Health Care and Society

Cystic Fibrosis

By Jack Barrington

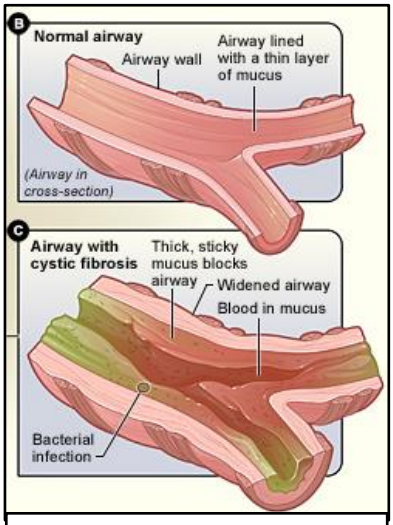
Cystic Fibrosis is not only something that I have enjoyed learning about during my A Levels but is something that I have experienced first-hand whilst on my work experience on a local paediatric ward. Whilst shadowing the consultant paediatrician on a ward round, I came across a 14-year old boy who at first glance seemed like a normal teenager. However, he suffered from chronic cystic fibrosis which meant that he was very different to his friends. It was clear that he was small for his age, caused by malnutrition as his body struggled to digest and absorb nutrients, and he therefore had a gastrostomy (a surgical opening through the abdomen into the stomach) for overnight feeding in order to maintain his weight. Also, he was required to have numerous nebulisers and inhalers with twice daily physiotherapy due to his chronic chest complaints.

Every week 5 babies are born with Cystic Fibrosis and 2 people will die from it. Approximately 3 million healthy people in the UK are carriers of the gene for cystic fibrosis, many of whom are unaware. This rare genetic disease is ever present throughout the modern society that we live in and so I feel that it is a fitting topic to write about.

What is Cystic Fibrosis?

Cystic fibrosis (CF) is a life-limiting genetic condition that causes the lungs and digestive system to become clogged with thick, sticky mucus. This is caused by a faulty gene which is responsible for the movement of salt and water into and out of cells.

The cystic fibrosis transmembrane regulator (CFTR) protein is made by instruction from the CFTR gene. The function of this intrinsic protein is to act as a channel across a cell membrane that produces mucus. When functioning normally, the CFTR protein transports negatively charged chloride ions out of epithelial cells into surrounding mucus. This causes the water potential of the mucus to decrease and so water moves into the mucus by osmosis from the epithelial cells. However, in a person suffering from cystic fibrosis the protein does not form correctly and so cannot function properly. This results in no chloride ions being transported out of the epithelial cells into the mucus. Therefore water does not move into the mucus and so it becomes thick and sticky, causing blockages, infections and inflammations in the respiratory, digestive and reproductive systems.



https://upload.wikimedia.org/wikipedia/commons/9/9a/Cysticfibrosis01.jpg

The build-up of mucus can cause a plethora of symptoms - mainly in the lungs and digestive system. The symptoms of cystic fibrosis can be generally separated into two categories; lung problems and digestive system problems.

Lung Problems	Digestive System Problems
• Recurring chest infections • Bronchiectasis *(abnormally widened airways due to persistent inflammation)* • Increased coughing • Occasional wheeziness and shortness of breath.	• Bowel obstructions • Jaundice • Diarrhoea • Malnutrition leading to problems putting on weight and growing. • Diabetes

http://www.nhs.uk/Conditions/cystic-fibrosis/Pages/Symptoms.aspx

The symptoms that a person suffering from cystic fibrosis will experience can vary as the individual's genotype ultimately decides how much the sufferer will be affected. Additional complications include infertility, sinusitis, nasal polyps, arthritis and osteoporosis.

Symptoms usually begin during early childhood however advances in modern medicine mean that cystic fibrosis can be diagnosed soon after birth through screening tests. The NHS offers a newborn blood spot test to all babies in order to try and detect early problems such as cystic fibrosis. This occurs when the baby is 5 to 8 days old and involves a prick in their heel in order to collect drops of blood which will be examined for abnormalities in a laboratory. The newborn screening is not completely accurate and so in order to confirm a diagnosis, further tests such as a sweat or genetic test will be carried out.

Cystic fibrosis is a genetic disorder and so cannot be caught or develop later on in life.

Cystic fibrosis is the most common inherited disease in white populations with 1 in 25 people carrying a faulty cystic fibrosis gene. For a person to suffer from cystic fibrosis, both parents must carry a faulty gene. In the punnet square on the right **C** represents a normal gene and **c** represents the gene for cystic fibrosis.

	C	c
C	CC	Cc
c	Cc	cc

http://www2.kumc.edu/genetics/risk/images/punnett.jpg

CC – unaffected
Cc – carrier
cc – cystic fibrosis

If both parents carry the gene for cystic fibrosis there is a 25% chance the child will suffer from cystic fibrosis. There is also a 50% chance that child will be a carrier of the cystic fibrosis gene and a 25% chance that they will not have the CF gene at all. Blood tests can be used in genetic screening to determine if an individual carries the faulty recessive gene that causes cystic fibrosis. This can help to find out if somebody is at risk of having a child with cystic fibrosis. Genetic counselling can then be used to support and advise on the possible implications and options available for future pregnancies.

The Cystic Fibrosis Trust say that:
"With advances in care, treatment and understanding of the condition, people with cystic fibrosis are living longer and healthier lives than ever before."
https://www.cysticfibrosis.org.uk/life-with-cystic-fibrosis

The prognosis for a person suffering from cystic fibrosis is certainly better in today's society than in previous decades. Life expectancy for babies born today is between 40 to 50 years. This is considerably more than the average life expectancy of under 10 years during the 1960s where people who suffer from cystic fibrosis were considered lucky to live past the

age of 5. Over many years, the lungs of a person suffering from CF become increasingly damaged and eventually may even stop working correctly. Despite the number of treatments available allowing patients to reduce the problems caused by the condition, unfortunately average life expectancy is reduced for people who suffer for it.

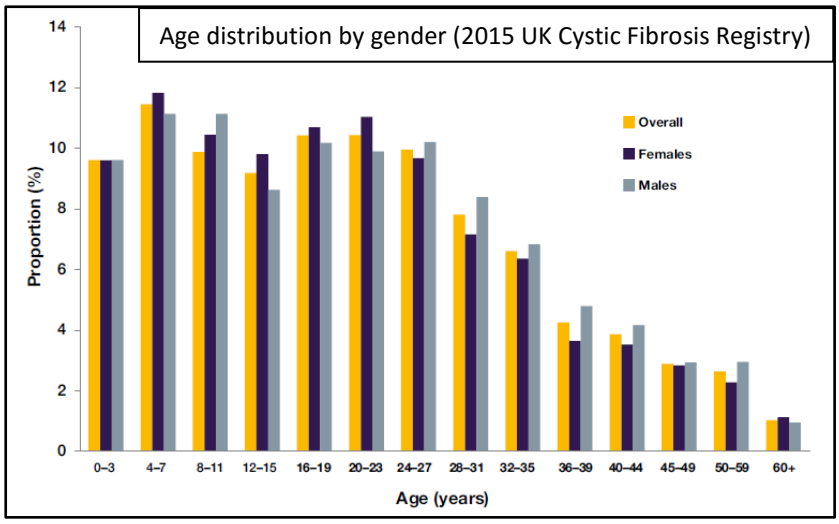
Prevalence and Epidemiology of Cystic Fibrosis

In the 2015 UK Cystic Fibrosis Registry it was documented that just over 10,800 people in the United Kingdom suffer from cystic fibrosis.

Summary of the 2015 UK Cystic Fibrosis Registry - https://www.cysticfibrosis.org.uk/the-work-we-do/uk-cf-registry/reporting-and-resources

	2011	2012	2013	2014	2015
CF patients registered[1] Excluding diagnoses that year	9749	10078 9804	10338 10076	10583 10356	10810 10586
CF patients with "complete" data; n(%)[2]	8679 (89%)	8794 (87%)	9052 (88%)	9432 (89%)	9587 (89%)
Age in years; median[3]	18	18	18	19	19
All newly diagnosed patients[4] (newborn screening and other)	261	285	301	291	224
Number of patients born identified by newborn screening[4]	203	213	177	164	112
Age at diagnosis in months; median[3]	3	3	3	2	2
Adults aged 16 yrs and over; %[3]	56.8	57.6	57.6	59.3	59.9
Males; %[3]	53.2	52.9	52.9	53.0	53.0
Genotyped; %[3]	95.6	96.2	97.2	97.7	98.1
Median predicted survival in years (95% Confidence interval)[5]	41.5 (35.7, 46.0)	43.5 (37.8, 49.9)	36.6 (34.4, 41.6)	40.1 (34.6, 46.7)	45.1 (39.9, 49.1)
Total deaths reported (%)[5]	118 (1.2%)	106 (1.1%)	146 (1.4%)	132 (1.2%)	125 (1.2%)
Age at death in years; median (95% CI)[3]	26	28 (25, 29)	29 (27, 31)	28 (25.5, 32)	28 (27, 33)

The number of CF patients registered seems to be increasing year on year. I believe that this could be caused by modern advances in treatment and care allowing more people than ever who suffer from cystic fibrosis to live for longer. This is explored in a study published in the European Respiratory Journal where it discusses how an increase in life expectancy will bring a large influx of adult-aged CF patients in health care systems across Europe. It predicts that the amount of CF patients living into adulthood is expected to increase approximately 75% by 2025. This observation is again confirmed when looking at the data for the median age. The table above shows a perhaps insignificant increase of one year between 2010 and 2015, however, on looking at earlier versions of the report it is clear that the median age is increasing gradually. It has increased from 16 in 2004 to 19 in 2015, confirming that more CF patients are now living into adulthood.



From the data in the UK Cystic Fibrosis Registry there are consistently slightly more male patients than female. I decided to investigate why this occurs and discovered that cystic fibrosis is equally as common in men and women. However, the severity of the symptoms that the individual experiences can vary in men and women. For example, young females who suffer from cystic fibrosis experience more problems meeting growth milestones and lung-related issues in comparison to young males. As a result of these more severe symptoms, females who suffer from cystic fibrosis have a greater chance of dying due to cystic fibrosis complications and so have shorter life expectancies than men. Therefore the prevalence of male adults with CF is greater than that of female CF adults – especially in adulthood.

The age at death in years seems to be fluctuating and remaining constant however on looking at earlier versions of the report it shows that people are dying at a later age. It has increased from 24 in 2007 to 28 in 2015 showing the positive impact that modern advances in treatments and medicine are having.

Summary of the 2010 UK Cystic Fibrosis Registry

	2004	2007	2008	2009	2010
CF patients registered	7046	8080[1]	8513[1]	9029[1]	9385[1]
CF patients with "complete" data; n(%)	5561 (79%)	4408[2] (55%)	6082[2] (71%)	7377[2] (82%)	7937[2] (85%)
Age in years; median	16	18[3]	18[3]	17[3]	17[3]
All newly diagnosed patients (newborn screening and other)	164	239[4]	235[4]	261[4]	301[4]
Newly diagnosed patients identified through newborn screening					189
Age at diagnosis in months; median	5	5[3]	4[3]	3[3]	3[3]
Adults aged 16 yrs and over; %	51.4	56.7[3]	56.2[3]	55.1[3]	55.5[3]
Males; %	53.4	53.9[3]	53.3[3]	53.1[3]	53.1[3]
Genotyped; %	95	92.6[3]	93.7[3]	94.3[3]	95.2[3]
Median predicted survival in years (95% Confidence interval)		35.2[5] (31.0, 42.6)	38.8[5] (34.2, 47.3)	34.4[5] (30.7, 37.0)	41.4[5] (36.8, 46.7)
Total deaths reported	123	106	100	141	103
Age at death in years; median	26	24	27	27	29

On looking at both the 2010 and 2015 CF registry, the median age at diagnosis has decreased from 5 months in 2004 to 2 months in 2015. This reflects the advances in newborn testing and diagnostic techniques, allowing the condition to be diagnosed at an earlier age. In the report, the Chief Executive of the Registry, Ed Owen, agrees with this observation and explains how the report "demonstrates the positive impact of national newborn screening for cystic fibrosis with more than 9 out of 10 five-year-olds with cystic fibrosis in 2015 having been diagnosed at birth."

The median predicted survival age in 2015 is 41.4, as opposed to 35.2 in 2007. This once again shows how modern treatments and medicines are proving more effective and having a real impact on the lives of people with cystic fibrosis. These new advances have also allowed people who suffer from cystic fibrosis to try and live as normal life as possible. The 2015 Registry shows that 71% of people over 16 with CF are in work or study, with nearly one third in full-time employment. This is a slight increase from 69.7% in 2010, again reflecting the effectiveness of better and more advanced treatments.

Treatment of Cystic Fibrosis

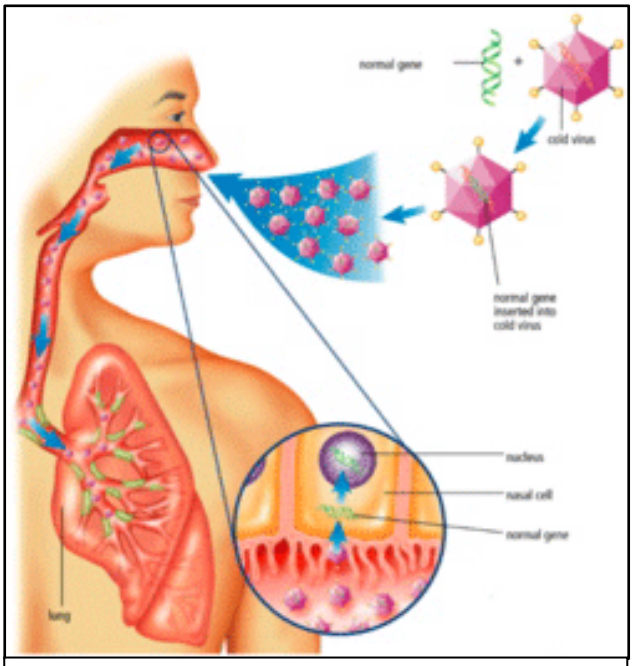
Unfortunately there is currently no cure for cystic fibrosis. However a range of treatments is available making it possible for people to control their symptoms, therefore preventing serious complications. Antibiotics, physiotherapy and in severe cases a lung transplant can all be used to help make the condition easier to live with.

Each person who suffers from cystic fibrosis has their own unique range of symptoms and hence treatments. For example, some people require enzymes with every meal to aid digestion whilst other people do not. This comes back down to the fact that the individual's genotype ultimately decides how much they will be affected by the condition.

Modern treatments and drugs allow many solutions to the problems that cystic fibrosis can cause. People who suffer from CF often require over 50 tablets a day, in addition to a couple of hours of physiotherapy at home together with some nebulised treatments. This allows people to manage their symptoms and get on with their lives, however, regularly taking numerous tablets and allowing time for treatments can be time consuming and have an effect on the patient's lifestyle, preventing some individuals from going into education or full-time employment.

Trials are currently underway to attempt to treat cystic fibrosis using gene therapy. This technique could be used to replace the faulty CFTR protein which is causing the condition with a healthy gene. This is done by transferring correct copies of the DNA involved in the CFTR protein into the epithelial cells that line the airways.

In order to deliver the correct gene to the patient's cells, a vector has to be used. This could be a virus or a liposome which contains the healthy gene. The vector is then introduced into the respiratory system of the patient through the use of an inhaler. If successful, the vector will then fuse with the epithelial cell membranes and the correct gene will travel to the nucleus of the cell becoming incorporated into its DNA. If this cell then undergoes cell division, the correct



http://genetics.thetech.org/sites/default/files/GeneTherapyCF.gif

CFTR protein will be produced, therefore alleviating the symptoms the patient experiences. However, repeated treatments will be required as the faulty CFTR gene causing the CF will still be present in future generations of epithelial cells. A further potential problem of this treatment is that the vector may cause side effects itself.

Results of a trial on 136 patients published in Lancet Respiratory Medicine in July 2015 showed that gene therapy had "stabilised and slightly improved cystic fibrosis" in some of the patients. These promising results came after the patients inhaled healthy copies of the CF causing gene once a month for a period of one year. The lungs of the patients showed, on average, no decline and the lungs most affected by the build-up of mucus showed a 3% improvement. This is opposed to a 3-4% decline in the lungs of patients who did not take the gene therapy over the same period.

Professor Eric Alton of Imperial College who led the trial said that "this is the first evidence worldwide which shows that if you give gene therapy to CF patients it has a protective effect".

Although the results of this trial look promising in improving the treatments available for patients with cystic fibrosis, Professor Alton also stated that "it is not ready to go straight into the clinic yet" and that "the effect…is variable". Future trials will be carried out by the scientists at the UK Cystic Fibrosis Gene Therapy consortium in order to try and build on the successes of this trial.

However, Professor Stuart Elborn from Queen's University, Belfast said that the results of these trials are "encouraging but the therapy had been no more effective than some of the drugs currently available." He suggested that perhaps the use of a larger dose or the combination of this treatment with other drugs would be more effective and that these should be tested in further small-scale clinical trials.

The Cystic Fibrosis Trust describe clinical trials as "the bedrock of translational research" and "are essential to establish the evidence base for clinical practice". The Trust is the UK's largest charity funder of research into cystic fibrosis and in the last year invested over £3 million into ground-breaking research – with plans to increase this to £3.5 million by the end of this financial year. This investment is essential to support the early-stage pilot studies of future treatments and helps to set the foundations for research in later-stage trials. All of this is crucial into the fight against cystic fibrosis.

Conclusion

Cystic fibrosis is described as the most common inherited condition amongst white populations. It is widely known as is part of the national biology curriculum both at GCSE and A Level. Despite there still being no cure for CF, there have been huge advances in recent times which is making the future discovery of a cure even more promising.

Data from the UK Cystic Fibrosis Registry shows the positive trend being set by advancing medicines and treatments. Life expectancy for CF patients has increased dramatically from under 10 years during the 1960s to around 45 years today. Even over the last decade it has increased from 35 to 45 years. In today's world, more and more CF patients are living into

adulthood, with nearly three-quarters of individuals over the age of 16 in work or study. Hopefully, this trend is set to continue allowing more and more people with the condition to be able to live with their symptoms.

The title of this work is “Health Care and Society” and I feel that cystic fibrosis is a perfect issue to write about. This year in the UK over 260 babies will be born with cystic fibrosis. This new generation will stand the best chance yet of having as ‘normal’ life as possible thanks to the ever changing and improving care for people suffering from the condition. Approximately 3 million healthy people within UK society are carriers of the gene for cystic fibrosis, most of whom are unaware of this. Cystic fibrosis also has an effect on society, with people now being able to effectively manage their symptoms they can play an active role in their community through study and employment. People who suffer from CF are now living longer and healthier lives enabling more than ever to attend university and be in employment.

Gene therapy is currently one of the most optimistic treatments being developed as it attacks cystic fibrosis at the core and has the potential to reduce the daily routine of drugs and treatments that CF patients have to go through every day. It also offers the potential of improvements to the long-term health of the patient, ultimately being able to change their lives. The results from the clinical trials show an encouraging start to this modern treatment and further research and trials may hold the key to finding a better treatment or perhaps bring us one step closer to curing cystic fibrosis once and for all.

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