

News investigation Popular antibiotic ciprofloxacin linked to UK deaths

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Millions of us are successfully treated with ciprofloxacin and other fluoroquinolone antibiotics each year. But for some patients the drugs are linked to severe adverse reactions involving terrifying physical and mental health impacts. Andrew Wasley reports

Patients who say they've suffered severe adverse reactions to a common antibiotic are calling for action to prevent others from experiencing a 'frightening' number of alleged physical and mental side effects.

The victims, who say they were poisoned by ciprofloxacin, want more research into the drug's side effects, greater education of health professionals and clearer warnings for consumers.

The calls come as an *Ecologist* investigation revealed the antibiotic has been linked to more than forty deaths in the UK in recent years, and been the subject of hundreds of suspected adverse reactions.

Ciprofloxacin, part of the fluoroquinolone class of antibiotics, is prescribed to treat a range of medical conditions, including bacterial infections. Fluoroquinolones are also – controversially – used to treat diseases in poultry, pig and cattle farming.

Symptoms associated with fluoroquinolone reactions include – according to victims – chronic fatigue, tendonitis, joint pain, muscle weakness and spasms, bladder pain, heart palpitations, depression and anxiety problems, panic attacks, tinnitus, unexplained buzzing and tingling, electric shock-type sensations, insomnia, numbness, impaired vision and sensitivity to light.

Some victims say problems begin immediately after taking the medicine, others weeks or even months later. Some experience minor side effects, others a pattern of debilitating symptoms.

Doctors say however that the percentage of patients who suffer is tiny compared with the overall volume of people successfully treated with the drugs. Millions of prescriptions of ciprofloxacin are administered annually with no reported side effects.

All drugs have to go through a strict testing and licensing procedure in order to be approved, and medicines are constantly reviewed by drug manufacturers. Antibiotics kill bacteria and prevent them from reproducing, and the drugs are credited with saving many lives.

Experts also caution that proving that a drug caused an adverse reaction is fraught with difficulty and point out that possible side effects are clearly listed on prescription medicines.

In the US however, there have been growing calls for fluoroquinolones to be restricted, and manufacturers have been forced to improve warnings on packaging. In 2001 a leading consultant, Dr Jay Cohen, published a groundbreaking if controversial article on the 'severe and often disabling' reactions some people sustain whilst taking fluoroquinolones.

Cohen said: 'It is difficult to describe the severity of these reactions. They are devastating. Many of the people in my study were healthy before their reactions. Some were high intensity athletes. Suddenly they were disabled, in terrible pain, unable to work, walk, or sleep.'

The precise number of US cases is unclear but figures have suggested some fluoroquinolones have generated more than 14,000 adverse reaction reports, and been linked to as many as a 1000 deaths. Public Citizen, which successfully sued the US Food and Drug Administration for clearer warnings and a patient guide, says it took action after around 1,000 individuals suffered tendon rupture after taking fluoroquinolones. Clinical studies

have linked the drug to this condition.

Electric shock symptoms

'I loved life, exercise and movement, my wife, son, friends and work colleagues. Now I am crippled [and] the medical establishment appear to not be able to help me or take me seriously... struggling to keep sane and get through this,' wrote Geoff Robinson in his diary documenting an apparent adverse reaction to ciprofloxacin.

The 39-year-old, from Sussex, was prescribed the drug last year as a precaution against a suspected urinary infection. The married father of one and fitness enthusiast told the *Ecologist* he has 'gone from being uber fit to absolutely crushed with physical and nervous system damage' after taking the antibiotics last November.

Following a month of unexplained pain in his abdomen and testicles, and after visiting his GP and hospital throughout October, Robinson was prescribed ciprofloxacin 'just in case' by a urologist unable to pinpoint the cause of his pain.

Several days after beginning the medication, Robinson found blood in his faeces, developed a mouth ulcer and had inflamed gums, as well as dizziness. In the following days he suffered panic attacks, feelings of disorientation and had growing pains across his perineum, penis and anus.

'The pain had become unbearable,' says Robinson, so much so that he had laid on the floor 'in agony'. At one point 'I was barely able to walk.' The next day Robinson began experiencing cold sensations in his feet and calves, pins and needles in his hands, and - he maintains - his wedding ring 'retracted and moved on its own.'

These symptoms evolved to include burning and crawling sensations on his skin, and an 'electrical buzz' type feeling - 'shocks into eyes, teeth, head, face, legs, feet [and] parts of my body [were] jumping, twitching, spasms so significant [it] made me itch,' Robinson recalled. He says he experienced an altered heart beat at night, with it feeling 'very slow then speeding up.'

Just before Christmas Robinson reported pains in his armpits, his lymph gland under his chin became inflamed and he felt 'pressure' in his head. In February, his ankle joints and shoulder began 'cracking', and his spine and right hip began 'clicking', alongside bouts of tinnitus. He went to hospital eight times - on three occasions in an ambulance. He also paid to see private practitioners. All struggled to diagnose him, despite a multitude of tests.

He was convinced the problems were down to the antibiotics, but several doctors ruled out ciprofloxacin, others were doubtful. One conceded that the antibiotic could have been responsible whilst another - a leading consultant - told him in person that he believed ciprofloxacin was probably to blame, but didn't confirm this in later correspondence.

Robinson says that other medications he was prescribed alongside ciprofloxacin may have exacerbated the reaction: he was given diclofenac - a non-steroidal anti-inflammatory drug - to take with the antibiotics but chose not to take it until three days after he'd finished the ciprofloxacin. Fluoroquinolones and non-steroidal anti-inflammatory drugs can be a potentially toxic combination, according to some experts. Although his adverse reaction began days before taking the diclofenac it's possible, he believes, that the anti-inflammatory worsened the symptoms.

Robinson reported his condition, via the Yellow Card scheme, to the [Medicines and Healthcare products Regulatory Agency \(MHRA\)](#) - which oversees drug licensing in the UK - and says they confirmed his symptoms were similar to side effects associated with ciprofloxacin.

Although he has recently carried out some work - he was previously signed off sick - he blames the reaction for putting huge pressure on his mental and physical health.

'My son is 12 years old and was used to his dad taking him out and generally being very active,' he says. 'That's not been possible.' Robinson says that the toll on his wife has been huge and that it's affected their

relationship: 'I cannot work, I cannot exercise, I cannot drive, which makes day to day trips difficult,' he says. 'No alcohol, multiple food allergies, no sex life, sensitivity to sound... it's miserable.'

Excruciating pain

Rebecca Smith, 36, from London, describes a similar experience after being prescribed ciprofloxacin to treat a suspected urinary infection in October 2009. She told the *Ecologist* that her adverse reaction to the antibiotic has 'limited anything I can do; I used to be very active, hiking [going on] holiday, singing in a choir' and says that she's suffered months of poor health.

She initially suffered a panic attack and shaking, experienced sharp pain in both of her heels, buzzing, cold sweats at night, numbness and a tightness in her chest. She also says the reaction has caused the veins in her feet to become much more prominent and for the hairs on her legs to fall out.

Smith was hospitalised for three days after taking the drug: 'The pain was excruciating and spread; aches and pains in my arms and heels, my toes kept going numb... my GP said this was not side effects [of ciprofloxacin]... they suggested the pain in my heels was because "I was on my feet too much"'.

Seven months after the initial symptoms, Smith suffered a major flare up that she puts down to 'residual damage' caused to her nerves, tendons and muscles. She describes clapping a music holder during a concert in which she was singing and felt a burning and tingling in her forearms. Additionally, the backs of her elbows started to hurt. She was suffering from tendonitis, a side effect associated with ciprofloxacin.

'At A&E they didn't acknowledge this – [even though] I had mentioned the ciprofloxacin'. Later, Smith says her hands swelled up and went blue as a result of a ruptured tendon in her elbow: 'I had to sit at home for a week, was off work for three weeks, I couldn't type,' she says.

Despite having much of her strength back Smith believes the reaction has weakened her; she had been due to undergo surgery for another condition but was taken off the list after the reaction as 'I couldn't cope with being on the crutches.' She says that even carrying out everyday tasks – like lifting her suitcase when on holiday recently – can still bring on unexpected pains and aches.

Smith says the majority of doctors she dealt with didn't recognise her symptoms as an adverse reaction, although one said it was 'possibly ciprofloxacin'.

Others who say they have been poisoned by ciprofloxacin complain that doctors discount – and appear to disbelieve even – that the drug can cause such severe reactions.

'Apart from the pain of the reaction itself, getting people to listen and consider [ciprofloxacin] as an option is so challenging I almost gave up bothering', Paul Jones, now recovering after an apparent reaction, recalls. "'You shouldn't believe what you read on the internet' is a typical reply from the doctor, or, "you must listen to your doctor as they are right 99 per cent of the time" is another.'

The 32 year old, from Bristol, lost his job after reacting to a prescription of ciprofloxacin for suspected orchitis. Despite suffering a range of symptoms similar to Robinson and Smith he said his doctor 'did not want to know' and admits even trying to convince his family that ciprofloxacin might be responsible was hard.

The patients unanimously believe they were not warned about the possible side effects of ciprofloxacin. Although conceding that notes accompanying the medication do outline reactions they maintain it's the doctors responsibility to educate themselves and pass this info onto patients – and, crucially – to research links when problems are reported.

'Doctors need to be better educated and shouldn't be handing out drugs [they] know nothing about,' says Smith. She believes the medical profession has treated her 'terribly, it's terrible when they've not listened to you,' and – whilst acknowledging that there is a need for the drugs – says they should be more restricted.

Robinson argues more research needs carrying out into the side effects of ciprofloxacin and in the meantime says warnings with all fluoroquinolones should be made more prominent, as in the US.

He also says he believes that residues of fluoroquinolones in meat he has consumed may have caused his reactions to flare up significantly, raising concerns over the possible [health implications of treating livestock with antibiotics](#).

Wider pattern of adverse reaction

All three are amongst a larger number of UK patients who have been reported for suspected adverse reactions to ciprofloxacin in recent years; figures obtained by the *Ecologist* reveal that 1,210 adverse reaction reports relating to the drug were submitted to the MHRA between January 2000 and March 2011. Forty-six deaths in the UK in the same period were also linked to ciprofloxacin.

The figures in turn form part of a wider pattern of adverse reactions to medications, with many people being admitted to hospital each year. A 2004 study by the University of Liverpool suggested that as many as 10,000 patients annually were dying in the UK because of adverse reactions. The researchers stressed the overwhelming majority taking medication do not suffer side-effects.

The researchers estimated – at the time – that adverse reactions were costing the NHS £466 million. More recent research by think-tank Compass put the figure at nearly £2 billion.

As in the US, those who say they suffered adverse reactions to fluoroquinolones believe the true figure is higher, as not everyone affected attributes symptoms to antibiotics, and doctors do not always make the link.

Experts caution however that establishing the precise cause of adverse reactions – and even proving that described symptoms are indeed an adverse drug reaction as opposed to an underlying medical condition – can be difficult.

Jeffrey Aronson, President Emeritus of the British Pharmacological Society, told the *Ecologist* that ‘only in a very few – and rare – cases [of adverse reactions] can you be sure. In 99.9 per cent of cases you don’t get obvious proof.’

Aronson says there is an assumption that people ‘take a tablet, get an effect’, and therefore that the two are linked. But the reality is that ‘things happen coincidentally, there is a tension here as [drugs] can cause adverse reactions but whether it was directly to blame for specific symptoms, that’s different.’

He said he was aware of tendonitis and tendon rupture being associated with fluoroquinolones.

In a statement to the *Ecologist*, the MHRA said: ‘All medicines have side effects - no effective medicine is without risk. The priority of the MHRA is to ensure that the benefits of medication outweigh the risks. It is important to note that a report of an adverse drug reaction does not prove that it was caused by the drug. Other factors such as the underlying disease or other medicines may contribute to suspected adverse reactions.’

The body acknowledged that ‘as with any medicine, ciprofloxacin and other fluoroquinolones may cause side effects in some people.’ The MHRA confirmed that it had ‘received 46 reports of suspected side effects with a fatal outcome in association with ciprofloxacin via the Yellow Card Scheme’ between 2000 and the present day, but said ‘whilst such reports may relate to true side effects, they may also be coincidental events due to factors such as underlying or undiagnosed illness or infection.’

‘Such figures must also be considered within the context of the serious infections ciprofloxacin is used to treat, and the number of people treated. For instance, in 2010 alone around 1 million prescriptions for ciprofloxacin were dispensed by community pharmacists in the UK,’ the statement continued.

Does the benefit outweigh the harm?

Aronson says the onus should be on doctors to explain possible side effects of drugs. “‘I’ll look it up” – that would be what would be expected of a good doctor,’ he said. He added the first port of call would ordinarily be a ‘summary of product characteristics’ document, followed by a package insert containing warnings of adverse affects – known as a ‘patient information leaflet’. He also said all doctors have access to the British National Formulary, a database that provides practical information and guidance on the use of medicines, and the [Electronic Medicines Compendium](#).

[Claudia Louch, a Harley Street-based natural skin care expert with a background in pharmacology and allergies](#) said it was hard to be certain how widespread recognition of the problem amongst healthcare professionals was.

‘This is difficult to estimate as it depends on what practitioners prescribe to their patients, how this is monitored by the practitioner, as well as symptoms reported to the practitioner by the patient; there are a lot of grey areas, as the patient may have other pre-existing conditions, which may confuse the general picture and terms of symptoms as causing similar types of symptoms in the first instance.’

The MHRA says it believes current drug labelling is adequate, and that the patient information leaflet ‘is a useful basis to aid a discussion between prescribers and patients on the risks and benefits of a medicine’. The body said health care professionals were kept updated with any developments.

Medical experts say that tackling adverse reactions is complex. ‘It’s a case of asking, “what’s the benefit, does it outweigh the harm?,”’ says Aronson. He cites the example of someone suffering a headache and someone suffering from cancer: ‘In the case of cancer one might be prepared to [to risk] a severe adverse reaction, with a headache that might not apply.’ He admitted that work to ‘improve prescribing’ needed to be done, as some doctors are ‘not well enough trained in prescribing.’

In the event of a pattern of serious reactions to a specific drug being reported, health officials have a number of options – amendments to labelling, voluntary withdrawal by the medicine’s manufacturer, or a recommendation by the MHRA for the drug’s licence to be withdrawn.

Bayer, manufacturer of ciprofloxacin, declined to respond to the *Ecologist*.

**The names of some patients have been changed*