Wilson's
Wilson's Disease Support Group – UK

NEWSLETTER

APRIL 2018

The Wilson's Disease Support Group - UK (**WDSG-UK**) is an all volunteer organisation which strives to promote the wellbeing of patients with Wilson's disease.

It publishes an annual newsletter with informative articles written by medical professionals, and also articles written by patients, their families and friends about their experiences of the disease.

It promotes networking of Wilson's disease patients and their families by helping and encouraging contact with one another.

And the Group strives to promote a wider awareness of Wilson's disease within the medical profession.

AFFILIATED TO :

BRITISH LIVER TRUST

LPTC The Liver Patients' Transplant Consortium

GENETIC ALLIANCE UK

RARE DISEASE UK

Children's Liver Disease Foundation fighting childhood liver disease

Climb Children Living with Inherited Metabolic Diseases

Hello everybody and welcome to another edition of the newsletter. I am so grateful to all those who contribute and should like to start by thanking the following people in particular. First of all, thank you to **Dr Sam Shribman** and **Mary Bythell,** who have not only written articles for the newsletter but have also agreed to speak to us at the meeting in the summer! Next I should like to thank **Dr Alan Stevens** for being cajoled into writing yet another excellent medical article, and **Dr Oliver Tavabie** for kindly agreeing to give a medical perspective on one of our more upsetting patient stories written by **Stacy**. Stacy has been honest and open in providing her story and I wish her all the best for the future and hope that her struggle will serve as a warning to other non-compliant young patients. On a happier note, I should like to thank **Stephen, Ellie, Anusha** and her mum, **Hilda,** for also sharing their patient journeys with us. For those of you who haven't yet written your stories, I hope it's just a matter of time!

Photo: Courtesy Anusha Joseph

As always, we owe a huge debt to our fundraisers who this year include **Angharad, Grace, Samantha, Andy** and **Giuseppe.** In addition, we are grateful to **Rushden & Diamonds Youth Football Club** who nominated WDSG-UK to benefit from their charity fundraising events and to all their players and supporters who have raised so much money for us. Currently, **Ann-Marie** is getting in training for her upcoming *Colour Run* and should you wish to support us through her, please follow the details on the notice board at the back of the newsletter. We are always interested in the innovative ways you find of raising money for the Group and look forward to hearing of any forthcoming ventures. Sadly, we lost one of our most prolific fundraisers last summer, when **Sylvia Penny** died unexpectedly at the age of 87. She will be sadly missed.

The Facebook Group continues to thrive and amongst our **750** members we have a new member, ***Cupri,*** a biochemist with a special interest in Wilson's. Every Wednesday she posts a short YouTube clip on some aspect of the disease, which is well worth following. I, also, communicate with patients via Facebook, as well as e-mailing, talking to and visiting them when I can. Recently, I received an invitation to attend the premiere of a short musical called ***Brothers***, written by Arnoud Breitbarth and based on a book by a Dutch author, Ted van Lieshout. It was all about Ted growing up with a brother who becomes progressively ill, finally dying in a mental hospital from undiagnosed Wilson's disease. It was so reminiscent of my own childhood, that I was jolly glad I'd remembered to take my handkerchief! By contrast, in June this year, **I** will be both glad **and** grateful to **Dr John Walshe** to be celebrating **50** years of successful treatment with *penicillamine*.

The following month, on **Sunday 15 July**, you are all warmly invited to our annual meeting in **Cambridge**. Booking forms and agendas are enclosed with the newsletter. There will be the usual raffle and **Belinda** and Samantha have kindly offered to run stalls to raise funds for the Group. If the day is half as good as last year's, then it would be a great shame to miss it!

Meanwhile, please remember to renew your subscriptions promptly. You will see that I have enclosed another *Dingbats* quiz, this year on the theme of London stations. I hope it provides you with a little light entertainment as well as proving a money spinner for the Group. I wish you all a very happy spring and an even happier summer to follow.

Valerie

IN THIS ISSUE ...

Chairman's Report for 2017-18

In my new role as chairman of the WDSG-UK, I am pleased to report that it has been another busy and exciting year for us. As patient representatives, the committee continues their existing links with Genetic Alliance and Rare Disease UK, and with the NHSBT Organ Donation & Transplantation Directorate and the Liver Patients' Group. It has also recently become involved in new initiatives led by the British Association for the Study of the Liver and Public Health England, which have the potential to develop new methods of treating patients as well as supporting our current objectives to improve healthcare for them. The coming year is likely to be as busy, and we thank you and our medical advisers, **Drs Godfrey Gillett** and **James Dooley**, for your continued support. On a personal note I would also like to thank **Rupert Purchase** our past Chairman for his counsel and support over the past year, which has been invaluable. Below I highlight some of the more important activities that have taken place this past year.

Donations and Fundraising

I would like to take the opportunity to thank all members for your continued support. WDSG-UK does not receive any formal sponsorship and appreciates all donations by members and their associates. We also appreciate the extraordinary efforts and imagination of those who raise funds for us, which this year have amounted to over **£2,600**. In particular, I would like to thank **Samantha Panchal** who raised **£454** through the innovative and very successful sale of *WDSG-UK* wristbands, and **Sam Fitzgerald's** former Football Club, *Rushden& Diamonds,* who raised **£1000** from events that they organised throughout the 2016-17 football season. **Grace Carter** generated **£110** from a produce sale and her friend, **Angharad Morgan,** ran a half marathon and raised **£300**. For further details of these events please see *pp6-7*. My thanks also go to **Valerie** for organising another successful Dingbats competition with the newsletter last year which raised over **£350**.

Finally, WDSG-UK was approached by two members who wanted to take advantage of their workplace *Charity Matching* programmes by nominating us as beneficiaries. We thank **Andy** and **Charlotte Forster** for completing a sponsored walk along the Thames-Footpath and raising **£250** for us and Andy's employers, ***Price Waterhouse Cooper,*** who matched this sum with a donation of **£250.** Later, **Giuseppe Cardone,** a Facebook member who works in London, approached us and through the *google.org.giving* programme, he and a couple of colleagues raised a further **£900** for us.

British Association for the Study of the Liver (BASL's) Wilson's Disease Special Interest Group (WDSIG)

BASL has taken the initiative to form the **WDSIG** for specialists across the country. The first meeting was held in December 2017 and Valerie and I were invited to attend on behalf of WDSG-UK. This collaborative group aims to provide input into national organisations such as NICE (National Institute for Health & Care Excellence), NIHR (National Institute for Health Research) and the NHS and be a forum for discussing, promoting and enabling research into Wilson's disease. Data is needed to facilitate research and support new methods of healthcare and through the approach of BASL, Public Health England (PHE) is working with the WDSIG in ground-breaking work to provide accurate information about the Wilson's Disease population in the UK (see below).

Public Health England (PHE): Wilson's Disease Pilot

PHE took over the responsibility for the registration of rare diseases (National Congenital Anomaly and Rare Disease Register) in 2015 and soon appreciated how difficult it was to collect data about rare diseases. Due to the structure of the NHS it is very difficult to establish accurately the population of WD patients in the UK. Consequently, as part of their approach, PHE has designed a proof of concept for collecting rare disease data and we are delighted that Wilson's disease is the **first** rare disease to be selected to pilot this concept. We are working with PHE over this and look forward to the results in due course. (For more details see *p19*)

NHS England Specialised Commissioning Policy Working Group: Trientine

This Group was initiated by NHS England to develop a policy *to inform* the NHS England commissioning responsibility in relation to the future prescribing of trientine for patients with Wilson's disease in England. A policy is required as the price of the drug has increased so much it was recognised that it has to be funded separately. In order for NHS England to do this, a policy setting out the use of this drug has to be agreed. A policy working group led by **Dr James Dooley** and made up of clinical specialists, a specialist in public health, a pharmacist, patient representatives (Valerie and I) and a lead commissioner has been reviewing the evidence and drafting a policy for consideration by the NHS England Clinical Panel. It is hoped that as a result trientine will continue to be available to those who need it.

NHS Blood & Transplant Organ Donation & Transplantation Directorate & Liver Patient Groups' 8th Meeting

Caroline Simms attended this meeting in London on behalf of the Group on Tuesday, 11 July 2017. It was reported that liver donation numbers have continued to rise as have the number of transplants being undertaken. However, it is still too early to assess the impact of the Welsh "opt out" legislation in relation to organ donation numbers as family members still have the ability to veto the wishes of the deceased. The National Liver Allocation scheme will shortly be adopted in stages meaning that when certain livers become available in the UK for transplantation, they will be offered to patients on a needs first basis anywhere in the UK rather than first offering them to the nearest transplant hospitals as is the policy currently.

Cambridge Rare Disease Network (CRDN) 3rd Conference—23 October 2017

Mary Fortune and Valerie attended this day conference in Cambridge with other representatives from Rare Disease Patient Groups. There were speakers talking about public engagement and drug repurposing as well as individual patients giving personal accounts of either having or living with a rare disease. At lunchtime some Groups presented *Patient Journey* posters, including the French WD Support Group, while representatives from bio-tech and pharma companies were on hand to discuss patient register software, orphan drug manufacturing and gene therapy. For interested parties, CRDN produces a newsletter called *Rare Disease Revolution.*

Clinical Research

The UCL Institute of Neurology, under the leadership of **Professor Tom Warner** and **Dr Sam Shribman** and in association with **Professor Oliver Bandmann** in Sheffield, have put together a proposal seeking NIHR funding to examine a wide range of possible, new, previously unrecognised, modifier genes which may influence the clinical features and severity of Wilson's disease, ultimately leading to potential gene therapies for both hepatic and neurological aspects of the disease. UCL has asked for our input and we have been delighted to assist them in supporting this proposal. This is an exciting project and we hope UCL will be successful in gaining research funds from the NIHR, and that you will consider joining the WD Patient Register, if you haven't already. (For more details see *pp14-15*.)

Implementation of UK Rare Disease Strategy

We are members of Genetic Alliance UK and I currently represent WDSG-UK on the Rare Disease UK *Patient Empowerment Group* in which I put forward ideas of what type of service would be needed in the future to best suit the needs of Wilson's patients. A key area for discussion is the implementation of the UK Rare Disease Strategy and in January 2018 NHS England and the Department of Health published their plans for the implementing of this Strategy. We have documented our requirements and are waiting to find out how the Strategy will deliver a modern service for the treatment of Wilson's disease.

Clinical Genetics

An important element of the *Rare Disease Strategy* is the rapid adoption of genetic techniques to provide new methods of treating rare diseases. Two organisations have published information on gene therapy products for the treatment of Wilson's disease and we are seeking further information and advice about its potential use in Wilson's disease.

WDSG-UK Committee Meetings and 7th AGM 2017-18

The WDSG-UK management committee met on two occasions in 2017 during March and November. Our annual Support Group Meeting for our members and friends and incorporating the 7th AGM was held in Cambridge in July 2017 and we thank all those members and doctors who attended. A report of the meeting appears overleaf.

WDSG-UK Annual Meeting and 8th AGM

The 2018 Support Group Meeting will be held on **Sunday, 15 July 2018** at our normal venue in Cambridge, the clubhouse of *Cambridge Rugby Union Football Club*. As part of this meeting, we will hold the 8th WDSG-UK AGM at which the election of officers and members of the WDSG-UK Management Committee for 2018-19 will take place. All members of the current committee have submitted their names for re-election for the coming year.

I would like to take this opportunity to thank the current members of the Management Committee, Mary Fortune, Caroline Simms and Valerie Wheater, who have served with diligence and commitment over the last year. Valerie, through her commitment to WDSG-UK which includes running our thriving Facebook group, has once again played a key role in the daily functioning of the group which ensures it will continue to be recognised as the leading charitable group in the UK dedicated to Wilson's disease patients and their families.

Looking at the range of activities we have been involved in during the last year the workload has been significant and is likely to continue for the forthcoming period. Consequently, we are seeking new committee members. The work is varied and interesting and will undoubtedly increase your knowledge of Wilson's disease, the challenges the NHS faces in treating a rare disease and how small charitable organisations can make an impact in the digital age. If you are interested, please contact Valerie or me.

Jerry Tucker
March 2018

Wilson's Disease Support Group Meeting & 7th AGM

Cambridge Rugby Union Football Club, Sunday 23 July 2017

The largest ever gathering of **WDSG-UK** members had assembled promptly for the start of our 2017 meeting, thereby avoiding a downpour of rain, which arrived shortly after midday.

Many new members were able to attend this year, both from the UK and overseas. We were particularly delighted that **Dr Walshe's** first UK Wilson's disease patient, **Shirley Wylie**, was able to join us. Dr Walshe first treated Shirley in 1955, and she remained a patient of his until he retired in 2000. Her remarkable story is recounted in last year's Newsletter. From overseas, we were pleased to welcome **Priya Joshi** and family from Zurich, **Kumari Bahall** and husband from Trinidad & Tobago and **Regine Bielecki,** who had taken a day return ticket from Germany just to thank Dr Walshe in person for discovering penicillamine and thereby saving her life. From the UK, it was lovely to meet older members **Andy Forster** and **David Pereira** together with younger members, **Oliver**, **Izzy, Sam J** and **Sam F**. Many regular members of the Group who have supported us over the last decade had also made their way to Cambridge, and the audience was completed by the presence of **Drs Godfrey Gillett** and **James Dooley**.

Dr Walshe with Shirley Wylie, his first UK patient — treated with penicillamine since 1955

Rupert Purchase opened the meeting by thanking **Valerie** for organising this event, and then introduced **Jerry Tucker**, Vice-Chair (WDSG-UK), who summarised some of the committee's work over the past year on behalf of members. The committee regularly attend meetings organised by Rare Disease UK, who are active in promoting the *UK Rare Disease Strategy* and **Caroline** has recently attended an NHSBT meeting reviewing liver transplantation in the UK. Jerry and Valerie are members of an *NHS England Working Group* who are examining issues regarding trientine, and we continue to develop the *WDSG-UK Patient Register*. Jerry also spoke about plans to improve and expand the WDSG-UK website.

Disease models, whether *in vivo*, *in vitro*, or *in silico*, are a means of understanding the causes of diseases and finding treatments and cures. **Dr Emily Reed** from the Sheffield Institute of Translational Neuroscience, University of Sheffield, has summarised the available animal models (*in vivo* methods) for Wilson's disease in last year's WDSG-UK Newsletter. Current rodent models are inadequate for understanding neurological Wilson's disease. In a presentation before lunch, Emily described some of the exciting research she has embarked on to find better ways of modelling neurological Wilson's disease. Zebrafish have been successfully used to study other neurological disorders, and Emily has begun to use zebrafish who carry the ATP7B mutant (Wilson's disease) gene as an *in vivo* model of Wilson's disease. Emily is also developing an *in vitro* technique of transforming skin cells into neurons, and hopes that skin cells taken from Wilson's disease patients and transformed in this way will offer an insight into copper transport in the brain.

Our speaker, Dr Emily Reed

Lunch was followed by the 7th **WDSG-UK AGM** and the election of the WDSG-UK management committee for 2017-2018. Jerry Tucker replaced Rupert Purchase as Chairman, with Rupert leaving the committee after seven years. Jerry presented Rupert with a small gift in recognition of his work for WDSG-UK. The other committee members, Valerie Wheater, Caroline Simms and **Mary Fortune** were re-elected for a further year. In his Chairman's report, Rupert thanked the committee for their support over the past year, and highlighted Valerie's commitment to helping Wilson's disease patients and their families through her work on the Group's Newsletter and Facebook page and by meeting up informally with WDSG-UK members during the year.

After the AGM, and preceding the raffle, **Anusha Joseph** read a poem in memory of Charlie Watsham, who died in 2015. This year's raffle was run by new member **Ruth Morgan** and raised **£104** to support WDSG-UK. It was supplemented by the sale of *Wilson's disease* wristbands, produced and marketed for us through another new member, **Samantha Ryan Panchal**. Details of how to purchase these elegant blue wristbands may be found on *p7.*

Anusha reading a Poem in memory of Charlie

Following the discussion at the 2016 WDSG-UK annual meeting on the repercussions of the recent price increases for trientine dihydrochloride, Rupert gave an update of some recent developments. *The Times* newspaper has been following the steep increase in price of so-called unbranded generic medicines, and these reports show that the price of trientine is part of a general problem of the sale of out-of-patent drugs needed for relatively small groups of patients. To counteract unscrupulous price increases for these drugs, the UK government has enacted new legislation – the *Health Service Medical Supplies (Costs) Act 2017*. To quote from the government's guidance note on this Act, "the government's intention is to use these new powers where, due to a lack of competition in the market, companies charge unreasonably high prices for unbranded generic medicines."

Some of our Members

The meeting concluded with a question and answer session between the audience and the three consultant physicians present. Questions were raised on whether trientine capsules could be emptied into water, fruit juice, or yogurt if patients have difficulty in swallowing capsules (or whether smaller capsules could be produced by the manufacturer); genetic testing to check that a partner is not a carrier of Wilson's disease; and the advisability of co-administering D-penicillamine and a zinc salt to treat Wilson's disease.

Drs James Dooley and Godfrey Gillett

Following the close of the meeting, Anusha, our photographer for the day, finished by taking Group photographs before we dispersed into the warmth of a Cambridge summer afternoon. We hope that members feel that these annual meetings are helpful and informative, and look forward to an even greater attendance next year! (More photos of the day on *p22.)*

Rupert Purchase
July 2017

Rupert delivering his Report

The Patients' Group Photograph

Fundraising 2017-18

Sylvia Penny

Sylvia

Sylvia Penny has been one of our keenest supporters and fundraisers over the years and it is with **great sadness** that we have to report that she died suddenly aged **87** in July last year, just three weeks before she was about to hold her eleventh coffee morning and bring and buy sale in aid of the Group. For regular members of the Group, you will know that Sylvia's granddaughter **Emma** was diagnosed with Wilson's disease in 2007 aged 26, since which time Sylvia and the entire family have kindly raised over **£4,000** for us. The funeral took place in Torquay in August last year (See notice on *p 23.)*

AFC Rushden & Diamonds—Youth Section

We are grateful to the **AFC Rushden & Diamonds Youth Section** for nominating WDSG-UK as their chosen charity for the **2016-17** and **2017-18** seasons. The Club has so far raised **£1,000** for us, which is a truly outstanding amount. They have over 300 youth team players representing 20 different teams as well as a flourishing over 50s' section. **Sam Fitzgerald**, one of our younger patient members, was an outstanding player at the Club before Wilson's disease took its toll on him in 2015. The Club wished to show their support for Sam by raising funds for WDSG-UK. The following initiatives have been implemented by **Mark Cullen,** Chair of the Youth Section of the Club, to raise awareness of Wilson's disease and WDSG-UK, and by **Tracy Stephen** to raise funds for the Group:

- WDSG-UK logos have been put on all youth team players' shirts;
- WDSG-UK logos have also been added to the shorts of 1st team players;
- WDSG-UK logo has been added to the AFC official website, youth site, Fb pages, Twitter and official match day programmes and Club publicity;
- A write-up about WDSG-UK has appeared in the *Nene Valley News;*
- Write-ups have appeared in the 1st Team programmes;
- A fundraising Charity Auction was held on 16 Sept 2016;
- A LADIES –v– LADIES football match was held on 1 May 2017;
- A Community Fun Day was held on 20 May 2017.

1st Team Shorts!

Tracy Stephen, who was head of fundraising, wrote at the end of the 2016-17 season:

"As Head of Fundraising for the club for the past two years, I have been responsible for the usual fundraising events and have created new events to raise more money and more awareness for both the Football Club and our chosen charity, WDSG-UK. The football season started off in Sep 2016 with a Michael Jackson Tribute Evening and a Charity Auction, held around a 3 course dinner. We asked for items to be donated and also invited local company *Sporting Gold,* who auctioned off sporting memorabilia.

Every year we hold a *FIFA* night where the entrance money is split between the Club and our chosen charity. This year the event took place in February and attracted a good turn out.

A Sponsored Walk was held at the end of the football season in April. Teams walk for a certain distance between one and five miles depending on their age. This year we began the walk from our new grounds on Hayden Road and completed it for the last time at our old ground, the *Dog & Duck* Stadium. Dan Richards organised this event for the third consecutive year.

On 1 May we held our annual Ladies Charity Football Match for which we sold advertising and raised sponsorship in advance and sold programmes on the day, which all raised money and awareness for local charities and WDSG-UK. In addition, we held a raffle during the match and took collection buckets around the ground.

Finally, we held a Fun Day around the annual presentations of cups to players for their achievements, and to say thank you to everybody for their hard work throughout the season. At this event we have popular activities such as a bouncy castle and *Soak the Coach*, and also run another raffle. By the end of the season through the goodwill of our families and supporters, we were pleased to have raised **£1,000** for WDSG-UK.

By the end of the 17-18 season we hope to have again exceeded the £500 target we set for ourselves to raise for WDSG-UK. We shall be holding a Community Fun Day on **28 April** and another Ladies' charity match on **29 April.**"

Angharad's Half-Marathon

From Lothwithiel in Cornwall and a friend of **Grace Carter, Angharad Morgan** kindly raised **£300** in sponsorship through *Just Giving* by running in the Edinburgh Half-Marathon last June. Apparently, she had never run such a distance before, but actually quite enjoyed the whole experience. Asked how she came to compete in this event so far away from home and how she chose to raise funds for us, she says:

"I wanted to show my support for Grace. I first met her when we started college together six years ago. I was struck by how determined she was, and only found out that she had Wilson's disease further into our friendship. Despite this and the tiredness and memory loss that came with it, she showed how resilient she was by working hard and achieving two grade A*s.

I remembered how much Grace had enjoyed meeting other patients at the annual WDSG-UK meeting in Cambridge in 2014, so when I found myself working up in Newcastle on the other side of the country, I decided to think of a way of raising money for the Group. Edinburgh was close and convenient and I'd heard great things about the atmosphere of the race. It was a beautiful run, half of which was along the coast."

Angharad at the end of Race

* * *

Meanwhile, **Grace** has been busy making chutneys and selling them to raise funds for the Group. She very kindly credited our account with **£110** in July and posted the following message on Facebook:

"Thank you to everyone who has bought my homemade chutney over the last few months. So far I have raised **£110** for Wilson's Disease! I have made a variety of chutneys: apple, apple and rhubarb, spicy pumpkin, and pear. I pick the apples and pears from a friend's garden and use recycled jars."

* * *

Samantha's WD Wristbands

Samantha Ryan Panchal kindly offered to fundraise for us last July by selling silicon wristbands to help raise awareness of Wilson's disease and to publicise the Group. To date, she has credited our account with **£454** nett. These wristbands are still available, should you wish to buy one (details below). Sam's brother, **Ben**, was diagnosed with Wilson's disease in 2016. She writes,

"Our family first found *WDSG-UK* in August 2016 and through this connection we have been able to have a better understanding of how we can best support Ben, my brother. The Group's Facebook page is also invaluable to many people.

Ben was diagnosed with neuro Wilson's in August 2016, age 28. Unfortunately, the disease has hit him hard with every side effect. He has been in hospital since December 2016. He has battled pneumonia and weight loss and is now on a PEG feed. Ben's primary medicine is penicillamine and more recently he has had a course of Dimercaprol injections to try and help with his dystonia. These he has tolerated well and we have noticed a difference in his movement together with maintained weight gains. Although small, there are improvements. Ben is also taking Baclofen to help with his dystonia.

The Wilson's disease wristband

Over the months, we have felt helpless. We have arranged various fundraising events to help Ben in his care and with his needs. Along with these events we also wanted to spread awareness of Wilson's disease and support WDSG-UK, so in June 2017 the Wilson's Wristbands were born! I sell these at **£2** each **plus** postage with payment to myself via Paypal (as gift friends/family) (https://www.paypal.com/uk/home).

If you would like a wristband you can contact me via the WDSG-UK Facebook group. Money for the wristbands is then transferred direct to the WDSG-UK current account less postage costs. The wristbands will also be available for sale at the next Group Meeting & AGM in Cambridge on **15 July 2018** or direct from me via Valerie."

A Cautionary Tale

by Stacy Shakespeare

I'm **Stacy.** I am aged 30 and currently live in Burgess Hill, West Sussex with my son and partner. I have two siblings: a brother aged 32 and a sister aged 23. Wilson's disease came to light in my family when my brother became very ill at the age of 17 (which made me 15). He began being sick every day and had jaundice and fluid in his tummy, legs and ankles. He was initially taken to *Good Hope Hospital* in Sutton Coldfield, but the doctors could not figure out why his liver was beginning to fail so he was transferred to the *Queen Elizabeth Hospital,* Birmingham. Eventually, he was diagnosed with Wilson's disease but by this time it was too late to treat him for it and instead he was given an *urgent* liver transplant. The transplant was successful and he is now a healthy 32 year old with six children and no more WD.

The diagnosis prompted doctors to refer me and my sister to the *Queen Elizabeth Children's Hospital* to undergo tests to see if we had Wilson's disease, too. The tests were a 24 hour urine test without medication then another 24 hour urine test while taking penicillamine, the medication used to treat Wilson's disease. We also had numerous blood tests and an eye test to look for Kayser-Fleischer rings. The results came back that my little sister was clear of Wilson's but I had a high content of copper in my body, although no K-F rings. I was then introduced to Professor Kelly at the *Children's Hospital* who suggested that I have a liver biopsy to see what condition my liver was in. The results confirmed that I had liver cirrhosis and Prof Kelly confirmed that I had WD. I was started on medication straight away (penicillamine and pyridoxine) and advised to stick to a low salt/copper diet. I had regular check ups for about a year but then my parents split up and I went to live on my own. I was so unsettled. By the age of 21 I had lived in nine different houses. At the age of 19 I had begun to neglect all doctors' and hospital appointments and had stopped taking my medication. I believed I didn't have WD and if I did, it wouldn't matter because I'd been ok so far. Although I stopped taking medication, I stuck to the low salt/copper diet and drank no alcohol. At the same time I had a baby boy and continued moving around until I ended up in West Sussex in 2014. Everything seemed ok until I got to 29 and that's when it all changed.

In August 2017 I started being sick in the mornings, then after every meal my tummy felt bloated. I thought I might have been pregnant, so I did a test and I wasn't. My symptoms carried on getting worse and I had that much fluid in my body that I looked as if I was nine months pregnant. I visited my GP who sent me straight to A & E. I told them that I had WD but that I had neglected any medical help. It was confirmed that my liver had started to fail. I was immediately started back on penicillamine and had the dose increased every two weeks. My liver was showing no signs of getting better. The fluid in my tummy formed a bacterial infection called e-coli. I had the fluid drained three times and it just kept coming back. By this point I knew that it was all my fault and I felt that I deserved to suffer the consequences. I wanted to give up fighting to stay alive so many times: the drains were painful and I just wanted to be at home with my little boy. I had several blood transfusions, two endoscopies countless ultrasound scans and x-rays.

The hospital I was at was only a local one, *The Princess Royal* in Haywards Heath, so they got in touch with King's College, London, deciding that I needed to be assessed by them straight away. I was taken to London where I had to undergo a week of tests to see if I was mentally and physically prepared for a liver transplant. At the same time they now found K-F rings in my eyes. I was allowed home after a week but was told I would need to return to King's every six weeks to see my consultant, Prof. John O'Grady. Once home, I got no better. I couldn't get out of bed. I couldn't sit upright for any longer than five minutes. I started to get severe pains in my chest and was rushed back to the *Princess Royal* by ambulance, where an x-ray confirmed that the fluid in my tummy had found its way into my right lung. Doctors didn't want to drain my lung so they hoped another tummy drain would help clear the fluid, and it did.

I eventually got to go home just before Christmas last year. My symptoms had stabilised to a certain extent. Two months later and I'm now 30 and waiting for a liver transplant. I'm unable to return to work. I'm still sick a lot, have no appetite, and have tremors in my hands when I'm tired or stressed. I only leave my bed to attend hospital appointments. I'm alive, but because of my neglect I am not living. Thankfully, I am still here but I have learnt a very hard and valuable lesson. I never skip a dose now. As a teenager I thought I knew better and I'd be ok. *How wrong was I?*

A Cautionary Tale—*the hepatology perspective*

Wilson's disease is a chameleonic disorder characterised by a myriad of presenting symptoms. Given the strong association with mutations within the ATP7B gene, it is surprising that individuals can present in acute liver failure, decompensated liver disease, a varying degree of neurology and psychiatric disorders or a combination of the above. For this reason, it can be difficult to diagnose. A survey I conducted through the WDSG-UK Facebook site found the mean time between patients presenting to healthcare services and diagnosis was just over 2 years. Many individuals are diagnosed through a family member's diagnosis. Even within family members, the condition can behave differently which suggests that the association between genotype and outcome is not straight forward. For these reasons, it is difficult for specialists to predict clinical outcomes for patients and it can be difficult for non-specialist clinicians and the general public to appreciate the disease fully. Further work is required to understand the association between genotype and clinical outcome and I would strongly recommend signing up to the *Wilson's Disease Patient Register—UK* (if you haven't done so already) to help research into this poorly understood area.

Stacy's story is sadly not an uncommon one. The development of chronic liver disease can be insidious. The liver has a fantastic ability to compensate for damage without showing any sign to the outside world. It is common for a particular trigger, such as in Stacy's case with an infection, to cause the liver to tip over the edge leading the individual to present to services. At this point, the liver struggles to perform its functions;- to perform its role in the immune system making the individual more likely to get infections, to perform its role in metabolism causing the individual to lose weight and develop blood clotting disturbances (**synthetic failure**), and to break down toxins and medications which leaves the individual at risk of confusion associated with liver disease (**encephalopathy**). The liver has a blood supply directly from the gut called the portal vein. This blood supply is slowed due to the liver's poor function, which in combination with other immunological phenomena and a low protein level, can lead to a high pressure in the gut (**portal hypertension**). The consequence of this is potential to bleed from dilated veins in the digestive track (**varices**) and the development of fluid within the abdomen (**ascites**) as in Stacy's case. This can be difficult to man age, with diuretics and drainage used depending on the individual's clinical case.

The introduction of a copper chelator, such as *penicillamine* or *trientine*, can be associated with the liver being able to 're-compensate' and allow reversal of hallmarks of end-stage liver disease such as portal hypertension, encephalopathy, jaundice and synthetic failure. Sometimes doses need to be gradually increased to achieve the necessary effect and individuals require repeat 24 hour urine collection, blood copper and caeruloplasmin levels measured to review the rate of copper loss and the free copper in their blood. However, for some individuals like Stacy, liver transplantation provides the only survival benefit and is accompanied with lifelong immunosuppression. It is a cure for hepatic Wilson's disease, the effect on neurological and psychiatric Wilson's disease is limited.

> *"Stacy's story is sadly not an uncommon one"*

Liver transplantation is performed at only seven centres within the United Kingdom: *King's College Hospital (London), Royal Free Hospital (London), Addenbrooke's (Cambridge), University Hospital Birmingham, St James' University Hospital (Leeds), Freeman Hospital (Newcastle) and Edinburgh Royal Infirmary*. Organs are donated by individuals who have sadly passed away and have either consented themselves or their families have consented for them to be used in transplantation. The country is now moving to a national allocations list which should ensure equal distribution of livers around the UK. The procedure is associated with a significant risk of mortality both during and post-transplant, but many individuals who are complication free by year 5 can expect up to 20+ years from their transplanted liver. The longest survivor at King's College Hospital is now entering their 4th decade post transplant.

Stacy's story will hopefully improve following her transplant. She has been courageous in sharing it with us as a demonstration of the subtle nature of the development of chronic liver disease in Wilson's disease which should provide a cautionary tale to us all.

Dr Oliver Tavabie
Hepatology Registrar
The Liver Unit, King's College Hospital.

THE BRAIN IN WILSON'S DISEASE – A Basic Account

In previous articles in these Newsletters, I have tried to explain, in simplified terms, the structure and function of the liver, the abnormalities that occur in the liver in cirrhosis, what blood tests for liver function mean, the reasons for oesophageal varices, and one of the more important skin diseases that occurs in Wilson's disease, all subjects within my comfort zone. I am now persuaded/coerced to write something about the brain changes in Wilson's, a topic close to the limit of my comprehension.

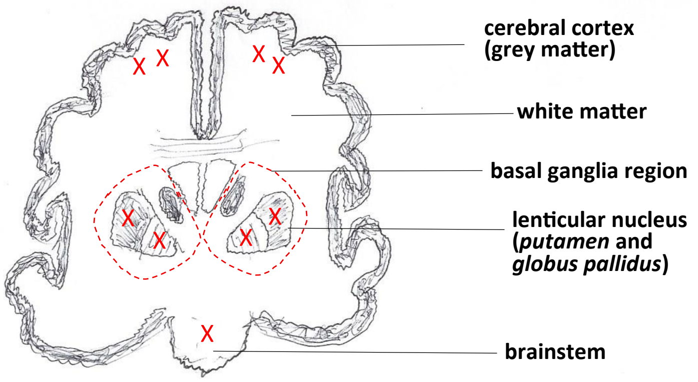
Before I start, a few words about the brain. It is a very complex organ, and a full explanation would take 500 pages and 50 diagrams, so I shall give a highly simplified version. The main cells of the brain are:-

- the nerve cells themselves, called **neurones,** the "thinking" and "doing" cells. Each neuron has a main cell body from which arise long, thin extensions called **axons** and **dendrites** analogous to wires in a telephone exchange. Neurones communicate by passing electrical signals down these connecting extensions.
- the **astrocytes**, which are cells that provide support and nutrition to the neurones, particularly supporting the cell body and the many connections.
- the **oligodendrocytes** which protect the axons by producing **myelin**, a waxy substance (proteolipid) which wraps round the axons and acts as an electrical insulator so that the electrical impulse passes down the axon rapidly.
- the **microglia** which are cells of the defensive immune system and can react to mop up damage once it has been caused.

Two main types of tissue can be recognised by naked eye examination of the brain; these are called *grey matter* and *white matter*. Grey matter contains great concentrations of neurones, whereas white matter is largely made up of axons surrounded by myelin. The (very rough) diagram below of a slice through the brain shows the location of grey and white matter. Much of the grey matter is on the outer region of the brain, in the **cerebral cortex,** whereas the inner part of the brain is largely white matter. However there are islands of grey matter deeper inside the brain, including the structures known collectively as the **basal ganglia.** These basal ganglia are an important target in Wilson's disease.

Copper is a vital trace element for the proper development and functioning of the brain, and the concentration of copper in the brain is finely controlled within strict limits by various mechanisms. If the copper level rises above or falls below these strict limits, then brain damage can occur. **Astrocytes** can take up, store and eliminate copper from the brain.

Wilson's disease was once called *hepato-lenticular degeneration*; the *hepato* bit is easy to understand, referring to the liver involvement in Wilson's. What is the *lenticular* bit? It refers to a part of the brain formerly called the lenticular nucleus which is a component of the **basal ganglia region;** the lenticular nucleus has two components, the **putamen** and the **globus pallidus**. The illustration below shows the location in a slice through the brain.



Rough Diagram *of a slice through the brain (right and left cerebral hemispheres) showing basal ganglia, lenticular nucleus and distribution of grey and white matter. Areas commonly involved in Wilson's are indicated by red crosses.*

The lenticular nucleus was the first part of the brain noted to be involved in patients with Wilson's disease with neurological symptoms, in Samuel Kinnear Wilson's doctoral thesis entitled *Progressive lenticular degeneration: A familial nervous disease associated with cirrhosis of the liver*. Wilson described areas of softening and degeneration in the lenticular nucleus region, a finding that has been noted subsequently at post-mortem examination of the brain in patients with neurological Wilson's, particularly those who have movement disorders such as tremor, ataxia (poor physical coordination), and dystonia (involuntary, often repetitive, movements caused by sustained muscle contractions). The various components of the basal ganglia are known to be responsible for control of movement, particularly of the limbs.

> *"Molecular genetics is having an impact in understanding disease"*

We have learnt much more about brain involvement in Wilson's using modern imaging techniques, particularly MRI scans (Magnetic Resonance Imaging). These have shown that considerably more areas of the brain are involved than originally described by Kinnear Wilson. It is true that the basal ganglia regions on both sides of the brain are frequently affected, particularly in those patients with severe movement disorders, but abnormalities are also found in other regions, including the **brainstem** and **midbrain**, and in the white matter of the brain. In simple terms, MRI shows variations in texture of tissues, and in the brains of Wilson's patients it demonstrates where the abnormal areas are situated, but gives little clue as to what is going on at a cellular level in the affected areas. This requires examination of the tissues under the microscope (histology).

Examination under the microscope shows that in early affected areas fluid accumulates between brain cells, giving rise to a spongy texture that pathologists refer to as **spongiosis**. Why this happens is not fully understood. As disease progresses, the neurones in the affected regions die, and the supporting astrocytes show a variety of degenerative changes. Affected areas become soft with development of larger fluid-filled cavities. An abnormal cell is also seen in affected areas and occurs only in Wilson's disease. These are called **Opalski cells** and appear as large cells with a foamy appearance and a small, shrunken nucleus. There is still debate if these cells are derived from astrocytes or derived from the microglia. It is not clear whether the high copper levels damage the neurones directly, or whether the copper first damages the astrocytes which are then unable to support the neurones which then in turn die.

A further change which has been described is areas of loss of myelin (**myelinolysis**), particularly in the brainstem region. It is not known to me whether the myelin loss is a direct effect of copper damage on myelin, or on the cells which produce it (oligodendrocytes), or whether it is secondary to the death of the neurones with loss of the axons which the myelin surrounds. MRI scans are very good at detecting changes in the fluid content of tissues, which is why scans can readily show areas of affected brain in patients with Wilson's disease.

There are many unanswered questions about the brain involvement in Wilson's disease, including:-

- why do some patients develop neurological symptoms, and others do not?
- assuming that the excess copper enters the brain throughout, why are certain parts of the brain affected and others not? This question of selective vulnerability is something that applies to many other diseases of the nervous system.
- is the severity of the brain damage directly proportional to the concentration of copper in the brain tissue, or are other factors involved?
- how does the copper cause damage at a cellular level? Studies are being performed in a range of experimental systems and the cell biology of copper accumulation in Wilson's is starting to be understood. It will take time for this to be applied to all of the different cell types that may be involved in the brain.

Molecular genetics is having an impact in understanding disease. It is very likely that some of the mutations in the gene for the copper transport protein that causes Wilson's disease carry higher risks for involvement of the brain than others. So far, studies using MRI scans in families with the same mutation do not show a simple association. Other factors are therefore involved; some will be genetic some not. The participation of patients in studies that link their genetic details with their clinical case information should build the large series necessary to get these answers. I shall be interested to follow the research proposed by Dr Sam Shribman et al *(see **p15**)*.

Dr A Stevens
(Retired Consultant Pathologist and Medical Author)

I am grateful to my friend, former colleague and co-author, Jim Lowe, (Retired Professor of Neuropathology) for his advice and assistance with this article.

Anusha's Story

by Anusha Joseph

Hello, my name is **Anusha;** I am single, live in Harrow west London and am 38 years old. My close family consists of my beloved parents, my sister and I. I attend the WDSG-UK meeting in July every year and for the past three years have been the "official" photographer for the day. The meeting is a good opportunity to meet other patients and doctors. I miss Charlie Watsham, another patient, who sadly died in August 2015. Unfortunately, my parents and I have a family wedding to attend in Canada this year, so we won't be able to come to the meeting, but I hope to see you all there again next year.

Well I am going to tell you about my struggle and challenging experiences of living with long-term illnesses and disability. I have neurological Wilson's disease but I also have Epilepsy, tonic/clonic seizures and learning difficulties. Epilepsy is a condition that affects the brain and causes repeated seizures. Tonic/clonic seizures are the classic type of an epileptic seizure consisting of two phases called the tonic phase and the clonic phase. In the tonic phase the body becomes entirely rigid, and in the clonic phase there is involuntary movements of your arms and legs. Tonic/clonic seizures may or may not be followed by an *aura,* which may consist of flashing lights, a gleam of light, blurred vision, a smell, the feeling of a breeze, numbness, weakness or difficulty speaking and is often followed by headache, confusion and sleep. They may last mere seconds, or continue for several minutes. If a tonic/clonic seizure does not resolve or if such seizures follow each other in rapid succession, I have to seek emergency help. Learning difficulties is the same as a learning disability. This affects the brain's ability to receive and process information. Any individual with a learning disability has trouble performing specific types of skills or completing tasks, if left to figure them out themselves. It describes a group of disorders characterised by inadequate development of specific academic languages and speech skills. About 1.5 million people in the UK have this disability.

What I remember of my medical story is that back in August 1993 when I was 13 years old, I went to *Great Ormond Street Hospital For Children* to have an MRI. Nobody knew what was wrong with me. While I was having an MRI scan of my brain, I was given sedation to make me sleepy but it had no effect at all and I remained wide awake. When the scan finished I tried to get up but I couldn't. I was paralysed from the waist down. My parents wanted answers, but they just said that the sedation didn't work. I was terrified and crying all the time and didn't know how to express my feelings to anyone. I was admitted to the hospital and my parents stayed beside me all the time, but I missed my friends and the rest of my family.

At home, I have been attending *Wiseworks* since May 2014. *Wiseworks* is a local mental health pre-vocational work centre provided by the Disability Day Services of Harrow Council. For more than 20 years, the service has worked with people recovering from mental health problems by assessing their work skills, providing comprehensive work rehabilitation and arranging training at local colleges. I am happy there as my friends and staff members understand my illnesses and disability and treat me with dignity. Unfortunately, I have been unable to attend since before Christmas as I have severe problems with my left hand. I have an appointment to have it x-rayed, so I am hoping that they will find out what is wrong so that I can return to *Wiseworks* shortly.

> *"When the scan finished, I tried to get up but I couldn't"*

So what if I have Wilson's disease, epilepsy and learning difficulties, nobody can cure me. I will always have to take various medications every day. I feel like a normal human being because others can see me for who I am, not what I have. Some of my relations and close friends did not want to know me because of my illnesses and disability but others supported me and I am so lucky to have had my parents by my side as I could not have managed without them. I ask myself occasionally why I had to get these illnesses and live with a disability? The reason is it just happened. I was living a normal life before and then suddenly I have these long-term illnesses and disability and life has never been the same since."

I found this history curious, so with Anusha's permission I rang her mum Hilda and asked her for more details.

Hilda started the story from the beginning. "When Anusha was eighteen months old, she had a febrile convulsion. The doctor told me this was not uncommon in young children and that she would probably grow out of them in time. Within a year, she had another more severe convulsion and this time she was rushed to hospital and given meds to keep these episodes under control. She did grow out of them by the time she was six. The next five years of Anusha's childhood were unremarkable. She had done well at First School and had settled in well at Middle School. She was a bright girl, popular with other pupils and liked by her teachers. She was good at Maths and English and was keen on sport. Her handwriting was beautiful and she was gifted at art. She was also musical and took piano lessons, passing her Grade 3 exam. By the time she was eleven we had begun to notice that things were slowly changing. She started to get teased at school as she seemed to be drooling a lot. Then other things happened like she was slurring her words and her handwriting was becoming scratchy. Her coordination was deteriorating and she was having difficulty walking and buttoning up her shirt. We took her to see the GP on many occasions and also consulted a paediatric neurologist at *Northwick Park Hospital* (our local hospital), where she was examined but they could find nothing wrong.

In 1992 she transferred to secondary school. Her symptoms got worse. She was bullied so we decided to take her out and send her to a smaller, private school nearby. But the bullying continued, so in desperation we transferred her to yet another school. It was the summer term of 1993 and I got a telephone call from the school one day saying that they were worried about Anusha. She was tall and had been a good netball player, but on this particular day she had been bumping into all the other players on the court. We asked our GP to arrange for us to have a second medical opinion and an appointment was made for us to see a paediatric neurologist at the *Clementine Churchill Hospital* in Harrow. The doctor there ran lots of tests but the results were all unremarkable, including, we found out later, her caeruloplasmin test. He then referred us privately to Dr John Wilson, Consultant Paediatric Neurologist at *Great Ormond Street Hospital* (GOSH), to see if he could help.

Dr Wilson examined Anusha and was puzzled and said that he would book her in to have an MRI scan and treat her on the NHS. He mentioned Parkinson's disease and Motor Neurone disease to us but Wilson's disease was not mentioned. Anusha returned to the hospital in August 1993 to have an MRI and when it had finished her whole body was very, very floppy. We never found out why. She was admitted for three or four days and given *haloperidol* to control her movements. We then all returned home and her condition got worse, so we took her back to see our G.P. He took one look at her and rang GOSH and arranged for her to be readmitted straight away. She stayed there under the care of Dr Wilson for about a month. During this time, many tests were done including blood tests, 24 hour urine tests and CT scans and eventually an ophthalmologist found Kayser-Fleischer rings in her eyes. At last we were given a diagnosis that Anusha had Wilson's disease and were reassured that the prognosis was good. She was put on penicillamine and allowed to return home.

Around three months later, one evening in December, Anusha was watching television when we heard a commotion and rushed in to see what was happening. We found her fitting in a way we hadn't seen before. We called an ambulance and she was rushed back to GOSH again. It was very frightening as her fitting lasted for nearly twenty-four hours. Once under control, GOSH discharged her into the care of *Northwick Park* where she stayed for a further twelve days.

For eight months after her diagnosis, Anusha didn't attend school. She couldn't get to the lavatory even without help. We had a full-time carer for her and a private tutor and an occupational therapist. The occupational therapist helped her with her speech and Anusha also had physiotherapy to get her legs working again. Anusha's arm was put in plaster from her wrist to her elbow in an attempt to arrest her dystonia. Gradually she started to improve and walk again, much to our relief. After Easter 1994 she returned to school, but she struggled in every aspect of school life, and the school discouraged her from staying on after taking her GCSEs in July 1997.

Meanwhile, in 1995, we were going to visit relatives in Toronto in Canada and Dr Wilson, who was concerned about Anusha's low platelet levels and neutrophil count at that time, suggested that we see Dr Diane Cox, who was a Wilson's disease specialist there. Dr Cox repeated the tests and agreed her platelets and neutrophil counts were low. She suggested Anusha change her treatment to trientine, which she did. She also suggested that on our return to the UK we ask to see Dr Walshe who was the world authority on Wilson's disease. Dr Walshe thereafter looked after Anusha at Queen Square, London, until he retired in 2000 and handed over her care to Dr Gillett. We often wonder whether Anusha's epilepsy is connected to her Wilson's disease, but nobody has ever said that it is. All we can do is to continue to support her in every way we can."

WD Research Notes

In this and subsequent Newsletters, we hope to keep you informed of research projects related to Wilson's disease and to share any announcements which appear in the public domain and might be of interest to you. If you are a researcher and would like to advertise any studies that you propose, or if you wish to make use of our Patient Register, then please contact either **Jerry Tucker** or **Valerie Wheater** by email (details on the back cover of this newsletter).

The following are three current research projects relating to Wilson's disease. The first two are under way and the third, which is detailed further in **Dr Sam Shribman et al's** article opposite, is awaiting funding.

University of Sheffield, Dept of Neuroscience

Prof. Oliver Bandmann and his team are investigating mitochondrial biomarkers in Parkinson's disease and other neurodegenerative diseases, including Wilson's disease. If abnormalities are found in mitochondria, there is the possibility of using so-called "mitochondrial rescue" drugs as treatment. Cells obtained from patients by skin biopsy will be investigated for their mitochondrial function, and will also be processed to convert them into neurones (brain cells) on which further studies can be performed.

Royal Surrey County Hospital and University of Surrey, Guildford, Surrey

Following the recent publication in *The Lancet Gastroenterology & Hepatology.2017;2(12):869-876,* of the open-labelled **Phase 2** Study using bis-choline tetrathiomolybdate(WTX), a **Phase 3** Randomised, Rater-Blinded, Multi-Centre Study to Evaluate the Efficacy and Safety of WTX101 Administered for 48 Weeks Versus Standard of Care in Wilson Disease Subjects Aged 18 and Older with an Extension Phase of up to 60 Months has recently gained approval in approximately 30 sites across the USA, Israel and Europe. If you would like further information of the trial, please contact Prof. Aftab Ala at Royal Surrey County Hospital, Guildford, UK. Email aftabala@nhs.net

National Hospital for Neurology, Queens Square, London

Prof. Tom Warner of the National Hospital for Neurology, Queens Square, London, is planning a research project into Wilson's disease.

In summary, he and his team will be looking at the genetic abnormalities in WD patients to determine why there is such a variation in the features of neurological disease, and variations in severity, progress and response to treatment. If these variations can be ascribed to genetic differences, it will lead to better understanding of optimal therapy in each case. Ultimately it is anticipated that specific gene therapy will be developed for the disease.

The study will also try to identify markers in blood and cerebro-spinal fluid that indicate how the neurological damage occurs and could be used to measure the effect of potential treatments in the future. For more information, please see opposite.

The Wilson's Disease Patient Register—UK

WDSG-UK strongly supports research into all aspects of Wilson's disease. In **2015**, we launched the *Wilson's Disease Patient Register—UK* for exactly this purpose, i.e. so that patients could make a contribution to research. We have over fifty patients registered with us already. We wish to reassure you that no patients' names will ever be passed on by us to researchers. Should we be approached to provide details of patients on our Register who could participate in a particular study, we will **always** write first to the patient direct, giving them details of the study and inviting them to take part. Should the patient choose to participate, **then and only then** on receipt of a signed undertaking will their names be forwarded to the researchers. If you have not joined the Patient Register already, then please consider doing so. A pamphlet and information sheet is available to download off the WDSG-UK website <*www.wilsonsdisease.org.uk*>, together with a registration form. We look forward to hearing from you soon, and increasing our number!

Why do some patients get neurological or psychiatric problems?

Everybody with a diagnosis of Wilson's disease is different. We know that without treatment some people tend to develop liver problems, whereas others develop neurological or psychiatric problems. Some people develop a combination of these. We don't understand the reasons for this but we think it is related to genetics. In this article we are going to discuss why understanding this is important, some of the current theories and how we can try to answer this question:

Why is this important?

Understanding *why* some people with a diagnosis of Wilson's disease develop neurological or psychiatric symptoms will allow us to understand *how* the brain is affected. This could lead to a means to predict who is at risk of developing neurological or psychiatric problems and, through further research, might lead to the discovery of new treatments for Wilson's disease.

Current theories

The gene that causes Wilson's disease, the ATP7B gene, was discovered in 1993. The disease occurs when both copies of this gene malfunction. Over the last 25 years, researchers have discovered more than 500 different alterations, i.e. mutations, in the ATP7B gene that can cause it to malfunction.

One theory is that different mutations in the ATP7B gene might determine whether someone will develop liver, neurological or psychiatric problems. Several researchers have tested this by comparing the mutations in those with predominantly liver problems and those with predominantly neurological problems but no clear pattern emerged. There are a few specific mutations that seem to cause liver failure early in childhood, but these are not common. Some argue that, given the large number of possible mutations, it would be very difficult to find any clear patterns using this approach. In order to overcome this, other researchers have repeated this work while grouping similar mutations together. They still did not find any link between the ATP7B mutation and the type of Wilson's disease.

What is a gene? *A gene is the basic unit of heredity. Genes are made up of lengths of DNA, which act as instructions to make molecules known as proteins. Humans have around 25,000 genes and every person has two copies of each gene, one inherited from each parent.*

An alternative theory is that a different gene, other than ATP7B, might be in some way contributing. There is some subtle variation in many of our genes and it seems plausible that one or several other genes could alter how Wilson's disease affects a given individual. These genes are referred to as modifier genes. Researchers have therefore looked at mutations in genes such as COMMD1, ATOX1 and XIAP, which are known to be involved in copper handling within cells, to determine if these could be modifier genes. Again, they did not find any correlation with liver, neurological or psychiatric problems. Genetic modifiers for other diseases that can affect the brain have also been studied. The ApoE gene, which affects Alzheimer's disease, does not affect the type of Wilson's disease either.

How can we try to answer this question?

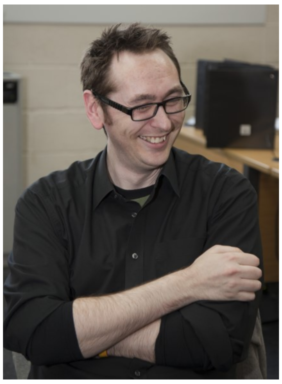
The previous attempts to find genes that might determine the type of Wilson's disease have focussed on a few specific genes only. It is possible that the modifier gene, or genes, we are looking for are not currently known to be related to processes that involve copper. **Our team is therefore currently planning a research study** where, using saliva samples collected in the post, we will look at thousands of unselected genes in people with a diagnosis of Wilson's disease. We hope to start inviting people from the **Wilson's Disease Patient Register UK** to participate in the next few months.

If you are interested in taking part in any research on Wilson's disease please go to www.wilsonsdisease.org.uk to find more information about joining the ***Wilson's Disease Patient Register UK***

Dr Sam Shribman, Ms Maggie Burrows and Professor Tom Warner
UCL Institute of Neurology

Stephen's Story

by Stephen Ginever



My symptoms (tremor) began to present in 1996 when I was 16 and deep into studying for my GCSEs, transitioning into Post-16 and thinking about which universities to apply to. My GP diagnosed me with anxiety due to all the pressure of school and prescribed me beta blockers for a few months. My mum was not convinced of the diagnosis, so after a couple of weeks on the beta blockers with no improvement, she took me to see neurological specialist, Dr Pall. We chatted about my situation and symptoms and he said there was a test he wanted to have done on my eyes (slit-lamp test to look for Kayser-Fleischer rings) that could confirm the diagnosis without the need for intrusive tests. The slit-lamp test came back positive and I began treatment for Wilson's disease. I was put on to 250mg penicillamine daily and I continued my studies and all the fun and challenging stuff teenagers go through whilst also coming to terms with the implications of being on medication for the rest of my life.

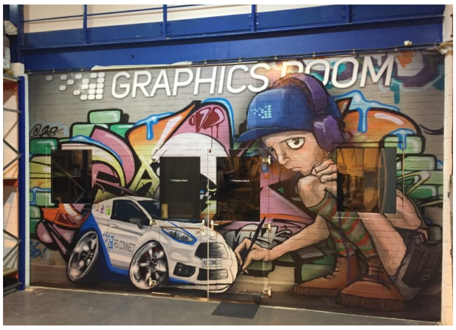
Studying Visual Communication at UCE Birmingham, I had always enjoyed success at school. Now I found myself failing classes, despite my best efforts, and it affected me a lot. My symptoms were becoming more exaggerated. Not my tremor, but I was mumbling and slurring my words. I found my left arm often crept around and up my back working its way upwards toward my head (I later discovered this is called dystonia). I also, occasionally, without realising it, stopped swallowing saliva as it was being produced, allowing it to collect in my mouth. On one occasion I was working on a drawing and I asked a classmate who was sitting next to me if I could use one of his pens but when I opened my mouth to speak I dumped a substantial amount of saliva on to my shirt, lap, desk and all over my drawing. Mortified, I had to rush to the bathroom to quickly clean myself up.

My parents also observed these developments and took me back to the GP. He contacted Dr Pall, and I was admitted to QE Hospital, Birmingham, with the plan to increase my medication and run a full series of tests. In the days leading up to going into hospital, my deterioration continued and by the time I was due to go in I had lost almost all control of my motor functions. I was rocking and writhing all over the place, unable to sit or lie still, I found it difficult to speak coherently and I couldn't write what I wanted to say because my handwriting was illegible. I couldn't feed, dress or wash myself. It was surreal. It was like a dream; I wasn't in pain and in my head I was fine. I just couldn't do anything that required physical coordination.

Once admitted into QE, I stayed there for a week and was put on a much higher dose of penicillamine (2 x 250g twice daily), given 220mg Zinc Sulphate and instructed to follow a low copper diet. I had MRI, CT and Ultrasound scans and countless blood tests. Within 2 days my exaggerated symptoms were all but gone leaving just a tremor in my hands and head. After I was discharged, I had to visit my GP twice a week for monitoring purposes and had blood tests taken regularly. Check-ups at the QE were also scheduled at 3 month intervals.

All seemed ok health-wise with the regularly scheduled check-ups so I began to look at what I was going to do with my life. The tremor I was left with prohibited me from traditional, manual art, so I felt I couldn't go back to my course at UCE. Instead, I decided to take a part-time computer aided art course at my local college. I'd always had an interest in technology as well as art and it was here that my love affair with Adobe PhotoShop began. I completed the 2 year part-time course in a little over 4 months.

After I completed my course I got a job as a Desktop Publisher making marketing material for a Post Grad Law Training company and discovered design as a discipline. With my Wilson's disease under control, I worked there for 10 years, learning many skills such as layout and graphic design for print and screen, web design and management, video recording and editing for webinars and email marketing. I now work for an aftermarket auto installations company called RS Connect as the in-house graphic designer. I am responsible for all visual representations of the company, from company uniform, vehicle livery, and building signage to internal documents, company events and monthly newsletter and also website design and maintenance. I also have a roster of freelance clients for whom I have built websites and created logos, invitations and flyers together with various other private projects. Check them out here http://stevegdesign.co.uk.



Stephen's In House Artwork at RS Connect

I should mention that through it all my family was super supportive. My amazing girlfriend, Emma, who I'd been dating for about a year at the time I went into hospital, could have said "Sorry - this is too intense for me." She could have cut and run. She didn't. She stuck with me and we're still together 20 years later. Last October we celebrated our 11th wedding anniversary.

Ellie's Story

by Ellie Gurnett

My name is **Ellie** and I have been living with Wilson's disease for 16 years. From the stories I have read so far, my route to diagnosis is quite unusual. My journey started in **2000**, when I was **18** years old, with what I thought would be a routine optician's appointment. During the visit my optician thought he could see Kayser-Fleischer rings in my eyes. He immediately wrote a letter to my GP and recommended I saw him as soon as possible. Prior to this, I was unaware of anything being wrong.

Photo: Courtesy Anusha Joseph

My GP said it could be something called Wilson's disease but it was very rare and he would have to be a doctor for 500 years to see it! However, he ran a variety of blood tests and a 24 hour urine test. The blood tests were unremarkable, but my urine copper was 590mcg/l (normal is <80). Also my urine copper:creatinine ratio was 420mcg/g (normal <80). After these results my GP sought advice from the Biochemistry department and then my GP referred me to my local hospital for further investigation.

I was seen in July 2000 at *Maidstone Hospital*. On the initial examination my Consultant (Dr Bird) noted my hand tremors, and clonuses (involuntary muscular contractions) of both my ankles. My Mum and I had noticed my hand tremors, but didn't think it was anything to worry about. He made a referral to a specialist optician so they could check my eyes with a slit lamp to confirm the presence of Kayser-Fleischer rings. Never having treated a patient with Wilson's disease before, Dr Bird also sought the advice of another consultant at the *Kent & Sussex Hospital*. In Sept. 2000 the specialist optician confirmed the presence of Kayer-Fleischer rings in both my eyes.

The next test I had was a liver biopsy. Microscopic evaluation of my liver showed it to be normal in appearance and no copper deposits were seen, even after staining. However the copper content of my liver biopsy was very high at 668 micrograms per gram dry weight. Again Dr Bird sought further advice, this time from a liver specialist, Dr Bomford, at *King's College Hospital*, London. Dr Bomford suggested an MRI scan to search for basal ganglia copper accumulation. The MRI results showed some changes of generalised copper deposition, which the radiologist thought would be reversible with treatment. Then came the penicillamine challenge test, which was thankfully the last test before diagnosis. This showed without a doubt that I have Wilson's disease and with it came the news which my older brother didn't want to hear, **he** would have to undergo tests to make sure he didn't have it, too. I am pleased to say all his tests were clear.

I was started on 1000 mg penicillamine a day increasing to 2000mg over the next few weeks. Here came the biggest challenge of all. To start with I took the penicillamine without a second thought. Unfortunately, once on the higher dose I lost my sense of taste and felt nauseous all the time. Dr Bird decided to reduce the dose to 1500mg a day and encouraged me to persevere with the treatment. After a few months I got used to the penicillamine and the nausea subsided. I currently take 1000mg a day, have a blood test every four months and see Dr Bird once a year. My hand tremor settled after a few months of treatment and now only occurs if I am feeling under the weather.

Whilst all of this was going on I had started a new job as a trainee Veterinary nurse. I was very lucky to have understanding employers who did not mind my many trips to the hospital. To be honest they were all quite interested in the disease. I had been on my treatment for some time before I actually started my college course, so it did not interfere with my training. I am happy to say I passed my exams and have been a registered Veterinary Nurse for twelve years now.

> *"he would have to be a doctor for 500 years to see it!"*

For me the hardest part of having Wilson's disease is the damage the copper has done to my joints. I have early onset osteoarthritis in all my joints which the rheumatologists suspect has been caused by the build up of copper in my joints over the years. I manage this condition fairly well although it has put a stop to my mountain walking. Over the years I have managed to climb the *Three Peaks* at various times. However, walking down Snowdon last year (I cheated and caught the train up), I was in a lot of pain so I have since hung up my walking boots for good. I do still keep active, though, with lower level walking and yoga.

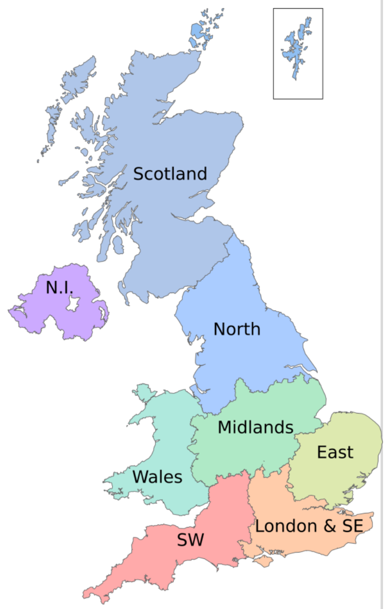
I have a very supportive fiancé and family who have been with me throughout my diagnosis and the ongoing challenges it throws my way. After reading some of your stories, I feel I am one of the lucky ones. My symptoms and damage has been very limited in comparison to others.

Which WD Meds are prescribed to Patients in the UK?

Last year's newsletter had a map of the UK showing where WD patients known to the Group, either through membership of WDSG-UK and/or belonging to the WDSG-UK Facebook Group, lived. This year, I thought it might be interesting to see what meds we, as patients, are taking to manage our copper levels and whether or not there are regional variations. Of course, with Wilson's disease being a rare condition many of our patients live in one part of the country but are treated and have their medication prescribed by doctors in another part, so it is difficult to draw clear conclusions from the chart.

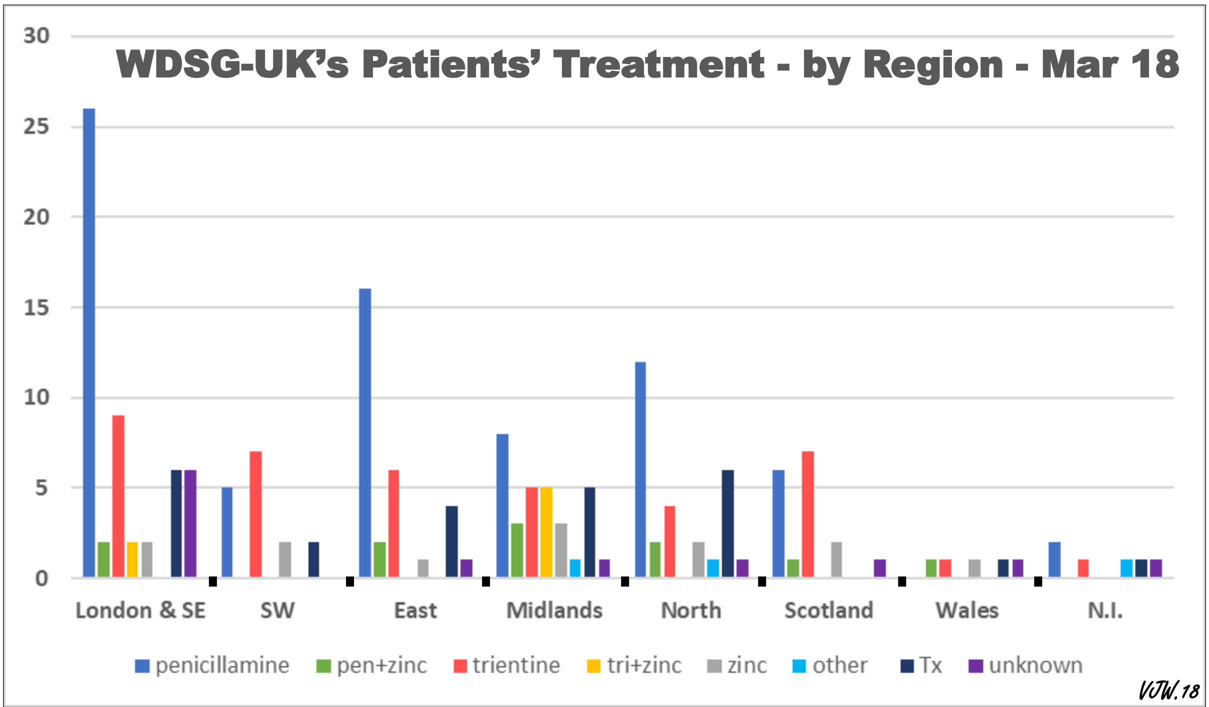
There must be many more patients in the UK unknown to the Group. The incidence of Wilson's disease is roughly 1:30,000. That being the case, one would have expected there to be around 2,000 patients, but that's highly unlikely and I've only managed to contact **186** of them! For the sake of this study, I have split the UK into 8 regions: **Greater London and the South-East**, the **South-West**, the **East**, the **Midlands**, the **North**, **Scotland**, **Northern Ireland** and **Wales**. I provide a key underneath showing which counties are included in each region.

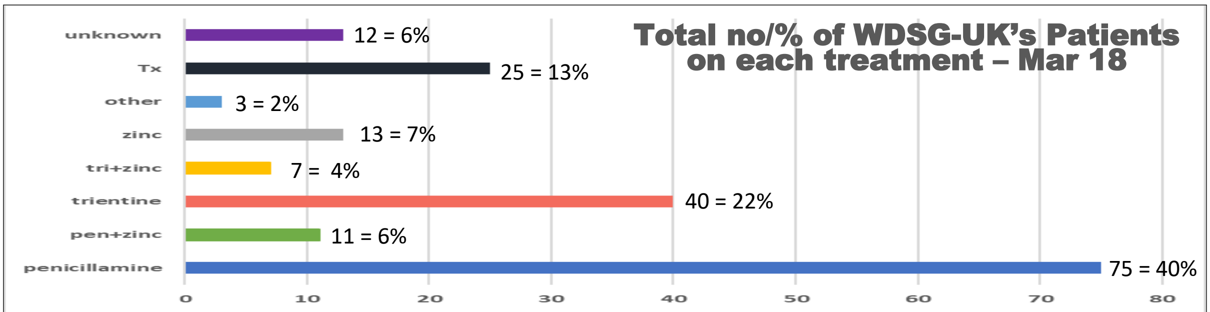
This year it won't be immediately apparent if you have been included in the chart or not. If you didn't pass on your medication details to me, then you will be classed as "unknown" for the purpose of this chart. And so that statistics from this year equate to those from last, I have included a bar representing patients who have received liver transplants (**Tx**). It was quite an undertaking I can tell you: thanks to everybody who took part!



*With special thanks to **Giuseppe Cardone** for this wonderful map*

Key to English Regions	
London & SE	Greater London, Kent, Sussex, Surrey, Hants., Berks., Bucks, Oxon.
SW	Cornwall, Devon, Somerset, Dorset, Wilts., Avon & Glos.
East	Norfolk, Suffolk, Essex, Cambs., Hunts., Beds., Herts.
Midlands	Herefords., Worcs., Warks., MK., Northants., Leics., Salop, Staffs., Derbys., Notts., Lincs.
North	Greater M/c, Ches., Lancs., Cumbria, Humberside, Yorks., Durham, Northumberland.





How many Wilson's Disease Patients live in England?

Mary Bythell, Head of Rare Disease Registration, National Congenital Anomaly and Rare Disease Registration Service—*NCARDRS* within **Public Health England** (PHE) is working on a project to identify people with Wilson's disease in England thereby providing a national prevalence rate for the disease. At the same time, information will be collected about diagnosis and treatment to help commissioners make the right healthcare decisions and improve patient care. Please contact NCARDRS phe.ncardrsrd@nhs.net, if you want to discuss any aspect of the project with her. This is the first project of its kind that NCARDRS is carrying out and Mary took the opportunity on Rare Disease Day — 28 February 2018 to post the following blog:

"Public Health England (PHE): *Wilson's Disease Pilot*

RAREDISEASEDAY.ORG

Why we need to count the people who have rare diseases?

The National Congenital Anomaly and Rare Disease Register (NCARDRS) has been working with stakeholders in the rare disease community to find out what our rare disease priorities should be. The answer that comes up again and again is "to count the number of people living in England with rare disease x".

Although each of the **6000+** recognised rare diseases affect **less than 1 in 2000** of the UK population, collectively rare diseases are not rare and approximately **3.5 million people** in the UK suffer from them.

More data is being collected about our health than ever before. Some data sources contain a small amount of data about a lot of people, like Hospital Episode Statistics and prescription data. Other sources meanwhile contain a mind-boggling amount of data on a smaller number of individuals, like molecular genetic data. Naturally people might imagine that with all of the available data, questions like that have already been answered and if they have not, shouldn't it be just a matter of looking for the answer in the right place?

The challenges of collecting data on rare diseases

There are many challenges associated with collecting data on rare diseases. Fragmented data systems pose logistical obstacles and routine health data is coded in a way in which rare diseases cannot be identified easily or at all. People are diagnosed with rare diseases throughout their lifetime – from before they are born until well into old age and the diversity of rare disease means that people can be under the care of virtually any medical speciality. Finally, because there are between 6000—8000 rare diseases, of which over 4000 fall under the remit of us in the NCARDRS, the sheer number makes the task extremely onerous.

As a result of these challenges, very little is currently known about a large proportion of rare diseases, including the number of individuals who have been diagnosed with a particular condition. The national registration of these conditions and collection of information about them is crucial in advancing our knowledge, and subsequently enabling improvements in the care and medical treatment of people living with a rare disease.

The role of NCARDRS

NCARDRS has made great strides in data collection of congenital anomalies, some of which are rare diseases, since Public Health England took over congenital anomaly registration in 2015. This has been done by building up records from multiple data sources until the clinical narrative is complete. This approach will be the same for other rare diseases, but will take time.

In the meantime, we are taking a pragmatic approach and are collaborating with others in the rare disease field so that our work is joined-up. We are identifying where relevant data is less difficult to collect and starting there. For those diseases where data collection is more difficult, we are harnessing the energy and curiosity which drives many of those in the rare disease field to help us find new, sustainable means to collect the information we need.

For example, our current work includes a proof of concept project on **Wilson's disease,** a disorder of copper metabolism which can have a devastating effect if it is not diagnosed early. Working with the British Association for the Study of the Liver: Wilson's Disease Special Interest Group, we are carrying out a project to identify **all** current cases of Wilson's disease in England and finding a way of making the reporting of future cases to NCARDRS routine. This is a first, and the data we collect will help inform how healthcare is delivered to patients with Wilson's disease as well as how data can be collected on similar rare diseases.

Addressing the challenges of collecting data on rare diseases is still very much in its infancy. We need to continue to collaborate with organisations in the field to identify approaches we can take to obtain the necessary information. The ultimate aim is to facilitate better, more targeted healthcare, benefiting those living with rare disease and their families."

Members' News 2017-18

Our President **Dr John Walshe** would like you to know that he is still alive and kicking (not to mention ticking over quietly) and that business goes on as usual in the Walshe household! He can look forward to being ninety-eight next month and we very much hope that he stays the course for another couple of years, at least, in order to hear from the Queen!

Dr Walshe at Wimpole Hall — Christmas 2017

I speak to him regularly and try and visit him when I can, but we haven't been very far together over the past twelve months. In fact, the only excursion of note was that of a short trip to another National Trust property, the nearby Wimpole Hall. Unfortunately, we chose a day just before Christmas, when not only was the soup **cold**, but the restaurant was teeming with people and hearing one another speak was practically impossible! However, we did manage afterwards to commandeer somebody to drive us around the gardens in a buggy, and although slightly on the cold side it still proved a worthwhile experience.

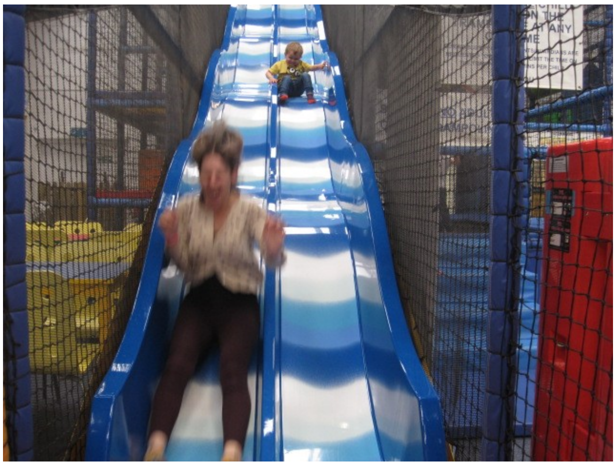
Occasionally I am called upon to facilitate a visit from one of Dr Walshe's fan base and recently it was the turn of Dr Sam Shribman from UCL, London, who had been encouraged to come by Dr Godfrey Gillett (with whom he runs a Wilson's clinic at Queen Square every month). He arrived with a barrage of questions that Dr Walshe fielded admirably. On this occasion, we lunched at home and enjoyed banter around the kitchen table, but normally when I see Dr Walshe, we pop across the road to the Community Hall where we avail ourselves of **hot** soup and paninis provided by the ladies in the village.

Since my last visit to see him I understand that the *Wellcome Foundation for the History of Medicine* has taken all his important clinical data, amassed since he arrived back in the UK from America in 1955 at the beginning of his clinical career. Apparently, it is going to be stored in a cave in Wales, but we have no plans to visit — at the moment! For those of you who are not familiar with Dr Walshe, he is a world authority on Wilson's disease and discovered penicillamine and, through his friend Hal Dixon, trientine, as effective chelating agents for copper. He has devoted his entire professional life to the management and treatment of over three hundred patients worldwide and he continues to take an interest in all of us today, offering advice and encouragement, when needed. He looks forward to attending our meeting in the summer and catching up with patients, old and new.

As a maths teacher, **Katie Hibbard's** husband Ryan has to attend an examiners' meeting in Cambridge every year, so Katie takes advantage of this and joins him for a mini break, away from the family home in Blyton, Lincolnshire.

On this occasion last year, she and I met up again with the aim of entertaining her two year old son, Jacob, with a trip to the Farm at Wimpole, where there are a range of activities popular with young children. Unfortunately, the weather was not in our favour so we resorted instead to visiting *Whale of a Time,* an Indoor Soft Play area nearby.

Katie enjoyed this somewhat drier experience enormously, as can be seen here in the photograph. Shortly after this picture was taken, however, it was pointed out that there was an upper age limit for playing on this equipment which, it is fair to say, Katie had exceeded – *significantly*!



Katie in playful mood with Jacob coming a gallant second!

Ashok Pandit is a 27 year old Wilson's disease patient from Kathmandu in Nepal, who has become familiar to us all through his articles in the newsletter. He was the youngest of three children and in 1993, when he was only three, his older sister who was nine and brother who was seven both died within a month of one another and nobody knew why. Four years later, Ashok also became ill. He was admitted to hospital and as luck would have it a visiting American doctor saw him and suggested a diagnosis of Wilson's disease. He has been treated with penicillamine ever since, although from time to time obtaining his tablets has been challenging to say the least. Yet another misfortune befell the family, when in 2015 their house was badly damaged in the country's devastating earthquake.

Ashok—March 2018

Ashok writes,

"Greetings from Nepal to everyone! 2017 brought three main events in my life which I share with you:

Inspiration:

The year started with my encounter with Mrs Asha Goel, a very inspiring lady. She is originally from Haryana, India, but is currently living in Kathmandu. Her son, Anuj, is 22 years old, and I got the same thing in common with him as I have with you all i.e. Wilsons disease. The only difference between her son and me is the kind of medication we are on. Her son is on trientine and me on penicillamine.

She must have found me through *YouTube*. Her daughter 21 years old emailed me and mentioned their problems getting trientine and asked if I could help them. I had recently been through the trauma of not getting my penicillamine again. I immediately contacted them and was invited to her house in Kathmandu. I was so happy to see her so as she. She treated me like her son; I could feel her love towards me. She knew most things about Wilsons disease. I told her about my connection with WDSG-UK and she was happy for me to add her to your Facebook Group. I was wishing to see her son but he was out of the house. We talked about family. She told me she is Indian and have a business in Nepal. Although she couldn't get hold of trientine from India at that time, she said she could easily get me penicillamine from there, if I need. When she knew about my financial condition and how I am being funded for my medicine, she said , "Please don't worry; if you don't have money for medicine then I will provide it." I told her not to worry about trientine. I would help her every way possible. She then said that she would like to see me doing any work which would help me earn my living. I told her what I am doing and she showed confidence in me and said, "Go for it; you can do it!" Her every word inspired me more for working..

I came home and sat in front of the computer, trying to help her. I found the reason behind the shortage of trientine was its price hike, because of which the supplier in India stopped importing it. I was in regular contact with her. Finally, I found the solution. The solution was getting the licence on the personal level for her to import the medicine. I told her about it and shared the procedure for applying to get the licence. Meanwhile, she got medicine for next six months. Last time I talked to her, she said somehow the problems of medicine is solved now. She said she got a licence for importing it.

Career:

I took the first step in my career this year. As you know, I graduated from high school and began college, but then dropped out. So I needed to take a step forward to build my career. When I met Aunt Asha, I was learning graphic design. While learning graphic design, I showed my writing skills and revealed my knowledge of search engine optimization (SEO). I was offered a 3 months internship in SEO which I happily accepted and completed. I need to work, but at the same time we are about to rebuild our house and I am expected to help. I have registered the domain on my name <www.mustbedigital.com> and have started to work on it and I run a blog.

Building House:

As you know, the 2015 quake hit Nepal and with it our house. We continued to live there just in one room but in November 2017 the house was about to collapse. We had to move out. We used the materials from our old house and built a hut in which we started living. We are now able to sell the land and we got advance payment of 10 million Nepali Rupees. The cost of land is 25 million. We are all set to build our new house, which should begin in a week's time from now. The budget for our new house is 23-24 million Nepali Rupees.

We have hired the contractor on the condition that he will build the house with the materials we supply him. I am busy finding quality materials at the lowest possible price. We all are very happy and excited about our new house. I hope I will have photos of it to show you this time next year."

Members' Photo Gallery

Photos: Courtesy Anusha Joseph

Sam Panchal and friend

Kumari and her husband from Trinidad & Tobago

Andy and Lottie with Katie

Olivia with her cousins from S. Korea and Sam F's younger brother and sister

Linda with David & Keith Pereira

Jane Ridley

Oliver and his family

Maria with her mum and sister

Linda Asher and Ruth

One big happy family

A Date for your Diary — 2018-19

Date	Time	Event
Saturday 2 June 2018	**1000 - 1300**	**Colour Run MK—Ann-Marie Collcott will be taking part in this event to raise funds for the Group. To sponsor her, see** *https://uk.virginmoneygiving.com/AnnMarieCollcott*
Sunday 15 July 2018	**1100 - 1530**	**WDSG-UK Meeting and 8th AGM – Cambridge Rugby Union Football Club (52) Grantchester Road, Cambridge CB3 9ED.**

WILSON'S DISEASE MULTIDISCIPLINARY CLINICS

The Birmingham WD Clinic

Prof Gideon Hirschfield (Consultant Hepatologist) and **Dr David Nicholl** (Consultant Neurologist) hold a one-stop Wilson's disease clinic at **University Hospital Birmingham** on a Friday morning four times a year. This clinic offers patients the opportunity to have their management reviewed by a hepatologist and a neurologist at the same time and is intended to supplement otherwise established care. Referrals must come from the clinician looking after the patient and should be addressed to *Prof Hirschfield* at *Queen Elizabeth Hospital, Mindelsohn Way, Edgbaston, Birmingham, B15 2WB.*

The Sheffield WD Clinic

The Sheffield clinic is jointly run by **Prof Oliver Bandmann** (Consultant Neurologist), **Dr Godfrey Gillett** (Consultant in Clinical Biochemistry, Inherited Metabolic Disease, and Adviser to WDSG-UK) and **Dr Barbara Hoeroldt** (Consultant Hepatologist). Clinics take place every six months at the **Royal Hallamshire Hospital, Sheffield** on a Tuesday morning. Patients may be seen in interim clinics by arrangement. Referrals should be addressed to *Prof Oliver Bandmann, Department of Neurology, Royal Hallamshire Hospital, Glossop Road, Sheffield, South Yorkshire S10 2JF*. Either GPs or hospital specialists may refer to this Sheffield WD clinic.

Royal Surrey County Hospital NHS Foundation Trust & University of Surrey, Guildford

The Centre based from the Royal Surrey County Hospital (RSCH) is running a regular multidisciplinary clinic to assess and manage patients with Wilson's disease. The Team includes expertise in liver, movement disorder, chemical pathology and eyes, with access to international clinical trials. If you would like further information please contact the Centre Clinical Director, Professor Aftab Ala (aftabala@nhs.net).

Children's Clinic at King's College Hospital, London

There is a Wilson's disease clinic for children and young people at King's College Hospital which is run by **Prof Anil Dhawan** (Paediatric Liver), **Dr Tammy Hedderly** (Paediatric Neurologist) and a psychologist. The clinic is directed at patients who are complex with both liver and neurological involvement and referrals should be made via the Paediatric Liver Centre at King's or enquiries sent to **Kathleen Meader,** (kathleenmeader@nhs.net), PA to Prof Dhawan.

IN MEMORIAM

It was with great sadness that we heard of the unexpected death of **Sylvia Jean Penny** on 28 July last year aged **87**. Sylvia had lived in Torquay all her life and her funeral, which took place at the Victoria Methodist Church (where she ran so many fundraising events for our benefit), was packed full of family, friends and neighbours whose hearts she had touched. The eulogy described her as a lady who had devoted her entire life to helping others. Valerie attended the funeral on our behalf and we thank Sylvia's daughter, **Sheila**, for holding a collection in her memory which raised **£185** for the Group.

Wilson's Disease Support Group – UK

CONTACTS:

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Caroline Simms	Group Co-Founder, Committee Member and Liver Transplant Patient Adviser email: **caroline@wilsonsdisease.org.uk**
Mary Fortune:	Committee Member and Liver Transplant Patient Adviser email: **mary@wilsonsdisease.org.uk**
Dr John Walshe	Honorary President, World Authority on Wilson's disease
Dr Godfrey Gillett	Group Adviser, Honorary Member
Dr James Dooley	Group Adviser, Honorary Member
Dr Rupert Purchase	Group Adviser on trientine
Linda Hart:	Group Co-Founder, Adviser

Tell others about WDSG-UK

Please encourage anybody else that you know with Wilson's disease to join **WDSG-UK**

Inform your family, friends, consultant physicians, general practitioners and local MPs about the work of **WDSG-UK.**

The more people who know about **WDSG-UK**, the more we can promote a better awareness of Wilson's disease within the community and the better the chance of an early diagnosis.

If more copies of this newsletter or patients & families' correspondence lists are required, please contact Valerie.

We're on the web
www.wilsonsdisease.org.uk