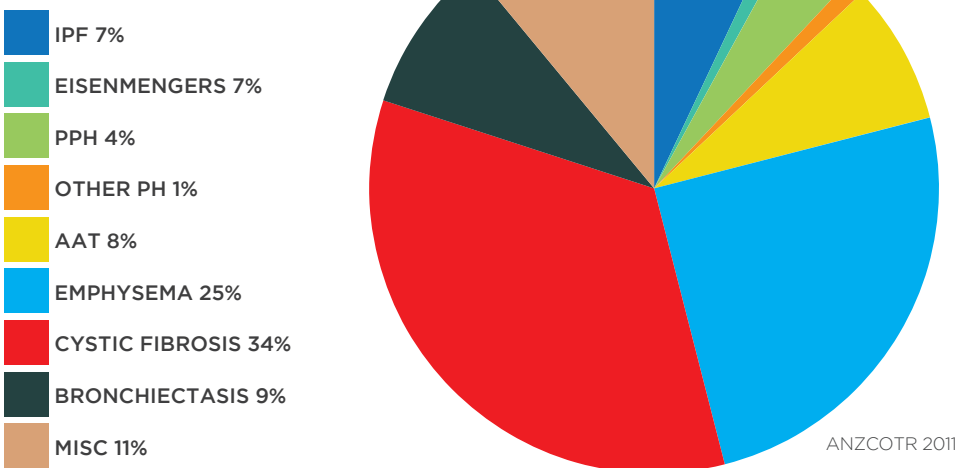
- Admit to single room
- Order high energy, high fat diet. Consider nutritional supplement
- PERT capsules should be available for the patient to self- dose
- Refer to dietician
- Refer to physio

9.

Lung transplantation

Lung transplantation is an option for some patients with declining lung function, limited life expectancy and poor quality of life. It is a non-curative procedure but may offer the best treatment option available. CF patients with rapidly declining lung function or an FEV<sub>1</sub> near 30% of predicted, exacerbation requiring ICU, frequent use of intravenous antibiotics and haemoptysis not controlled by embolization without other major organ dysfunction will usually be referred to the Royal Perth Advanced Lung Disease Program for consideration and discussion of transplant. Influences upon transplant eligibility include age, BMI rehabilitation potential, respiratory infections and resistant organisms. In 2012 the Australian CF data registry reported 24 lung transplants amongst the Australian CF population (CFA, 2013).

Reason for Bilateral Lung Transplant, 1992 - 2011





## 10. Continuing care in the community

### COMPREHENSIVE HOME CARE (CHC) PROGRAM

The CHC program administered by CFWA is funded by the West Australian Department of Health. It is designed to provide continuation of treatment and /or assistance in the home for individuals and families with CF, thus promoting early discharge and reducing hospital admissions. CHC is available by referral from a CF centre and is described as an early intervention or early discharge package of care. It covers several areas:

- assistance with airway clearance
- supervision of intravenous antibiotics
- newly diagnosed support and airway clearance education
- counselling

## 11. CF centres Western Australia

If you have any questions about any information contained in this booklet please contact your health care team or Cystic Fibrosis WA.

### SIR CHARLES GAIRDNER HOSPITAL (SCGH)

Sir Charles Gairdner Hospital is the Adult CF centre for WA. It provides both inpatient and outpatient services. Outpatient clinics are run twice per week. The Adult CF service is run by a Medical Consultant who specialises in CF care, and it is co-ordinated by the Nurse Practitioner. Contact with this service can be made through the Department of Respiratory Medicine.

**P** | (08) 9346 3333 **W** | [www.scgh.health.wa.gov.au](http://www.scgh.health.wa.gov.au)

### PRINCESS MARGARET HOSPITAL (PMH)

Princess Margaret Hospital is the Paediatric CF centre in WA. It provides both inpatient and outpatient services. Outpatient clinics are run twice per week. PMH have five Consultants who care for CF patients. This service is co-ordinated by the Clinical Nurse Consultant, Respiratory Medicine. Contact with this service can be made through the Department of Respiratory Medicine.

**P** | (08) 9340 8626 **W** | [www.pmh.health.wa.gov.au](http://www.pmh.health.wa.gov.au)

**In 2015 paediatric and adolescent services will be relocated to the Perth Children's hospital on the Queen Elizabeth Medical Centre site Nedlands.**

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## CFWA services and support

CFWA employ a team of professionals to provide short and long term support for individuals, families and carers in the CF community.

These are some of those services:

- ☒ **Home based airway clearance support and exercise programs**
- ☒ **Occasional respite**
- ☒ **Exercise and equipment loans: physio tables, nebulisers, running and rowing machines**
- ☒ **Counselling, life coaching, general support and advice**
- ☒ **Nursing consultation and community support**
- ☒ **Education to schools, workplaces, community groups, allied health and nurses**
- ☒ **Social and recreation events**
- ☒ **Regional support**
- ☒ **Community fund raising opportunities**
- ☒ **Quarterly newsletters, fortnightly e news**
- ☒ **Fundraising for research**

**For more information contact:**

### **CYSTIC FIBROSIS WESTERN AUSTRALIA**

Niche Building, Suite C 11 Aberdare Rd  
Nedlands WA, 6009

Postal Address:

PO Box 959

Nedlands, WA 6909

**P** | (08) 9346 7338

**F** | (08) 9346 7344

**W** | [www.cysticfibrosiswa.org](http://www.cysticfibrosiswa.org)

**E** | [info@cysticfibrosiswa.org](mailto:info@cysticfibrosiswa.org)

[www.cysticfibrosis.org.au/wa](http://www.cysticfibrosis.org.au/wa)