Wilson's Disease Support Group-UK

NEWSLETTER, **FEBRUARY 2008**

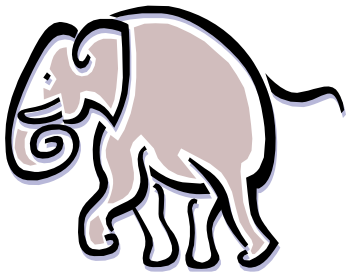
Welcome!

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, their families and friends.

The organisation aims to provide informative articles about the nature of the disease, articles written by patients, families and friends, about their experiences of the disease, recent progress in treatment and much more by way of an annual newsletter. The organisation also aims to promote networking of Wilson's disease patients and their families by helping and encouraging them to correspond with one another.

The organisation also strives to promote a wider awareness of Wilson's disease within the medical profession.

2007 was a busy and eventful year!



The good news is that at last, and at Dr Gillett's recommendation, we have now employed the services of a professional web designer, Black Cat, to redesign our website.

Last year Valerie and I attended two meetings of the EuroWilson UK forum in London; both were very interesting and informative. Doctors, academics and representatives from other liver charities and drug companies also attended. Professor Tanner, coordinator of the EuroWilson project, has kindly written an article for us in this issue of the newsletter

WDSG - UK

Currently, we have just under £5,000 in group funds; our main expenditures being the newsletter, new website and hiring of the University of Nottingham Staff Club for the *At Home* with Dr Walshe. May I take this opportunity of thanking members who have raised funds for the Group and also those who have given a donation with their annual membership.

During the year we have welcomed new patients and their families to the Group, but have also, sadly, lost to cancer one of our longest standing members and friend in Linda McGibbon. Valerie and I attended her funeral in November and flowers were sent on behalf of the Group.

Earlier in November Valerie and I took a short break in the Peak District, which on reflection was not the best time of year to visit the area! Nevertheless, it was very pleasant, although I am looking for a new walking partner for next year!

We are planning an annual meeting of the Group at the Cambridge Rugby Union Football Club (CRUFC) in Cambridge for Sunday, May ? 2008. It should prove an ideal venue with a newly built conference room, disabled facilities, ample parking and easy access from the M11. We hope to see you there!

I hope you will enjoy reading the newsletter and, as always, many thanks to all our contributors. Please note that subscriptions are now due for 2008.

Best Wishes, Linda

(Membership and booking forms for meeting enclosed)

IN THIS ISSUE…....

Wilson's Disease Support Group (UK) – Website Update

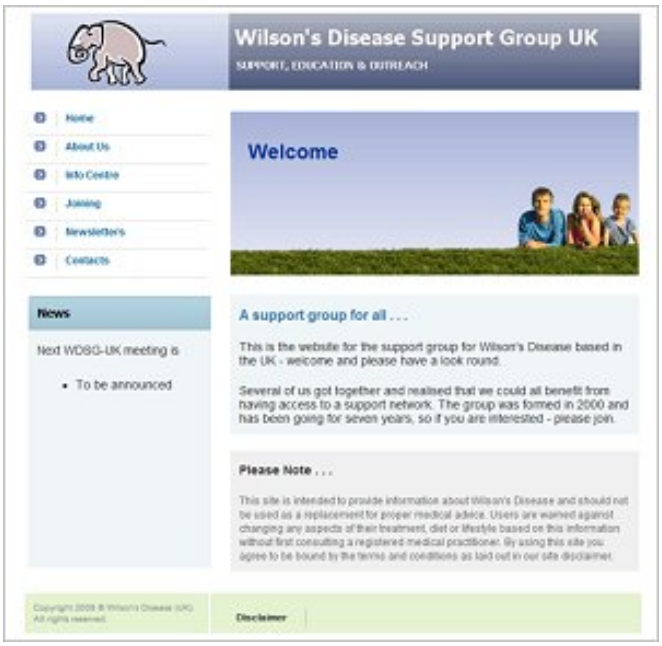
The Wilson's Disease Support Group website has now been redesigned and has a new web address:

www.wilsonsdisease.org.uk

Please take a look and let Linda know if there is anything you think should be added or changed. Please send all comments to: linda.hart37@ntlworld.com

We would like to thank James Beckett for all his hard work and effort in maintaining the website since 2001.

Unfortunately, due to ever increasing commitments, James has kindly passed on maintenance of the website to *Black Cat Websites*.



Fundraising

We would like to thank Sylvia Penny for all the fundraising she has done for the group this last year.

Firstly, Sylvia approached the Reverend Valerie Price, vicar of Victoria Park Methodist Church in Torquay, to request a collection plate be left at the back of the church after a Sunday service to raise funds for the Support Group. She was taken aback when the vicar appeared to refuse. However, the vicar offered instead to ask the Church Council if a Bring and Buy Sale and Coffee Morning could be held in which Sylvia could tell everybody about her granddaughter, Emma.

The event went ahead and £130 was raised for WDSG-UK and a thoroughly enjoyable day was had by all.

In addition, Sylvia through various collections, has raised a further £150.

Once again, we would also like to thank Belinda and Barry Diggles for their fundraising contributions in the last year. They raised £190 through their efforts last Christmas (2006) from the sale of Belinda's home-made Christmas puddings and also by holding a barbecue at their home last summer.

Donations

Thank you to Joan Smith for the contribution of £155. Joan's father-in-law, the late Mr Edward Charles Smith, requested that rather than flowers be sent to his funeral, mourners make a donation to a charity. Joan and the family very kindly suggested WDSG-UK.

"AT HOME" WITH DR WALSHE
September 2007

Last year there was no formal structured meeting of the Support Group. Instead, and at Dr Walshe's suggestion, we held an informal meeting, so that he could keep in touch with old patients and also make himself available to any newly diagnosed patients.

The meeting took place on September 22 at The University of Nottingham Staff Club, which had been the venue of three previous meetings of the group.

Amongst those present was a new patient, Matthew Rose, together with his fiancée and his mother. Of the regulars who attended there were the *terrible twins* (David and Paul Chiswell), David Groome, Helen Lothian, Linda and her partner, John, and Valerie.

The weather was kind, the setting was beautiful and a good time was had by all.

Dr Walshe with left to right: Matthew's mum, Pat, Matthew and his fiancée, Katie.

A few smiling faces: left to right - David & Paul, John, Dr Walshe, David & Val. Front Linda & Helen

About Emma…….

by Sylvia Penny

Hello: I am Sylvia Penny of Torquay, grandmother of Emma who is now 27 years old. Emma has a partner called David and they have been together for twelve years. They have two lovely children; Amy who is nine and Thomas who is six.

In around November 2006 Emma started to become ill. She started to fall about and her legs and arms would twitch and kick uncontrollably. We could not understand what was wrong with her, so I took her to the doctor's and he examined her, but really did not know what was wrong even despite carrying out various tests. She gradually got worse and a few months later I found her in bed suffering from a fever and appearing extremely ill.

David sent for the doctor, who immediately arranged for Emma to be admitted to Plymouth Hospital some thirty miles away. It was only then that they diagnosed Wilson's disease. After a week's stay in hospital Emma was sent home, having been prescribed penicillamine. After a couple of months she got so much better that she and David started to talk about getting married. However, the penicillamine started to affect her kidneys and her medication had to be changed. She is now on trientine dihydrochloride. Unfortunately, her condition has worsened and we are now waiting for her to improve again.

She is not quite as bad as she was when first diagnosed, but we are having to help feed her, and her speech has deteriorated. Her balance has also been affected and she is falling down inside and outside the house.

The past fifteen months has been heart breaking for us all to see Emma become so ill, then improve and then get poorly again and we are now just hoping and praying that these new tablets will make her better.

Emma's mum, (my daughter) Sheila, has been wonderful in every way. She has cooked special food for Emma and has helped with household chores as well as taking Emma's children to school. Amy has been found to have an enlarged liver, but does not have Wilson's disease. She has to visit Birmingham Children's Hospital each month and is on steroids.

The other great help we have had is our contact with Linda and the Support Group. We had been worried and in low spirits, but when Linda made contact with us for the first time and talked about Wilson's, we realised we were not alone. She has been a tower of strength to us all.

Left to right:
Back: Sylvia, Emma and Sheila.
Front: Amy, Thomas and Emma's sister, Daisy

Journey - Liver Transplant and beyond

by Caroline Simms

When I look back on the last four years of my life, it has been like a roller coaster ride.

I decided to go on the waiting list for a liver transplant on February 17th 2004. My friend Joan Smith, who some of you may know from the WDSG-UK group, had recently come through hers and this had prompted me to have my much needed surgery in the hope of a better quality of life and also of alleviating some of the more serious and potentially life threatening symptoms my Wilson's disease had left me with, such as oesophageal varacies, caused by portal hypertension and thrombocytopenia (low platelet count).

My family and I attended the clinic at the Queen Elizabeth Hospital, Birmingham, to have a final low-down on what might be in store for me and them, and I was put on the list as I said on 17th February. They said I could expect to wait up to six months for a suitable donor liver.

I suppose I went home that afternoon not feeling that different. I went back to work as normal and the next day life felt just the same.

It wasn't until I got a call from Peter, one of the transplant coordinators, only six weeks later on Wednesday night at 11.15pm, the 7th of April. "Hi Caroline; can you get your bag and be ready in 15 minutes as we think we have found a suitable donor liver for you".

Sure enough it was at this point I realised what was ahead of me, or at least I thought I did. Shortly after the ambulance arrived at my home to take me over to Birmingham. I can only say I felt deeply sad for the person who had just lost their life, but at the same time immensely grateful that they were giving me the chance of a new life with improved health and also the chance to live a reasonable length of time.

It's hard to describe what emotions passed through me during that eight hours or so, between the call and actually walking into surgery. I must admit I felt very sexy in the support tights!

That morning (8th April 2004), I told my Dad and Calum (my boyfriend at the time) that I'd see them later and my mum and Linda came into the pre-med room with me. The last thing I remember is hugging and kissing them both and saying something about saving me some supper!

My surgery lasted eight and a half hours and the next thing I remember was waking up in recovery in the ICU and feeling like I had been hit by a truck. I cannot describe the pain, but it was dulled somewhat by morphine. My operation had been successful, but I now had the hardest part of the journey to come.

I was only in the ICU for about two-and-a-half days; I seemed to be making a really good recovery, the staff were fantastic, and on Sunday I was moved to a high dependency ward, Liver West 3. I think I was up out of bed after about four days, my belly was HUGE, I went from size 12 up to size 18 pants due to water retention, and my feet looked like sausages! It was my ambition to get back to size 12 and fit into the dress for my brother Mike's wedding in July, for which I was to be a bridesmaid, and to get my feet into those very slim shoes which we had found back in February up in Chester, when Zoe, Sonja and I had spent the weekend looking for the bridesmaids' dresses.

But unfortunately I had an acute rejection about one week after the surgery, and this started a chain of events which prevented me

from attending the wedding and from returning home to Mum and Dad's for some time.

I was treated with high doses of steroids, used to combat the rejection, which incidentally can be quite common following transplant.

Some people can have unusual reactions to the high doses required to counteract rejection, including steroid psychosis.

I don't wish to go into much detail regarding what happened to my mind for the next six months, but just to say it was an unfortunate experience for myself and those close to me and also for some of the staff whom I battered, but who hopefully understood that I was not well. Most people were fantastic, (all apart from Calum, now my ex, who went off with another woman whilst I was under section).

However, I did recover; it just took some time.

Almost four years on, I have a fantastic new job in London, I feel like a new person, life is AMAZING, and looking back on how I was before my liver transplant, I don't know how I managed to keep going. I have energy which I haven't known for many years, which allows me to live a pretty normal life. I have been on holiday abroad and can eat pretty much what I like apart from grapefruit. So many years without chocolate, but can you believe it, now I'm allowed to eat it, I don't bother! Why do we always want the things we can't have??

Anyway, if any of you good people are facing the dilemmas of possibly needing a transplant now or in the future, feel free to contact me for support via Linda who has my details.

I hope to be at the next meeting of WDSG-UK later this year, and will be happy to show off my very neat, very big mercedes scar.

Competition

Aubrey Morris has suggested an idea for a competition, which we think is an excellent one.

He suggests that we invite patients to submit an amusing anecdote of a stay in hospital, while being treated for Wilson's disease. The prize will be an original, framed, 'woolly mammoth' drawing created and signed by Dr John Walshe.

All entries will be judged by Dr Walshe and the funniest two will appear in the next edition of our newsletter. Please limit your article to no more than 500 words.

Closing date for the competition is 30th November 2008.

We are looking forward to being inundated with entries!!

WHY I GOT THE NEEDLE!

Aubrey Morris ©

I shall be 80 in May, and I have Wilson's disease. My doctors are reluctant to affirm that I am the oldest patient in the world with the illness but, as they don't know of anyone older, it seems likely to me that I am. This is my story:

At the end of the war, in 1945, I was 17 years old and at school. I obtained my BA degree at university and was then called up for two years' National Service. The MO found me in good nick, I did my square-bashing, was selected for an OCTU (officer cadet training unit), where they really put you through the wringer (assault course and all that) and ended up as a flying officer. During this time, there was never the smallest hint that I was anything other than fully fit, whereas in fact there was this time-bomb ticking away within me, a liver slowly accumulating more and more copper.

It was early in 1969, when I had been editing a well-known weekly magazine for 11 years, that I began to get symptoms. It started with a tremor in my left arm. As it began to get worse and other bits of me started to shake, I went to see my GP, who was baffled. All he could suggest was that it was the stress of my job and that I should take it easy. By September, I was shaking uncontrollably in every limb and my speech was slurred. I was horrified to discover that friends and colleagues were whispering behind my back that I had become an alcoholic. I returned to my GP, who referred me to a Harley Street specialist, Dr Parsons-Smith.

Dr Parsons-Smith did some routine tests and, getting no answers, said he would have to take me into hospital for observation and further tests. He was the consultant at a tiny hospital in Dean Street, Soho, devoted solely to neurology. It was part of the Charing Cross group of hospitals, but it had only three wards, each of twelve beds (six facing six), and minimal facilities. There Dr Parsons-Smith led a team of a Registrar and four other doctors, all of them neurologists.

A few months before I was hospitalised, I had read a book entitled *Struggle to Return* by a woman called Carol Bunker. It was a narrative of her operation for a brain tumour and her subsequent rehabilitation. She was undoubtedly a brave woman, but she did tend to make a meal of the various medical procedures she had undergone. Particularly harrowing was her account of a lumbar puncture. I remember thinking "Oh, please God, don't let this ever happen to me!" And now the very first thing Dr Parsons-Smith proposed for me, after I had settled in, was a lumbar puncture!

I had not yet discovered what all of you know: that nothing is as bad in reality as it seems in the prospect. So I was very surprised when the expected ordeal caused me very little discomfort. My surprise, however, was not nearly as great as that of Dr Parsons-Smith, who had been convinced that this test would yield up the answer to my problem. My spinal fluid was entirely normal! Dr Parsons-Smith simply couldn't believe it and ordered that the puncture should be repeated! When the result was again negative, the doctors all got into a huddle and reached no conclusion whatever.

You have to remember that in the 60s medical students were not taught about Wilson's disease, except perhaps for a passing mention. Certainly, they were not told - as they are today - that they should always consider it a possibility. The doctors at Dean Street, being all of them specialist neurologists, did know about it, but none of them had ever had a patient who suffered from it.

Meanwhile, my tremor worsened, and my head began to nod up and down, like a mechanical doll's ("titubation," the medics called it). I had to be fed like a baby, because otherwise any food would be shaken from my fork into my lap in its passage from plate to mouth. Anything in a spoon, of course, slopped all over me. I have been told that no two cases of Wilson's are exactly the same, and it does seem to me that my tremor was worse than that of any other Wilson's patient I subsequently saw on the wards, but that my other common symptoms (slurred speech and jerky rigidity when walking) were comparatively mild.

I believe it was one of the less senior doctors who suggested they test me for copper. She was the daughter of New Zealand's foremost neuro-surgeon and she had been in touch with papa to discuss the perplexing case that was me. Of course, the moment they discovered the abnormal copper levels in my blood and in my urine, they knew what to do. They sent me to Moorfields Eye Hospital to have my eyes looked at through a slit-lamp, which showed the inevitable Kayser-Fleischer rings; and "to make assurance double sure" they submitted me to a liver biopsy (expertly performed under local anaesthetic by Dean Street's Registrar, Dr Weinstein) which caused me no discomfort and offered final confirmation. So now they had the diagnosis, but did they have a cure?

"You have Wilson's Disease," said Dr Parsons-Smith." It means your liver doesn't eliminate copper. It has been retaining your copper ever since you were born, and eventually it had more than it could hold, so the copper spilled out into your nervous system. That's why you've got the shakes. As it's a congenital defect, we can't cure it, but we can reverse it. There's this drug called penicillamine which latches on to copper and flushes it out when you go to the loo. However it's a drug with very dangerous side effects, and the maximum safe dose is 500mg a day . So that's what we'll give you and we look forward to you improving."

It was now nearly Christmas 1969, and they thought I might go home, with my tablets, for a couple of weeks. My mother moved in to look after me (my mother was a widow, and I was - and still am - a bachelor). I have a very extensive home reference library, and I searched high and low for a mention of Wilson's. At last, I found it, and this is what I read: "Those with Wilson's disease are doomed to die in coma, bleeding, mute, immobile or demented, unless the correct diagnosis is made and treatment given." I thought a scientific publication should not use emotive words such as "doomed", but that was by-the-by. I had been shaking for a whole year and I had been nearly three months in Dean Street. The diagnosis had been made and treatment was being given, but what exercised my mind was whether this breakthrough had come soon enough. Only time would tell.

Meanwhile I thought of a way to capitalise on my pitiable state. There was a girl I fancied who had always snubbed me and told me quite bluntly how unattractive I was. I now phoned her (my mother held the receiver because of my shakes) and told her I was doomed to die, which brought her rushing to my side. She never forgave me when I failed to pop my clogs! "False pretences," she said (quite rightly).

Returning to Dean Street in January, I lingered for a couple of months, and then something really terrible happened. One reads all the time in the papers these days of MRSA and c. difficile, and the report is always accompanied by some comment about how this never happened "in the good old days." Well, it may have been rarer, and it may not have been the same bugs, but the washroom for my ward was certainly unsanitary, and that must have been where I caught the bug which attacked my left kidney. In next to no time, my temperature shot up to an alarming 104 degrees and I became delirious.

As nightfall approached, the hospital phoned my mother and asked her to come. They gave her a little room at the top of the building, because they thought I might not make it through the night. There was no intensive care unit in that little place, and throughout the night two nurses sat at my bedside, one placing ice-packs on my forehead and the other pushing ice-packs up my rectum. By morning the crisis was over and my temperature was coming down. Not that the bug had been killed off, of course. I was fixed up with a catheter (and for a while with a drip-feed) and confined to my bed, where it was decreed that for the next seven days I was to be injected every four hours, day and night, in my rear, with I know not what. "Wake up, Mr Morris! Time for your injection!" At the end of this period (my backside like a pincushion) they thought I might be okay. It is ironic that the closest I ever came to death was not through the illness that "doomed" me but through being in a place whose aim was to fight against that illness.

Still, they were a great bunch of people in Dean Street. With no special knowledge of kidney disease, they had got me through this nasty episode. Now, they took away the catheter, and Dr Parsons-Smith said: "I have arranged a bed for you in Fulham Hospital. That's the best place for kidney illness, and they will give you a final check-over." How I wished, later, that he never had!

In Fulham, the "arranged" bed was not there, and I was put temporarily in the bronchial ward, full of elderly men suffering from pneumonia. I was kept awake all night by the sound of their coughing up sputum and, twice in the day, the curtains were drawn around my bed while a corpse was trundled out. Eventually, I was seen by the kidney specialist, who said he would give me a kidney biopsy. I awaited this with equanimity, because my liver biopsy in Dean Street had been such a doddle. I was greatly mistaken. Despite the local anaesthetic, I felt the needle go in and considerable pain as the morsel of kidney was extracted. For a long time after, there were blood clots in my urine.

After these tribulations, Dr Parsons-Smith felt I might benefit from a complete break and some fresh sea-air and permitted me to spend a fortnight in Torquay with my mother. Entering the ward on my return to Dean Street, I did a very strange thing: I walked round the ward and gave a £1 note to each occupant - and Sister, following close behind me, collected them all up again!

In subsequent years, I told this story many times as a joke against myself. I knew that what I had done was barmy, but I thought it was a barminess peculiar to myself. It was not until some thirty years later, when I succumbed to full blown manic-depression ("the Stephen Fry illness") and did some research into it that I discovered that unwarranted generosity and a general spendthrift attitude to money were classical symptoms of mania (in the clinical sense). Why this should be, no one seems to know.

There were no longer any blood clots in my urine. I am convinced that these had been caused by internal bleeding after a botched biopsy and were not the first symptoms of a new misfortune which was about to befall me. For now I began to see that my urine had a reddish tinge, as though of blood, and I experienced pain on urinating, which I wanted to do with unusual frequency. I reported these symptoms to Dr Parsons-Smith, and he sent me to the Middlesex Hospital for a cytoscopy. This is a procedure whereby, under general anaesthetic, a narrow tube is pushed up one's urethra and into the bladder.

A fortnight later I had an interview with the consultant. Sitting behind his desk, he eyed me sternly, "What have you been doing to yourself?" he demanded.

I stared at him blankly.

"I said, what have you been doing to yourself?" he repeated.

"I'm sorry," I faltered, "but I don't understand your question."

Seeing he was getting nowhere, he took the bull by the horns and said: "You have pushed a pencil-stump up your penis, haven't you?"

I was astounded. I had never heard of such an aberration, much less practised it. It sounded a very painful thing to do and I couldn't imagine what pleasure anyone could get from it.

"Certainly not," I said.

"Well, you have a large stone in your bladder," he replied, "and it has formed around a foreign object. If *you* didn't push it there, how did it get there?"

"You tell *me*," I retorted angrily, and our interview ended.

I returned to Dean Street to await a date for an operation at the Middlesex to crush the stone. But before this could be fixed, I went completely out of my mind.

My clothes were in my locker, so I got dressed and discharged myself. I got it into my head that I wanted to see a performance of Son et Lumiere at Blenheim Palace, but on my way to the station (I was later told) I barged into the office of a friend and threatened to throw his typewriter out of the window. I made it as far as Woodstock (between Oxford and Blenheim) and checked in at the *Bear Hotel*, but I began to feel tired and my waterworks were painful, so I took a bath and went to bed.

The next day I called on an old friend, an Oxford professor, and requested that he and his wife put me up for the following night. I have no idea what mayhem I caused in his household, but when, some time later, I wrote to apologize, he replied, "Plainly, you were ill, so forget about it."

My final act of madness before I left Oxford was to call into a furniture shop and order £200 worth of furniture (about £3,000 today) to be sent by road to my home in Wembley. After having no income apart from my invalidity benefit for two years, £200 was all I had in the bank, and I had spent it on furniture I didn't need.

When I reported back to Dean Street there was a hullabaloo, and it was decided to treat my mania before I could have the operation for my bladder stone. There ensued several hazy weeks of sessions both with a psychologist and a psychiatrist, and the latter said he would have me committed if I didn't cooperate. It all seemed a waste of time to me, since I felt quite normal. I did notice, however, that people were giving me a wide berth!

At last came the operation and my stone was crushed. When the surgeon came to see me afterwards, of course my first question was: "What was the foreign object?" "Oh," he replied, quite casually, "it was the snapped-off end of a catheter." How times have changed! In today's litigious times, he would have been more guarded. I had only once had a catheter and I remembered which doctor had taken it out. But I would no more think of suing that dedicated man for negligence than I would of flying to the moon.

It was now nearing the end of 1970. I said to Dr Parsons-Smith: "I have been taking penicillamine for a year. It is true I've got no worse, but I don't seem much better either." His response, a few days later, was: "I've arranged for an expert in Wilson's disease to come and see you in January. If we're very lucky, he'll take you back with him to his hospital in Cambridge and give you his personal attention."

Enter Dr John Walshe, of Addenbrooke's, knight in shining armour . . .

EuroWilson

EuroWilson: www.eurowilson.org

We have several effective drugs for the treatment of Wilson's Disease (WD) – penicillamine, trientine, zinc sulphate and acetate, and possibly ammonium tetrathiomolybdate (TM). Many patients with WD have benefited from these drugs, and we are grateful to pioneers such as Dr John Walshe who developed them. Yet a number of questions remain for which it is difficult to find answers, such as

- Some patients treated with penicillamine may initially deteriorate before improving; what proportion, how may this be prevented, and is the same true of the other treatments?
- Trientine is reported to have fewer side effects; are we sure this is so, and that it is equally effective?
- TM is reported to be effective in neurological patients, but it has some important side-effects and is not generally available
- It is now possible to diagnose WD very early with genetic tests, but at what age should treatment start?

To answer these questions, we need clinical trials. Because WD is a rare disease, such trials could only occur if a very large population was involved, namely the whole of Europe. To design trials, we need to know exactly how many new diagnoses of WD are made each year, and how many patients are in the different categories of liver disease, neurological or psychiatric disease, or other.

This was the thinking behind EuroWilson, which is a clinical database of WD patients diagnosed in Europe since January 1 2005. A great deal of work has gone into designing the database, making sure that there are secure methods of maintaining patient confidentiality, producing patient information and consent forms, and setting up a network of "Specialist Country Coordinators" (SCCs). SCCs are doctors (neurologists, paediatricians, liver specialists, geneticists) working in each country, responsible for identifying the patients, obtaining consent, and entering data. This is funded by a grant from the European Commission.

As we know, WD may cause liver disease (usually in younger people), or neurological or other problems. In the UK, most children with serious liver disease are seen at one of the nationally funded paediatric liver centres at King's (London), Birmingham or Leeds. This means that it has been quite easy to ensure that the families of these children have been told about EuroWilson. However, adults with WD under the care of a consultant neurologist may be seen in many different hospitals, so it is quite difficult to ensure that they all hear about EuroWilson. Fortunately, we have been helped by the British Neurological Surveillance Unit, which circulates a monthly electronic questionnaire to all neurologists in the UK on the occurrence of a number of rare neurological disorders.

Even though there is more work to be done to ensure that we are 'capturing' all new cases, and to improve the quality and completeness of the records, some very important things have emerged

from the first three years of data collection. Although WD is often thought of as an adult disease, the average age of diagnosis is 20 years, the youngest being an infant and the oldest 58 years. Severe liver disease occurred as young as 7 and as old as 56, whilst serious neurological symptoms were seen in patients diagnosed between 18 and 50 years. Many of the younger cases were diagnosed through family screening following the diagnosis of WD in a family member. These cases had usually not developed significant problems, and we expect them to remain completely well on treatment. We believe that EuroWilson has raised clinicians' awareness of WD, and this may cause cases to be diagnosed earlier, and thus to have a better outlook. This is obviously a very good thing.

WD appears to be more common in the eastern European countries than the west. We need to make sure that this is not because doctors in Poland and Hungary are more conscientious at entering their patients into the database! A more likely explanation is that a particular genetic mutation which causes WD is more common in the east.

The EuroWilson project has had a number of valuable spin-offs.

- A DVD of neurological features of WD has been produced for neurologists who may not be familiar with WD, to assist them in assessing and monitoring patients
- In order to check that laboratories doing genetic tests for WD are operating at a high standard of accuracy, the European Molecular Quality Network (EMQN) has agreed to set up a quality assurance scheme, which is now in its second year
- As one of several national initiatives, a "UK WD Forum" has now met twice. It brings together patient representatives (Linda Hart and Val Wheater from WDSG-UK and Catherine Arkley from the Children's Liver Disease Foundation), doctors and laboratory scientists.

Patients with rare diseases like WD can sometimes feel rather isolated. This is recognised in a document called "Rare diseases: Europe's Challenge" which is calling on the European Commission to do more for patients with rare diseases in member countries. It is open for public consultation via the web until February 14, and the website for this is: http://ec.europa.eu/health/ph_threats/non_com/cons_rare_dis_en.htm.

We have some challenges for the future, including finding funding to continue the database once the EU money comes to an end. But we have come a long way, and would like to thank everyone who has helped to make EuroWilson such a success.

Stuart Tanner
EuroWilson Coordinator
Emeritus Professor of Paediatrics, Sheffield Children's Hospital

Trientine.

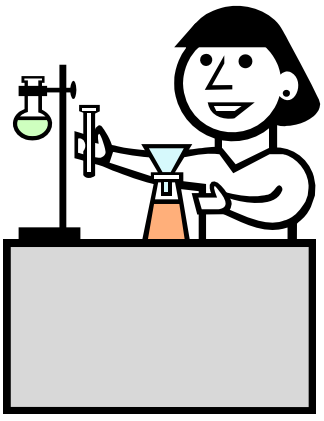
(Triethylene tetramine 4 hydrochloride)

by Dr J.M. Walshe

Patients with Wilson's disease now have a variety of treatments available. In order of development they are BAL (dimercaprol), penicillamine, zinc salts, trientine, liver transplant and tetrathio molybdate. BAL, penicillamine and trientine all act by removing copper from the body and promoting its excretion in the urine. Zinc salts act by blocking the absorption of copper from the gut and molybdate acts both by blocking copper absorption (more effectively than zinc) and also by locking up copper already present in the tissues in an inert form that is not toxic. I will deal with this in a later number of the newsletter. In previous numbers of the news letter I have described BAL and penicillamine and Linda has asked me to write about trientine.

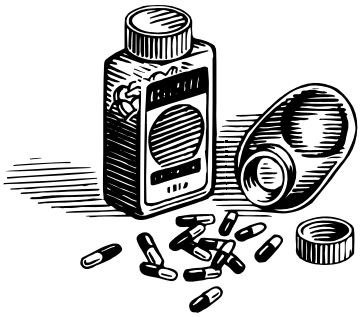
BAL was first used for Wilson's disease in 1948 by professor Cumings at the National Hospital for Nervous Disease in London, penicillamine was introduced in 1955, zinc salts in 1961 and trientine in 1969. The reason for this is probably unique. Trientine was designed for a single patient who had developed penicillamine intolerance, the drug was destroying his kidneys and to have continued with it would have killed him, so an alternative had to be found. My first thought was to get hold of a catalogue of laboratory chemicals and see which, if any, had a formula that might bind copper and was not toxic.

I bought a number of these and with the help of Kay Gibbs, I fed them to rats. None looked very useful. Then I had a stroke of luck. Cambridge University circulated a document listing the various research projects going on in different University departments. In this I spotted that Dr Hal Dixon, in the Department of Biochemistry had interests which might help. I went round to see him and explain my problem. He immediately suggested that triethylene tetramine had the right formula to bind copper and should not be toxic. All that was available was a crude industrial chemical, an oily liquid, only about 60% pure, used as epoxy resin hardener! It was strongly alkaline and highly corrosive. What we had to do was to find a salt and recrystalise out the compound we wanted. Unfortunately none of the acids available gave the desired result and we had to settle for hydrochloric acid to make a safe salt for use. We tried this on rats and it worked just as Dr Dixon had predicted. Unfortunately there was more chloride than we liked, we had to use the 4 hydrochloride salt, not the 2 as we would have wished and the end product remained impure but it was well tolerated by our rats and as no action was an unacceptable approach for my patient, I decided to give it a trial. It proved an immediate success.



This meant that Kay Gibbs had to prepare the salt in my laboratory as there was no commercial source and no drug company was interested in making a new drug for a single patient. The cost of introducing new drugs, at that time, was many millions of pounds. All went well for several years and more and more patients were referred to my clinic for this new treatment. The load of preparing this new drug was becoming impossible to carry out as a 'do it yourself' exercise. Then disaster struck. Our source of supply was suddenly cut off. We had to find a new chemical company from which to buy the crude compound. For some reason which was never explained this new source, using the same preparation, gave us an end product which seriously damaged the kidneys of two new patients just referred to my clinic. Even the best chemists in Cambridge could not isolate the toxic ingredient but it meant recalling all supplies recently posted out until a safe product could be found. Here Dr Dixon came to the rescue and he pioneered a method of recrystallising the pure compound we wanted from absolute alcohol and from then on there have been no more problems with this treatment. About the same time I called a small specialist conference in Cambridge with representatives from the Department of Health, the pharmaceutical industry and interested physicians and as a result the Department of Health took on responsibility to monitor purity, to take on legal responsibility for a product license and a chemical company, Aldrich Chemicals, agreed to manufacture triethylene tertamine 4 hydrochloride to government specifications. Dr. Rupert Purchase, their chief chemist, worked out a method of purification which could be used on an industrial basis. My problems were solved after many

years of frustrating negotiations. We now had a second powerful copper binding drug which could be safely given to patients on a regular legal and supply basis.



It was given the trade name of Trientine. Trientine is now used worldwide as a very effective treatment for patients with Wilson's disease. It has very few side effects and, in this respect, is probably safer than penicillamine though, probably not quite so good at mobilizing copper. But those of you who are now taking it can think that you are taking a drug which was originally developed for a single patient who had developed a rare complication of treatment for a rare disease.

Probably a unique situation and one which is unlikely to be repeated.

Patients with Wilson's disease are warned about an advertisement on the web under the heading Wilsotab.

To the best of my knowledge there is no publication in a peer review journal about the clinical or bio-chemical results of treatment with herbs

As you probably all know, Wilson's disease is caused by the body's inability to excrete copper and the metal accumulates in the liver and brain causing symptoms of the disease'

To effect a cure this excess copper must be removed. This is achieved by treatment with penicil-lamine or trientine. Absorption of copper from the gut can also be achieved by treatment with zinc salts or tetrathiomolybdate.

There is no evidence that herbs can give such results, much less so in forty days at a cost of $230 for a months supply.

To stop your regular anticopper treatment will be courting disaster

J.M. Walshe

The Intrepid Explorers

by Valerie

Linda and I managed a few days' holiday in the middle of November in the tiny village of Litton in the north-west of the Peak District. Litton is a mile outside Tideswell, which is famous for its church known as the *Cathedral in the Peaks*.

Having been born in Derbyshire, Linda is familiar with the area and was able to suggest two good walks that we could take in the short time that we were there.

So, the first day we drove out to Lathkill Dale. We had decided the night before to take a circular walk which would allow us to stop half-way round at a pub in Youlgreave. Not being morning people, we were already late setting off, but it was downhill all the way and we managed to get there in time for a late lunch.

The weather was very frosty and we warmed ourselves up in front of the open fire, before attempting the return leg. Unfortunately, thereafter, the Ordnance Survey map proved inaccurate! Fields and roads had been moved and public rights of way just didn't exist.

Now I should like, at this point, to mention Linda's and my different approach to walking. Whereas I like to get from A to B in as quick a time as possible, returning via C and ignoring contour lines on maps, Linda enjoys stopping for flasks of coffee, admiring the views, appreciating the wildlife, indulging her artistic talent behind a camera lens and generally adopts a more respectful attitude towards maps! What should have been a relatively quick walk turned into rather a long one and we were lucky to get back before darkness fell.

That evening, we decided to pit our wits at a pub quiz in nearby Tideswell, confident of our superior intellect. However, beset by misfortunes and misunderstandings, we ended up coming last of twelve teams competing. I blame Linda for not knowing all the answers!

The following day, full of optimism, we set off to explore Monsal Dale. We parked at a disused railway station at Millers Dale and headed east towards the River Wye. No sooner had we started than we had to cross an enormous viaduct, where Linda dutifully stopped and lent over to photograph the road many feet below. I, on the other hand, kept my feet firmly planted on the ground, resisted going anywhere near the edge, continued walking with my eyes focussed on the path ahead and yet still suffered an appalling attack of vertigo.

Beyond, the walk turned out to be lovely, albeit a trifle muddy along the river bank. Eventually, we climbed up the 180 steps to the café at Monsal Head, where we stopped for a wholesome lunch; it being the only option. I was resolute that we should return a different way. I persuaded Linda, by showing her the map, that rather than returning the way we had come, it would be just as easy to continue for a couple of miles along the river and then turn right, picking up an alternative path which would soon take us back to the station at Millers Dale.

Linda's Indulgencies!

Val & I outside our humble abode

Appreciating wildlife!

OK Mrs Smarty-pants….. Where to next?

Unfortunately, the right turn we needed to make was in fact a vertical ascent, which was taxing, to say the least, for the unseasoned walker not to mention Linda and me! We made it to the top, amazingly, but it was getting late and distances proved deceptive. Cameras were confiscated, birdwatching forbidden and flasks of coffee confined to rucksacks. An SOS to a friend was treated as a joke. Eventually, we met a very nice farmer, who, taking pity on us, directed us to the nearest main road along which we finally limped back to camp in the pitch dark.

The next and final day we went shopping in Bakewell!

WARNING-WHEN I AM OLD

When I am an old woman I shall wear purple
With a red hat that doesn't go, and doesn't suit me.
And I shall spend my pension on brandy and summer gloves
And satin sandals, and say we've no money for butter.
I shall sit down on the pavement when I'm tired
And gobble up samples in shops and press alarm bells
And run my stick along the public railings
And make up for the sobriety of my youth.
I shall go out in my slippers in the rain
And pick the flowers in other people's gardens
And learn to spit.

You can wear terrible shirts and grow more fat
And eat three pounds of sausages at a go
Or only bread and pickle for a week
And hoard pens and pencils and beermats and things in boxes.

But now we must have clothes that keep us dry
And pay our rent and not swear in the street
And set a good example for the children.
We must have friends to dinner and read the papers.

But maybe I ought to practice a little now?
So people who know me are not too shocked and surprised
When suddenly I am old, and start to wear purple.

Jenny Joseph

Wilsons Disease Support Group UK

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WDSG-UK

Tell others about the WDSG-UK

Please tell others whom you may know who have WD, who might benefit from the support group and what we are doing.

Inform your family, friends, consultant physicians, GP surgery, local MPs about WDSG-UK

The more people who know about us , the more we can promote a better awareness of Wilson's Disease within the community and the better the chance of early diagnosis of WD for future WD patients.

If more copies of this newsletter or patients & families' correspondence list are required, please contact:
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We're on the web
www.wilsonsdisease.org.uk