



ERS School Course Cystic Fibrosis

Treatment of advanced stage CF lung disease

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Educational aims

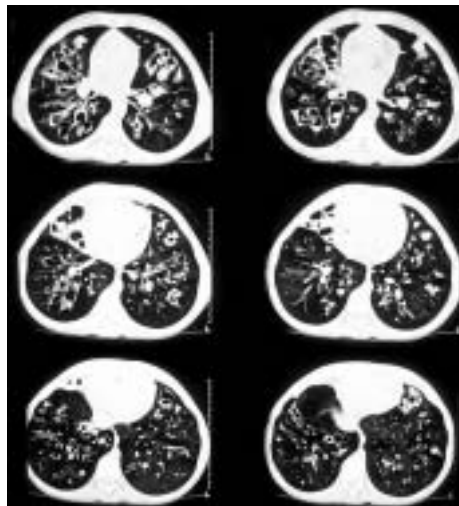
- ▶ To identify patients with advanced and rapidly progressive lung disease.
- ▶ To discuss how to best optimise standard therapies.
- ▶ To understand the different approaches appropriate to patients who have and have not decided that lung transplantation is an option.
- ▶ To detail innovative strategies which may be worth attempting if conventional means failure.

Summary

More than 90% of CF patients will eventually die of advanced lung disease, despite everything that has been attempted. This article will discuss strategies that can be adopted when a patient is doing badly.

▶ The definition of advanced cystic fibrosis (CF) lung disease can be debated, but if forced expiratory volume (FEV₁) <30%, arterial oxygen tension <7.3 kPa (55 mmHg) and arterial carbon dioxide tension >6.7 kPa (50 mmHg), then, as a working definition, mortality is 50% at 2 years [1]. Of course, these figures also mean that 50% will survive for >2 years. A number of other more sophisticated indices have been proposed [2], which allow for sex differences, but the individual predictive value is still poor. The strategies that will be described in this article are also applicable to less severe lung disease where the patient is deteriorating rapidly; in particular, beware of rapid deterioration for no obvious reason in adolescent females. There is no uniformly accepted definition of rapid deterioration, but recognition that

all is not going smoothly, followed by prompt action, is essential.



CT scan of a patient with severe end-stage CF. There is extensive bronchiectasis in all areas.

This article is adapted from the ERS School Course on Cystic Fibrosis organised in Vienna, November 11–13, 2004. Original slides, web casts and additional material can be found at www.ersnet.org/elearning.

Get the basics right

Before undertaking therapeutic trials of what are, at best, experimental therapies, it is essential to ensure that all standard therapies are being carried out as well as possible and pushed to the limit. This includes therapies directed at all organ systems affected by CF and not just the lungs (see section CF and other organ structures on page 326). In particular, vigorous nutritional support must be instituted, and insulin deficiency, even in the absence of overt diabetes, should be actively sought and treated if present.

First, missed diagnoses, such as allergic bronchopulmonary aspergillosis and non-tuberculous mycobacterial infection, should be looked for as a cause of deterioration.

Chest radiograph of a CF patient with allergic bronchopulmonary aspergillosis. There are bilateral wedge-shaped shadows in the mid zones.



Antibiotics should be used effectively: regular and prolonged intravenous anti-pseudomonal antibiotics; optimised nebulised antibiotics, including the use of a regime with alternating months of TOBI™ and colistin, so the patient always inhales antibiotic; and macrolide antibiotics.

In order to ensure successful airway clearance, chest physiotherapy and other techniques as an aid to physiotherapy, including positive-pressure devices and nasal ventilation, should be reviewed. One extremely important point that should be noted is that some young females with bad CF will deliberately suppress their cough because of stress incontinence. This will be missed unless enquires are made in privacy; a sympathetic and senior colleague, usually the CF nurse, is often the best person to ask about this embarrassing problem. There is anecdotal evidence from the authors' centre that the cough in/exsufflator [3] is beneficial in some; however, care must be taken, because there is the potential for airway collapse and sputum retention if a "too vigorous" negative

suction is applied.

In addition, mucolytics, such as rhDNase (two trials show benefit in end-stage CF lung disease [4, 5]) and hypertonic saline (up to one third of rhDNase non-responders may benefit from hypertonic saline [6]) should be efficiently utilised.

Prednisolone or pulsed methyl prednisolone is another therapeutic strategy to be considered.

Nutrition should be monitored, and gastrostomy feeding is usually needed to maintain any sort of adequate nutritional status. Total parenteral nutrition has been occasionally used with marked success in children with advanced disease and severe nausea and vomiting.

Insulin deficiency is almost always present and should be treated when detected. Sometimes this alone may result in improvements [7].

Any major haemoptysis should be dealt with [8]. These are almost invariably caused by hypertrophied bronchial arteries as a result of chronic airway inflammation and bronchiectasis. Most patients with massive haemoptysis will have established severe lung disease. Haemoptysis must be distinguished from haematemesis secondary to varices. The patient should be admitted to hospital, reassured and given intravenous anti-pseudomonal antibiotics; infection with resistant organisms is common. Cautious chest physiotherapy should be continued. Clotting studies and a full blood count should be performed and blood cross matched. Bronchoscopy is not generally useful, as it is technically difficult during active bleeding and does not influence management. If bleeding does not settle, or recurs, then bronchial artery embolisation should be considered. If it



Digital subtraction bronchial angiography in a CF patient who has suffered a major haemoptysis. Note the hypertrophied bronchial arteries, which will be occluded during this examination. There is also a Vascuport visible.

fails, and the area of haemoptysis can be identified, lobectomy may be needed, but this carries the risks of high morbidity and mortality. There are occasional reports favouring the use of tranexamic acid therapy in massive haemoptysis.

Any pneumothorax should be treated [9]. This usually complicates severe lung disease and carries a high subsequent mortality from respiratory failure as a result of the underlying disease. A high index of suspicion is needed, and a chest radiograph or even a computed tomography scan should be performed if there is unexplained deterioration, breathlessness and pleuritic chest pain. This complication should always be taken seriously in all but the most minor cases. The patient is usually admitted, given intravenous anti-pseudomonal antibiotics and cautious chest physiotherapy is continued. Minor pneumothoraces need not be drained, but larger ones require a chest drain, which may make chest physiotherapy difficult. If there is no rapid re-expansion, surgical consultation should be sought with a view to pleurodesis. A second episode of pneumothorax on the same side is a firm indication for surgery.



Right-sided pneumothorax in a CF patient with very severe lung disease.

Adherence is often a major issue. The patient may become disillusioned with time- and labour-intensive therapies that are burdensome and, despite which, there is relentless deterioration. Sometimes a period of intensive, in-patient therapy may enable the patient to get better and prove to him/her that being well is possible. It may also be that local services need to be mobilised to

provide help for the family in doing the treatments, for example a session of chest physiotherapy at school.

Palliation or persistence?

A key decision to be made is whether a patient is eligible for lung transplantation. Ineligibility may be due to physical criteria, such as active tuberculosis or infection with pan-resistant Gram-negative organisms, or because the child and family do not wish to be considered. In the latter case, in particular, it is important to assess the appropriateness of different treatments and discontinue those that are intrusive and no longer helpful. Such discussions need sensitivity. The results of such discussions may also determine the approach to other complications, such as bone disease. Clearly, energetic treatment with potential toxicity is appropriate if lung transplantation is a possibility, but might not be correct if the patient has declined.

Novel potential rescue therapies

By definition, these therapies have been employed in desperate situations and there is little more than anecdotal evidence to suggest their use. They are options that might be considered after discussion with the child and family to ensure that they understand that these therapies are experimental.

If a previous rhDNase trial had failed, then the use of more modern and powerful nebulisers to deliver medication or twice-daily treatment should be considered.

Long-term (many months), twice-daily, intravenous colistin has been used by the author's group on an anecdotal basis. In this case, urea, electrolytes and serum creatinine should be monitored regularly. An implanted vascular access device is essential for this strategy to work. The use of pre-packaged antibiotic infusions, such as the Intermate™, may assist with this strategy.

Monthly infusions of intravenous immunoglobulin (ivlg) have been used in CF patients [10]. The index case [11], a child who had severe non-bronchiectatic distal airway obstruction and was dependent on high-dose corticosteroids, responded dramatically to ivlg. Steroid treatment could be stopped while maintaining lung function, although, to date, the patient has had to remain on monthly infusions for >6 years; attempts at weaning have led to return of airflow obstruction. A case series [10], published more recently, has confirmed that, in a few patients, this strategy may improve lung function while allowing

reduction of steroid dosage. Before trialling this medication, the current author's practice has been to perform a bronchoscopy, bronchoalveolar lavage and a pH study to exclude reflux and aspiration as a cause of the problem.

Whether the CF airway is pro-inflammatory in the absence of infection, or infection merely results in an exuberant inflammatory response, is irrelevant in advanced CF lung disease. At this stage, there is massive airway neutrophilia, with release of neutrophil elastase and other toxic chemicals. There is logic for the use of immunosuppressives. Unfortunately, there is no evidence that non-steroidal anti-inflammatory medications, such as ibuprofen, are of use in advanced, as opposed to more early-stage, CF lung disease. There is anecdotal evidence that steroid-sparing agents, such as methotrexate and cyclosporin A, may be beneficial for selected patients. It would seem logical to trial either the anti-tumour necrosis factor (TNF)- α monoclonal or the receptor blocker given the high levels of sputum and serum TNF- α reported in severe CF [12], but there is no data from advanced CF lung disease.

There is no doubt that work of breathing is considerably increased in advanced CF lung disease. Hypoxaemia is common, especially during sleep. Although hypoxaemia can be corrected by oxygen therapy, at the risk of worsening hypercapnia, the work of breathing and gas exchange can be improved by using nocturnal biphasic positive airway pressure (BiPAP). Considerable improvements in nutrition have been reported with this approach [13, 14]. BiPAP may also be used during the day and as an adjunct to physiotherapy.

Advanced CF lung disease is often characterised by chronic infection with multi-resistant organisms. Combinations of antibiotics are often used. Detailed synergy testing may have a role, but is as yet unproven. It should be noted that

there is no correlation between *in vitro* antibiotic sensitivity test results and clinical outcome [15]. However, it should also be noted that, at least *in vitro*, combinations of antibiotics to which a resistant micro-organism is sensitive when used as a single agent may be additive, synergistic (the two together are better than the sum of the two alone) or actually antagonistic [16]. Macrolides may antagonise the effect of some anti-pseudomonal antibiotics, for example meropenem [17]. These facts should be noted, while the clinical relevance is unclear. Further studies of the role of synergy testing are awaited.

Other innovative uses of antibiotics include extended sensitivity testing for compounds, such as minocycline, to which, surprisingly, *Pseudomonas* may be sensitive [18]. Resistant *Pseudomonas*, *Burkholderia* and *Stenotrophomonas* species have been reported to be sensitive to a combination of nebulised amiloride and tobramycin [19].

Conclusions

The management of advanced lung disease in CF is a challenge. If transplantation is an option, aggressive therapy should be maintained, provided quality of life is not compromised, and the success of transplantation is not compromised by, for example, therapy with large doses of systemic corticosteroids. The time may come, however, when the patient is too sick to be considered for a transplant, and it takes skill and courage to recognise this. Failure to do so, however, may mean that intrusive and burdensome treatments are continued inappropriately. Terminal care for those who have declined transplant also needs careful and sensitive planning. On a positive note, not infrequently, the application of aggressive and anecdotal treatments can bring substantial benefits to really sick children.

Educational questions

- The following apply to most children with advanced CF lung disease, true or false:
 - FEV₁ <15% predicted.
 - Elevation of plasma pro-inflammatory cytokines cause cachexia.
 - Increased work of breathing contributes to malnutrition.
 - Good nutritional status is usual despite poor lung function.
 - Poor adherence to treatment is never a factor in this severe group.
- The following are known to be useful in the management of advanced CF lung disease, true or false:
 - Synergy testing for antibiotic combinations of multi-resistant organisms.
 - rhDNase.
 - Prednisolone.
 - Ibuprofen.
 - Macrolide antibiotics.
- There is anecdotal evidence for the following rescue therapies for advanced CF lung disease, true or false:
 - Monthly intravenous immunoglobulin infusion.
 - Methotrexate.
 - Cyclosporin A.
 - Oral manganese supplementation.
 - Ω-3 fatty acid supplementation.

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Suggested answers

- False
 - True
 - True
 - False
 - False
- False
 - True
 - True
 - False
 - True
- True
 - True
 - True
 - False
 - False

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CF and other organ systems

CF is a multi-organ disease affecting all organ systems with epithelial cells, and this results in a wide range of diseases in several organ systems. Some of the issues relevant to CF patients are highlighted here.

CF-related diabetes mellitus (CFRD)

Pancreatic cells are damaged in CF because of pancreatic fibrosis resulting in gradual loss of islet cells. The diagnosis of diabetes is important as delay can result in avoidable deterioration in pulmonary function and body weight. CFRD has been shown in studies to be associated with reduced survival. The prevalence increases from ~1.5% in those aged 10 years, to 13% at 20 years and 50% in those over the age of 30 years.

Diabetes is defined by World Health Organization criteria as a random venous plasma glucose concentration ≥ 11.1 mmol·L⁻¹ or a fasting

plasma glucose concentration ≥ 7.0 mmol·L⁻¹ or an oral glucose tolerance test 2 hour value >11.1 mmol·L⁻¹. This leads to a diagnosis of insulin-dependent diabetes mellitus. Impaired glucose tolerance is a state of impaired glucose regulation, with a fasting plasma glucose <7 mmol·L⁻¹ and an oral glucose tolerance test 2 hour value >7.8 mmol·L⁻¹ but <11.1 mmol·L⁻¹. Screening for CFRD should be undertaken by annual glucose tolerance testing. Random blood glucose measurements and HbA1c are not sufficiently sensitive to be used as screening tests. Symptoms of diabetes, weight loss or falling lung function should trigger appropriate investigations for diabetes. During pregnancy or while on oral corticosteroids, blood glucose should also be carefully monitored.

The treatment of CFRD should focus on improving symptoms and prevention of complications. This usually involves treating with insulin, but appropriate dietary advice should also be given. Diet should not be restricted, but insulin should be prescribed to allow adequate energy intake. Sulphonylureas and glitnides may also be used for those with modest elevations in glucose. However, there is very limited evidence to support their use. The dose of insulin may need to be adjusted during pulmonary exacerbations and again this should account for increased energy requirements at these times. People with CF can develop microvascular complications.



Rib fractures are very difficult to diagnose.



Thoracic cage abnormalities affect respiratory function: lower back vertebrae cross-fractures due to osteoporosis.

CF-related bone disease (CFRBD)

CFRBD has only been recognised as a significant complication in CF over the past 10 years. CFRBD is important because of the risk of fracture, particularly to ribs, which can interfere with airways clearance. However, studies have demonstrated that, overall, fractures are more common in patients with CF.

CFRBD is a form of osteoporosis and diagnosis is made by measuring bone mineral density by dual-energy x-ray absorptiometry. Other methods are available, but are less frequently employed. Bone mineral density is significantly lower in patients with CF compared to controls and is

lowest in older patients and those with more severe lung disease. Reduced bone mineral density is particularly important in patients going for lung transplantation, as they are frequently treated with large-dose glucocorticoid therapy, which can cause further loss of bone mass.



Bone mineral density measured by quantitative computed tomography.

A number of factors contribute to the development of CFRBD. The malabsorption of fat-soluble vitamins, particularly vitamins D and K, is important as they have a role in maintaining bone matrix and calcification. Reduced physical activity due to limitation of exercise tolerance because of impaired lung function is another significant contributor. Delayed puberty is also important, and any teenager with hypogonadism should be considered for testosterone replacement.

Glucocorticoids have an important effect on bone metabolism by decreasing calcium absorption, increasing renal excretion, depressing gonadal function and decreasing osteoclast numbers. Glucocorticoids have been associated with reduced bone mass and are an important factor in the development of CFRBD. Chronic infection is also another important factor and it is likely that cytokines, such as interleukin 6, have an effect on bone, favouring the development of CFRBD.

There are now guidelines for the assessment of patients with CF for bone disease. It is important that all patients with a FEV₁ <50% predicted and chronic lung infection have regular scans for bone mineral density measurement. If their bone mineral density is satisfactory (T or Z score >1), these can be safely repeated every 3 years.

If the T or Z score is <-1, treatment should

include an adequate calcium intake and a check of vitamin D levels, although there is little evidence that this is effective. Exercise and sun exposure should be encouraged. If the T or Z scores are <-2, then they should be considered for bisphosphonate therapy. This can be given conveniently as a weekly treatment (35 µg risedronate or 70 mg adedronate weekly). Intravenous pamidronate every 3 months is also attractive to any patient, although it causes bone pain if infused too rapidly.

There are still significant issues to be addressed in the management of CFRBD. It has still not been determined when bisphosphonate treatment should be exactly initiated, and the mode of treatment in children who are pre-pubertal with evidence of CFRBD is not clear. There is a need for some further randomised control trials in this area.

CF arthropathy and vasculitis

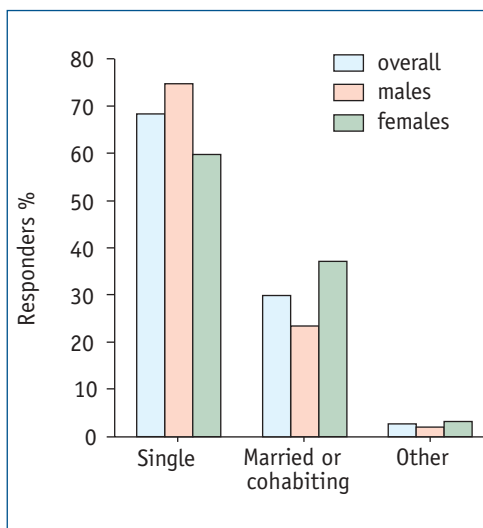
Joint symptoms are relatively common in CF, affecting up to 9% of patients. Finger clubbing is associated with hypertrophic pulmonary osteoarthropathy, although this is relatively uncommon. People with CF can also develop transient episodic arthritis, which is rarely erosive to the joints and is usually rheumatoid factor negative. This form of arthropathy is often exacerbated during pulmonary exacerbations. CF arthropathy can occasionally become more severe and erosive and may require treatment with steroids and immunosuppressive agents. However, major treatment should include analgesia and aggressive treatment of lung disease.

Fertility in males

The vast majority of males with CF are infertile due to bilateral absence of the vas deferens. Sexual potency, however, is not affected by CF *per se*, although it may be reduced due to ill health. Infertility in males is an issue that should be addressed at the appropriate age in people with CF and, generally, this should be in the early teenage years. Males and females with CF should be encouraged to practice safe sex if they are sexually active.

Recent advances in microscopic epididymal sperm aspiration (MESA) and intracytoplasmic sperm injection (ICSI) have made it possible for males with CF to have their own children. This is a very difficult and expensive method, with most centres reporting a 25–30% successful pregnancy rate. Issues on screening partners and longevity of a partner with CF need to be addressed.

A large proportion of patients are engaged in long-term relationships (from the adults CF survey in the UK) and want to consider having children.



Pregnancy and fertility in females

Females with CF are said to be less fertile than healthy females. However, the evidence for this is

limited. It is likely that females with CF who have normal lung function are as fertile as those in the healthy population. Pregnancy presents many challenges and is best managed if it is discussed prior to becoming pregnant. Partner screening is a significant issue, as is discussion as to the future if the partner with CF becomes ill.

A recent review of >600 pregnancies in the USA has indicated that pregnancy is more likely to occur in females with better lung function and that, in this group, pregnancy has no adverse effect on lung function or survival in the mother and there is no increased risk of foetal malformation, although premature birth is more likely. Careful management of lung disease, malabsorption and nutrition is important during pregnancy. CFRD may present for the first time during pregnancy.

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Suggested further reading

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Psychosocial aspects of CF

To most parents, the diagnosis of CF in their children represents a severe blow, as they are confronted with an unwanted and unexpected disease that completely changes their whole life and affects the whole family. Living with a chronic disease and adjusting to the necessary life changes is very often predominantly a psychosocial affair. If the implications of a disease are to be understood, the facts must be considered, a meaning from the facts deduced, and then considerations and potential interventions sought.

Shifting focus

Frequently, questions asked by patients with cystic fibrosis (CF) and their parents refer to fate and the injustice of having a chronic disease. Many parents complain that it is unfair that their innocent child has to live with such a burden. Admittedly, there is no truly comforting answer and that is what the parents are told. However, one positive step is to shift the emphasis from a question that cannot be sufficiently answered to another where there is much more to offer. This question is: what can be achieved despite the disease or what is possible despite this particular condition? This is one of the key questions, as many children have the potential to develop favourably in many ways. In other words, the focus should be shifted from the threat caused by the facts to the possibilities that are available.

Providing comprehensive information

When patients and their parents learn about CF they face unfamiliar medical information and they experience fear. In this situation, can people with a lack of medical knowledge, who are also in an emotional state, be expected to understand medical explanations that refer, for example, to pathophysiological terms and genetics? Whenever new information is given, parents are put into a learning situation that is not labelled as such and, very often, does not fulfil the fundamental requirements for optimum learning. Although health professionals (HPs) expect patients and their families to understand and to retain given information, this will only seldom be achieved. The HP often provides explanations that are comprehensive and upsetting, which, in turn, evokes intense emotions that are incompatible with optimum learning and diminish a person's ability to understand, think coherently and retain the information given. Irrespective of whether it is during the informing interview or later over the course of the disease, fear-provoking information may result in trauma that leads to

retrograde or anterograde amnesia. In general, it is advisable to present information auditorily and visually, which means that written and illustrated material should be provided with ample time for digestion. With regard to "difficult" topics, the presence of both parents should be mandatory.

Adjusting to reality

Individuals with a chronic disease and their families have to live with the illness, there is no choice. The HP, as well as society, expect the patients and their families to learn to accept the disease. This may be an unjustified and unrealistic expectation. Generally, patients and families do prove successful in adjusting to the disease, although this is often only due to the lack of alternatives.

In the case of a genetically transmitted disease, three particular feelings are likely to be evoked in the parents: guilt, blame and family-planning worries. When parents are healthy, but manage to pass a severe disease on to their child, they often feel guilt. They also sense blame, because someone must have caused the disease. Family planning is another big issue: whether or not to have further children, the many concerns surrounding prenatal testing and pre-implantation genetic diagnosis, the fear of decision-making, the anticipation of guilt feelings in case of termination, ethical considerations, religious beliefs, *etc.* The provision of counselling and information is the major intervention strategy in this case.

It is very likely that the HP will describe CF to both the patient and their parents as a manageable condition. However, the patients and their parents will predominantly hear the terms "no cure" and "incurable". The fact that a disease is incurable drastically and negatively alters a family's view of the future and many are shocked to the core. The parents, in particular, will have had some image of how their healthy child was going to be. This loss of potential provokes intense feelings, such as anxiety, despair, disappointment and anger. So what can be done? First, they may all

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benefit from having a professional shoulder to unload some of the pain onto. Later, when the parents have seen their child grow and when they have seen older patients, their worries concerning incurability will probably lessen.

An HP can support a family by teaching them the difference between having a disease and being ill. They need to learn that many children, over many periods of time, perceive themselves as relatively or totally healthy. Therefore, the presence of a chronic disease is not necessarily associated with either the constant objective evaluation (doctor) or the constant subjective perception (patient) of being ill.

Towards a therapeutic alliance

Life-long treatment means exactly what it says: for many families, no matter how well the child, there will be no more days without restrictions. The common factors in many components of therapy include: intrusion, unpleasantness, boredom, resentment and sometimes little obvious immediate effect. Amazingly, the majority of families are willing to create a therapeutic alliance with the treatment team. However, the team must not expect complete adherence because this is truly unrealistic.

Parents need education with regard to management skills and the many practical aspects of CF. The HP should put great effort into motivating both parents to share the responsibility for the child's health needs. The development of a "therapeutic subsystem" that only includes the mother and the child with CF should be avoided wherever possible. If the father is left out and not involved in parenting and disease management they will not learn enough about CF and will not be able to support the mothers appropriately.

Time-consuming treatment also affects the sibling system, as it results in transient disruption and the absence of a playmate. Well siblings will probably encounter periods of time where they are outside the central focus of their parents' attention. The parents should be made aware of this potential problem, as it enables them to develop strategies in advance and to compensate for less attention and time. In addition, the spouse relationship may be endangered, especially when the demands of the ill child make the parents lose sight of their needs as a couple. It may help them to learn that sustaining a loving partnership will strengthen their parenting qualities rather than lessen them, and it may ease their worries to hear that their needs as a couple should be recognised irrespective of the presence of CF.

In the case of a progressive disease, uncertainty is one of the most painful aspects. Very often, no one can tell whether the child will follow a smooth progression into adulthood or whether he or she will deteriorate relentlessly. Hoping for the best while preparing for the worst may well characterise the reactions caused by progression.

The child and their parents need to learn that much of the medical treatment is based on the necessity of preventive care, that the HP are not only aiming at immediate benefits but also at long-term benefits and that many researchers all over the world are assiduously trying to improve treatment in order to improve quality of life. In addition, in case of severe deterioration, lung transplantation is a promising treatment option.

Life span

When life expectancy is discussed, it must be realised that only a few individuals reflect on the length of their lives. Rather, life seems to be viewed as something ending in old age. In contrast, patients with CF and their families are forced to confront the issue of mortality sooner and more intimately than other people. The particular fears of the parents are that their child may die early, and they even may consider the distant future and confront themselves with the incredible possibility that they may outlive their own child.

The crucial point when discussing diminished life expectancy with parents is to initiate reflection that will enable them to develop their own philosophy. This may be difficult, because reflecting on life in any other way than the general "how life should be" consideration is something only few people have done previously. However, when parents are willing to reflect, they may find answers, new considerations and new ideas. For instance, they may realise that every day counts or that their own health is currently an under-appreciated gift. Even if it is difficult to reflect on life span and on life-limiting circumstances, this may bring new insights and new perspectives into their lives.

Conclusion

Psychosocial services should be embedded in a multidisciplinary team according to the saying "together everyone accomplishes more". All members of the nuclear team should provide their services from diagnosis onwards and all should put an emphasis on preventive care. Ward rounds and team conferences are essential for appropriate communication. The amount and intensity of support required will vary among HP, but the aims

of the caregivers are identical: to help achieve, maintain and improve physical health, mental health and social functioning. This includes the

never-ending task of helping the families to find or re-find new or old strengths as a means to meet many of the ongoing demands.

Suggested further reading

Abbott J, Dodd M, Gee L, Webb K. *Ways of coping with cystic fibrosis: implications for treatment adherence. Disabil Rehabil* 2001; 23: 315–324.

Developed a coping scale and examined the relationship between coping styles and treatment adherence.

Abbott J, Gee L. *Contemporary psychosocial issues in cystic fibrosis: treatment adherence and quality of life. Disabil Rehabil* 1998; 20: 262–271.

A comprehensive overview which focuses on the two major psychosocial areas currently topical in cystic fibrosis research.

Bluebond-Langner M, Lask B, Angst DB, eds. *Psychosocial Aspects of Cystic Fibrosis*. London, Arnold, 2001.

A comprehensive book that covers a wide range of topics surrounding CF care and research.

Dodd ME, Webb AK. *Understanding con-compliance with treatment in adults with cystic fibrosis. J R Soc Med* 2000; 93: Suppl. 38, 2–8.

Deals with the benefits of compliance and the consequences of non-compliance. Describes reasons for and management of non-compliance.

Götz I, Labenbacher I, Eichler I, Wojnarowski C, Götz M. *Health-independent lung transplantation information of parents of children with cystic fibrosis. Transplantation* 1997; 64: 742–747.

Investigated parents' attitudes and anxieties toward provision of information about lung transplantation and describes which information parents would want to receive.

Götz I, Götz M. *Cystic fibrosis: psychological issues. Paediatr Resp Rev* 2000; 1: 121–127.

Introduces significant topics that are of relevance to all healthcare providers, such as the impact of CF on family structures, adherence, team approach and controversially discussed issues.

Henneman L, Bramsen I, Van Os ThAM, et al. *Attitudes towards reproductive issues and carrier testing among adult patients and parents of children with cystic fibrosis (CF). Prenat Diagn* 2001; 21: 1–9.

Investigated approximately 70% of the Dutch adult CF population and 53% of the parents of children below 16 years of age with regard to carrier testing, family planning, prenatal diagnosis and termination of pregnancy.

Jedlicka-Köhler I, Götz M, Eichler I. *Parents' recollection of the initial communication of the diagnosis of cystic fibrosis. Pediatrics* 1996; 97: 204–209.

Investigated parents' emotional and cognitive reactions to the diagnosis of CF in their children. Describes the incompatibility of emotional distress and optimum learning.

Joralemon D, Fujinaga KM. *Studying the quality of life after organ transplantation: research problems and solutions. Soc Sci Med* 1996; 44: 1259–1269.

Addresses methodological and theoretical items, points to the saviour effect in quality of life research, reports contradictory findings and suggests an alternative approach.

Lavery SA, Aurell R, Turner C, et al. *Preimplantation genetic diagnosis: patient's experiences and attitudes. Hum Reprod* 2002; 17: 2464–2467.

Investigated English and Spanish couples who actually have undergone pre-implantation genetic diagnosis (PGD). Reports participants' views of advantages and disadvantages and compares PGD with prenatal diagnosis.

Quittner AL, Espelage DL, Ievers-Landis C, Drotar D. *Measuring adherence to medical treatments in childhood chronic illness: considering multiple methods and sources of information. J Clin Psych Med Settings* 2000; 7: 41–54.

Uses CF as a model for studying adherence. Addresses the characteristics of three types of adherence measures (self-report questionnaires, daily diary reports and electronic monitors). Gives specific recommendations for future research.

Staab D, Wenninger K, Gebert N, et al. *Quality of life in patients with cystic fibrosis and their parents: what is important besides disease severity? Thorax* 1998; 53: 727–731.

Investigated adolescents, adults and parents, and describes significant relationships between coping styles and health-related quality of life.