

Surviving Wilson's disease

Lisa Yonetani

Comments by Dr J M Walshe

Lisa Yonetani BA

J M Walshe

ScD, FRCP

Clin Med JRCPL
2001;1:72-4

Her story

It is difficult to say when it all started. Several years before I was diagnosed as having Wilson's disease I experienced a sense of 'impending doom'. My mother recalls me saying that I thought something terrible was going to happen to me and I told my best friend that I was fated to die in my youth from some kind of illness. Fortunately, that premonition was only partially correct and I am here to tell my story.

Wilson's disease is a rare neurological disease caused by an abnormal recessive gene. The normal gene controls the metabolism of copper. As I have the full abnormal gene I cannot excrete copper, which accumulates either in the brain or in the liver. Wilson's disease can also cause serious psychological damage. Copper accumulates in the body from birth yet its effects usually do not become apparent until later in life, most often during adolescence.

Hepatic Wilson's disease is sometimes misdiagnosed as hepatitis. The neurological form has many different symptoms, some of which I experienced myself. Damage to the brain can cause slow speech; slurred speech; no speech; the gradual deterioration of writing; lack of concentration; personality change; tremors; dystonia and the inability to chew or swallow. These are but a few of the numerous symptoms that can puzzle doctors for years before a correct diagnosis is made.

In the school year of 1989-1990 I involved myself in numerous activities and pushed myself to the limit. It seemed to be a consequence of this that I spent the whole of the following summer in an arm-chair with no energy to do anything. I even refused to go out in the sun as it tended to wilt me like a flower.

Long before that summer, some of the first symptoms could be observed in the way that my singing voice, previously quite good, seemed to be breaking rather like a boy's voice does during puberty. Gradually, as time went on, my speech became slurred. I also lost some dexterity in my fingers and was taking longer to learn new piano pieces. My hands were becoming stiff and many of my teachers complained about my writing being illegible in my exams in June 1990. By the following September it had shrunk to almost pinhead size. Mornings were often difficult as I found it increasingly difficult to

open my eyes and drag myself out of bed, and sometimes severe leg cramps during the night left my legs unable to support me the next morning. Also by this time my head had begun to manifest a distinct Parkinsonian tremor. I was scared and yet strangely gratified that my presaged destiny was not derived from some crazy hypochondriacal fantasy. The most frightening thing was not knowing what was wrong with me.

When it became clear that the summer's rest had brought no improvement, I was taken to see the doctor. After numerous blood tests left me without a definite diagnosis, the possibility of myalgic encephalomyelitis (ME)/post-viral syndrome was suggested, though the search for a more conclusive answer was continued. In November 1990 my mother requested that I have a CT scan. Dark patches on the scan gave evidence of brain damage.

In an eye test on 24 January 1991, Kayser-Fleischer rings – rings of copper around the cornea of the eyes – were immediately spotted. Wilson's disease, one of the few symptomatically curable neurological diseases, was diagnosed that day and a great feeling of relief and triumph washed over me. My mother wept and I held her hand, comforting her.

The following day I started penicillamine treatment. The usefulness of this drug was first described in 1956 by J M Walshe, a consultant physician at Addenbrooke's Hospital in Cambridge, who, although retired, still gives up his time to see his patients with Wilson's disease. The drug is a derivative of penicillin and acts by forming a bond with the copper ions so they can be excreted from the body.

Three days later I had a painful liver biopsy to determine how much damage had been caused to my liver by the copper. The biopsy revealed some liver scarring.

On 1 February I developed a reaction to the penicillamine – a rash resembling measles and a soaring temperature. When the rash died down a couple of days later, penicillamine was reintroduced in a smaller dosage. My temperature started to rise again and I was immediately taken off it and put onto trientine. Trientine had to be refined and packaged in Dr Walshe's own laboratory for some years before a regular manufacturer could be found.

One night about three weeks later I began having

horrendous muscle spasms. I spent the next few days in hospital. I remember lying helplessly in the hospital bed the first night while overwhelming waves of muscular tension washed over my face and entire body every few seconds. I remember the look of pain on my mother's face as she watched mine. She was as helpless as I was and could do nothing. I was physically drained but somehow my body, which was completely out of control, managed to find the strength to continue tormenting me. For the first and only time up until the time of my depression, I shed a few tears – tears of desperate and utter exhaustion.

The next few days are a black hole in my mind as I was put on a drip and heavily sedated to relax my muscles. After a night in the intensive care unit, I was taken to another hospital in London. I settled in well and befriended all the nurses and other patients by means of an insatiable desire to hug everyone in sight, and a communication aid which the hospital loaned me so that I could type what I wanted to say.

By this stage I was on various tranquillisers and muscle relaxants including benzhexol, which is used in Parkinson's disease, and I suffered no more muscle spasms. However, when conscious, my body was in a constant state of dystonia, like a rigid statue of deformity. The dystonia left no trace when asleep and I appeared to be normal.

The doctors also added zinc to my therapy. However, the combination of zinc and trientine blocked my intake of iron, making me very anaemic. During the next seven months my condition deteriorated rapidly.

When I could bear it I wore a neck brace as I could no longer support my head and it hung down, involuntarily and rhythmically swinging to and fro like the pendulum of a clock.

I started going to a school for disabled children in June 1991. This was mainly to give my mother a break as I was completely dependent on her for everything and she was nursing me around the clock at home, having to get up during the night to give me medication and to tend to my spontaneous, heavy nosebleeds that sometimes lasted several hours. I never really felt I belonged at the school as I did not feel that I was 'disabled' – I was 'ill'. Neither did it stimulate my mind, for I lacked concentration.

By mid-September my mother was desperate as she could see how much worse I was becoming. We discovered that there existed another Wilson's disease specialist in New York and as my father happened to be working out there at the time we decided to go. Seven days later and three weeks after my sixteenth birthday we were on a plane to New York.

There we were to meet one of the most inspiring men I have ever met – my doctor, Dr Scheinberg. He has dedicated his life to the study and treatment of Wilson's disease and he and his associate, Dr Sternlieb, who treats the hepatically affected Wilson's disease sufferers, showed me such sincere care and affection that I am eternally grateful. Dr Scheinberg immediately took me off the trientine and put me on corticosteroids for about four days before gradually reintroducing penicillamine. Over a period of about six weeks he weaned me off the steroids until I was just taking penicillamine. By then I had also started my treatment of BAL (British antilewisite). This was used during wartime in Britain to get rid of heavy metal poisoning from bullets and was

found to be effective in getting rid of copper accumulated in the brain from Wilson's disease. However, there was only a 60% chance of recovery with BAL. It was given by intramuscular injections which were excruciatingly painful. I received three courses, each one of twenty injections.

At the end of the first course I started to walk upright and my dystonia lessened. To others I was noticeably improving. However, midway through the second course in late November I became deeply depressed. This was triggered by my own personal realisation that I was, actually, going to be all right. The psychological change was striking, seeming to occur almost immediately, and overnight I lost many of the memories from the previous three or four years, since my illness had started subtly to manifest itself. I even forgot what I had been like and how I had behaved towards people as recently as the week before.

All this time I had been half denying that I was ill and now my rapid improvement was forcing me to face up to reality. I could not keep up with myself. I had accepted death with the courage that kept me going throughout the whole ordeal and now that my life had taken such a dramatic turn I had to accept living again. The concept of life was harder to accept than death. I was terrified of everything, especially the future and that long, bleak road to rehabilitation that I would have to face.

During my illness my personality had changed. I appeared to revert to a much younger age, behaving in a playful, light-hearted manner, telling jokes on my communication aid and being extremely, and often inappropriately, affectionate. It was not that I was not aware of the gravity of my situation – I was; my apparent frivolity was just my way of dealing with it, trying to make things easier and less traumatic for those around me, whilst showing them that I was at peace with death. Depression left me in a sort of limbo. I didn't know who I was anymore. I wasn't the old healthy me and I wasn't the merry ill version either.

For two or three weeks endless sentences poured out of me full of the confusion I was experiencing. My doctor was very patient and generous with his time, seeing me every day after my injection for up to two hours. But this constant flow of emotions also continued at home with my weary mother. She was worn out reading everything that came into my mind. I selfishly hated it when the phone rang because it was an intrusion and it was taking my mother away from me. If I knew someone was coming to visit me, I would vomit with nerves the day before. I wanted to hide myself and my ugliness from the world.

The memories I had lost came back in pieces and each recovered memory was a triumph and a step towards my renewed inner strength and acceptance of life. A final course of BAL, which finished at the beginning of February 1992, brought my speech on greatly and the following day I put away my communication aid, resolving never to use it again.

The first six months after my treatment ended were highly gratifying as every day granted some improvement, whether big or small. Once I had re-mastered the intricate art of using cutlery I began to have the courage to eat out in a restaurant without feeling self-conscious. All the basic activities that I used

to take for granted, such as eating, talking, dressing myself and brushing my teeth, had to be relearned. Brushing my teeth was one of the harder things to relearn because of the rigidity in my arms and wrists. I spent the month of May that year teaching myself how to write again. It was, and still is, not as fast as it was before my illness, but remains almost as attractive. The hardest thing to perfect, to this day, however, is my speech. It tends to fluctuate between good and bad patches according to how tired or lazy I am at the time. The main difficulties are with projection and articulation. However, I am improving all the time, and although progress is slower now than in the first year, I have not given up yet.

I also, inevitably, lost a lot of self-confidence through my illness, and this has fluctuated over the past seven years. Although I still become anxious or nervous occasionally, I have not experienced a panic attack in a long while. Generally things have improved enormously and can, as I see it, only continue to do so.

In the first year of this new era of my life I relearned other important skills that, at the time, I was not even aware that I had forgotten – social skills. I had completely forgotten even the concept of tact and, among other things, how to go about making friends. Despite this I did make some wonderful friends and had a very active social life. I went back to a private sixth form college in September 1992 and undertook five GCSEs in a year, followed by three A-levels over the next two years, achieving straight As. I then went on to Leeds University, where I read psychology and sociology joint honours. The three years I spent in Leeds were particularly important as it was the first time that I had lived away from home for any significant amount of time and I desperately needed to break away and learn to be independent after being so dependent while I was ill. I graduated successfully two years ago and am now pursuing a BSc in herbal medicine.

It is not easy living with Wilson's disease. Almost every day is a battle. It becomes very frustrating at times, for myself and for others listening, when I cannot express myself the way that I want to, and it does hold me back in some ways and make me feel impatient with myself. However, I do not really resent the disease – how can I when it was my fate? It is a part of me, and although I may feel frustrated or sorry for myself at times, it is difficult to express how much I have gained through it. It is a huge, ongoing lesson. I went from a young, carefree teenager who had just about everything, to a young, disabled teenager who lost just about everything, and had to fight her damndest to win it all back.

I am eternally grateful to all the doctors, nurses, friends, relations, my parents and my sister who stood by me and helped me to get to where I am now. Although it may be years more before I am rehabilitated to my maximum ability, I am winning the battle.

Comment on Lisa Yonetani's story by Dr J M Walshe

This patient's story illustrates several important aspects of the management of patients with Wilson's disease. First is the almost inevitable delay in making the diagnosis, some 18 months in this case. The initial symptoms were those of vague ill health and a 'sense of impending doom', not an uncommon story; neurological signs were only present for about six months. Thus the delay probably did not contribute significantly to the severity of the illness. Her initial response to treatment with penicillamine was a febrile, urticarial reaction. My experience suggests this type of early reaction can always be managed with steroid cover and cautious reintroduction of the drug. In this case an attempt was made to restart penicillamine without steroids and, inevitably, resulted in failure. Trientine was then given, a logical second step, and though not apparent from the patient's story, was followed by some slow improvement. However, her doctors, anxious to speed her recovery, made the cardinal mistake of adding zinc sulphate to the regimen. This resulted in the development of a severe sideroblastic anaemia. I have noticed previously that the development of significant anaemia is likely to result in deterioration and must be corrected as quickly as possible.

This case history also illustrates the continued value of dimer-caprol (BAL) in the management of severe neurological Wilson's disease, particularly the dystonic syndrome. It is obviously impossible to say, in this case, whether the remarkable improvement achieved by Dr Scheinberg's regimen was a result of the successful reintroduction of penicillamine, the use of dimer-caprol, or a combination of the two. This is always a problem when two variables are introduced at once but in clinical medicine controlled studies of one variable at a time may not be ethically justifiable, as in this case when the patient's very severe illness required urgent management.

The lessons to be learnt therefore are (1) always consider the possible diagnosis of Wilson's disease in a youngster with failing performance at school and vague personality changes; (2) never try to correct early penicillamine allergy without steroid cover; (3) never add zinc sulphate to a chelation regimen. Dimercaprol can be a valuable addition to therapy in severe neurological Wilson's disease.

Address for correspondence:

**Lisa Yonetani, 96b Pinley Oaks Road, Sanderstead,
South Croydon, Surrey CR2 0NS;**

**Dr J M Walshe, Broom Lodge, 58 High Street,
Hemingford Grey, Huntingdon, Cambs PE18 9BN.**