This is the story of the world's first ever successfully treated Wilson's disease patient— written in April 2017 by Valerie ©

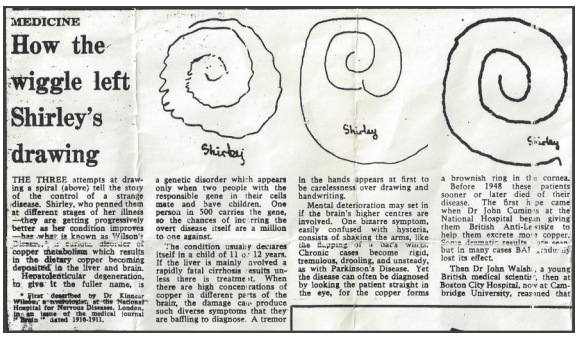
At the end of October last year (2016) I received an email out of the blue from a lady living in London. The email was headed *How the Wiggle left Shirley's Drawing* and it continued, "My name is Jennifer and I manage a small community hall in Westminster, London. What is really fascinating is that the above caption is about my coffee morning attendee **Shirley** who lives here. She was one of the first people that Dr Walshe saw in the 1950s when he first discovered penicillamine..."

Now that was an email that I wasn't likely to ignore. Dr Walshe has on several occasions asked the Group if it had ever heard from a lady called Shirley who was one of the first patients that he ever treated. None of us ever had. Surely it was too big a coincidence that two ladies called Shirley had been treated by Dr Walshe in the 50s. There was only one way to find out - a trip to London!

With Christmas intervening it was quite a while before I could arrange a visit. I had had no direct contact with Shirley at all but Jennifer and I continued to email one another, she acting as the intermediary. She assured me that if I turned up at 2.00 o'clock on a particular afternoon, she would make sure that Shirley would be there to see me. On an uncharacteristically sunny St Valentine's Day afternoon, I presented myself in the courtyard of a grand Victorian building set in the shadows of the Houses of Parliament, to be greeted by Jennifer and later by Dr Walshe's seventy-seven year old former patient, Shirley. What a treat!

Jennifer had kindly opened the hall especially for us and we went inside for coffee. Shirley began by handing me a copy of a 1964 cutting from the *Sunday Times* headed *How the wiggle left Shirley's drawing.* This obviously was the explanation for Jennifer's subject heading in her emails. Above the article were pictures of three spirals, the symbol Caroline and Linda adopted for the welcome section on the front page of the newsletter. Historically, Dr Walshe used to ask all his patients to draw spirals when they were first diagnosed and to repeat them on subsequent visits to see if motor control had improved. Their presence in this newspaper cutting indicated that Dr Walshe was associated with the article.

So what exactly was Shirley's story? She told me that she was born in Islington in July 1939 as the youngest of six children, all of them girls! There were twenty-two years between her oldest sister, Mary, and her although Mary had died as a child so she never actually knew her nor what she had died of. War broke out less than two months after Shirley's birth and although she remained with her parents in London throughout the War, narrowly escaping several bombs, she was lucky enough to have survived the period to now tell the tale!



MEDICINE

How the wiggle left Shirley's drawing

THE THREE attempts at drawing a spiral (above) tell the story of the control of a strange disease. Shirley, who penned them at different stages of her illness—they are getting progressively better as her condition improves—has what is known as Wilson's Disease, or Kinnier Wilson's disease of copper metabolism which results in the dietary copper becoming deposited in the liver and brain. Hepatolenticular degeneration, to give it the fuller name, is

* First described by Dr Kinnier Wilson, a neurologist, at the National Hospital for Nervous Diseases, London, in an issue of the medical journal Brain " dated 1910-1911.

a genetic disorder which appears only when two people with the responsible gene in their cells mate and have children. One person in 500 carries the gene, so the chances of incurring the overt disease itself are a million to one against.

The condition usually declares itself in a child of 11 or 12 years. If the liver is mainly involved a rapidly fatal cirrhosis results unless there is treatment. When there are high concentrations of copper in different parts of the brain, the damage can produce such diverse symptoms that they are baffling to diagnose. A tremor

in the hands appears at first to be carelessness over drawing and handwriting.

Mental deterioration may set in if the brain's higher centres are involved. One bizarre symptom, easily confused with hysteria, consists of shaking the arms, like the flapping of a bird's wings. Chronic cases become rigid, tremulous, drooling, and unsteady, as with Parkinson's Disease. Yet the disease can often be diagnosed by looking the patient straight in the eye, for the copper forms

a brownish ring in the cornea.

Before 1948 these patients sooner or later died of their disease. The first hope came when Dr John Cumings at the National Hospital began giving them British Anti-Lewisite to help them excrete more copper. Some dramatic results were obtained but in many cases BAL undersupply lost its effect.

Then Dr John Walsh, a young British medical scientist, then at Boston City Hospital, now at Cambridge University, reasoned that

▲ ***The Sunday Times article 26.01.1964***

Asked about her memory of childhood, Shirley remembers doing well at school and specifically being around third from the top of her year in her teens. She considers herself to have had a normal childhood and good health apart from a stay in hospital when she was about ten. She had developed pneumonia and had a collapsed lung. She made a speedy recovery and returned to school. The only other health problems she can recall in her adolescence were several very severe nosebleeds. In 1953 she vividly remembers attending a Street Party that was held to celebrate the coronation of Queen Elizabeth II, and it was around that time that people began commenting to her parents that they thought something was wrong with her. On one day in particular, she had been out food shopping as was her custom and she remembers having difficulty walking home, staggering along the street in an erratic fashion. Thereafter her memory of events is hazy and Dr Walshe takes up the story.

"Shirley was the first patient that I ever treated. I returned to the UK in August 1955, after a 12 month scholarship at the Boston Hospital in the States, with 50 grams of penicillamine, a drug which I had discovered while working over there as a possible chelating agent for patients with Wilson's disease. On my return I went back to work at University College Hospital (UCH), London, in search of patients on whom to trial my new medication. My father was a leading neurologist at the National Hospital for Nervous Diseases (now known as the National Hospital for Neurology and Neurosurgery (NHNN)) at Queen Square, London, the same hospital where Dr Samuel Kinnier Wilson, who first described Wilson's disease in 1912, had worked. I asked my father if he would en-

quire among his professional colleagues whether any of them had patients with Wilson's disease in their care. My father found three such patients, two that were based at NNHN and another that was in the care of Dr Ashby, a consultant neurologist at Whittington Hospital in North London. This last patient turned out to be sixteen year old Shirley.

I visited her in hospital and with the agreement of Dr Ashby, gave her a low dose of penicillamine. I had taken some myself previously and had suffered no ill effects. Shirley had been at *The Whittington* for some time and had received no effective treatment. She was bedridden, had to be fed and dressed, was shaking uncontrollably and her speech was practically incomprehensible. She tolerated the penicillamine I gave her very well and Dr Ashby agreed for her to be transferred into my care at UCH. There she remained for some time until she gradually started to improve. The chief biochemist at *Distillers* kindly agreed to make further quantities of penicillamine for me and I went on to use it successfully on many more patients. In 1957 I moved to Addenbrooke's Hospital in Cambridge and Shirley remained my patient until I retired in 2000.

On 7 January 1956, roughly six months after starting her on treatment, I was able to write up Shirley's case in *The Lancet: Wilson's disease new oral therapy (pp25-26)* based on her positive response to penicillamine. Thereafter penicillamine was accepted by other doctors in the treatment of Wilson's disease."

I asked Dr Walshe about the article Shirley had shown me from the newspaper. He said that he had been approached by the Medical Correspondent of *The Sunday Times* who had been reading through past issues of *The Lancet* and had read the story of Shirley. The medical correspondent had promised Dr Walshe fame and fortune once his article had been published. As it was Dr Walshe waited for the telephone to ring on the day of circulation, but he received only one call, from the daughter of Samuel Kinnier Wilson, who pointed out that her father's name had been spelt incorrectly in the article! So much for the fortune and fame that had been promised!

Shirley's memory of events since she started to get better are a lot more clear. She was discharged from hospital at the end of 1955, continuing to improve by the day. She returned home to her parents and tried to make up for the time that she had spent in hospital. Seven years later, in October 1962, she married her husband, Harvey, and they are still happily married today. The wedding took place at Caxton Hall in Westminster, a venue favoured by the rich and famous and near which they still live today. She had been a regular churchgoer but decided that a church service would take too long and would not be conducive to her wearing a new lilac coat and dress which she had recently bought! She and Harvey took the train to Southend afterwards where they spent a very happy honeymoon.

Shirley and Harvey - 1962

She was worried about starting a family, as in 1962 few treated Wilson's disease patients had done so already, but by 1971 at the age of thirty-two, she gave birth to her first child, a son, followed by two further healthy children at two yearly intervals. At that time, of the few children that had been born to Wilson's disease mothers, all had turned out to be boys. Dr Walshe had speculated that penicillamine might have been responsible for this. Unfortunately for him, in April 1975 Shirley produced her third child, a daughter, and any commercial interest in him having discovered a drug which determined male selection had been eradicated in one. My producing a daughter six months later didn't help!

Shirley has remained on penicillamine throughout her life, and will have been taking it for 62 years at the end of the summer, longer than any other patient in the world. She has had good health and has worked throughout her life. She has asked me through this article to pass on her personal thanks to Dr Walshe in the knowledge that, without him, she is unlikely to have been here today to tell her remarkable story.

This article has been uploaded on to the medical section of the WDSG-UK website in November 2020. Shirley continues in good health, is now eighty-one and is in her sixty-sixth year of receiving penicillamine to treat her Wilson's disease. We wish her well.