Wilson's
Wilson's Disease Support Group - UK
www.wilsonsdisease.org.uk

NEWSLETTER

#wdsguk APRIL 2025

A very warm welcome to the 2025 newsletter on this our silver jubilee. It hardly seems like twenty-five years since Caroline and Linda founded the Group and arranged our first meeting at The Peacock in Nottingham. I reminisce a little later in the newsletter by writing about the history of the Group. We have grown from strength to strength since then, thanks to you, our members.

Nowadays, we have Bill as chairman about to start his third year. He has been a great asset to the Group representing us wherever he can. In August, he organised and hosted the educational video which has been a long time in the making, details of which he gives in his report. Before then, he gave a poster presentation on drug adherence in WD patients at the conference held by the European Association for the Study of the Liver (EASL) in Milan. We thank those of you who completed the questionnaire we circulated, the data from which he used in his talk.

Meanwhile, a big thank you to everybody who has contributed to the newsletter this year. In the medical section, Rupert has researched and written about a possible new treatment for patients—methanobactin, and Peter Bull, following on from his talk at last year's AGM, gives an account of how the ATP7B Wilson's disease gene was discovered in the early 1990s. Tom Shaw, a newly diagnosed patient, shares his patient story with us—or at least the first half of it which is five pages long. There is more to come! Tom is an English student at Durham University and clearly has a gift for writing. Should he become a best selling author one day, remember you read it here first!

Moving on to the news section at the back, we are delighted to report that love has certainly been in the air during 2024. Congratulations to all concerned. Also well done to committee member, Claire Stapleton, who has conducted some clinical research exploring the lived experiences of Wilson's disease patients, for which she has been awarded a Masters degree from the University of Manchester.

Seasoned members Sue and Anne-Marie write about their different holiday adventures, each of which has been of great interest to me. First of all I've never heard of a *quokka* before which Sue encountered in Australia and, after a lifetime of listening to the Shipping Forecast on Radio 4, Anne-Marie solves the mystery for me of the place name mentioned between the Mull of Kintyre and Cape Wrath: Ard-na-mur-chan Point. Never having seen it written down before and not speaking Gaelic, I couldn't decipher if it was a name made up of one word of four syllables, four words of one syllable or simply just a name made up!

What is clearer though is that this is the second year without anybody holding any fundraising events for us. Not that it matters, we are well in funds, but I do enjoy reading about them! I thought I might do some more Dingbat quizzes, but online clipart as was, is no more! I have, however, managed to scrape a few together for Abby's bumper puzzle page—which you'll find at the end of the newsletter. My thanks to Abby for the variety of puzzles that she offers: there should be something for everybody. But, if her puzzle page isn't enough, try naming all the faces on page 13. A prize to the first one who can name them all.

I am pleased to report that as far as we are aware there have been no shortages of penicillamine nationally in the past twelve months. This is welcome news. However, it did come to our attention that one of our members had amassed several unused bottles of trientine having been switched back to her original medication. At around £3,000 a bottle, trientine is too expensive to waste. Please let your consultant know if medicines you no longer use are still being prescribed to you.

Sadly, our webmaster, Michael McConnell, who has been running the website since 2008 is retiring at the end of July next year (2026). He has been wonderfully helpful over the years and we thank him for all that he has done. Should you have the expertise to host and maintain our website and be interested in doing so, please could you get in touch with one of us to discuss terms and our requirements.

Finally, our meeting and 15th AGM has been booked this year for Sunday, 20th July at our usual venue in Cambridge — details on *p4*. Please complete the form enclosed if you would like to attend (and we would love you to) and also please remember to renew your subs at the same time. The one form covers both and should be returned to me either through the post or by email—even if you pay by Bacs.

So all that is left is to wish you a very happy Eastertime. Good health, and we very much look forward to seeing you in the near future.

Valerie

IN THIS ISSUE ...

Chairman's Report for 2024-25

Another year has flown by and the WDSG-UK committee has been busy. The AGM last July was well attended and regular Zoom meetings continue. We had the inaugural *World Wilson's Disease Awareness Day* in December on the birthday of Samuel Kinner Wilson and in conjunction with this was the hosting by WDSG-UK committee member Claire Stapleton of the third international meeting of WD associations in January with 24 representatives attending from at least 16 different countries. The plan is to form a steering committee with task forces appointed to address individual topics such as aiming to standardise copper content in food, co-ordinating the WD International Awareness Day, communications and funding initiatives. There will be further meetings in 2025. In keeping with international collaboration, Claire also attended the WDA (American association) annual conference in October 2024.

An important accomplishment for WDSG-UK in conjunction with the Pharma Company, Orphalan, was the recording in London and publication of a 5 minute educational video on early diagnosis in Wilson's disease. It has been viewed over 400 times but more work is needed to ensure it is reaching the intended target audience, namely general practitioners and physicians. The video is accessible via the WDSG-UK website (WDSG-UK :: What you should know about Wilson's disease), but is also on *'X'* (previously Twitter).

The idea is to ask various medical societies to 'retweet' it to their membership for maximum coverage. It is hoped at the very least that it will enable a few patients to be diagnosed before they run into trouble. I should like to formally thank my colleagues (*from left to right above*) Sam Shribman, David Okai, Tammy Hedderly and Aftab Ala for their kind participation in the making of this video.

Various other educational events have occurred over the year including the 3rd International Wilson's disease meeting at Aarhus in Denmark last May, which Val and Claire attended, and an invited speaker on WD at the annual British Association for the Study of the Liver (BASL) meeting which took place in Harrogate last October (Peter Ott from Denmark). There is a plan for a Rare disease masterclass at Kings, London, in June which will feature WD as one of four topics up for review and discussion.

The BASL Wilson's Disease Special Interest Group (BASL WDSIG), had its 9th meeting in London on 6th December which was organized by Prof. Aftab Ala, BASL's Chair for Rare Diseases and the Wilson's Disease sub-SIG lead. It was an all day event with 12 speakers and by coincidence took place on the *World Wilson's Disease Awareness Day* mentioned earlier. There are 379 people registered with the WDSIG of whom around 35 attended the session. These included representatives from neurology, hepatology, psychiatry, metabolic disease, clinical science, genetics, chemistry, ophthalmology, imaging and ourselves.

The WD SIG is continuing its pursuit of a better understanding of the importance of psychiatric symptoms which are often present in patients years before WD is diagnosed. We are fortunate to have in our midst Dr David Okai, Consultant Neuropsychiatrist at the Maudsley Hospital, London which recently celebrated its centenary. David features on our educational video and through him James Liu Yin has been able to investigate the diagnosis of WD amongst thousands of patients who have been through the Maudsley. This should pave the way for improved awareness and testing in younger people with mental illness.

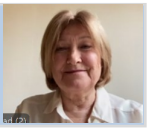
Following on from the WD SIG Guidance published in 2022, EASL has updated its clinical practice guideline on WD previously published in 2012. The 2025 guideline, hot off the press, includes new recommendations for 'asymptomatic' WD, emphasis on 'relative exchangeable copper', if available as a laboratory test to improve diagnostic accuracy, additions to the management of WD presenting as acute liver failure and updated evidence for monitoring patients on therapy. As progress in diagnosis and management of WD continues year on year this is a valuable addition for clinicians. All newer guidelines (UK, European and American) emphasise the importance of initial brain MRI, even in the absence of overt neurological symptoms, and the role of genetic testing which is now more readily accessible.

There is a lot of interest in the naturally occurring compound 'methanobactin' as a potential new treatment for WD which Rupert Purchase has written about later. You will also hear more from Dr Peter Bull who spoke at the AGM about his seminal research pinpointing the gene for WD (ATP7B). On the research front, WDSG-UK is helping fund a study in Sheffield (Professor Bandmann) on a novel angle in WD. Gene therapy trials continue but just Ultragenyx at the moment as Vivet has put their trial on hold. One uncertainty is the planned disbanding of NHS England through which trientine is centrally commissioned. New opportunities may arise though to argue for financial support for multi-disciplinary WD clinics.

Finally, I would like to thank my fellow committee members for their contributions to WDSG-UK over the past 12 months and I wish everyone well for the remainder of 2025.

Bill Griffiths, March 2025

Notices



Donations and Fundraising—Income

Thank you to everybody who made generous donations with their subscriptions last year and those of you who have set up regular standing orders to us. A special mention is made of Elizabeth Nicolson for collecting £500 from family and friends in lieu of presents at her recent special birthday celebration, Maddy Joseph for raising funds of £1,750 through the ***GoodHub*** online platform, John Turley's family for holding a collection in his memory and donating the proceeds of £133 to us and to Tanya Parker and Giuseppe Cardone for donating £425 between them through their workplace non profit schemes. Thank you too to Joan Smith.

Should you wish to hold a sponsored fundraising event, then please remember that our online fundraising platform *GoodHub* is an easy and efficient way of collecting sponsorship. They are now also accepting ApplePay and Google Pay through their website. *GoodHub* also collects Gift Aid on our behalf, where appropriate. Of course, all donations made to WDSG-UK can be Gift Aided. Gift Aid forms can be downloaded from our website or obtained from Valerie direct.

Discretionary Gifts & Research Funding —Outgoings

WDSG-UK gave discretionary gifts totalling £750 to members at Christmas 2024. It has also recently given further funding in the sum of £12,500 to SITraN, Sheffield, towards their research into bioenergetic dysfunction in WD (see p 5).

HSBC Bank Charges for Charity Accounts

Now that our bank HSBC has introduced bank charges on charity accounts for over the counter transactions, we thank those of you who responded to our request to make payments to us electronically rather than by cheque. If you are able to pay your annual membership by bank transfer or even better by setting up a standing order, that would be much appreciated.

WDSG-UK Meeting for Families and Carers of WD Patients— 17 November 2024

A suggestion was made at our AGM last July that a virtual meeting be convened solely for carers so that they could come together to discuss their individual concerns. All relevant members of the Group were invited by email to attend and the meeting, run by Claire and hosted by Liz Wood, went ahead with 10 attendees. Those who had been living with a family member with the condition for many years kindly joined us to share their own experiences and give advice to those for whom Wilson's disease has only recently become a reality. The subject of anxiety was a strong feature in discussions, together with difficulty obtaining meds periodically and accommodating all the different appointments involved in regulating patient health. We hope to run another such session in due course. Please let us know if you are interested.

WDSG-UK Rare Disease Coffee Morning via Zoom — Sunday, 23 February 2025.

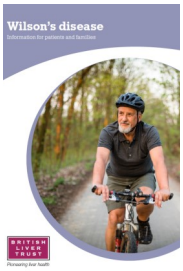
The 5th WDSG-UK Rare Disease Day Coffee Morning Zoom hosted by Liz took place on the last Sunday in February. Rare Disease Day was first introduced in 2008 (which was a Leap Year) by the European Organization for Rare Diseases. It takes place globally on the last day of February, which every four years is indeed a rare day! As we as a Group are spread out all around the UK and beyond, it is nice to have the opportunity to come together informally once a year.

This year we had 15 attendees together with Drs Godfrey Gillett, James Dooley and Sam Shribman, to whom we are indebted. At the invitation of Godfrey we were delighted to welcome also Dr Flori Savi who runs the paediatric genetic services in Sheffield. Flori took an active part in discussions (we were split into 2 *break out* rooms to begin with and then came together for the rest of the session), advising on the importance of and how to request genetic testing for close family members. Flori is planning to attend our AGM in the Summer, should you have further questions for her.

Other topics discussed included prescription charges, exemptions, pyridoxine (Vit B6) deficiency and seizures in WD patients. And finally, Laura told us about the Viking Genes Study that is running in Shetland, Orkney and the Western Isles, with which she is closely involved *(see p19).*

Liver Patients Group (LPG) and The British Liver Trust (BLT) - Meeting 4 October 2024 via Zoom.

Valerie attended this meeting which represents different liver patient advocacy groups and is chaired by Paula Hadford, CEO of the PSC (Primary Sclerosing Cholangitis) Group. Pamela Healey (CEO of BLT) and Chair of the UK Liver Alliance (UKLA) reported on their work over the previous twelve months. BLT joined forces with the Children's Liver Disease Foundation (CLDF) in April 2024 and together they are working on a strategy over the next five years to influence national policy on liver disease to help improve early detection, treatment, management and outcome in patients. BLT continues touring towns and cities with a high prevalence of liver disease offering from their mobile units free screening and fibroscans (non-invasive machines for detecting liver disease) to all. Detecting liver disease early is crucial for improved outcomes in all patients and would certainly benefit patients with Wilson's disease whose symptoms have not yet become manifest.



Don't forget that the British Liver Trust, which is an umbrella group for all liver disease patients in the UK, has produced an excellent booklet on Wilson's disease which can be downloaded from their website https://britishlivertrust.org.uk/wp-content/uploadsWilsonsDiseaseweb DEC.21.pdf or alternatively a single hard copy can be ordered free by emailing info@britishlivertrust.org.uk or by asking us.

NHS BT (Blood & Transplant) Organ and Tissue Donation & Transplantation Directorate (ODT)

There was no meeting this year between NHSBT and Liver Patient Groups. However, NHSBT has reported that there were 10 liver transplants carried out on WD patients between 2020-2023 inclusive.

Cambridge Rare Disease Network (CRDN) RAREfest 24

CRDN was set up in 2015 to address the challenges faced by people affected by rare diseases and to find ways of improving lives and bringing hope to those affected by rare conditions. To this end patient groups, scientists, researchers, clinicians, pharma and biotech companies come together to learn about and share the latest in innovative science, cutting-edge technology, patient histories and new treatment regimes.

I attended the 9th meeting of RAREfest on Saturday, 23 November, at the Guildhall in Cambridge at which there were short films, talks and panel discussions—with hands-on exhibits to educate and entertain.

Wilson Aarhus 2024 Symposium— 2-5 May 2024

The Wilson Aarhus Symposium is an International meeting held in Denmark every two years for WD specialists across the globe to come together and discuss the latest findings in the diagnosis, treatment and management of Wilson's disease. The third such meeting in May was held in Aarhus at The Cornwell Hotel and was superbly organised by Prof Peter Ott and Dr Thomas Sandhal, WD specialists at Aarhus University Hospital.

There was a good representation of doctors from the UK including Prof Oliver Bandmann, Dr Sam Shribman, Profs Aftab Ala and Anil Dhawan and Dr Chris Harrington (all of whom gave short talks), together with Dr Godfrey Gillett, Prof Tom Warner and Miss Maggie Burrows. The Symposium is sponsored through a Memorial Foundation set up by a Danish Engineering Company in 1968 which has a family connection with Wilson's disease.

Claire and I attended the meeting (together with patient representatives from Germany, Spain, Poland and the US) as guests of Wilson Patientforeningen, the Danish Patient Association. Our hosts, Lisbet Ottesen, Susanne Nielsen

and Brien and Astrid Laursen put together a varied and engaging patient programme. We had a pizza supper on the first evening, attended various medical sessions throughout the conference, went sightseeing around Aarhus and took part in the first international virtual meeting of patient representatives with the aim of better collaboration between associations in the future.

Wilson's Disease Global Alliance formerly *The International Wilson's Disease Community*

Originally set up for Spanish speaking countries as a WhatsApp Group in 2022 by Rodrigo Valdez of the Argentinian WD Association, the WD Global Alliance gathered momentum around the time of the Aarhus meeting and now has a membership of 25 different Support Groups and Associations worldwide. Claire and I are UK participants with Claire taking a leading role in its running.

It held its first Zoom meeting on August 31st, hosted by our friends in Spain and supported by Rhonda Rowland in the US. At the meeting, amongst other things it was agreed that communities would come together to mark the 6th December as *World Wilson's Disease Awareness Day,* being the birthday of Samuel Kinnier Wilson who first described our disease. Posters were created by each community and circulated on social media, and included the letter "W" formed by a patient's hands under the slogan *Leave No-one Behind.* WDSG-UK publicised the day on our website and in our Fb Group.

Since then, Claire has hosted the second Zoom meeting on 18th January 2025 from which the new name of the Group — Wilson's Disease Global Alliance—was agreed. If you would like to get involved in some way in this year's *Wilson's Disease Awareness Day*, please let us know.

WDSG-UK Management Committee Meetings

During 2024-25 the management committee met three times via Zoom—in May, October and January.

WDSG-UK Annual Meeting & 14th AGM—7 July 2024.

The 14th WDSG-UK AGM took place at Cambridge RUFC, on Sunday, 7thJuly 2024. The accounts for 2023-24 and the Minutes of the 13th AGM were circulated and agreed and the election of officers and members of the WDSG-UK Management Committee for 2024-25 took place. **Bill Griffiths, Mary Fortune, Liz Wood, Debbie Buckles, Claire Stapleton** and **Valerie Wheater** put their names forward to serve on the committee and were duly elected**.** For more details of the day please see the report on *pp 6-7.*

Debbie Buckles will be standing down this year after serving on the committee for 5 years. We thank her for all her support and dedication. If you would like to join the committee, perhaps feel that you could offer advice and expertise in areas we don't cover, then please get in touch with me at val@wilsonsdisease.org.uk.

WDSG-UK 15th AGM— Sunday, 20th July 2025

This year's AGM will take place at the Cambridge Rugby Union Football Club, Grantchester Road, CB3 9ED on Sunday, 20th July from 1130—1530. We would love you to join us. The booking form is enclosed with this newsletter. Please complete and return it as soon as possible. Thank you.

Bioenergetic dysfunction in Wilson's Disease—A Research Project

by the University of Sheffield/Sheffield Teaching Hospitals NHS Trust

This study, which is looking at mitochondrial function in people with Wilson's disease, was launched in January 2025. Mitochondria are found in almost every cell in the body and are responsible for producing energy. This study aims to identify whether we can detect mitochondrial dysfunction in people with Wilson's disease using brain imaging and blood tests, and is being carried out in **Sheffield** by **Dr Sophie Voase** under **Prof Oliver Bandmann.**

What do we know about how the mitochondria function in people with Wilson's disease?

Mitochondrial dysfunction has been heavily implicated in Wilson's disease. The build up of copper has been shown to cause mitochondrial dysfunction in both liver cells of humans with Wilson's and animal models of Wilson's. However, so far there has been limited research looking at how mitochondria work within the human brain of people with Wilson's.

What do we hope to find out?

The aim of the study is to identify whether mitochondrial dysfunction can be detected in brain tissue and in the blood in people with Wilson's disease, as so far, most of the evidence is limited to animal and cell models. The secondary aim is to compare people with neurological, hepatic, mixed neurological-hepatic, and presymptomatic Wilson's disease, as well as with healthy controls, to determine if there are differences in mitochondrial function between these groups. If differences are found, this could help to explain why there is such a range of symptoms in people with neurological Wilson's and may also help to explain why there are different responses to traditional therapy options. If we are able to reliably identify these changes in mitochondrial function in people with Wilson's, this could allow us to design future medication trials using 'mitochondrial rescue' medications in addition to existing medications for Wilson's.

What does the study involve?

People with Wilson's disease:

The study involves three main parts - clinical assessments including neurological examination and cognitive tests, an MRI brain scan and blood tests.

1. ***Clinical Assessments***

   The Unified Wilson's Disease Rating Scale (UWDRS) will be used to quantify the symptoms and signs of Wilson's disease in each person. This scale looks at neurological symptoms and signs on neurological examination, symptoms of liver disease and psychiatric symptoms related to mood and cognition. Each participant will also undertake a cognitive test which looks at different areas of cognition, including language, spatial perception, short-term and long-term memory. The clinical assessment will take around 2 to 2.5 hours to complete.

2. ***MRI Scan***

   All participants will undergo a special type of brain MRI scan. This scan involves looking at the amount of energy produced in different parts of the brain. We will also look at changes in the structure of different areas of the brain and how they connect to each other. The MRI scan will take around 1 hour to complete, with at least one break built in.

3. ***Blood Tests***

   The aim of this part of the study is to identify whether we can detect changes in how the mitochondria function on blood tests. We will also look at changes in the specific type of DNA found in the mitochondria, the mitochondrial DNA.

We hope to compare these between the different types of Wilson's disease. We hope to recruit around 10-15 people with neurological, 5-10 people with hepatic, and 5-10 with mixed or presymptomatic Wilson's disease.

Healthy controls:

To ensure that the changes detected are due to Wilson's disease, we also hope to recruit up to 10 healthy controls. Healthy controls will undergo a neurological examination and cognitive tests (around 1 hour) and an MRI scan (around 1 hour).

Where?

The study visits are carried out at the Royal Hallamshire Hospital in Sheffield. The visits can be split into two separate visits (clinical exam and bloods, and MRI) or all completed in one day. We can work with you to plan visits around other commitments such as work or family.

We can refund travel expenses (standard rail fare, petrol costs etc) and reasonable hotel expenses. Recruitment commenced in January 2025, and we hope to continue recruiting throughout 2025.

Who do we need and how do I get involved?

We are keen to ensure that we have a good representation of people with Wilson's across different age groups, sexes and ethnicities. We would also like to recruit more people who have been diagnosed with Wilson's disease in the past 2-3 years or have had a relapse of symptoms (either hepatic, neurological, or psychiatric) within the past six months. Finally, we need more healthy, female volunteers to act as controls for the Study. If you are at all interested in participating, please email sophie.voase@nhs.net.

We would like to thank all patients and family members who have put themselves forward already, as well as WDSG-UK for contacting patients on their WD Patient Register-UK and who are supporting the work very generously financially.

WDSG-UK Meeting & 14th AGM
Cambridge, Sunday 7th July 2024

Another very successful AGM took place in Cambridge last Summer with 50 members in attendance. Amongst them, we were very pleased to welcome four new faces, the youngest of whom had travelled all the way from Norway; the oldest from Scotland. Others came specifically to support newly diagnosed patients by sharing their own stories with them. To them, we are particularly grateful. Unfortunately, committee member Debbie Buckles was too unwell to travel that day but we thank her for sending the fabulous flowers as centre pieces for the tables.

Refreshments were served on arrival and Claire manned the reception downstairs greeting everybody as they arrived. She is the mother of a 19 year old patient whose Wilson's disease journey has been fraught with difficulties such that she is still in hospital four years after diagnosis. Despite this, Claire has thrown herself into helping the Group in whatever way she can attending the biennial International Wilson's disease meeting in Denmark last May, the Wilson Disease Association conference in North Carolina in October and taking a key role in the newly formed Wilson's Disease Global Alliance as mentioned on *p4.* And when nobody else came forward to act as photographer for the day, Claire kindly stepped into the breach.

Vice-chair, Liz Wood, slickly ran the meeting. She began by welcoming everybody and thanking Drs. Godfrey Gillett, James Dooley and Sam Shribman for giving up their valuable time to join us yet again. We were especially pleased to welcome Dr Georgeta Taylor, neurologist at the Salford Royal Infirmary, who had made the journey down from Manchester to be with us for the day.

Liz then introduced our speaker, Dr Peter Bull, who with the help of many props gave us a wonderful and entertaining overview of his involvement in the discovery of the ATP7B Wilson's disease gene while doing a post-doctoral fellowship in the early 1990s at the Sick Children's Hospital in Toronto. For those who were not at the AGM, he has written an equally interesting article about this which you can read on *pp 9-11.*

Our chairman, Dr Bill Griffiths, then convened the short 14th Annual General Meeting in which he gave us his annual report on the activities of the Group, before asking members to agree the Minutes of the 13th AGM and accounts for 23-24, which had been audited. Committee members for the following twelve months were then proposed and seconded *(see list on p 4).*

An hour and a quarter was set aside for a delicious buffet lunch provided by in house caterers Cantab Catering. This interlude gives everybody plenty of time to mingle, make new friends and catch up with old. It is particularly gratifying to see recently diagnosed patients coming together and

Peter Bull giving his talk ...

to an attentive audience

lunching

making friends. Two such patients had, by coincidence, both been diagnosed the previous year while in their first term at University. Even more of a coincidence was that out of all the weird and wonderful subjects available for students to study nowadays, they had both embarked on the same degree — that of English Literature!

Also during the lunch break raffle tickets were sold. This year we had a fantastic range of prizes. These were generously donated by friends and family with Group members adding to the mix. We thank Anusha for donating one of her diamond paintings expertly crafted, Katie for sharing one of her *Cakes and Bakes* (as highlighted in last year's newsletter) and absent members who sent money orders from which we bought prizes of their choosing. The grand sum of £244 was raised in total and we thank everybody who contributed to the raffle's success. The best ever!

After lunch, the doctors, with Rupert Purchase—former chairman of the Group and trientine specialist—came together to form a panel to answer patients' questions. This year they were asked if and when gene therapy might be available on the NHS, was ongoing fatigue a common feature of Wilson's disease, will Dimercaprol be available in future in the UK and should medication be calculated according to the weight of a patient or based on the patient's dietary copper intake. We thank the doctors for giving their expert opinions on these subjects.

The meeting finished at 1530 with the customary Group photograph of patients and doctors. Unbeknown to us, while the meeting was taking place the Rugby pitches were filling up with vans and trailers. It turned out they were there for the filming of a new thriller set in Cambridge called *After the Hunt* in which Julia Roberts stars. I found this out the following morning when I also learnt that Julia had been present briefly the day before. What a pity we hadn't known; she could have joined us for tea!

This year's meeting will take place on Sunday, 20th July. We hope you'll be able to join us. You never know who might be there!

The Doctors Answering our Questions

The Raffle Table

Hollywood comes to Town

Our customary Group Photo courtesy Vishaal Ranjitsingh

Methanobactin – a new drug for Wilson's disease?

Introduction

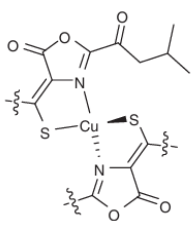
By studying the chemistry of the natural world, we can better understand and utilise nature's diversity. One major benefit of these investigations has been the discovery of new drugs from chemicals biosynthesised in nature – its 'natural products'. Many examples spring to mind, for example quinine (an antimalarial), penicillin (an antibiotic) and paclitaxel (an anticancer drug, first isolated from the bark of Pacific yew trees (*Taxus brevifolia*)). To this list we can now add **methanobactin**, which is secreted by some methane-oxidizing bacteria whose powerful copper-binding properties have attracted the attention of clinicians with Wilson's disease patients.

What is methanobactin?

A methane-oxidising bacterium is an example of a **methanotroph**. *Trophē* is the Greek word for nourishment (nutrition). Using methane as their 'nutritional' (carbon) source, methanotrophs can convert methane into methanol with the assistance of methane monooxygenase (MMO) enzymes. One of these MMO enzymes has a dependence on copper for its enzymatic activity. In order to satisfy this need for copper, it was realised in the 1990s that some methanotrophs can secrete a chemical that can 'capture' i.e. chelate copper from the bacterium's environment for use by MMOs. This copper-chelating chemical is named **methanobactin**. The methanobactin isolated from a methanotroph – a mutant strain of the bacterium *Methylosinus trichosporium* – was characterised in 2004 as a small peptide with specific attachments which can strongly bind copper with an exceptionally high stability constant.

More methanobactins have since been discovered in other methane-converting bacteria, but all have similar distinctive copper-binding features.

Because of the detrimental effects of anthropogenic methane, the methane-consuming properties of methanotrophs are of much interest to environmental scientists.But the role of methanobactin in methanotroph activity was noticed by the Wilson's disease community, and in 2011 work with methanobactin in an animal model of Wilson's disease was published leading to the conclusion that "the outstanding affinity and selectivity for copper [in rat liver] makes methanobactin a promising candidate … for the initial treatment of Wilson disease patients presenting with hepatic symptoms".



Copper-binding site of a methanobactin

Methanobactin and Wilson's disease. Can methanobactin make the transition from animal model to patient?

Since 2011, investigations of methanobactin in animal models of Wilson's disease have continued. Rapid depletion of hepatic copper overload in these animals and its elimination in faeces *via* biliary excretion is observed. Discussions of the benefits of treating Wilson's disease patients with methanobactin are taking place. But there are several obstacles before methanobactin's therapeutic potential can be realised:

1. There is currently no viable method for the production of gram / kilogram batches of methanobactin. This suggests methanobactin will be an extremely expensive drug to administer.
2. Methanobactin cannot be given orally (because its peptide bonds will not survive the conditions of the gastrointestinal tract). In animal work, methanobactin is given intraperitoneally. (Intraperitoneal refers to the administration of a substance by injection into the abdominal cavity, and it is often used in laboratory studies and clinical settings to achieve high local concentrations while minimizing systemic side effects).
3. In the absence of copper, methanobactin can bind other metals, notably iron and zinc.
4. The effect of methanobactin therapy on hepatic copper enzymes and the drug metabolising cytochrome P-450 enzymes will have to be considered.

Conclusion

Methanobactin belongs to a class of natural products called **metallophores** ('metal carriers'; 'phore' from the Greek *phérō*, "to bear, to carry"). Many other metallophores have been discovered which are capable of sequestering a wide range of metals. Understanding the biosynthesis and chelating properties of metallophores is yet another facet of the chemistry of the natural world.

Rupert Purchase
February 2025

Finding ATP7B

by Dr Peter Bull

When I was doing my PhD in London in the late 1980s, I remember being fascinated by the ongoing drama of two groups of scientists racing to identify the gene lesion causing cystic fibrosis. Robert Williamson at St Mary's Hospital in London led one of the groups and Lap Chee Tsui in the Genetics Department at The Hospital for Sick Children Research Institute in Toronto, led the other. In August 1989 we heard that Lap-Chee Tsui's group had identified a lesion in a gene, later called CFTR, in a patient with cystic fibrosis. I was extremely excited by this. At the time I was studying in the Department of Biochemistry at UCL and was spending my days growing small chunks of human DNA in viruses that are able to infect and multiply within bacteria.

Shortly after the discovery of CFTR, I noticed an advert for Postdoctoral Fellowships in Toronto, in the same department where the CFTR gene had been discovered. I applied and shortly heard back from them inviting me for an interview. After I finished my PhD, I saved up some money from a temporary job at a lawyer's office and flew to Toronto. I talked to several different scientists. One of them was Diane Cox. She excitedly told me about the work she was doing on Wilson's disease. They had found 'linkage disequilibrium' between the Wilson's disease locus and one of their genetic markers. She was such a pleasant and friendly person and this sounded great, so I accepted an offer to work in her group. To explain why she was excited let me first explain what linkage disequilibrium is and how inheritance works:

We look like our parents. It is intuitively straightforward why we look a bit like both our parents. It's because their DNA mixes together when the sperm meets the egg. But why do all brothers or all sisters not look identical? This is because we inherit DNA in chunks called chromosomes, selected at random from the DNA supplied to the ovaries and testes where our gametes are made. Each egg and sperm cell receives an individually shuffled selection of chromosomes like a hand of playing cards that represents half the full pack.

DNA varies between individuals. What is it that makes the DNA from one person different from the DNA from another person? Differences in the DNA are called "alleles". Alleles are usually small differences in the sequence of chemical subunits that make up our DNA. More about this later. Unless we have a rare condition caused by the deletion of a very large piece of DNA, we all have the same set of genes as each other. Indeed we share these genes with chimpanzees, gorillas and many other animals. However, unless we are identical twins, we all have many differences in our alleles. This is what makes us unique as individuals.

Much of the variation in our DNA is hidden. Surprisingly, most of our DNA is not located in a gene. In other words, not all of our DNA plays a role in telling our cells how to make specific proteins. This means that most of the alleles found in our DNA, though they can be detected in the laboratory, do not lead to physical differences between us. Many alleles are apparently just sitting there and going along for the ride as they pass from one generation to the next. This hidden variation in our DNA is what makes DNA fingerprinting possible.

Chromosomes also recombine to make new chromosomes. As well as chromosome shuffling discussed above there is another level of mixing called recombination. This happens because, while we are manufacturing our gametes in testes or ovaries, the chromosomes we originally inherited from our mum and dad join together in a kind of embrace that is so tight that the chromosomes exchange sections of DNA with each other, generating unique new chromosomes that are like a patchwork made from pieces of our parents' chromosomes.

Hidden variation in DNA can be used to find alleles causing disease. The individual pieces of DNA that make up this patchwork in a recombined chromosome can provide useful information about where different alleles are located in relation to each other. In the case of Wilson's disease (WD), we knew that there must be an allele that adversely affects the function of the gene. We did not know where the gene was, until the scientific community started making a large collection of pieces of DNA that contained alleles. It was like a large stamp collecting exercise in which the fascination lies in the small variations between the stamps made in any particular year. The rationale behind this exercise was: if we could collect enough pieces of DNA carrying enough alleles, we would eventually start finding two alleles on the same piece of patchwork. We could then start to know if two alleles are close to each other on the chromosome by how often they are inherited on the same piece of patchwork.

Alleles that are physically close to each other on our chromosomes tend to get inherited together. Alleles that are on the same chromosome will tend to be inherited together through families, but occasionally get separated by a recombination event described above and end up on different pieces of patchwork. The closer alleles are together, the less likely they are to get separated as they are passed from generation to generation. This kind of loose connection between alleles is called "linkage". Moreover, alleles that are extremely close together always tend to be inherited together on the same piece of patchwork. In other words they are "associated" or are in "linkage disequilibrium" in the human population. It was linkage disequilibrium between an allele detectable in the lab and an allele that causes WD that Diane Cox was excited about when I went for my interview. This allele was located on a piece of DNA called D13S31 and was work led by a visiting researcher, Roderick Howen (J. Hepatol 16, S15, 1992). D13S31 was on chromosome 13.

I arrived in Toronto in November 1990, just as it was starting to get cold. I had temporary accommodation just near to the

lab at Hospital for Sick Children. I liked Toronto, but missed my friends and family. However, Diane's research group was friendly and I soon felt at home. The whole group would go for coffee each morning, and Diane would lift our spirits with her positivity and sense of what might be possible. She would often ask: "What's new and exciting?" She treated people well and made you feel like your work was worth something even at times when it seemed to be going nowhere. My project was to make a physical map of the important pieces of DNA that we had available to us in the lab that were known to be near to where we thought the gene lesion implicated in WD was. We wanted to know where all the significant pieces of DNA that carried alleles associated with WD were located on chromosome 13. As I explained above, the most exciting of these pieces of DNA was given a rather unexciting name: D13S31.

A physical map of a chromosomes is just like a map of a country such as UK. The map needs to include all the rivers, hills and the coastline. These are the bits that have been around for thousands of years. You need the physical map before you can add in the exciting details about things that change over shorter periods of time. Things like Margaret's Vegan Burger Restaurant in Cambridge might appear and disappear over a relatively short time scale, but we need the physical map to locate them. Similarly, a physical map of a chromosome is very useful as a framework for anchoring the position of alleles and describing their relationships to each other. To home in on the alleles that actually cause WD we needed to map the alleles that have a tendency to be inherited on the same pieces of DNA in people with Wilson's disease. This is how it is done:

There are several properties of DNA that make physical mapping of DNA possible:

DNA is made from long strands. The DNA strands are made from only four different chemicals subunits called bases. These bases are often represented by letters A,C,G and T. An example of a short strand of DNA might have the following sequence of bases: **AGGCGAAAGGTT**. Some, but not all, DNA sequence acts as the code for determining the structure of proteins in our bodies.

DNA is double-stranded. This means that every DNA molecule is made from a strand together with a complementary copy of itself. Imagine keeping with your door key an exact mould of its shape. If you lost your key, you could make a new one using the mould. The reason we can reproduce is that our DNA has the same feature built into it.

The rules are simple. In the double-stranded DNA molecule, A always sticks to T and G always sticks to C. So the double-stranded DNA for the sequence above would read:

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AGGCGAAAGGTT
||||||||||||
TCCGCTTTCCAA
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The vertical lines represent the weak chemical bonds that hold the two strands of DNA together.

DNA strands can unzip so that each strand can be used as a template to make a new copy of itself. This happens whenever a cell divides. Furthermore, DNA can be unzipped easily in the lab.

Individual unzipped stands of DNA will stick to their complementary strand. If we unzip the two strands of DNA we can use the binding rules above to find pieces of DNA with the same base sequence. We can easily unzip DNA strands in the laboratory and use them like invisible ink on pieces of paper. We can make the invisible DNA 'ink' visible by preparing another sample of DNA called a probe, that is labelled with radioactive "ink" and see where it sticks to the invisible DNA 'ink' on the paper using a piece of X-ray film.

DNA can be cut in specific places with enzymes. These enzymes called "restriction enzymes" evolved in bacteria to destroy foreign DNA from invading viruses. They do this by finding sections of DNA with specific sequences, such as GCGGCCGC which, in this case, is cut by the enzyme called "Not I". These enzymes can artificially generate large fragments of DNA in the lab. We can use these fragments as sections of artificial patchwork and ask: which pieces of DNA carrying known alleles lie on the same piece of patchwork? If alleles are close together the piece of DNA in which they are found will lie on the same piece of patchwork. If they are further apart they will tend to lie on different pieces.

DNA fragments of different sizes can be separated. When dissolved in water DNA is negatively charged. In the same way, if you rub a balloon on your hair it will pick up electrons from your hair and become negatively charged. The balloon and hair then stick to each other because your hair wants those electrons back. In the same way, we can attract negatively charged DNA strands to an electron-deficient piece of wire using electricity and force the DNA to move through a slab of jelly-like material. The technique is called *electrophoresis*. Small pieces of DNA move faster through the jelly than large pieces, in the same way as bikes move faster than cars in a traffic jam. After carrying out *electrophoresis* we can then transfer the DNA exactly where it ended up, on to a piece of paper. As described above, we can then make visible just the piece of DNA we are interested in by making a radioactive probe using this DNA of interest and seeing how it sticks to the DNA on the paper. The result is something like this:

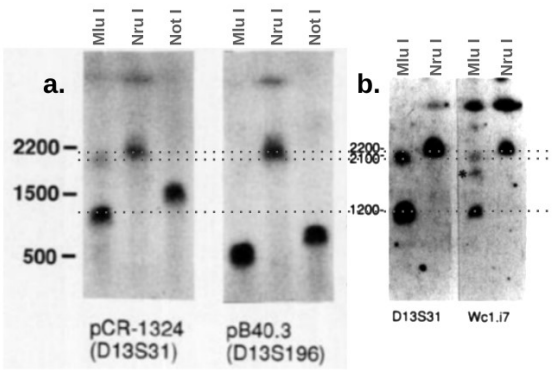


Figure 1. Two results that gave us some key information

a. Fragments of DNA cut using three different enzymes MluI, NruI and Not1, then separated by size and transferred on to paper, then sequentially made visible using two different radioactively labeled pieces of DNA (probes): D13S31 on the left and D13S196 on the right (from Genomics 16, 593-598, 1993).

b. Fragments of DNA cut using MluI and NruI, then sequentially made visible using two different radioactively labeled pieces of DNA: D13S31 on the left and a piece of the gene we had isolated (Wc1.i7) on the right (from Nature Genetics 5, 327-337, 1993). The three horizontal dotted lines pass through the bands that lit up in more than one experiment.

The result in Figure 1a shows the same bit of paper on which was bound DNA fragments separated using *electrophoresis*. The numbers along the left side are the lengths of the DNA measured in thousands of bases, so 500 means 500,000 bases. The words along the top are the names of the enzymes used to cut the DNA, Mlu I, Nru I and Not I. The figure shows the same bit of paper in which the DNA is visualised in two different ways. The result above shows that the pieces of DNA called D13S31 and D13S196 lie on the same fragment that is 2,200,000 bases long, generated through digestion by the enzyme Nru I, but they lie on different smaller fragments generated by the enzymes Mlu I and Not I. The fragments of DNA were made visible using the technique described above: DNA we had isolated that contained the D13S31 and D13S196 alleles were radioactively-labeled one at a time. In each case the radioactively-labeled DNA probe found its complementary strand on the paper. We were able to see its location by placing a piece of X-ray film on it. The radioactive DNA probe that stuck to its complementary piece on the paper gave off particles that darkened the X-ray film where it ended up. After doing this we just washed the probe off and started again with the next interesting piece of DNA.

We used this approach to determine where we needed to focus our work. Everything relied on collecting these fragments of DNA and seeing where they were located in relation to each other. While I focused on this, Gordon Thomas, a PhD student in Diane's lab, would see if he could find new alleles to use to study the inheritance of Wilson's disease. As we refined the collection of DNA fragments we could, at the same time, refine our collection of new alleles.

Collections of DNA fragments can be made in various ways.

1. For the small pieces, insert pieces of DNA into viruses, called *bacteriophage* that multiply and make new copies of themselves in bacteria.

2. Insert large pieces of DNA into yeast. This was a great way to grow very large pieces of DNA called yeast artificial chromosomes (YACs).

3. Fuse hamster and human cells together to make extremely long fragments. The resulting cells contain random segments of human chromosomes. Such hybrid cells provided us with a rich collection of useful DNA pieces that I isolated through a technique called 'Alu PCR' (Cytogenetics and Cell Genetics, 64, 12-17 (1993).

Peter at the American Society of Human Genetics Meeting in Washington DC, 1991

In early 1993 we were fortunate that two research groups isolated a gene ATP7A containing alleles associated with Menkes disease. Menkes disease is caused by disrupted copper uptake by cells. Interestingly, the predicted protein encoded by ATP7A contained sections similar to those found in bacteria growing in places polluted with heavy metals. Since copper is a heavy metal too, it appears that humans manage the transport of copper in our bodies using proteins that are similar to those that evolved in bacteria well over a billion years ago. The existence of such proteins in bacteria suggested there are only a limited number of ways of constructing heavy metal-binding proteins. It was therefore possible that WD was caused by the disruption of another version of such a protein.

We had all the tools needed to test this idea. I made a radioactive probe using just the portion of the ATP7A gene that coded for the copper-binding section of the protein. As I described above, DNA strands with the same or similar base sequence stick together, and excitingly, some of the DNA fragments (in this case YACs) in our collection stuck to the probe. Gordon then used the same probe to isolate other fragments of cloned DNA. We then collaborated with Johanna Rommens who had developed a new technique for quickly isolating fragments of DNA that lie specifically within regions of the chromosome that encode proteins. One of the DNA fragments we isolated was called Wc1.i7. Notice in Figure1b how the fragments that appear when using Wc1.i7 as a probe are the same as those picked up by D13S31.

Further analysis of Wc1.i7 by John Forbes, an undergraduate student in the lab, showed that it was part of a gene that was very similar to ATP7A. Gordon, John, and I soon isolated and assembled the remaining parts of a gene that was later given the name ATP7B. Gordon then found evidence for an allele within the ATP7B gene in a patient with WD, so we had all the evidence we needed to publish our findings. Our paper appeared in the December 1993 edition of Nature Genetics, back-to-back with two beautiful papers from another group led by Conrad Gilliam, who had isolated the same gene.

1993 was certainly an exciting time. I will always be grateful for the privilege of working with Diane Cox and her group and look back with great fondness to my time in the Genetics Department, which was always buzzing with news of a recent discovery or anticipation of one that might lie just around the corner.

Diane Cox in her office at SickKids, Toronto 1993

25 years The History of WDSG-UK 25 years

Exactly 25 years ago, Caroline Simms and Linda Hart came together to start the Wilson's Disease Support Group—UK. Linda was diagnosed in 1964 at the age of 9 by Dr John Walshe, the World Authority on Wilson's disease, and when 23 years later Caroline received her diagnosis from Queen's Medical Centre in Nottingham, her then consultant put the two in touch with one another as they lived not far apart. Concerned by the lack of patient support in the UK, in the year 2000 they opened a bank account in the name of WDSG-UK, deposited £73 of their own money into it and then, with the help and encouragement of Dr Walshe (who was just stepping down from his WD clinic in London at the grand old age of 80), set out to enlist members. Dr Walshe approached all his patients past and present inviting them to join from which there was a good response. A meeting was arranged at The Peacock Hotel in Nottingham, which I, and many others, attended.

In 2000, few households owned computers and even if they did, the World Wide Web was still in its infancy. Social media was unheard of. The chances were that a patient would receive a Wilson's diagnosis and know nothing more than what their physician could tell them. Families would often be left feeling isolated and stigmatised. Emotions would inevitably run high with feelings of guilt and uncertainty about the future. The Group was a perfect way of bringing everybody together, sharing experiences and supporting one another. It also maintained a link with Dr Walshe.

Over the years, it has attracted members from all over the country—indeed from all over the world. From the humble beginnings of a function room above a smoky bar in Nottingham to our current venue in the spacious grounds of the Rugby Club in Cambridge, meetings have taken place, Covid permitting, every year since. And at these meetings, as well as having speakers covering different aspects of the disease, we have had the unwavering support of our medical friends, James Dooley, Godfrey Gillett and more recently Sam Shribman. They sacrifice their weekends to join us, and with expertise and compassion answer any medical concerns that we have.

Back in early 2004, Caroline's health unfortunately deteriorated and she was given a liver transplant. Not well enough to continue fully in the co-running of the Group, I put myself forward to help. By this time I had introduced her and Linda to a close family friend and pathologist at nearby Queen's, Dr Alan Stevens. He quickly took an interest in the Group organising and hosting some of the earlier meetings on the Nottingham University campus and delegating technical matters to his friend and younger colleague, Jim Lowe. Feeling the need for the Group to be put on a more formal footing, Alan suggested that a committee be formed and Rupert Purchase (the chemist responsible for purifying the first ever commercial preparation of trientine) be invited to be its chairman. Rupert kindly accepted this offer and through him in 2010 charitable status was obtained. He remained chairman until 2017, handing over to his deputy Jerry Tucker before Graeme Alexander took the lead in 2019 followed by Bill Griffiths in 2023.

Every year the Group puts together a newsletter with as varied a content as possible. Patients contribute generously to this, especially through sharing their medical histories — with over 50 published to date. These are a great educational resource and show Wilson's disease in all its different hues. On the housekeeping front, membership fees have been kept to a minimum rising by only £5 in 25 years! We wish to be inclusive to all. Through donations and fundraising over the years, we have raised a significant amount of money, which we use to support patients and fund research.

So what apart from meetings and newsletters has the Group done over the past twenty-five years to benefit patients? As we are all volunteers, we are limited in what we can offer. We are contactable by email and 'phone at any time and will happily visit patients in their homes or hospital whenever appropriate to do so. One of our greatest accomplishments is our Facebook Group which Caroline set up in 2013. It has a thriving worldwide community of 1500 members and is monitored on a daily basis. Through it, news and information about the Group can be disseminated quickly, such as alerting patients to potential medicine shortages, letting them know about forthcoming events or advertising research opportunities that have come to our attention. People are joining the Facebook Group all the time, but we look out in particular for patients newly diagnosed. If living in the UK, we message them privately to offer support and check that they are receiving the best possible care. This is especially important for patients with a neurological presentation, knowing as we do how critical the first few months of treatment can be to outcome.

Meanwhile, we are representing patients in various forums both at home and abroad, ensuring that their voice is heard. At home, we attend meetings such as the BASL WD SIG (and previously The Wilson's Disease Network—UK), which under the direction of Oliver Bandmann and with a little input from us produced the 2022 UK guidelines for the treatment and management of WD in the UK. We also attend meetings run by the Cambridge Rare Disease Network (and previously Rare Disease-UK and Genetic Alliance—UK), the British Liver Trust and its many affiliated Liver Groups and the NHS BT (Blood and Transplant) ODT (Organ and Tissue Donation & Transplantation Directorate) where we check that national decisions made on liver transplantation don't prejudice our patients.

Abroad in the last twenty-five years, we have attended all International and European WD Specialist Meetings open to us. These include an International Conference in Leipzig in 2001, three EuroWilson meetings in Paris and Munich in the mid 2010s and the 3rd International WD meeting in Denmark last May. And in October 2012, London hosted an

International Symposium marking 100 years since the publication of Samuel Kinnier Wilson's seminal paper on Wilson's disease. All these meetings are attended by the leading WD specialists from around the world and so by being there we can keep up to date with and share their latest findings.

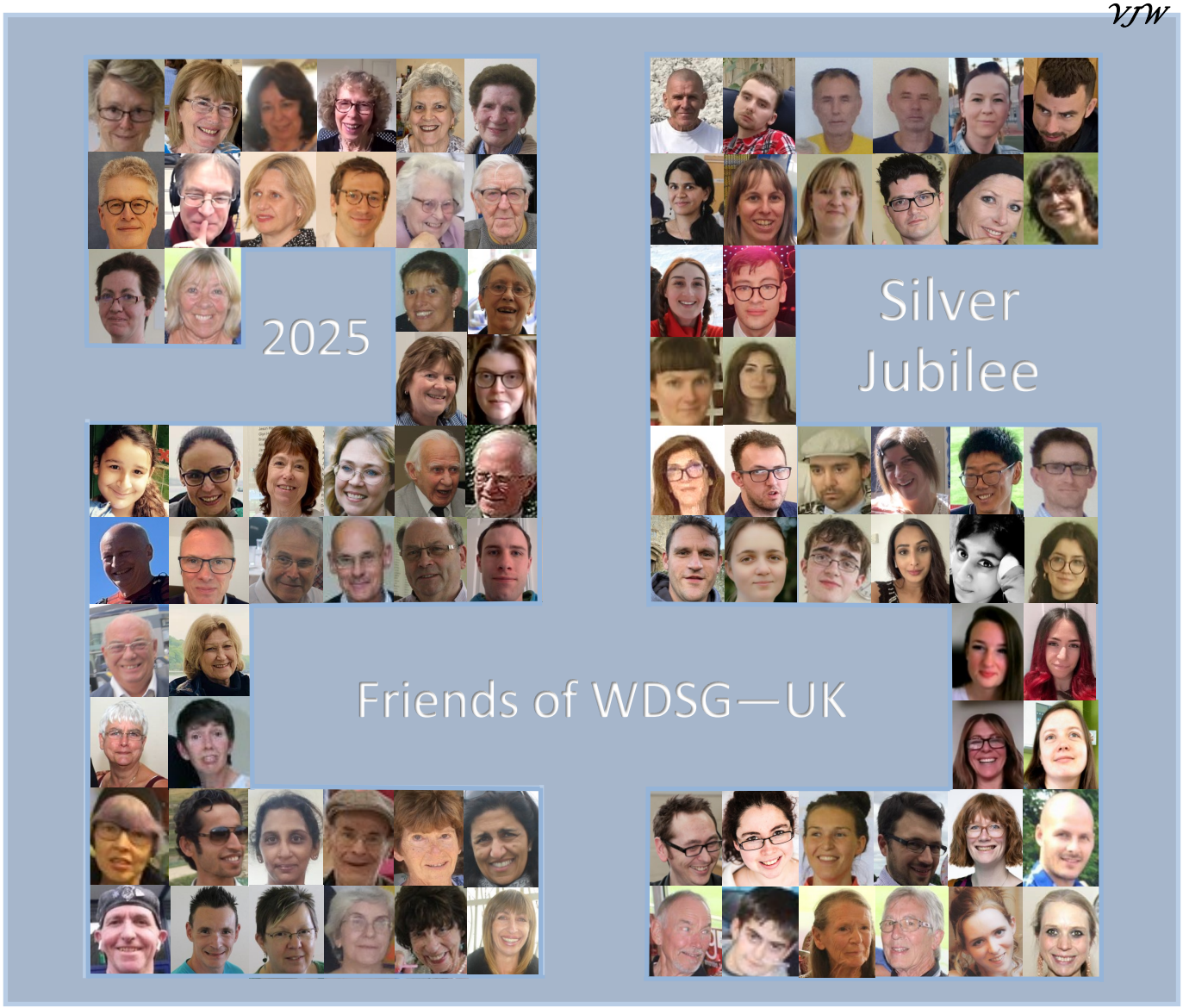
So what advancements have there been in the understanding, diagnosis and treatment of patients over the past twenty-five years? How have patients' lives improved? Firstly, there has been a lot more understanding of the mechanism of the disease. However, sadly little has changed as regards a timely diagnosis or treatment options. Patients still wait an average of two years before they are diagnosed. This is disappointing. The WDSG-UK's recent video initiative to publicise to general practitioners the tools needed for early detection of WD is a way of countering this. Educating primary carers in the signs and symptoms of WD is paramount. We can only hope that the video reaches its target audience, is watched, savoured and subsequently recalled.

The abandonment of the drug trial TTM was also disappointing and so, too, more recently Vivet's gene therapy trial. It is worth reminding ourselves that but for Dr Walshe and his discovery of penicillamine in the mid-1950s and subsequent introduction of a trientine preparation which was suggested to him by his colleague, Hal Dixon, a decade later many of us and indeed many patients across the globe quite probably wouldn't be here now. Indeed, our oldest member Shirley Wylie, certainly wouldn't be. She was the world's first recipient of penicillamine and is still alive and taking it today—aged 85!

So, how can we improve the outlook for future patients? Future successes in drug trials would obviously be helpful and we will watch with interest any developments on methanobactin. But, in my mind the only way of having the best possible outcome for Wilson's disease patients in the future is through routine genetic testing at birth. The old adage *to be forewarned is to be forearmed* is particularly pertinent here. At the Aarhus meeting last May, Dr Sihoun Hahn, a paediatrician at the WD Center of Excellence in Seattle, spoke about a screening test for WD that he has developed over the past 20 years. He is hoping it will be added to existing newborn screening in the near future. Let's hope one day that it will also happen here.

And while we wait, let's raise a glass (metaphorically of course) to Caroline and Linda thanking them for their vision in setting up the Group and their hard work in establishing it. Let's also remember Dr Walshe for his lifetime's dedication to us. Here's to another twenty-five years of friendship and mutual support. Cheers!

VJW



Tom's Story - Part I

by Tom Shaw

It's quite hard to say when it started. Was it when my voice started to slow? Or when my toes started to twitch? Or was it when I started drooling? Or even when I started experiencing anxiety? I guess the real beginning was when I had that first nosebleed, aged 5. I had them so regularly over the years that they became normal. I am constantly brushing off the concern of strangers.

"It's ok," I say, "I'm used to them."

I experienced frequent nosebleeds for the following 12 years or so, when, suddenly, in August 2021, in the summer before my final year of sixth form, I started experiencing anxiety. I had always been a worrier, but this was different. Before, the stress always had a logical explanation, now it was as though there was a pit of ineffable anxiety lying in my stomach. This persisted until I started seeing a therapist in December, who helped alleviate the anxiety greatly.

A few months earlier, when I had started Year 13, I had noticed something distressing. My grades in the sciences had begun to slip. Despite preferring the arts and humanities, I had always been good at the sciences, so this was highly confusing. I remember my mother reassuring me:

"Don't worry, love. Year 13's just more demanding, that's all," she said. I remember finding this reassurance quite odd, as I actually didn't find the work more demanding. There was a blockage that stopped me from translating my understanding of the work to solutions to problems in class. It was as though a dam had been built in my brain, blocking me from doing chemistry and physics to the best of my abilities. After struggling with sciences for a few months I decided it was time to drop chemistry (I took four A-Levels rather than the usual three) in the hope that my grades in physics would start to pick up again. When mocks came and I received an unusually low grade, my physics teacher reassured me;

"Tom, don't worry. Everyone has a bad day!" However, I knew that this was not just one "bad day" and my grades in physics had been slipping for some while. Never mind, I thought, willing myself to believe what my physics teacher had just said, I better work hard revising for the real thing.

A few weeks before the exams, my twin sister and I took a much-deserved break from our revision to meet up with our aunt in Leeds. We looked around the shops in the shopping centre for a while and after that, we had a coffee at a *Café Nero.* We were midway through a conversation when, suddenly, everyone started to look at me oddly. At first, I was bewildered, but then I saw they were looking at my chest. I looked down and saw a large globule of drool had landed there. We all laughed about it, despite my slight embarrassment:

"I can't believe I just did that. How embarrassing!" I exclaimed. I didn't think much of this at the time and soon forgot about it, as I came home and continued revising.

The exams came and went without any major issues, apart from one fiendishly difficult physics paper. Summer passed and before long it was time for results day. I walked into my school hall went to the table where my results were, picked up the brown envelope, and opened it. This is what it said inside:

*English Literature: A**
History: A
Physics: C

My feelings were a bizarre mix of pride, disappointment and a sense of "I knew this was going to happen." I had performed well in English and History and underperformed in physics. Whilst C isn't a bad grade by any means, it was well below the standard I had set myself for the last seven years at secondary school. Nevertheless, I had done just about well enough to get into my top choice of university, Durham.

Around this time, I had begun to experience a bizarre symptom: a toe in my left foot had started twitching intermittently. The sensation was similar to that of a twitchy nerve but different in a way I can't quite articulate. It became irritating, sometimes even to the extent that it took me a bit longer to get to sleep.

"Don't worry about it," I told myself. "Everyone gets bizarre symptoms like this from time to time. It's normal." Then, after several weeks of this, a more distressing symptom emerged; my voice had begun to slow down. My thought process had remained the same, sharp as ever, but my words had become more slurred. It was a subtle change, not even enough for anyone else to notice, but it distressed me. And then it got worse. And worse. Eventually, the change was significant enough for my family to notice:

"Tom, is your voice slower than usual? I didn't want to say anything, but I noticed it a few days ago and now I can't unnotice it, you get me?", my sister, Phoebe said one day.

"Er…yes…I suppose it has." I said, willing it not to be true.

It was around this time that I had begun preparing to study English at Durham. For the move to Durham, we had bought cups, mugs, cutlery, plates, texts for my course, posters for my room and photo frames for pictures of friends and family. I had even read what, in my opinion, is the worst novel ever written, *Moll Flanders*, by Daniel Defoe in preparation for my course. Despite all this, I couldn't escape the worry that my voice, which at this point had forced me to consider the number of words I used (I had begun to find talking tiring), would make life in Durham difficult. I couldn't escape the feeling that I would not be going to Durham after all.

The big day came. The day that I had been looking forward to for years had arrived, not with excitement on my part, but with a foreboding sense of anxiety. We packed the car with my things, and left for Durham.

I don't know how I coped as well as I did. I turned up to every one of my lectures and tutorials and even made a few friends. Nevertheless, I felt like Atlas, with the world on my shoulders every day. Each day that went by, my voice got a

little slower, a little more slurred. I remember one night I told my friends I was leaving the nightclub as I was tired.

"Do you want anyone to go back with you?", one of my friends asked. What kind of question is that, I thought? And then it dawned on me. She thought I was drunk! I had had a couple of beers, yes, but my head was clear and I certainly hadn't had enough alcohol to be vulnerable.

"No, I'm fine," I insisted, somewhat embarrassed. I went back to my halls and went to sleep.

As the next few weeks passed, my symptoms continued to worsen, particularly my voice. When I asked my friends if my voice sounded weird at all, they responded with assurances that it sounded perfectly normal. However, I do remember one interaction with a friend where I was told that I was shy and didn't talk much.

"You're a nice guy, but you don't talk a lot," my friend told me.

"I promise you, I'm usually a lot more talkative, it's just this weird thing going on with my voice I was telling you about." She gave a feeble nod. I could tell that she didn't really believe me. I didn't bother arguing.

Eventually, my symptoms had worsened to the point where I had become something of a recluse. I ate alone and didn't go out clubbing. I was, on the whole, quite miserable. The final straw came when a band me and many of my flatmates liked released a new album. In an effort to show my peers that I wasn't a reclusive weirdo, I came up with the idea that we could have a listening party. I asked people if they wanted to come to my room and listen to it with me once our lectures were over. I went to my room, turned my speaker on, and waited. And waited. And waited. Eventually, I had to admit that no one was coming. The humiliation was overwhelming. This was a new low.

"Hey, everyone, just to let you know, I feel a bit under the weather so I'll be going home for a few days. I'll be back by Wednesday."

The next day, on Saturday, I rang my mum, partially to complain about how miserable I was, partially just to hear a familiar voice. The call lasted about half an hour as I wandered from Waterstones to my favourite record shop. When it had become tiring talking, I hung up, walked back to my college, went to my room and shut the door. A few hours later, I received a call from my dad. He seemed concerned yet calm.

"Tom, mum and I have talked together about your call and we talked with mum's friend who used to be a stroke consultant. We're coming to pick you up to take you home." I thought they were overreacting. I feel well enough to stay, I thought. However, I had become so miserable over my short time in Durham, that I welcomed the opportunity to be sent back to the comfort of home.

"Do you mind packing some essentials you need for a few days at home?", my dad asked.

"OK, I'll do that," I said.

I waited for my parents to pick me up. In that time, I thought it was a good idea to tell my flatmates what was going on, so I sent a message to our group chat:

Hey, everyone, just to let you know, I feel a bit under the weather so I'll be going home for a few days. I'll be back by Wednesday.

I clicked *send* and then thought over my promise to return by Wednesday. I knew in my heart that I would be away from Durham for much, much longer than a few days. I pushed these thoughts aside and decided to stay positive.

I sat in my room, waiting to receive the text that my parents had arrived. After I had finished packing, I sat on my bed, listening to Radiohead's *In Rainbows*. I often listen to music to calm me down. It helps me feel safe. Ninety minutes passed, and then I received the all-important text that heralded comfort and security. I picked up my bag and opened the door. When I walked down the corridor, I bumped into the friend I had grown closest to.

"I saw your message," she said sadly.

"It's just this thing with my voice I was telling you about. I'm sure I'll be back on Wednesday," I insisted, not really believing the words I was saying.

"See you on Wednesday then, I guess."

I walked quickly to the car park and saw the reassuringly familiar sight of the family car. I got in, greeted my parents, and we drove off. Thankfully, my parents had understood how tiring it had become to talk, so we didn't talk much on the journey. My mother did express her joy at hearing my music in the car; we listened to *Lippy Kids* by Elbow, the *Detectorists* theme tune and *Sledgehammer* by Peter Gabriel. When we arrived home, my parents told me that my mum's stroke consultant friend had advised them to take me to A&E the next morning, as this was the quickest way to see a neurologist. My gran, whom I adore, came for dinner that evening and my dad and I watched Liverpool, the team I support, beat Manchester City 1-0 with a Mohamed Salah goal.

We woke early the next morning and drove to Harrogate Hospital. Luckily, the wait in the A&E department wasn't too long, and a nurse led us upstairs to see a doctor. After telling him about my twitchy toe and slowed voice (I hadn't yet connected the nosebleeds and my lower science grades with my other symptoms), he looked bemused, and paused for a while.

"Mr Shaw, your symptoms are very unusual." *Great*, I thought, *there's no easy solution*.

"I think it's best if you come in for a brain MRI scan. Come to the *Same Day Emergency Care (SDEC)* unit tomorrow." I was both relieved and fearful. On the one hand, I knew how difficult it was to get appointments for MRI scans, and on the other, I began to fear the worst. *Did I have a brain tumour*, I panicked. *Surely not,* I reassured myself. I tried to dismiss the worrying thought from my mind.

The next day, as instructed, my mother and I drove to the hospital and walked to the *SDEC* unit. A kind nurse led us to a curtained off room. What felt like years passed, with the nurse coming in every now and then to check on us. We learned her name was Ellie. She was the first of many wonderful NHS workers I would encounter over the next year. Eventually, a tall, formidable-looking woman with black, curly hair, entered the room.

"Hello, Tom. My name is Dr Buccoliero. I'm one of the neurologists here at Harrogate hospital." She spoke with a strong Italian accent.

"Do you mind if I take a quick look at you?" she asked. I responded in the affirmative, and she performed various tests, asking me to tap my thumb and forefinger together (a

task I would become very familiar with over the coming year) as well as her moving a pen around close to my face and watching my eyes follow it. She left the room, saying that someone would come soon to escort me to my scan.

A couple of hours passed before I was taken down a long hospital corridor for the scan. I was given some hospital garments to change into before being taken through a door into a second room, where the MRI machine was. I was asked to lie down and be as still as possible while the scan took place.

It was difficult to keep still for such a long time, because of my twitchy foot, which always seemed to pick the wrong time to start vibrating. The rhythmic beeps and whirrs of the machine were deafening. To pass the time, I started trying to name every player of my local football club, Harrogate Town: *Luke Armstrong; Sam Folarin; Josh Falkingham*. It took for ever and then a woman came into the room and told me that the scan had finished.

I was escorted back to the *SDEC* unit. I was told I could leave as long as I returned there the following day for the results.

When my mum, dad and I got to the hospital the next day, we went to *SDEC* and into a room we had not been to before. We were there for an hour before Dr Buccoliero entered the room carrying the scans of my brain. She sat down in front of us and began to talk:

"We've had a look at your scans, Tom, and it doesn't look like you've got a tumour." Relief coursed through my veins. "But there's definitely something abnormal there. It could be a metal, like magnesium or copper. Now, I think it's best if you go home and we can run some more tests another day. It goes without saying that you won't be returning to university tomorrow."

"Do you mind if you give us some time to think about whether or not we want Tom to be admitted," my mum suddenly said. *Why is she saying this?* I thought. All I wanted was to be back home.

"That's ok, I'll let you be alone for a while." When Dr Buccoliero had left, my mum explained:

"It's just something Sam (my mum's ex-stroke consultant friend) said. She says your swallowing mechanism sounds dodgy and that you shouldn't be allowed home until you have had a proper swallow test by the speech and language therapist." Dr Buccoliero returned, and my mum explained our wish to be admitted.

"Very well," sighed the neurologist. "Follow me."

After a few minutes of traversing the labyrinthine hospital corridors, we finally reached the ward that would be my home for the next 10 days. The Oakdale Ward, it was called. As we walked towards the room I would be sleeping in, we passed other rooms occupied by elderly, senile-looking patients. I later learnt that this Ward was used for stroke patients. I was by far the youngest there.

The next day, I was taken for an eye test in the ophthalmology department. After waiting in the waiting room for a few minutes, my name was called. I walked into a room with an ophthalmologist and a nurse. The ophthalmologist motioned for me to sit down in a chair opposite her and I obeyed. Leaning closer, she started to inspect my eyes. As she looked, an expression of puzzlement spread across her face.

"Surely not … it's never Wilson's," I thought I heard her mutter under her breath. She motioned to the nurse to fetch a senior colleague. *What could she have seen?* We waited for a couple of minutes until a rotund, balding man entered the room. The two ophthalmologists discussed something under their breaths together, too quiet for me to discern. The senior ophthalmologist exited, and then my ophthalmologist spoke:

"You have some copper rings in your eyes, Mr Shaw. This would indicate that you have something called Wilson's disease." Uncertainty flooded my thoughts.

"*Disease* is a scary word," I said. No one responded. Talking had become such an effort people often missed what I said.

"It was as though, deep down, I had always known"

"It's an extraordinarily rare genetic disease whereby your liver doesn't excrete copper from your body, meaning it builds up over time until you experience symptoms." Strangely, I was unsurprised by this description. Despite the disease being alien to me, hearing this description of what I might have was not shocking, but weirdly comforting. It was as though, deep down, I had always known.

"Of course, it is not certain that it is Wilson's that you have. We will need to confirm your diagnosis by running some tests over the next few days."

Over the next few days, I had to do various tests. Ultrasounds of my liver, urine collections, eye tests; there was scarcely a moment in the day where I wasn't doing some sort of test to confirm my diagnosis. I remember one test I did to confirm my cognitive ability. My cognition had never really suffered alongside my other symptoms, so this test was quite easy.

Now, it is important to understand for the context of this anecdote that this first week in hospital, far away in Westminster, the political world was quite turbulent. You see, Liz Truss's disastrous, short premiership was just imploding and everyone was expecting her to resign soon. The occupational therapist running the cognitive test asked me various questions:

"What day is it?"

"Thursday"

"What time is it?"

"Five past two"

"Who is the Prime Minister?"

"Who knows?", I said jokingly. "At this rate, it could be anyone!"

Sure enough, a few hours later, Truss resigned. I find it ironic that one of the most politically turbulent times in recent history ran parallel to one of the most turbulent times in my personal life.

The following day, Friday 21st October 2022, I was diagnosed with Wilson's disease.

"We'll let you go home for the weekend, but you need to be back here on Monday so you can start your treatment of penicillamine—the drug that excretes the excess copper from your body." Dr Buccoliero informed us.

"Now, I must warn you of something," she said. "You have eighteen years' worth of copper in your brain, so I'm

afraid your return to normalcy will be very gradual. You will likely worsen before you get better. It could take six to twelve months for you to even start improving." Upon hearing these words, I chose not to believe them. *You will likely worsen before you get better.* I didn't think it could get much worse, could it? How wrong I was.

We decided to collect the rest of my things from Durham that weekend. I returned just over a week after I had come home. As my parents loaded the car, I said my goodbyes to all of the people on my corridor: to Lydia, Molly, Harvey, Dan, Joachim, Emma, Georgia, Martha, Nick, Zac, Jed, Eliza. I said goodbye to every one of them. This was not without difficulty, however. Talking had become so difficult I had to resort occasionally to typing what I wanted to say on my phone. I finished saying farewell, helped my parents load the last of our things into the car, and we were off.

We had to rise early on Monday to go to the hospital in order to take my tablets in plenty of time before breakfast was served on the Oakdale Ward.

"He deserves a knighthood as far as I am concerned"

The next few days were a bit of a blur. Visitors came and went. Grandparents. Friends of mine. Friends of the family. It was really quite overwhelming to know that this amount of people cared about me and what I was going through. This is a feeling I have never got used to. By Friday, I was told that I could leave the hospital, which I welcomed as I was beginning to miss home. This wasn't before one conversation I had with Dr Buccoliero.

"Tom, as Wilson's is an incredibly rare disease, I think it is important that I put you in touch with the Wilson's Disease Support Group, as well as my colleague, the national expert in the disease, Dr Godfrey Gillett."

One of the few positives has been knowing Godfrey. He has not just devoted his life to one of the least known (at least among non-medical professionals) genetic diseases, but he is one of the kindest, most genuine people I have ever met. It has been a privilege knowing him and weirdly, I am glad that I have had the year that I have had, as I would have never have had the pleasure of knowing him. He deserves a knighthood as far as I am concerned.

"We'll let you go home for the weekend, but you need to be back here on Monday so you can start your treatment of penicillamine—the drug that excretes the excess copper from your body," Dr Buccoliero informed us.

The next month or so was a steady decline and by mid-November I could only speak one short sentence at a time. It had become difficult to communicate my ideas and thoughts, something that would persist for the next six months of my life. Now, in the hospital a month earlier, there was concern about my swallowing. The worry was that I was "silently" aspirating, which means fluids were going down the wrong way without me realising. Clearly, this concern had persisted amongst the speech and language team at the hospital to the extent that it was decided I should have a swallow test.

My amazing speech and language professional, Jo, explained that I would have to drink a chemical that could be seen by the x-ray. They would whisk in "thickener", a fine white powder that would make fluids thick enough for me to swallow safely. They would try various different thicknesses to find the safest one for me.

I went to the appointment, and a few days later Jo came to our house to explain what the outcome of the swallow test was. She explained that I was to have level 3 thickness, which meant three scoops of thickener was to be added to all my drinks. She showed my mum how the drinks should be thickened, practising first on some water. Once the drink was thick, I was told to drink it. It was as thick as wallpaper paste and not hydrating in the slightest. I didn't like it.

"I realise that probably wasn't the most refreshing drink you've ever had", Jo sympathised.

"But there is a protocol which will allow you to have thin drinks of water if you drink it half an hour after food and make sure your mouth is clean. Unfortunately, this will mean that you will have to have thickened drinks with meals. I recommend thickening juice to make it more appetising." She left our house soon after this, and I was condemned to drinking wallpaper paste for the next few months of my life.

As the weather grew colder, my symptoms continued to worsen. Christmas came, which was particularly difficult, as I was unable to eat Christmas dinner as normal — cutting and chewing food as tough as chicken had become difficult, so we had lasagne. What was especially difficult, was that my voice had now become so bad that saying one word at a time was a struggle, so it was difficult to thank my family for my Christmas presents.

In the weeks after Christmas, things continued deteriorating at a steady pace. Holding books to read began to make my wrists ache, which was particularly frustrating for someone who had decided to study English Literature at University. Another new development was I had begun to struggle to control my momentum when walking. After walking for a few minutes, I would start to stagger. This was quite upsetting, as one of the few things I felt that I still had control over was my walking. We informed my physio, Pam of the difficulties I was starting to have walking. Pam is yet another of the fabulous NHS professionals I have encountered over the last year. She spoke with a thick Scottish accent, and as with all the other NHS workers I have seen over the past year, she seemed to take my case with genuine interest. I have often been treated by people at Harrogate Hospital as a sort of micro-celebrity, on account of how rare Wilson's disease is.

Anyway, I reported to Pam about the difficulties I was having walking and she said that she thought I might find a walker helpful. My wheelie-walker was the sort you often see disabled people using to walk down the street. It made me self-conscious to use at first, but soon it gave me confidence when I walked, which was greatly appreciated.

February came, and with it, the death of my gran's beloved brother, Uncle John. Uncle John, who lived in Croydon had had a stroke ten years prior to his death, which had left him speechless and wheelchair bound, but had not robbed him of his intelligence. The obvious similarities between Uncle John and my own case made me desperate to attend his funeral.

There was only one problem. The journey to Croydon. One of the most painful symptoms had emerged around the same time that I had started to use the walker; whenever I sat or lay down, my toes started to curl involuntarily towards

my foot. If this doesn't sound painful, let me assure you that the sheer force with which they curled was excruciating. It made sleeping difficult to the extent that there were some nights where I would have been thankful for one hour of sleep. I was put on a drug called amitriptyline to help with nights. Unfortunately, this drug was only to be taken at nights, so on the long journey to Croydon, we had to stop at a service station about once an hour for me to walk around the car to stretch my toes out.

The funeral was a mixture of emotions. On the one hand, it was nice to see members of my extended family, on the other, it was difficult not to be able to talk to them. As an alternative to talking, I typed what I wanted to say on the notes app on my phone and showed what I had typed to whoever I wanted to talk to. It was not a solution to the problem. There was no flow to the conversation, because whoever I was "talking" to had to wait for me to type a response. They had to wait quite a while, as I typed a lot slower than I did pre-Wilsons's, due to the dystonia in my hands. Of course, I had got used to this as much as was possible – typing what I wanted to say had been my reality since November. Despite these difficulties, I was glad that I was able to pay my respects to my beloved great-uncle.

"In many ways, my entire experience of Wilson's disease has been like one very long out-of-body experience."

It was around this time that I had begun to become obsessed with something Dr Buccoliero had said when I was first diagnosed 5 months previously.

It will probably take at least six months for you to start improving, she had said. I had begun to fixate on the "six months" thing. And had started to take what she had said literally. I had sort of started to diarise that exactly six months on from when I first started taking penicillamine, on April 24th, I would start to get better. I would start typing the number of weeks left until the six-month-mark and showing it to my mum. I didn't really believe that I would start to improve on the 24th of April exactly, but it gave me something to hold on to. I had been worsening for about five months at this point, and it was very difficult to have hope. The six-month benchmark gave me a flicker of hope.

My hope was rocked slightly by the end of the time with my old therapist, Robin. I saw him through a mental-health charity, which only allowed you 12 months of time with one of their therapists. I had to look for another therapist. I was very nervous to start again with a different therapist, because I did not like meeting new people; I worried they would judge me because of my lack of voice. Eventually, we found a new therapist: a kindly Argentinian man, called Patricio, with a big beard. Fortunately, my fears were set aside when I found that Patricio was just as helpful in discussing my feelings as Robin had been.

I continued to fixate on the six-month benchmark. That was until one appointment with Dr Buccoliero. I came to the appointment armed with the question that I asked at every appointment with Godfrey or her, *When am I going to get better?* Usually, Godfrey or she would answer with *Well, Wilson's presents itself differently in every patient, it's hard to say.* However, when I asked her this time, she responded slightly differently.

I don't actually remember exactly what she said, but when she spoke, she seemed to suggest that if I had not started improving by now, I would likely not fully recover. Of course, she may not have actually meant to say this. Italian was her first language, not English. Nevertheless, this did not change the way what she said made me feel. This was probably the lowest moment in all of my Wilson's journey. I went numb. To get across exactly how I felt, I will quote one of my favourite Radiohead songs, *How to Disappear Completely,* written by the lead singer, Thom Yorke, about a breakdown he had at a show in Dublin:

I'm not here, this isn't happening.

In many ways, my entire experience of Wilson's disease has been like one very long out-of-body experience. It's the way I've coped, I think, to detach my feelings from my experience. It's not like I haven't felt emotional by the ordeal, it's more like I've had to accept my experiences as fact and "move on". In this moment that Dr Buccoliero was telling me that I may never get better, the intensity of this detached sensation was the strongest it had ever been. I still felt angry about the apparent lie of the "six-month" thing, but it was like I was angry on someone else's behalf. The weirdness of this anger probably makes that appointment with Dr Buccoliero both the darkest and strangest moment of my Wilson's journey.

Later that day, I organised a video call with Godfrey, to discuss what Dr Buccoliero had told me. As usual with Godfrey, it was a reassuring call. He told me that whilst it was not certain that I would fully recover, I would eventually start to recover, if not with penicillamine, then with other available treatment. Despite feeling a lot better after this video call with Godfrey, I stopped believing that I would start improving exactly six months from when I first started treatment. It is, therefore, one of the greatest ironies of my life, that the day I finally turned the corner, was on April 24th 2023, *exactly* six months after I started treatment.

It was in an appointment with my wonderful physio, Pam, that I discovered I had begun to improve. In most of my sessions with Pam, we would do a few exercises to track how I was getting on. In all previous appointments, I had got significantly worse since the previous time. However, this appointment was different. During one balancing exercise, we noticed that I was able to stand on my right leg for considerably longer than previously. We tried again to see if it was a fluke. And again. Each time we tried I could stand on my right leg for longer than before.

"Tom, I think you may have improved!" Pam said.

"Really?", I wrote on the new iPad that the speech and language department had given me a few days previously to make it easier for me to type.

"It must just be a fluke", I typed. The words would have sounded half-hearted had I been able to speak. I knew the evidence was irrefutable. Even though it was not significant in the grand scheme of things, it was a definite improvement. The thing was, I had got so used to worsening symptoms it felt bizarre that I had finally started improving. It felt both monumental and insignificant at the same time. Like I said earlier, Wilson's has been like one very long *out-of-body experience …* **to be continued** .

Members' News 2024-25

Love seems to have been in the air during 2024 …

First of all Laura from Shetland, who was diagnosed in 2019 and who shared her heart-wrenching story with us the following year, now writes:

Last year was certainly a busy year for us. Neil and I got married on the 18th May and we have welcomed our second child, Billy, mid-February this year. Shortly after my diagnosis of Wilson's disease I was unable to eat, talk or walk and at that time I never dreamt I would be able to look after or even have children as I needed care myself. Now, five and a half years later, I'm back to a full bill of health and am married with two children! So what I'd like to say to my fellow Wilson's disease patients is "Don't give up on your dreams!"

Other news from Shetland is they have found that Wilson's disease is far more common here than the rest of Britain. A study called *Viking Genes* which is headed by Dr Jim *WILSON* of The University of Edinburgh has identified a number of rare diseases (including Wilson's disease) are more prevalent in Shetland, Orkney and the Western Isles due to their smaller gene pools. The ATP7B WD gene could be 1000x more common in Shetlanders than the rest of the UK. I have been trying to raise awareness of Wilson's disease locally and have raised significant funds for the *Viking Gene Project*. For more information on the Study, please visit https://viking.ed.ac.uk/"

* * * *

James Manning wrote about his Wilson's journey in last year's newsletter. He now brings us up to date:

Firstly I would like to thank everyone who took the time to read my story last year. I hope it gave anyone struggling to come to terms with their Wilson's diagnosis hope and a lift that life continues despite being diagnosed.

Since writing my story I have continued to make improvements in my health, both mentally and physically. I have gone through therapy and maintained stable liver functions. In addition, the beautiful border collie cross puppy which we have recently acquired has helped me mentally (she loves a cuddle), and also physically by keeping me active with all the lovely walks we have been on. I have also joined a football team for the first time since my diagnosis, and despite a number of trips and falls, have thoroughly enjoyed playing again after a break of ten years.

I also have the absolute pleasure to report that last year I proposed to my girlfriend and best friend, Georgina, whilst on holiday in the Brecon Beacons. She was very shocked—mainly because I had managed to keep it a secret and not lose the engagement ring! She happily said "Yes!" We are busy planning and very much looking forward to our wedding on May 30th next year."

* * * *

After living with and looking after Dr Walshe for the last fifteen years of his life, in 2023 his daughter Susan and her partner Phil, moved away from Cambridge to live closer to their son Simon and his family in Bath.

And on 19th October last year, after forty years of courtship, they decided that it was perhaps time to tie the knot. Here is a photograph of them with their granddaughters Annabelle and Rose after their wedding ceremony at The Guildhall in Bath.

Sue and Phil are still enjoying getting to know their new surroundings in Somerset and the people in the village in which they now live. We wish them every happiness in their future life together.

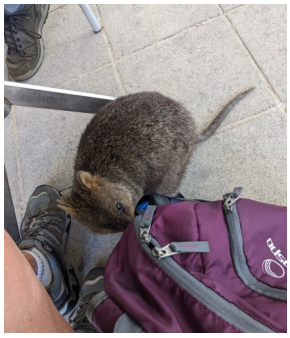
It seems we have another intrepid explorer in our midst. **Sue Boysons** has been a member of WDSG-UK since 2002 and has lived in places such as Shetland, Thailand and the Bahamas at various stages of her married life. She wrote her patient story for our March 2005 newsletter (available to read on our website) and she now writes:

Relaxing in Mauritius

I was diagnosed with Wilson's disease back in 1983 aged 26. I had been married for 3 years to Chris and was advised that I would not be able to have children as my liver was in such a poor state. Thanks to penicillamine and good care I am now 68 and have had 2 sons. I also have 3 grandchildren and another due in August. Both our boys live overseas and I like to think that our love of travelling has given them the wings to fly. However it is hard being a FaceTime grandma.

Our eldest son lives in Byron Bay on the eastern coast of Australia and we try to go out every other year to see him and the family while visiting different places, and parts of Australia on the way. Last September we flew out via Mauritius, a wonderful island on which to rest and get rid of some jet lag. We then continued to Perth in Western Australia, where we stayed with friends.

Pinnacles in Nambung National Park



A Quokka

While in Perth, we visited the offshore island of Rottnest, where there is a small marsupial called a Quokka. They have no predators on the island and hence have no fear of humans. They are very cheeky approaching you for food and looking for it in your rucksack as you aren't allowed to feed them!

From Perth we drove 175 miles south to explore the Margaret River wine region before heading back north to the Pinnacles Desert in Nambung National Park with its amazing structures dating back thousands of years. So many flies there!

The family down under

Australia is vast and it took all day across three different time zones to fly to the Gold Coast where our son met us. We then had two glorious weeks being grandparents in Byron Bay. Heaven!

* * * * *

Claire Stapleton first contacted WDSG-UK shortly after her teenage daughter was diagnosed with Wilson's disease at the beginning of 2021. She was co-opted on to the committee at the beginning of 2023 before being formally elected at the AGM later that year. She now writes:

After a decade of working as a Research Nurse, and driven by the devastating condition of my daughter, I was determined to better understand Wilson's disease – this prompted my return to further education.

In December 2024, I graduated from the University of Manchester with a Masters in Clinical Research (MClinRes). My research proposal aimed to explore the lived experiences of Wilson's disease patients utilising qualitative methodologies, highlighting my commitment to patient-centred research.

Now, as a Clinical Project Manager, Registered Nurse, WDSG-UK committee member and founding member of the Wilson Disease Global Alliance (WDGA), I continue to champion clinical research, advocating for advancements in understanding and treating this rare disease, raising awareness and addressing the unmet needs of those living with Wilson's disease.

Our past chairman, Graeme Alexander, introduced us briefly in last year's newsletter to his new life and surroundings in the north-west of Scotland which is where, by coincidence, former committee member and regular contributor **Anne-Marie** and her husband Steve, took a short holiday in November. She writes:

Discovering Ardnamurchan

Ardnamurchan is a beautiful peninsula on the spectacular west coast of Scotland. Located in the most westerly area of the UK mainland, it remains unspoilt and undisturbed. Last November we drove up and rented a house there for a week, looking forward to experiencing this remote area of the UK. We weren't disappointed.

From our home near Carlisle we headed north to Glasgow and then followed the eastern shores of Loch Lomond towards Fort William on the A82 as far as Corran where we hopped on the ferry, taking less than 10 minutes to cross Loch Linnhe to Ardgour on the A861. The ferry provides a lifeline connection for the communities to the west and at the same time, because there is no bridge, maintains an island feeling. Without it, motorists have to take over an hour's diversion by road.

The ferry

Our rental stood on the foreshore of Loch Sunart in the pretty village of Salen with its little community shop at the end of the jetty. The views from the house across the water and the hills beyond were amazing and somehow very calming. We were able to observe something of the life of the community. Every morning we watched a local fisherman sail out in his dinghy to board his fishing boat and set off for the day's catch. We were also on the lookout for wildlife. One early morning we were rewarded by the sight of two otters swimming and diving in the water just in front of the house. Otters had always proved elusive up till that moment, so it was a real highlight of the holiday.

View of the Loch from our accommodation

The lighthouse at Ardnamurchan Point

Setting out to discover the area by car, the roads are mainly single track so you can't rush. We wanted to visit some of the stunning beaches the peninsular is famous for and chose to go to Sanna with its glorious white sands. Amazingly, we had it all to ourselves except for a few local dog walkers. Another day we headed for rugged Ardnamurchan Point with its lighthouse. Designed by Stevenson, it is the most westerly lighthouse on the British mainland. From there we were able to see the isles of Rhum, Eigg and Coll in the distance.

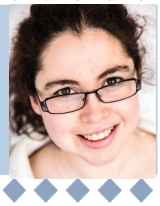
The white sands of Sanna

We also enjoyed walks in native oak woods festooned with lichen and mosses. We spent time birdwatching in a forestry commission hide overlooking Loch Sunart and spotted cormorants, oyster catchers and herons.

All in all a very special week. We came home refreshed and relaxed.

Anne-Marie taking a wee stroll!

Abby's Puzzle Page



With WDSG-UK celebrating its Silver Jubilee this year, I thought it would be good to theme the puzzles accordingly. However, easier said than done!

Hope you enjoy. Answers can be found at the bottom of *p 23* — opposite.

1. Wordsearch

P D A L G O L D H R E P A P X Y
B P N X F H E Y X L U M L K D O
T G L J C B O S Z I Z R U I R V
Y R D A P O J B J Q A T W N W F
V E I C T O T J F E O O Y I R F
D V A A K I S T P Z F J A A L K
O L M H Y E N A O Y T K A L A O
O I O R B K E U P N C H E E W K
W S N E U C M C M P Y P Q C Q R
H D D H R R O E J N H Z L R A J
A O Q T F Y C M B W E I W O U X
C M C A N S N E D H O L R P H G
Z F R E V T L R K D K O R E E N
I T N L P A P A K X J G E W I Z
O W U T B L V L P G K B Z T G N
B U B I F D O D O B H O P X M N

Find the following wedding anniversary celebrations in the puzzle above:

GOLD SILVER DIAMOND PLATINUM PEARL RUBY COTTON PAPER WOOD TIN SAPPHIRE EMERALD CRYSTAL

2. Sudoku

		8	2			4	7	
				8		3	1	
	9				4	8		
	3	4	6	1				
			4		7			
				5	8	1	4	
		9	8				3	
	1	2		9				
	7	3			1	6		

Sudoku provided by www.sudokuof theday.com

3. Find 6 x 3 letter words which fit in the brackets and are suffixes to words on the left and prefixes to words on the right making 12 new 6 letter words

e.g. ten (ANT) hem = tenant/anthem

a) bed (_ _ _) com
b) not (_ _ _) box
c) mis (_ _ _) men
d) vel (_ _ _) ted
e) imp (_ _ _) ear
f) ado (_ _ _) act

g) Taking the first letter of each of the words in brackets and reading from top to bottom, what 6 letter word is made?

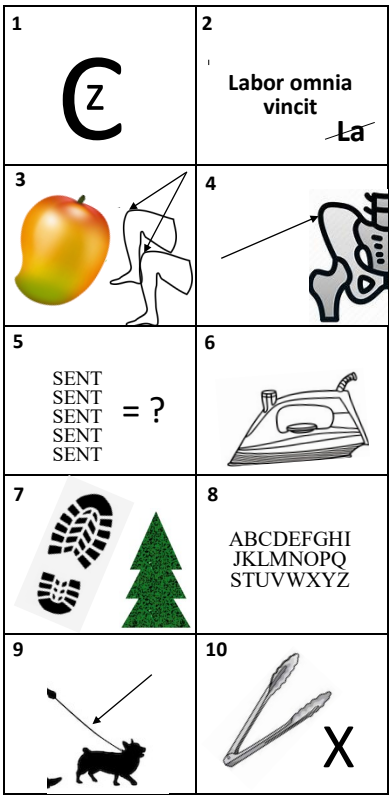
4. Crack the Codes Below

e.g. 24 H in a **D = 24 hours in a day**

1. **1 M W** to **M**
2. **6 W** of **H T E**
3. **7 W** of the **W**
4. **12 S** of the **Z**
5. **18 H** on a **G C**
6. **21 S** on a **D**
7. **29 D I F** in a **LY**
8. **52 C** in a **P (W J)**
9. **88 K** on a **P**
10. **360 D** in a **C**

5. Valerie's Dingbats

Below are the names of 10 elements in the periodic table. What are they?



6. Did they Exist in the Year 2000?

1. **McFlurry from McDonalds? y/n**
2. **Wikipedia? y/n**
3. **Netflix? y/n**
4. **Harry Potter? y/n**
5. **Facebook? y/n**
6. **Euro coins? y/n**

7. Anagrams

Brands/entertainment/things that turn 25 in 2025.

1. **he mists** (2 words)
2. **arnold front protons** (3 words)
3. **Plethora redo rex** (3 words)
4. **Hero tills** (1 word)
5. **Atlantis annotation piecers** (3 words)

WILSON'S DISEASE MULTI-DISCIPLINARY CLINICS

Adult Clinics

The Birmingham WD Clinic

Dr Andrew Holt (Consultant Hepatologist) and **Dr David Nicholl** (Consultant Neurologist) hold regular one-stop Wilson's disease clinics in the Centre for Rare Diseases at University Hospital Birmingham. 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 should be addressed to the clinic manager Richard Bayley Richard.Bayley@uhb.nhs.uk or to Dr Holt's PA, Ms. Maria Del Vecchio Maria.DelVecchio@uhb.nhs.uk.

For older teens under the care of Birmingham Children's Hospital, Ms. Catherine Stewart the Young Adult Nurse Specialist is happy to be contacted at Catherine.Stewart@uhb.nhs.uk and will help you make an appointment in clinic.

The Cambridge WD Clinic

Dr Bill Griffiths (Consultant Hepatologist) and **Dr Paul Worth** (Consultant Neurologist) run a joint clinic at Addenbrooke's Hospital as required on a Wednesday morning for patients with neurological manifestations of Wilson's disease. Dr Griffiths sees a number of patients with hepatic-only disease separately on Thursday mornings in his adult genetic liver clinic. Referrals from clinicians can be made to Dr Griffiths at the Liver Unit, Box 210, Cambridge University Hospitals, Hills Road, Cambridge CB2 0QQ.

The Leeds WD Clinic

Dr Joanna Moore (Consultant Hepatologist) and **Dr Jeremy Cosgrove** (Consultant Neurologist) run a joint clinic for patients with Wilson's disease at St James's University Hospital, Leeds. This currently runs on a Thursday morning. Referrals from clinicians can be made to Dr Moore at the Leeds Liver Unit, Merville Building, Beckett Street, Leeds LS9 7TF or Dr Cosgrove at Department of Neurology, F Floor, Martin Wing, Leeds General Infirmary, LS1 3EX.

The National Hospital Wilson's Clinic, Queen Square, London

A dedicated Wilson's disease clinic has been held at University College Hospitals for the past 38 years. It was set up in 1987 by Dr John Walshe after his retirement from Addenbrooke's Hospital, Cambridge. **Dr Godfrey Gillett** attended from the mid-1990s and ran the clinic after Dr Walshe stepped down in 2000 at the age of 80. Later the clinic was moved to the National Hospital for Neurology and Neurosurgery, Queen Square, continuing the long tradition of care for patients with Wilson's disease which began in 1913 with Dr Samuel Kinnier Wilson. Today the clinic has ~70 patients and is held on the third Friday of the month. **Dr Sam Shribman** joined the team in 2017 and now runs the clinic with the support of Dr Godfrey Gillett and **Miss Maggie Burrows**, Specialist Nurse. The clinic also benefits from access to the Neuropsychiatry, Neuro-Ophthalmology, Speech and Language Therapy, Physiotherapy and Vocational Rehabilitation services at NHNN. Referrals from across the UK are welcome, addressed to Dr Sam Shribman, Charles Dent Metabolic Unit, Internal Mailbox 92, NHNN, Queen Square, London WC1N 3BG, uclh.metabolic.enquiries@nhs.net.

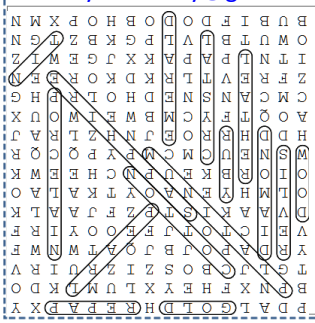
The Sheffield WD Clinic

The Sheffield clinic is jointly run by **Prof Oliver Bandmann** (Consultant Neurologist), **Dr Barbara Hoeroldt** (Consultant Hepatologist) and **Dr Godfrey Gillett** (Consultant in Clinical Biochemistry and Inherited Metabolic Disease). Clinics take place every six months at the Royal Hallamshire Hospital, Sheffield on a Tuesday afternoon. 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, S10 2JF. Either GPs or hospital specialists may refer to this clinic.

Children's Clinics

WD Clinic for Children and Young Adults at King's College Hospital, London

There is a multidisciplinary team 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), **Dr Jemma Day** (clinical psychologist) and **Ms Bethany Tucker** advanced nurse practitioner (ANP) in children's liver disease. The clinic is directed at patients who are complex with both liver and neurological involvement. Referrals should be made via the Paediatric Liver Centre at King's or enquiries sent to **Lucia DeBiase** lucia.debiase@nhs.net, PA to Prof Dhawan or to **Dr Tammy Hedderly** Tammy.Hedderly@gstt.nhs.uk.



ANSWERS: 3. a sit; b ice; c lay; d vet; e end; f red; g Silver; **4. Crack the Codes —** 1) 1 Man went to mow, 2) 6 wives of Henry the Eighth, 3) 7 Wonders of the World, 4) 12 Signs of the Zodiac, 5) 18 Holes on a Golf course, 6) 21 Spots on a die, 7) 29 Days in February in a Leap Year, 8) 52 cards in a pack (without jokers), 9) 88 keys on a piano, 10) 360 degrees in a circle; **5. Dingbats** 1 Zinc (Z in C), 2 Tin (Latin writing with La crossed out!), 3 Manganese (mango + knees), 4 Helium (the Ilium bone!), 5 Nickel (5 cents = a nickel!), 6 Iron, 7 Sulphur (sole + fir), 8 Argon (R gone from alphabet!), 9 Lead (a dog's lead), 10 Tungsten (Tongs + X = 10 in Roman Numerals); **6. Did they exist in the year 2000?** 1 Yes (first one in 1995), **2** No (founded in 2001), 3 Yes—founded in 1997, 4 Yes—the first book published in 1997, **5** No—founded in 2004, 6 No— Euro Coins came into circulation in 2002); **7. Anagrams** 1 The Sims, 2 Transport for London, 3 Dora the Explorer, 4 Hollister, 5 International Space Station.

1	6	8	2	3	5	4	7	9
2	4	7	9	8	6	3	1	5
3	9	5	1	7	4	8	2	6
7	3	4	6	1	9	2	5	8
5	8	1	4	2	7	9	6	3
9	2	6	3	5	8	1	4	7
4	5	9	8	6	2	7	3	1
6	1	2	7	9	3	5	8	4
8	7	3	5	4	1	6	9	2

A Date for your Diary 2025-26

Date	Time	Event
Sunday, 20 July 2025	**1130—1530**	**WDSG-UK 15th AGM – Cambridge RUFC, (52) Grantchester Rd, Cambridge CB3 9ED**

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 :

Wilson's Disease Support Group – UK
www.wilsonsdisease.org.uk

CONTACTS:

Dr Bill Griffiths:	Chairman email: **billgriffiths@wilsonsdisease.org.uk**
Elizabeth Wood:	Vice Chairman email: **lizwood@wilsonsdisease.org.uk**
Valerie Wheater:	Secretary, Treasurer, Patient Register Coordinator & newsletter editor email: **val@wilsonsdisease.org.uk**
Mary Fortune:	Committee Member and Liver Transplant Patient Adviser email: **maryfortune@wilsonsdisease.org.uk**
Claire Stapleton:	Committee Member email: **clairestapleton@wilsonsdisease.org.uk**
Dr Godfrey Gillett	Group Adviser, Honorary Member
Dr Caroline Simms	Group Co-Founder
Linda Hart:	Group Co-Founder
Rupert Purchase, DPhil	Group Adviser on trientine
Webmaster:	**Black Cat Websites**

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 are required, please contact Valerie.