WOLFRAM SYNDROME

A guide for individuals, families and carers

WOLFRAM SYNDROME UK

Inform, Support, CURE

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FOREWARD

Hello, my name is Tracy Lynch. I am the CEO and Co-founder, with my husband Paul, of Wolfram Syndrome UK. We started WSUK as a support group in 2010 following our daughter's diagnosis at the age of 8. Like many families we had looked it up online and came across some very medical sites but there was nothing or no one to support us apart from a worldwide support group; so WSUK was born. We became a charity in June 2013 so that we could fundraise in our own right, instead of via other charities, which gives us more of a say in how the money we raise is spent.

First I would like to assure you that receiving the diagnosis for Wolfram Syndrome (WS) does not mean the end of life as you know it. We have been through it, as have the families that have shared their stories in this information book. The diagnosis has made many of us that much stronger as we try to find a treatment with the help of many fantastic researchers around the World. It has also brought us many new friends, who are now like family.

Wherever you are in the world you can be assured that any member of the WS family is there to support you, whether by phone, Skype, email or Facebook.

Together we will *Inform, Support, CURE.*

Keep strong!

Tracy

WOLFRAM SYNDROME UK
Inform, Support, CURE

Introduction to Wolfram Syndrome

Wolfram Syndrome is a genetic disorder that can cause a set of conditions which includes Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness as well as several other conditions. It is a complex progressive neurodegenerative condition which is very rare. Every person affected is different and may only have 2 or 3 of the main features. Some do have all 4.

Why is it called Wolfram Syndrome?

A syndrome is the name given to a condition where features occur in a consistent pattern and where the cause is not understood. Wolfram Syndrome is named after a Dr Don Wolfram who saw 4 siblings from the same family with Diabetes Mellitus and Optic Atrophy in 1938 at the hospital he worked at in North America. Since then over 300 patients have been described in the world medical literature with WS. It is also sometimes referred to as DIDMOAD, which is an acronym for the main features associated with the syndrome (**D**iabetes **I**nsipidus, **D**iabetes **M**ellitus, **O**ptic **A**trophy, **D**eafness).

How common is it?

Wolfram Syndrome is very rare. It affects about 1 in 770,000 of the total UK population, or 1 in 500,000 children. There are currently about 120 people, adults and children, diagnosed with WS in the UK. A specialist doctor may only see one affected individual in their professional lifetime, many doctors will never come across it.

What causes Wolfram Syndrome?

It is an inherited genetic condition caused by a gene mutation. The gene that is usually affected is called WFS1 but other genes have also been identified. More information about the genetics of WS can be found further on in the booklet. (*The mutation in the genes affects the function of a protein called Wolframin. This protein is used in cells within the body including in the brain, pancreas, muscles, heart, liver and kidneys. The disruption in Wolframin is what causes the features associated with WS).*

The Wolfram gene was identified by the late Dr Alan Permutt from Washington University, St Louis, USA in 1998.

What are the chances of having another affected child?

The chances of parents having another child affected by Wolfram Syndrome are about 25%. WS is inherited as an autosomal recessive condition; this means that both parents carry one abnormal copy of the Wolfram gene, and one normal copy. For a child to be affected, they have to inherit both abnormal copies, one from each parent. It is possible to test if an unborn child is affected during pregnancy. (More information can be found on the Genetics page in this book).

What are the features of Wolfram Syndrome?

Wolfram Syndrome is very varied and presents differently in different people. The following is a list of the most common features:

Diabetes Mellitus

Most people with WS get Diabetes Mellitus, usually as a young child. This is when the body can't convert glucose (sugar) to energy, because the pancreas is not making enough of the hormone called Insulin. Glucose therefore stays in the blood or is passed out in urine which means that it isn't used up by the body. Symptoms of Diabetes Mellitus include thirst, frequent passing of urine and weight loss. This can normally be diagnosed from a blood test.

Diabetes Insipidus

Some people, but not everyone, with WS is affected with Diabetes Insipidus. This is when the body can not concentrate urine because the posterior pituitary gland in the brain is not making enough of a hormone called Vasopressin. Vasopressin usually regulates the amount of fluid in the body. Symptoms of Diabetes Insipidus often include being very thirsty and frequent passing of very dilute urine.

Optic Atrophy

Most people with WS will get Optic Atrophy. This is when the optic fibre nerves weaken causing vision to become disrupted. Symptoms often present as difficulty seeing in the classroom at school, colour blindness or everything "going grey". In WS the vision problems usually, but not always get worse and some people may be registered blind within about 8 years of the onset of eye problems.

Deafness

Some people, but not everyone, with WS will develop some degree of hearing loss. This can include difficulty hearing in a crowded room or space and difficulty hearing high pitched sounds.

Renal Problems

Renal problems can affect some people with WS. Renal problems include urinary tract disorders and may cause difficulties with controlling bladder function (incontinence) known as a Neurogenic Bladder.

Neurological Problems

Neurological problems may occur in some people affected with WS as the nervous system is damaged. These problems can include loss of balance, sudden jerks of the muscles, depression and breathing problems. Choking/swallowing problems may also occur in those affected, usually from the age of 20 onwards.

Diagnosing Wolfram Syndrome

As this condition is so rare not all doctors will be aware of it. Early diagnosis and the management of the conditions leads to better health outcomes for those affected and an improved quality of life. It is important that you share the information in this booklet with your doctor, so they know what information you have. The majority of the time you will be teaching the doctor. For further clinical information for you or your doctor, there is a clinical management guideline for WS which is available on the Euro-WABB website (www.euro-wabb.org) or a useful information pack which includes the guideline on the WSUK website (www.wolframsyndrome.co.uk/docs/infopack.pdf).

Most of the features will exhibit during childhood. Diabetes Mellitus occurs in almost everyone with WS during childhood. The latest onset is usually about 16 years old. Optic Atrophy also occurs on average at about 10 years of age and the latest onset is usually about 19 years old.

If both Diabetes Mellitus and Optic Atrophy are present by 15 years of age then an individual is likely to have Wolfram Syndrome. Your doctor can take a blood sample that can be genetically tested to confirm the diagnosis.

Managing Wolfram Syndrome

The current treatment involves treating the various conditions present separately:

- Diabetes Mellitus can be controlled with insulin injections or the use of an insulin pump. These replace the insulin in the body and allows glucose to be converted in to energy for the cells to use.
- Diabetes Insipidus can be treated by replacing the hormone Vasopressin in the body by using a nasal spray or tablets. This means the body can regulate it's fluids better.
- There is unfortunately no treatment yet for Optic Atrophy but research is being done for this.
- Deafness can be helped with the use of a hearing aid.
- Renal problems can be treated by tablets; or if severe, by passing a tube or catheter several times a day.
- Different Neurological disorders respond to different medicines.

Once a child has been diagnosed with WS, regular health appointments and assessments will be required. These assessments are to manage the presenting symptoms of the syndrome and also to test for the related symptoms that are known about so that they can be diagnosed and managed as early as possible.

For diabetes; diet and exercise advice will be given along with blood tests to look at the average blood glucose levels (HbA1c) over a few weeks and other treatments to manage any complications of diabetes.

Yearly tests for eyesight and "Audiometry" tests for hearing are recommended for those affected by WS to track the progress of Optic Atrophy and hearing loss.

Regular testing for any issues with the neurological system, kidneys and digestive system are also recommended. These will all be checked when you are invited to attend a Wolfram Multidisciplinary Clinic at either Birmingham Children's Hospital or The Queen Elizabeth Hospital (adult clinic) every 12-18 months but should also be checked

by your local doctor/hospital with your local routine appointments, to pick up any changes in between clinics.

Is there a cure for Wolfram Syndrome?

Unfortunately at the moment there is no cure. The current research that is taking place is to understand why mistakes in the Wolfram gene cause the syndrome. There are research groups in America, France, UK and Japan all investigating this problem. 2 drugs are currently being tested by researchers to identify if they can halt or slow down the progression of the syndrome, with hopes for clinical trials in the near future.

Clinicians and Teams within the Multi Disciplinary Clinics

Genetics-

My name is Denise Williams and I am a doctor specialising in genetic conditions. My role in the Wolfram syndrome clinics is to help individuals and their families by providing understandable information about the condition, explaining the way in which Wolfram syndrome is inherited and arranging genetic testing if this has not already been done. If appropriate I take the opportunity to discuss the risks to future children and / or other family members. The questions I am asked are very varied – I normally suggest you write them down before you attend the clinic as it is a long day and very busy, so

important things are easily forgotten. I hope to provide the information necessary to allow families to make informed medical and personal choices. The first time I meet a family I expect to spend about three quarters of an hour with them, but some people need more and some less. Subsequent appointments are usually shorter and sometimes I am not needed. I always think that people will want to 'dip in and out' of genetics services at different points of their lives. What's really important is that I offer to see the young people affected by Wolfram syndrome in their own right. Genetics is taught really well in school, most commonly in year 10 and year 11, so I like to start discussions at this time. The teenagers pick it up really easily and often ask me challenging questions!

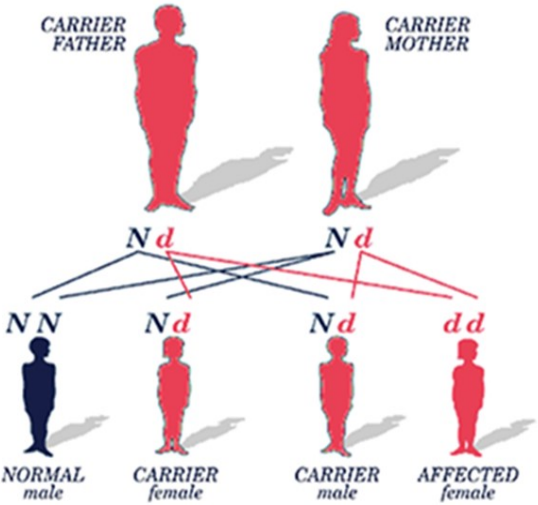
I work closely with the genetic counsellors, Shagufta Khan in the paediatric clinics at Birmingham Children's Hospital and Chris Platt in the adult clinics at the Queen Elizabeth Hospital in Birmingham. Both Shagufta and Chris have specialist training in genetics and counselling skills. Before your first appointment, either Shagufta or Chris will try to telephone you to obtain some basic information before you attend the clinic. They may ask about your family, so that a family tree can be drawn.

They may also ask your permission to obtain relevant medical information, including the results of any genetic investigations already carried out. Having this information ahead of the clinic allows us to make the best use of the time available in clinic.

Individuals and families attending the clinic have different knowledge, depending upon their previous experiences. I nearly always go 'back to basics' and discuss the way in which the condition is inherited assuming no previous knowledge. I feel more comfortable doing this as I know I haven't missed anything out and the concepts involved are quite complicated – many people find going over the same thing a second or third time is quite helpful. I use visual aids to help me; I have photographs of chromosomes and I draw diagrams illustrating the way in which genes are passed from the parents to their children. I also have some embossed charts to help me communicate effectively with individuals who have a severe visual impairment.

If I have been able to obtain the results of any genetics tests, then I will be able to discuss these in detail in clinic. If not then testing can

be initiated using a small sample of blood. Genetic tests are often complex and the results can take several weeks or months. We confirm the diagnosis of Wolfram syndrome when we are able to find 2 misprints, a bit like spelling mistakes, in the 'Wolfram syndrome' gene. This gene is known as WFS1. In the majority of families we have been able to confirm the diagnosis, but this is certainly not true for everyone. Like many rare conditions, Wolfram syndrome is not always straightforward so it is really important that everyone is assessed individually and regular evaluation and surveillance put in place according to that individual's needs. For example, we are starting to see some individuals with a few of the clinical problems we expect in Wolfram syndrome, but the pattern of these features is a bit different to those we recognise in the classic form of the condition. Some of these individuals have a 'misprint' in only one copy of their WFS1 gene and we say they have Wolfram syndrome-like disease. This seems to be very uncommon, but is important because it is inherited in a different way to the classic form of the condition. When this is important for a family I always discuss this carefully.



As mentioned already, part of my role in clinic is to discuss the 'risks' to other family members. From a practical point of view, finding the specific misprints responsible for causing the Wolfram syndrome in an individual means that we can use this information to test other family members who may be at risk of the condition or wish to know if they

are carriers. I normally suggest this is arranged with the advice and support of the local clinical genetics service and I am in a position to liaise with my colleagues around the country and facilitate this.

Although there is currently no cure for Wolfram syndrome and this may still be a long way off, Professor Barrett who leads the multidisciplinary team in Birmingham is working closely with research doctors across Europe and America. There is no doubt that a greater understanding about the different misprints in the gene and the different ways in which people are affected by the condition, may lead to novel treatments for different aspects of it in the future. This is something we are all hoping to discuss with you in time.

Dr Denise Williams.

Consultant Clinical Geneticist,

Birmingham Children's Hospital.

Neurological problems in Wolfram Syndrome

Wolfram Syndrome is a rare genetic condition which is characterised by insulin dependent diabetes mellitus, optic nerve atrophy and vision problems, diabetes insipidus and deafness. However neurological problems, apart from optic nerve atrophy and vision problems and deafness, can also occur.

On clinical neurological examination the most common other problems that are found are nystagmus (jittery eyes movements which may be very subtle) and difficulties with balance and as a result walking. Some individuals may also have impaired sensation/feeling in their hands and feet and this may also contribute to the balance problems.

Other problems which are sometimes seen are stiffness in the legs and feet and a tremor of the arms and hands. This tremor often becomes more pronounced when the individual is trying to do something a little fiddly.

The majority of people with Wolfram Syndrome do not have problems with cognition/learning. There is however an increase in risk of behavioural and psychological problems, which may include anxiety

and depression.

MRI brain scans are often normal in individuals with Wolfram Syndrome. However, in some people the brain size may be a little smaller and there may be some abnormalities seen in the brainstem (the lower part of the brain that becomes one with the spinal cord), the cerebellum (the balance centre of the brain) and/or the optic nerves and tracts (the nerves which carry information from our eyes to the part of the brain which analyses that information to make us "see").

As already noted Wolfram Syndrome is a rare condition and neurological problems, apart from optic nerve atrophy and vision problems and deafness, are often subtle or not always present. As yet we have not been able to identify why some people with the syndrome develop such problems and others do not. One aim of the Wolfram Syndrome Clinic is to regularly review individuals with the syndrome in order to learn more about their signs and symptoms and how these may progress. Such knowledge will then help us to better support individuals with Wolfram Syndrome and their families and hopefully help us to develop new treatments.

Professor Rajat Gupta

Consultant Paediatric Neurologist

Birmingham Children's Hospital

Visual Problems in Wolfram Syndrome

I am an eye doctor (ophthalmologist) with a particular interest in genetic eye diseases. I see patients with Wolfram syndrome in my specialist clinic at the Newcastle Eye Centre (Royal Victoria Infirmary) and at Moorfields Eye Hospital in London.

How is visual information sent from the eye to the brain?

The eye is a very sensitive camera that converts an image from the outside world into an electrical signal. At the back of the eye is the optic nerve, which is similar to a high-speed “broadband cable” that allows this electrical signal to be sent quickly to the vision centres at the back of the brain to be decoded. The figure above illustrates how visual information gets from the eye to the brain via the connecting optic nerve.

What is optic atrophy?

The majority of patients with Wolfram syndrome will develop optic atrophy. Optic atrophy means that the optic nerve has been damaged and it looks pale in colour when the eye doctor looks at the back of the eye with the appropriate equipment. Because the optic nerve is damaged, less visual information is sent from the eye to the brain, and this also happens more slowly with transmission errors. As a result, patients with Wolfram syndrome start to struggle with their central vision and they find it increasingly difficult to read small print and make out people’s faces (as in the example shown

below). Visual difficulties usually start in childhood and they tend to get progressively worse with time.

What other eye problems can you get in Wolfram syndrome?

1. Diabetes is very common in Wolfram syndrome, but fortunately diabetic eye complications tend to be rare. Nevertheless, patients with Wolfram syndrome need to take particular care that their blood sugar levels are well controlled to avoid further diabetic eye complications in addition to optic atrophy.

2. A small group of patients with Wolfram syndrome can develop cataracts at a young age. If the eye doctor spots that a cataract is present and vision is getting worse because of it, the option of cataract surgery can be discussed.

What treatments can we offer at the moment?

1. Depending on how severely their vision has been affected, patients with Wolfram syndrome can be offered the option of being registered as sight impaired (partially sighted) or severely sight impaired ("blind"). The eye doctor will carry out the assessment and complete the Certificate of Visual Impairment (CVI) if the inclusion criteria are met (http://www.rnib.org.uk/eye-health-registering-your-sight-loss/criteria-certification, accessed on 16 November 2015).

2. Unfortunately, there is currently no proven treatment to stop the damage to the optic nerve and loss of vision. There is a lot of research being carried out at the moment to look for drugs that can protect the optic nerve. Gene therapy is also being considered, but this strategy is still at an early stage of

development and so far, studies have only been carried out in mice .

3. As there are no effective treatments yet for the optic atrophy in Wolfram syndrome, visual and occupational rehabilitations are very important. An assessment in a Low Vision Assessment (LVA) clinic can be arranged and most eye departments will have an Eye Clinic Liaison Officer (ECLO) who can provide extremely useful practical advice to patients and their families.

Patients with Wolfram syndrome and their families must be very vigilant about various unproven "stem cells" treatments being offered on the internet.

How frequently should an eye check-up be carried out?

All patients with Wolfram syndrome should ideally have an annual check-up. Drops will usually be put in the eyes to dilate the pupils and make it easier to have a careful look at the back of the eye for any changes since the patient's last visit.

Mr Patrick Yu Wai Man

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Ophthalmologist

http://www.ncl.ac.uk/igm/staff/profile/patrick.yu-wai-man

http://www.moorfields.nhs.uk/consultant/patrick-yu-wai-man

What is Diabetes mellitus?

Diabetes Mellitus occurs when the cells in the pancreas (an organ in your body) that normally produces insulin are damaged. The pancreas produces less insulin than normal, or no insulin at all.

When we eat food containing carbohydrate (starch and sugar) it produces glucose, which is transferred from the stomach into the blood stream and then into the cells to provide energy and maintain normal blood glucose levels.

Insulin is responsible for this process and acts like a key. It opens the door to the cells in your body and allows the glucose to enter. The body's cells then convert the glucose into energy. Without insulin, more and more glucose will build up in the blood stream and your body will try to remove the glucose. This can lead to a chain of events including the following:

The body will try to get rid of the excess glucose by pushing it out in the urine– resulting in the need to go to the toilet more often

- Because more urine is being passed, there is increased thirst.
- Because your cells are not getting the energy they need, you will feel tired.
- Because your body still needs energy, it will start to break down fat stores, so there will be weight loss.
- If this continues for any length of time, there will be a build up of ketones, which are toxic to the body. This condition is called Diabetic Ketoacidosis or DKA.

Treating Diabetes mellitus

To maintain 'normal' blood glucose levels you need to do the job of your pancreas. This means injecting insulin several times a day/ or if on insulin pump therapy giving regular boluses, regularly monitoring your blood glucose levels, and making constant decisions about how much insulin to inject to keep your blood glucose as close to normal range as possible. One of the reasons to do this is to help you feel your best and give you more energy.

Blood glucose monitoring.

This is the best method of being in control of your diabetes, as it enables you to see how well your body is responding to your insulin, diet and activities, which in turn helps to keep you healthy and safe.

Susan Gleeson

Diabetes Nurse Specialist

Birmingham Children's Hospital

Diabetes Insipidus in Wolfram Syndrome

Wolfram Syndrome is a rare genetic condition which is characterised by insulin dependent diabetes mellitus, optic nerve atrophy and vision problems, diabetes insipidus and deafness. Diabetes insipidus means passing lots of urine that is not sweet, as it is not due to sugar problems.

In people without Wolfram syndrome, there is a gland in the brain called the Pituitary gland, which makes several hormones, one of which is Anti-diuretic hormone, or ADH. ADH travels round in the bloodstream to the kidneys, where it helps the kidneys to concentrate the urine.

About half of people with Wolfram syndrome will not make enough ADH, so that they are unable to concentrate the urine. Symptoms can be like sugar diabetes, with thirst, getting up at night to go to the toilet and passing lots of urine during the day. Sometimes this can make people feel extra tired.

There is a test that doctors do for diabetes insipidus – this is to ask for a urine sample first thing in the morning before having anything to eat or drink; and a blood sample also before any food or drink. These are used to check the concentrations of urine and blood. The urine should be concentrated first thing in the morning, and the blood a normal concentration. If the urine is very dilute and the blood is very concentrated, this suggests diabetes insipidus.

The treatment is to put back into the body, the hormone (ADH) that the body is not making enough of. This can be as a nasal spray, a tablet that dissolves under the tongue, or a tablet that you swallow. Most people manage very well with this medicine.

The medicine is sometimes called Desmopressin or DDAVP. There are not usually any side effects unless you take too much- in which case your body may retain too much water and you could get fluid overloaded. If you find you are not passing any urine, it is important to stop taking the tablets until you have had a good wee.

Your doctor will want to check your blood chemistry levels at least once every 6 months. It would be worth carrying a card with your

medicine written down on it in case you have to see a doctor.

Professor Tim Barrett

Consultant Paediatric Endocrinologist

Birmingham Children's Hospital

Family Stories

The Bennett Family

I live with my husband and two children, Naomi 22 and Jared 18 both who have Wolfram Syndrome. Naomi was unofficially diagnosed with WS when she was 6. She had started to have problems with her hearing when she was 4 and developed diabetes mellitus when she was 5 and it was her diabetes consultant who noted that it was unusual to have both and referred her to the eye clinic for an eye test. We felt confident that this would be OK and so were not worried. Unfortunately, they discovered that her optic nerve was unusually pale and when pressed said that it could relate to a condition called DIDMOAD syndrome. Despite our best efforts, no one was able to enlighten us further which added to our anxiety. We resorted to the only other course of action we felt we had – the internet. It proved very difficult initially but my husband persevered and eventually made the connection to WS, the other name for DIDMOAD.

Nothing prepared us for the devastating prognosis of the condition - we felt completely numb and it all seemed completely hopeless – my initial reaction was to take my daughter out of school and wrap her up in cotton wool. Our next thought was what to tell her – she was only 6 after all. We had no one to turn to. When my husband sent a copy of the internet information to my daughter's diabetes consultant, he said he had no idea. We didn't tell anyone because we didn't want them to let anything slip in front of our daughter. We didn't even tell her what the condition was called for fear of her looking it up on the internet at a later date as we had done. This may seem silly but we put WS from our minds, a form of self protection I guess, and simply focused on the individual parts of WS and supported her as best we could.

As implausible as it may seem, we pushed WS from our minds and

tried to carry on as usual. As time went on, Naomi's eyesight got worse and she was registered blind. Despite all this, she never asked questions. When she was 16 she was diagnosed with diabetes insipidus. When Jared was 6 he was diagnosed with diabetes mellitus and he too underwent hearing and eye tests and it became apparent that he also had WS. Initially, he too did not ask any questions but as time progressed he began to ask about the implications of the disease.

It was during a regular appointment at the audiology clinic that the audiologist there said she could put us in touch with a consultant paediatrician who may be able to support us in light of the diagnosis. She was so lovely and understanding and although she did not know too much about WS, she went out of her way to research it and it was through her that we were put in touch with Professor Barrett at the Birmingham Children's Hospital. It was only through meeting him that we were able to view WS in a more positive light. We went to visit him to discuss the prognosis and to ask his advice about explaining the condition to our children. He was so kind and reassuring that we felt that a huge weight had been lifted from our shoulders.

We felt that we could be much more open with our children but that we didn't have to focus on the negatives and to realise that the websites we had accessed on the internet were unregulated and gave the worst case scenario rather than focus on some of the more positive and encouraging cases.

I have always felt guilty that as each diagnosis was given, I cried and I felt bad because my children were present. They never mentioned it or asked me about it and even when we arranged counselling, neither child mentioned their condition at all as a source for their anxiety. It was only recently that Jared told me that he hadn't asked me because he was afraid to hear the answer. It made me realise that I should have explained at the time why I was upset rather than have my children worrying and believing the worst. It also made me realise how important it was to have the advice and support of an expert, Professor Barrett, who was well versed in the condition. Had we had this support earlier, we would have felt better prepared to deal with our own feelings and therefore be better able to support our children.

What do I wish I had known at the time of diagnosis? Several things.

I wish I had known how resilient our children are and that I should not have underestimated them. Their positive approach to WS and determination to not let it get in the way of their ambitions is an example to us all. They are truly amazing and inspirational young people (as all the people we have met with WS are).

I wish we had known about Professor Barrett and his amazing team at the time of diagnosis so that we could have shared our fears and received his invaluable support and guidance which would have saved us so much anguish.

What do we wish had been different? That the medical team supporting our children had been more knowledgeable about WS and to have properly counselled us about the condition.

And now? There is light at the end of the tunnel – research is underway and we all feel very hopeful for the future. We now have the support of Wolfram Syndrome UK and a way of linking up with other families to share experiences and provide mutual support. The annual conference keeps us informed of advances in medical science and it has also enabled Naomi and Jared to link up with other young people. There has also been so much work done to raise awareness amongst the medical profession across the UK, that I truly believe that our negative experiences will become a thing of the past and that newly diagnosed families will be given much better support and informed advice in future.

The Bassett's

My name is Stephen Bassett. I live in Leeds with my wife Kelly and guide dog Klint. I was diagnosed with Wolfram Syndrome when I was 16 years old by word of mouth, as I had all the characteristics of it. I was not formally diagnosed until I was 32. This was only because we wanted to know if our children, if we decided to have any, would be affected by it. We were told there is only a 1 in 700 chance of a child of ours being affected.

I would have liked to have known back then that I am not on my own living with Wolfram Syndrome, also not to have read internet pages as they tell you that life expectancy is 30 – 40 years old which makes you sad; I am now 34 years old!!!! Also I would have liked to have known that there were specialist teams at Birmingham Children's

Hospital and The Queen Elizabeth Hospital, Birmingham as I have never seen any specialist that has good knowledge of it. I always thought when I got another illness that they weren't related.

I am coping well with the syndrome; I have good days and bad days. Unfortunately it has affected my working life. After 17 years at Morrison's Supermarket I have become unable to do my job due to my failing health.

This syndrome should not stop you from living your life and being happy. Something else also is that you are not on your own. Wolfram Syndrome UK has loads of members and the only reason I know what I know today is from them. I have made loads of friends and for that I am eternally grateful; I am not on my own anymore and I feel so happy.

The Lynch Family

Jennifer seemed to be a normal toddler just like her older brothers although rather shy, even around family members. She had suffered with coughing attacks which was put down to possible Asthma, as her dad Paul suffers with it & was having some toileting accidents which they said was childhood constipation. At the age of 5 we took her to the optician where she was diagnosed with Rotational Nystagmus and being longsighted. This explained her 'shyness'. They referred her to the local eye hospital to investigate the cause of the Nystagmus. Tests and an MRI were done with no obvious diagnosis, so she was referred up to Great Ormond Street (GOSH); so started our 3 years of visiting there. Another MRI was carried out as well as an ERG (electroretinograph). This diagnosed her Optic Atrophy as well as an

issue on the brain so we were then referred to see Neurology. Whilst waiting for this appointment she was discharged by the local Paediatrician for the coughing attacks even though they were still happening and was diagnosed with diabetes, at the age of 6, which we had caught early through some concerns I had.

We met the Neurology Consultant who was very nice and explained all of her problems to him. He then requested a Lumbar puncture be done along with about 20 blood tests, the Endocrine Consultant also requested a load of blood tests be done, one of which was for WSF1. I looked this up on the internet and wished I hadn't. In the end the endocrine tests weren't done as she was newly diagnosed with diabetes but under control. We could have found out she had WS then, but had to wait another 23 months before she was diagnosed.

Tests were also being carried out for the coughing attacks and bladder issues which hadn't settled down since everything started. The childhood constipation was sorted as soon as the diabetes was diagnosed, it was her system reacting to the sugar, which we are aware for now if she has a long period of hypos. More tests, visits to GOSH and a skin and muscle biopsy followed. In March 2010, at the age of 8, we were asked to attend GOSH to see 2 of her consultants and were given the news that Jennifer had Wolfram Syndrome. One of the consultants had tried to find out more about it but had only been able to find the worldwide WS support group and a page of information about Professor Barrett.

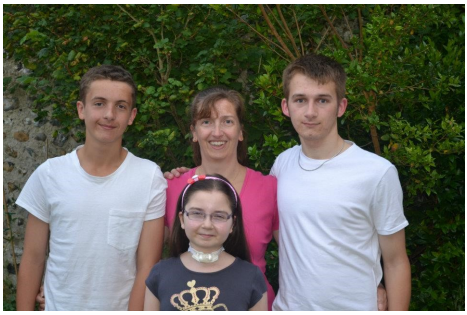
Like everyone we went straight onto the internet to find out what help and support there was, which was pretty much zilch. This was when we decided that we would start up the UK support group. We contacted Prof Barrett to ask for his help and support with this, which he was very willing to do. Before the website went live we asked him to check over the information on the site to ensure that it was all correct. Through the website we have met and come into contact with many amazing people both affected by WS as well as those helping to treat and research the condition.

This then helped us, when in 2012 Jennifer had a 2nd severe choking attack which put her into intensive care (PICU) and on a ventilator up in London and away from home and family. All our WS family were sending messages of support during those difficult days.

The staff tried taking her off the ventilator 3 times during the first 2 weeks but each time failed, the longest time off was 36 hours. The only way to get her off the ventilator was with a ‘temporary’ tracheostomy, which Jennifer adapted to really well and very quickly. A further 2 weeks were spent on PICU, 1 week on a general ward and then we were transferred back to our local hospital where she spent a further 4 weeks before being allowed home permanently.

Life is carrying on as normal, with Jennifer attending mainstream school, regular check ups with her individual consultants, the WS Clinic and all our charity work for WSUK. Life did change for the whole family when Jennifer was diagnosed with Type 1 Diabetes, we ‘grieved’ in a way for the life that we had lost. We could no longer decide to go somewhere spontaneously. We had to plan around her insulin injections, meals and snack times. With the diagnosis of WS this feeling of grief was slightly more intensified, but we feel that so long as we can keep her healthy and control her diabetes well there is no reason for her not to have a long and healthy life. The trachy does make life rather more restrictive now as we have so much more that we have to carry around with us when we go out and there are only a few of us that are trained for her care needs in an emergency, but we have her here with us and we are hopeful that the trachy may come out soon. We don’t know of anyone else with WS that has a trachy, so this isn’t a normal part of the syndrome. Her courage and strength have earned her 2 bravery awards

My motto to everyone is ’Even in the darkest times, stay positive. Keep strong and healthy. The WS family will always be there to support you when you need them.’



Amy Hawkins

I had to go into hospital for lots of tests before I found out that I had Wolfram Syndrome, which was when I was 16. I went through a time where I shut down because I did not see the point to try anything as I thought I was the only one who had this illness, so I felt on my own and alone. I could not think about the future as I did not think that I would have one. My education suffered as I was not concentrating on school at all and my GCSES were affected. I went to college though where I was supported and given extra time when sitting exams and the exam papers were enlarged to a format that I could read.

Living with WS is difficult because you cannot be as independent as you would like to be, and asking for help all the time is frustrating. I did not have many friends as I would not talk to anyone because I felt different. My mum and dad helped me to start socialising more with the church so I started going out with them and taking part in the youth club that they hold every three Fridays of the month.

I have been in contact with the WS charity and clinic. The Wolfram Syndrome charity has helped me so much as now I have a plan for my life and I know what I am able to do. I am able to speak to others who have this illness and am able to speak about my problems as well as theirs. We help each other to come up with ideas about fundraising and we bounce ideas off each other. We talk about the illness and we do not have to worry about what we say as everyone knows and understands. No one has to keep anything to themselves and can relate to one another. We also chat about subjects that are not to do with the illness, as talking about it all the time gets us down. We have a laugh and we talk normally about shopping and favourite comedians that are out and things that they have said.

Meeting up with these people helps me as I can meet someone face to face who understands completely. My mum and dad have been a great help whilst I have been going through this. They have taken me to places where I need to be and have supported me

when I go through bad stages. They are always there when I need to talk to someone.

Rachel Bates – WellChild WS Family Co-Ordinator

I am the WellChild Wolfram Syndrome Family Co-ordinator, and I support families with children and young people with Wolfram Syndrome. I help families attend the Specialist Wolfram clinics at Birmingham Children's Hospital by making sure they have all the information they need before coming and I also help with logistical arrangements such as transport to the clinic and accommodation. It is my job to make sure the families have all they need to ensure their visit is as stress free and pleasant as possible. When a new family is referred to the clinic I will visit them at home, to find out more about them and see how we can support them, and to answer any questions they may have about the clinic. I also attend every clinic to support the families over the two days.

Listening to families is at the heart of what WellChild does, and an important part of the Family Co-ordinator role is to connect with families and feedback their experience and opinions of the children's clinics to the team at the Birmingham Children's Hospital, to make sure the service is right for families.

Outside the clinic, I act as an advocate for families, helping them get the support and help they're entitled to; whether that be the right support for their child at school, or that they're getting all the benefits that they should be.

I also help organise the Wolfram Syndrome Annual conference.

For more information about the conference, clinics or just to find out how I can help you, please contact me on:

Tel: 01242 548762

Email: rachelbates@wellchild.org.uk

Web: www.wellchild.org.uk/families-area

Further Information

For further information on Wolfram Syndrome please see:

Wolfram Syndrome UK (www.wolframsyndrome.co.uk)

This website/charity is run by families affected by this rare genetic disorder and the aim is to raise as much awareness as possible, funding for research and to support those affected.

Wolfram Syndrome Organisation (www.wolframsyndrome.org)

This website provides more information on WS. Patients and their families can register and contact families all over the world.

WellChild WS Family Co-Ordinator (www.wellchild.org.uk/families-area/wolfram-families)

The WellChild WS family co-ordinator provides emotional, information and advocacy support to families with children affected by WS

Association Syndrome de Wolfram (www.association-du-syndrome-de-wolfram.org) Website for French Wolfram Association providing information and support for families.

Gene Reviews (www.ncbi.nlm.nih.gov/books/NBK4144/)

This article on Gene reviews provides a good review of Wolfram Syndrome.

Orphanet (www.orpha.net)

Orphanet is an online database of rare diseases and related services provided throughout Europe. It contains information on

over 5000 conditions and lists specialised clinics, diagnostic tests, patient organisations, research projects and clinical trials.

Euro-WABB (www.euro-wabb.org)

The Euro-WABB Project is a collaboration of doctors, scientists and patient support groups from all over Europe. This website provides information on Wolfram Syndrome and other rare genetic forms of diabetes.

Here is information about some useful organisations that may be handy too:

ABELIZE (http://www.ableize.com/)

ABLEize is the biggest UK disability resource directory offering the largest collection of disability, mobility and health resources in the UK and Europe.

ACTION FOR BLIND PEOPLE (https://www.actionforblindpeople.org.uk/welcome-to-the-action-for-blind-people-website/)

Action for Blind People is a national charity with local reach, providing practical help and support to blind and partially sighted people of all ages.

ACTION FOR BLIND CHILDREN, YOUNG PEOPLE AND FAMILIES
(8-17years)
Various organised activities
Tel: 0303 123 999
Email: sarah.Winch@actionforblindpeople.org.uk
www.actionforblindpeople.org.uk

ACTION ON HEARING LOSS (www.actiononhearingloss.org.uk)

UK charity for people who are deaf or have a hearing loss.

BLIND CHILDREN UK (http://www.blindchildrenuk.org/)

Formerly known as National Blind Children's Society's mission is to enable children and young people who are blind or partially sighted

to achieve their educational and recreational goals.

Tel: 0800 781 1444. email: services@blindchildrenuk.org

CONTACT A FAMILY (http://www.cafamily.org.uk)

Contact a Family is the only national charity that exists to support the families of disabled children whatever their condition or disability.

DIABETES UK (www.diabetes.org.uk)

Diabetes UK is the leading charity that cares for; connects with and campaigns on behalf of every person affected by or at risk of diabetes. We help people manage their diabetes effectively by providing information, advice and support.

FACE2FACE NETWORK (http://www.scope.org.uk) (www.face2facenetwork.org.uk)

Are all about changing society for the better, so that disabled people and their families can have the same opportunities as everyone else.

FAMILY FUND (http://www.familyfund.org.uk)

Are the UK's largest provider of grants to low-income families raising disabled and seriously ill children and young people. We help ease the additional pressures families face.

HOME FROM HOME CARE
Created by parents to make the difference
Tel: 01749 676924
Email: admin@homefronhomecare.com
www.createdbyparents.com

GUIDE DOGS FOR THE BLIND (www.guidedogs.org.uk)

Provide mobility and freedom to blind and partially sighted people. We also campaign for the rights of people with visual impairment, educate the public about eye care and fund eye disease research.

LOOK (www.look-uk.org)

Provides support, information and activities for families with visually impaired children and young people.

National Deaf Children's Society (www.ndcs.org.uk)

A national charity dedicated to creating a world without barriers for deaf children and young people.

National Parent Partnership Network (www.parentpartnership.org.uk)

PPS offer free, confidential advice, information and support to parents and carers about special educational needs.

RNIB (www.rnib.org.uk)

Royal National Institute of Blind People (RNIB) is the leading charity offering information, support and advice to almost two million people with sight loss.

SENSE (http://www.sense.org.uk/)

Sense is a national charity that supports and campaigns for children and adults who are deafblind.

Sibs (www.sibs.org.uk)

Sibs is the only UK charity representing the needs of siblings of disabled people.

SOS-SEN! (admin@sossen.org.uk)

SOS!SEN is a national charity aiming to empower parents and carers of children with SEN to tackle successfully themselves the difficulties they face when battling for their children's rights.

TURN2US (http://www.turn2us.org.uk/default.aspx)

Turn2us is a charity that helps people in financial need to access welfare benefits, charitable grants and other financial help.

VICTA (www.victa.org.uk)

Provides support, information, activities, breaks and holidays for families with blind or visually impaired children or young people.

EDUCATION

www.Load2learn.org.uk from RNIB provide educational material
Books on loan: picture, tactile, Braille books.
ClearVision: preschool onwards
Tel: 020 8789 9575
www.clearvisionproject.org
info@clearvisionproject.org

National Library Service
RNIB
Tel: 01733 375351

WESC Foundation, Exeter
The specialist centre for visually impaired Ages 5-25 years
Tel: 01392 454200
Email: info@wescfoundation.ac.uk

Scholarships:

http://www.afb.org/info/other-scholarships-and-grants-for-students-blind-or-visually-impaired/5

http://www.open.edu/openlearn/about-openlearn/try

Preschool

Books on loan: picture, tactile, Braille books
ClearVision
Tel: 020 8789 9575
www.clearvisionproject.org
info@clearvisionproject.org

Through Scarlett's eyes: online support for parents and families of visually impaired children 0-5 years
www.throughscarlettseyes.com

Primary School

Books on loan: for keystage1 and 2
www.rnib.org.uk/education

Keystage online for primary school maths and English work and online preparation for 11 plus exam
http://www.ksol.co.uk/contents/Free11Downloads.aspx

Secondary School

Books on loan: for keystage3
www.rnib.org.uk/education

New College Worcester, Worcester
Residential school and college for 11-19 year olds: supporting children and families prepare for exams, university and university applications.
Tel: 01905 763933
Email: info@newcollegeworcester.co.uk
www.ncw.co.uk

rnib.org.uk/startingcollege
rnib.org.uk/startinguniversity
rnib.org.uk/leavinghome

Queens Alexandra College, Birmingham for ages 16-25 years
Tel; 0121 4285041
www.qac.ac.uk/enterprises

The Royal National College for the Blind, Hereford
Supporting education, employment and empowerment
Tel: 01432 376621
Email: info@rnc.ac.uk www.rnc.ac.uk/ican

ASSISTIVE TECHNOLOGY

RNIB
Tel: 0303 1239999
onlinetoday@rnib.org.uk
www.rnib.org.uk/onlinetoday

RNIB support for one-to-one help with phone technology

1.DaVinci PebbleHD OCR: all in one HD Video magnifier with Text-to –Speech: www.enhancedvision.co.uk

2. Claria Zoom: all-in-one android application: www.claria-zoom.com

Cobalt speechmaster

SINDHI systems : www.sindhisystems.co.uk

3. Optelec low vision aids

4. Synaptic software
Tel: 0845 5760576 email: sales@synapptic.com
www.synapptic.comtware

SPORT AND LEISURE

BLIND CRICKET IN ENGLAND & WALES (www.bcew.co.uk)

The BCEW have been working in partnership with British Blind Sport and the England and Wales Cricket Board since 2006 to deliver competitive cricket for those who are blind or partially sighted running national and international competitions.

BRITISH BLIND SPORT (http://www.britishblindsport.org.uk/)

British Blind Sport (BBS) is a national registered charity based in Leamington Spa. Since its beginnings as a registered charity in 1976, British Blind Sport has become the leading voice for visually impaired people (VI) in the world of sport and leisure, both at home and internationally.

ENGLISH FEDERATION OF DISABILITY SPORT
(www.efds.co.uk/)

The English Federation of Disability Sport (EFDS) was established in September 1998. EFDS is a national charity, dedicated to disabled people in sport and physical activity. We support a wide range of organisations to include disabled people more effectively.

GOALBALL UK
Tel: 0114 2235670
enquiries@goalballuk.com
www.facebook.com/goalballUK

SPORT ENGLAND (www.sportengland.org/our-work/disability/)

Sport England is committed to helping people and communities across the country create sporting habits for life. They know that disabled people are less likely to take part in sport with only one in six playing sport regularly compared to one in three non-disabled people. Their work will seek to challenge and change this to enable disabled people to view taking part in sport as a viable lifestyle choice.

Performing Arts
Exant: performing arts for visually impaired
Tel: 020 78203737 www.exant.org.uk

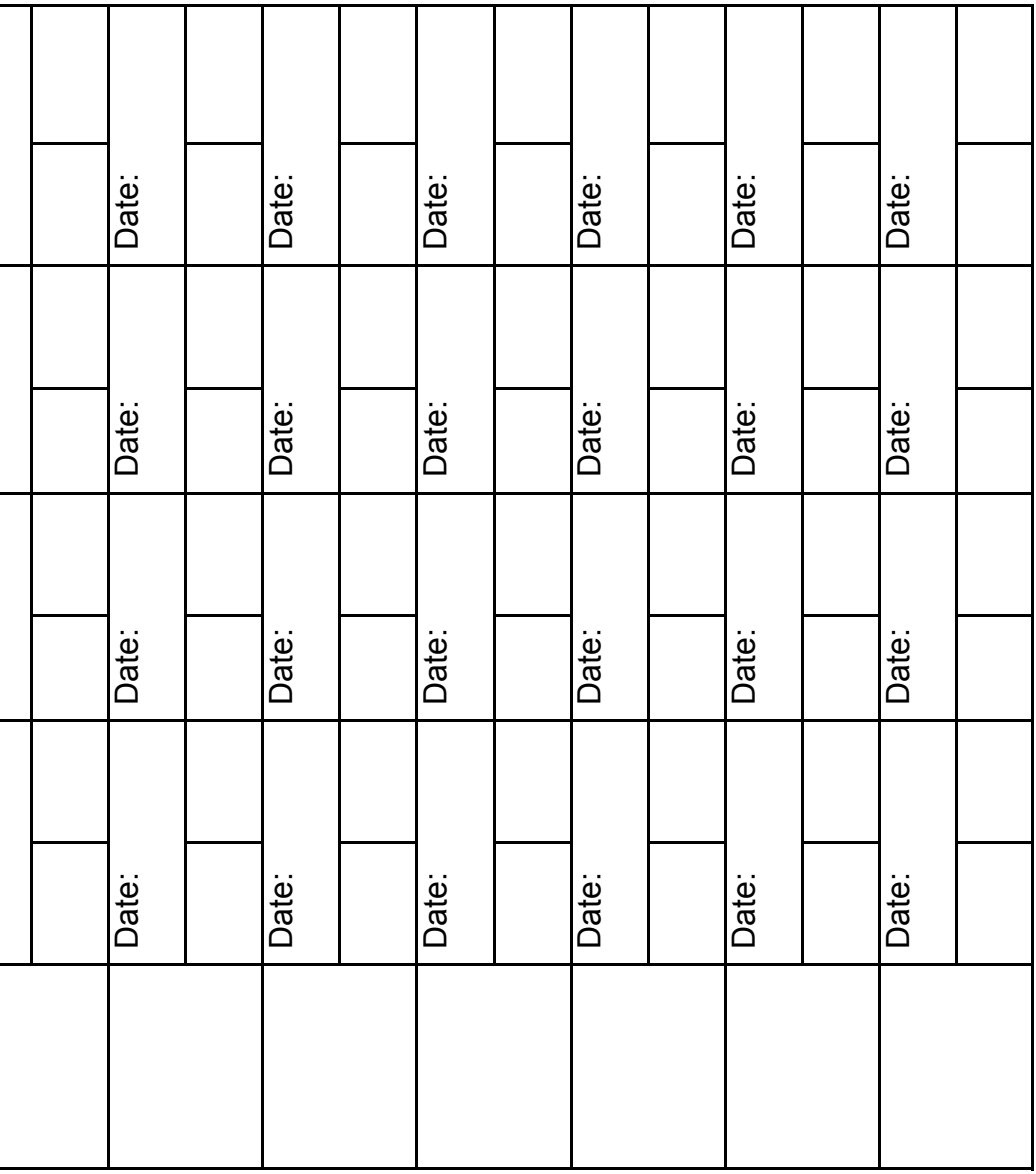
Medicines

You/ your child may be taking a variety of different medicines; you may

Name of medicine	Date started		Date changed		Date changed		Date changed	
	Dose	How often	Dose	How often	Dose	How often	Dose	How often
EXAM-PLE Thyroxine	Date: **3.2.12**		Date: **17.9.12**		Date: **21.3.13**		Date:	
	50 mcgs	**Once daily**	**75 mcgs**	**Once daily**	**100 mcgs**	**Once daily**		
	Date:		Date:		Date:		Date:	
	Date:		Date:		Date:		Date:	
	Date:		Date:		Date:		Date:	
	Date:		Date:		Date:		Date:	

OD – once daily. BD –twice daily. TDS- three times daily. QDS – Four

find it helpful to keep a record of the different medicines and the doses.



times daily. Nocte- at night

Appointments

The space below can be used to help you keep track of your hospital appointments.

Who you are seeing_____

Hospital/location_____

Date/Time_____

Who you are seeing_____

Hospital/location_____

Date/Time_____

Who you are seeing_____

Hospital/location_____

Date/Time_____

Who you are seeing_____

Hospital/location_____

Date/Time_____

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Hospital/location_____

Date/Time_____

Who you are seeing_____

Hospital/location_____

Date/Time_____

Who you are seeing_____

Hospital/location_____

Date/Time_____

Results record:

Test	NORMAL RANGE	DATE AND RESULT	DATE AND RESULT
HEIGHT/cm	N/A		
WEIGHT/kg	N/A		
BODY MASS INDEX kg/m²	N/A		
BLOOD PRESSURE/ mmHg	N/A		
URINARY MICROALBUMIN	2.5mg/mmol or less		
HbA1c	3.5-6.5		
FASTING GLUCOSE	3.9-5.2		
FREE THYROXINE	<5y 10.7-21.8 12-18y 9.8-19.2		
THYROID STIMULATING HORMONE	**Male**: **15d-10y** 0.2-4.0 **10-13y** 0.5-7.0 **>13y** 1.0-11.0 **Female**: **15d-10y** 0.2-6.0 **Other ranges as above**		

Blood osmolality mOsmol/L	275-295		
Sodium mmol/L	133-146		
Potassium mmol/L	3.5-5.0		
Lutenising hormone IU/L	10-12y 0.3-5.0 >12y 0.5-8.0		
Creatinine Micromole/L	Male **<6y** 18-46 **<11y** 18-51 **<15y** 37-60 **>15y** 37-80 Female **<6y** 18-46 **<11** 18-51 **<15y** 32 -55 **>15y** 37-70		
Urea Mmol/L	<5y 1.7-6.7 **>5y** 2.5-7.5		

Reference ranges taken from Pan Pathology website BCH (Accessed 07/14)

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WOLFRAM SYNDROME UK

Inform, Support, CURE

www.wolframsyndrome.co.uk