Unhappy Anniversary

Forty years ago, Valium was the new wonder pill. Today, the story looks different.

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Much has changed in Pat Edwards's life in the past 40 years. She has divorced, she has moved from London to the South Coast, she has become a grandmother. But one thing has stayed the same: she is still taking the Valium.

Pat Edwards was 25 when she was first prescribed the drug at the end of 1962, a few months before its official launch the following year. She had become unaccountably weepy after the birth of her second child, a condition we may now recognise as post-natal depression. Her local GP in Hackney gave her four days' supply of Valium, a suitably cautious amount for a new treatment, and four days later, after some improvement, Edwards was given another small supply. The drugs seemed to have an immediate effect, and she made plans to return to her job as a hairdresser. But then something else happened.

'One morning I was on my mum's doorstep crying my eyes out. My mother called the doctor, and he didn't come round to see me but upped the dosage of my tablets. They went up from one tablet of five milligrams to two, so I was on 10 milligrams a day. This went on for another month, until one day I simply couldn't leave my mother's house. My mother thought I was being silly, but I would have terrible panic attacks and start sweating if I couldn't see the front door.'

Agoraphobia was not a well-recognised medical condition in the early Sixties. The doctor was called again, but Edwards says he failed to visit. Instead, the dosage was increased again, to 15 milligrams. He also prescribed Marplan, an anti-depressant. Edwards's condition failed to improve. 'In those days you believed in what your doctor gave you without question. I used to send him a stamped addressed envelope every month and he sent me back a month's supply of tablets.'

Edwards is 65 now, and housebound. She is a heavy-set woman, and looked to me like the actress Kathy Burke plus 30 years. She lives alone in a bungalow in Durrington, a short distance from Worthing in Sussex. Her mother died nine years ago, and her principal support comes from her daughter and her neighbour. She has received disability allowance only for the past eight years, since her osteoarthritis necessitated use of a wheelchair.

'In the past 40 years I haven't had a life,' she says. 'No one can say they've seen me go up the street on my own, or take my children out on my own, or go on a bus. When my daughter was at primary school her teacher told her she couldn't understand why I never came to the parents' evenings. If my mum hadn't been there to look after them they probably would have been taken into care.'

She is still taking the tablets, now prescribed under the generic name diazepam. Her dosage has been greatly reduced in the past few months, but she had a

traumatic experience at Christmas after cutting down below five milligrams a day. When she first visited the local surgery in Durrington last summer her new GP greeted her with disbelief. He didn't think the drugs were doing any good. She told him she'd been on them for 40 years. He said: 'You shouldn't have been on them for more than four weeks.'

Valium and similar drugs in the benzodiazepine group are widely considered to belong to a previous generation, replaced in the treatment of insomnia, panic attacks and all manner of modern anxieties by more sophisticated drugs with side-effects of their own. The reality is somewhat different. In the year to March 2002, 12 and a half million prescriptions to benzodiazepines were written in England alone. In the previous year there were 13.028 million. The Department of Health has no indication as to how many patients are receiving repeat prescriptions, or for how long. But Professor Heather Ashton, a specialist in psycho-pharmacology at Royal Victoria Infirmary in Newcastle who ran a withdrawal clinic for more than a decade, believes there are half a million people in the UK who have been taking benzodiazepines for several years. The official guidelines issued to prescribing doctors 15 years ago advises continued use for no more than 28 days. The Home Office has other figures, for the amount of deaths in England and Wales in which drug poisoning is included in coroners' reports. Between 1997 and 2000, cocaine was included in 273 reports, while diazepam and tamazepam - only two generic types out of 17 available for prescription - were included in 795.

Campaigners claim that more than one million people in the UK may be addicted to benzodiazepines, a family which includes anti-anxiety tranquilisers such as Ativan (lorazepam) and Xanax (alprazolam), sleeping pills such as Mogadon (nitrazepam) and anti-convulsive muscle-relaxants such as Klonopin (clonazepam). This is a disturbing statistic for many reasons, not least because it is a problem inflicted by our own health service. Addiction may occur after only two weeks' use, and it is so common that it is often ignored in the big debates about drug policies and the funding of withdrawal treatment. It is an addiction whose victims largely suffer in silence, impeded by the symptoms that first drove them to seek medical help and worsened by long-term use of what should have been a short-term solution.

Most patients in receipt of tranquillisers or sleeping pills do not consider themselves to be addicts until they attempt to reduce their dosage and, like Pat Edwards, find complete withdrawal impossible. It is not hard to find people who have suffered from benzodiazepine use, or people who are happy to talk of their experiences as a warning to others. The several men and women I spoke to tell stories unique only in their early details; their tales of involuntary dependence on their medication all end with a common catalogue of suffering and distress. They all find it hard to understand why this state of affairs has been allowed to exist for so long, and why we ever thought that these drugs would be the answer to our ills.

Part of the explanation lies among the trial papers of an experiment conducted in Sheffield in the late Fifties. Alec Jenner and his colleagues at the United Sheffield Hospital were at the beginning of their careers in psychiatric medicine when they read in a newspaper of a Swiss circus trainer who had found something that would calm his lions and tigers. 'I was intrigued whether this would have any

human applications,' Jenner remembers. 'So I phoned up Roche, who produced this series of drugs in Switzerland, and they were already thinking about marketing it for people. They wanted people to do studies which would add to the conviction that it was worth giving to humans. So they jumped on us, really.'
Jenner believes he conducted the first double-blind controlled trial of both Librium and Valium (a trial in which neither the patient nor the doctor knows who's taking what until after the results are compiled). 'Before us, people had published their impressions of it,' he says 'but it was less scientific than ours. The way we did this - and now it looks naive, but then I didn't see it - we gave people two bottles marked A and B, and we told them what was in them without saying which was which. The bottles contained two of three things - either a barbiturate, or a benzodiazepine, or nothing - just chalk pills. They had to say which helped them most.'
Jenner is 73 now, and still lives in Sheffield. He speaks without the benefit of his notes from the trials, and he admits he cannot remember the exact number of patients he studied - he thinks it was about 200. But he is sure of his findings. 'The benzodiazepines came out heavily on top. The improvement of patients on the drugs was the only thing that came out strikingly - the side-effects were unconvincing. They were infinitely safer than barbiturates, which was what people had used to treat anxiety before, and which carried a great risk of fatal overdose. So we were enthusiastic. I myself took enormous quantities to see if there was any toxic effects, but my wife said I was just the same.'
But Jenner did not test his drugs, or those of his patients, over time. 'In those days drug addiction didn't appear to be a problem in Britain at all - I'd never seen a heroin addict, for example. It now seems rather mad that we didn't consider this. One of the most interesting things was that the side-effects experienced by those on the chalk was about the same as those on the drugs.'
Jenner's work came as a delight to Hoffmann-La Roche. Parallel studies, which also failed to consider the possibility of addiction, did find great uses for Librium and Valium (both drugs have a similar chemical formula, but Valium is five times as potent). In 1961 Roche's researchers in its laboratories in New Jersey published a report stating that Valium had only mild side-effects, including fatigue, dizziness and rash, but these were results based on only seven patients. The results from two other patients were not included because they considered their side-effects too severe to continue on the trial. On average, patients took Valium for only 12-and-a-half weeks.
The drug was launched globally in 1963, and it became, along with LSD, the smallest icon of its generation (taken together, the two drugs signalled a paradoxical age of peace, love and anxiety). By the time the Rolling Stones sang about 'Mother's Little Helper' in 1966, Librium and Valium and the sleeping pill Mogadon had helped Roche to become the biggest pharmaceuticals company in the world. Valium's triumph inspired every large pharmaceutical company to market a benzodiazepine of its own. Upjohn was soon competing with Xanax; Wyeth would grow wealthy on Ativan.
In Sheffield, Alec Jenner remembers feeling glad that his work was having some beneficial effects. 'I had no idea that it was going to be so enormously successful. We were quite excited that we'd backed a winner.' Financially his rewards were

scant. 'We weren't offered anything for doing it. They did pay for us to have a camping holiday in Vienna and they gave me money to buy a flame photometer for measuring lithium in blood which must have cost about £50.'

In 1979, about 30 million prescriptions for benzodiazepines were issued in the UK, while the worldwide figure was put at three billion. But by then problems with the drugs had been a regular feature of medical literature for more than a decade. As early as 1968 the Journal of the American Medical Association had noted how a number of psychiatric patients had become suicidal after only a few days' use, and noted how the condition of others worsened when they came off the treatment.

'The problems of addiction took me some time to believe,' Jenner says. 'But after a while it became obvious that that scepticism was not justified.' In the Seventies, Jenner subjected Valium to another trial, though not with Roche. He told 50 or 60 local people to come off the drug without a gradual reduction in dosage. About 30 per cent complained of problems. 'It was becoming obvious that we had been naive about the addiction potential. I was on the Committee on Safety of Medicines for a while, so I was getting more and more information through. One chap made a suicide attempt and we got a long letter from his wife saying, "Put him back on and use this letter as our permission that we feel it's the only way he can go on living." So we went on prescribing it.'

Jenner is now retired, but says he likes to keep in touch with developments in psychiatric care. He is interested in the mental healthcare drugs that followed his work on Librium and Valium, but notes that they too are beset with damaging consequences. (Upjohn's Halcion was banned in Britain in 1991 after many reports of amnesia, depression, and violent behaviour, while Rohypnol still receives adverse coverage for its illicit use as a 'date-rape' drug. The newer drugs such as Prozac and Seroxat target a different receptor in the brain, and despite the fact that one of their chief selling points at launch was that they were non-addictive, many users suffer severe symptoms when they withdraw.)

Jenner regards his researches with a combination of pride and embarrassment. 'I feel naive but not guilty,' he says. 'What seemed so good about the benzodiazepines when I was playing with them was that it seemed like we really did have a drug that didn't have many problems. But in retrospect it's difficult to put a spanner into a wristwatch and expect that it won't do any harm.'

Ten weeks ago in the Terrace Marquee at the House of Commons, Phil Woolas, a Labour government whip and MP for Oldham East and Saddleworth, spoke at a meeting to mark the tabling of an Early Day motion seeking redress for some of the damage of benzodiazepine addiction. 'So what's the scale of the problem,' he asked his audience of MPs, solicitors and current users. 'Statistics show that something in the order of 1.2 million people in this country are still in receipt of repeat prescriptions of benzodiazepines, some 20 or 30 years after the danger of that repeat prescription became well known.'

The motion, which has now been signed by more than 100 MPs, called for a review of the disability guidelines to ensure recognition of benzodiazepine addiction, and for greater support services for addicts. 'We are not just telling people to come off the drugs instantly,' Woolas said. 'Sometimes I have the nightmare that if we do have the breakthrough that we are all campaigning for,

whereby the Department of Health were to stop prescriptions, the problems that would cause would be horrendous. The key is phased withdrawal, and treatment and help for people coming off the drugs.'

That was not the first time the issue had been raised at Westminster. Woolas addressed the problem in a debate in 1999, and five years earlier, when he was Shadow Secretary of State for Health, David Blunkett wrote a supportive letter to a patient suffering withdrawal symptoms in which he called the issue of benzodiazepines 'a national scandal'. Since Labour came to power, however, progress has been slow at best, and there is still no specific funding for benzodiazepine withdrawal treatment. 'We shall not give up,' Phil Woolas maintains. 'In my view there's a conspiracy of silence ... I believe the problem exists because at a fundamental level, it is too huge and too horrific for people to cope with and grasp the enormity of.'

As well as political lobbying, redress has been sought through the courts. By the late Eighties 1,700 people had received legal aid to bring a class action against Roche Products Ltd and John Wyeth and Brothers Ltd, the makers of Ativan. Their principal claim was that the companies were aware of the dangers of addiction and other side-effects before making this information available to prescribers and patients. Roche and Wyeth denied this, and the action was discontinued in 1994 after the Legal Aid Board withdrew funding. The majority of the claimants' cases were complicated by the difficulty in proving the harm caused by the drugs as opposed to the psychological problems they may have had before they were prescribed them.

Seventy-five people subsequently tried to pursue their own cases against the companies, but were also hampered by lack of funds and their claims were struck out by the Court of Appeal in 1996. One case, begun in 1993 against Roche by a formerly successful Scottish businessman who claims his life was ruined by Mogadon, is under consideration for trial in the Court of Session in Edinburgh and may be heard in full next year. Another, brought by a woman against Wyeth, is under consideration in Dublin.

Last summer, benzodiazepine addicts did receive news of a legal success, albeit against a new target: overprescribing GPs. Ray Nimmo, the patient involved in the case, and his solicitor Caroline Moore of Keeble Hawson in Sheffield, were also present for the launch of the parliamentary motion in November, and Moore outlined the case. Nimmo was 32 when he was first prescribed benzodiazepines in the mid-Eighties, after an allergic reaction to another drug and stress brought on by illness to his father. He was given 90 milligrams of Valium a day, a prescription that continued at a reduced dosage for 14 years.

'The effects were shocking,' Caroline Moore recalled. 'Ray's personality changed, he became agoraphobic, and he became unable to cope with life. In 1986 he gave up his co-directorship [of a scaffolding company]. Ray and his wife planned to extend their family, but Ray became convinced he was not fit to be a father.'

When another doctor advised withdrawal in 1998, Nimmo underwent the usual problems, from which he believes he is still suffering. His legal action against his GPs, a husband and wife team, was settled out of court in June 2002 for £40,000 plus costs. Success was made possible by reference to a key report issued in January 1988 by the UK Committee on Safety of Medicines. This noted that

'withdrawal symptoms can occur with benzodiazepines following therapeutic doses given for SHORT periods of time' (the report's own emphasis). New guidelines were issued to all GPs. This document, only two pages long, advised clearly that benzodiazepines should not be prescribed for more than four weeks, including a tapering-off period.

Similar guidelines were adopted by the Royal College of Psychiatrists, and were swiftly included in the new literature from Roche. Caroline Moore says that anyone who has been prescribed benzodiazepines for a prolonged period since 1988 who wasn't part of the group actions may be able to bring a claim against their prescriber, although their chances of success may depend on what advice they received regarding addiction and whether they have been offered help with withdrawal.

Moore doubts whether Ray Nimmo's case was the first to reach a successful conclusion, but merely the first not to include a gagging clause. Since his case was made public, she has received many phone calls from people who have similar claims. 'More stories about ruined lives,' she says, 'including one case of a girl who was given benzodiazepines at 13.'

After her address at the House of Commons, Moore was congratulated by Barry Haslam, who also has a case against a former GP. Haslam, a qualified accountant from Oldham, spent 10 years on various benzodiazepines and is the driving force behind a charity called Beat the Benzos. His organisation has many aims, including the reclassification of the drugs from Class C to Class A, which would put them on a par with heroin. He is hopeful that the lead on this may come from the European Parliament. He shows me a report from the Hong Kong Medical Journal which notes a 50 per cent reduction in average yearly prescription of benzodiazepines since they were classified as dangerous drugs in 1992.

When Haslam came off Valium, Ativan and others he says some remarkable things happened. 'I couldn't believe the colour of the sky and the flowers, and the noise was so loud.' But his wonder has now been replaced by anger.

'For me, the Government Ministers are cowards,' he says. 'If they had gone through one-hundredth of what I've gone through then they would have done something about this long ago.

'Why have GPs and psychiatrists been allowed to ride roughshod over the advice of people more qualified to judge the drugs than they are? And why have the Government looked the other way? Why have they allowed so many people to get addicted to a legal drug and not put any money into services to help people?'

These are valid questions, and they are as valid now as they were 15 years ago. Used correctly, for very short periods, benzodiazepines may still provide a respite from common symptoms. But their overprescription has left a trail of misery for which no one will take responsibility and only a few seem prepared to confront.

Roche still makes three brands of benzodiazepine for the UK, but it discontinued its production of Valium last year. In its press release, the company explained how effective the treatment had been, how widely it was available in generic form, and of its pleasure that it was designated 'essential drug status' by the World Health Organisation. In what some may regard as a paradoxical statement, the Swiss firm also claimed it continued to be the second largest foreign investor in healthcare in the UK.

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