

August 4, 2015

Dear Colleague,

The broad spectrum fluoroquinolone antibiotics (FQs) are some of the most potent oral antibiotics in clinical use today. They are among the most often prescribed antimicrobial agents.¹⁰⁴ Initially they were recommended as drugs of last resort. FQs act by inhibiting bacterial DNA gyrase and topoisomerase IV. By doing so they are bacteriolytic instead of bacteriostatic.

In this letter I would like to give you additional information regarding the adverse effects (AEs) to FQs, which appear to happen with greater frequency and chronicity than previously known.⁷⁸ The adverse effects of FQs are multi-systemic in nature, co-occurring and therefore meeting the qualifications for a Syndrome: the Fluoroquinolone Toxicity Syndrome (FTS).^{76,77,78}

AEs to FQs can be either immediate or delayed.^{1,6} They also can become permanent in nature.²⁵ Tendonitis/tendinosis, gastrointestinal (nausea, diarrhea) and central nervous system AEs (headache, dizziness) are most common. The pathophysiology of the AEs to FQs are multifaceted: Inhibition to and/or disruption of the GABA receptor; Chelation of divalent ions such as magnesium with disruption of cellular function; Oxidative stress; Harm to nuclear DNA, harm to mitochondria and other cell organelles such as lysosomes; Depletion of mitochondrial DNA; Direct toxicity; From a recent Mayo Clinic article;⁸² Iron chelation leading to epigenetic effects through inhibition of dioxygenases, inducing global epigenetic changes and inhibition of collagen maturation leading to tendinopathy and liver injury.

A summary of possible adverse effects:

1. Fluoroquinolones may harm not only Achilles tendons, but also other tendons, ligaments, connective tissue, cartilage, bones and muscles.^{1-9, 98-103}
2. Fluoroquinolones may induce apoptosis of human body cells and thereby harm their mitochondria by several mechanisms including oxidative stress.²⁹⁻³⁷
3. Fluoroquinolones may harm human DNA and may therefore be genotoxic.³⁸⁻⁴⁹
4. Fluoroquinolones have been used as chemotherapy or as an adjunct to existing chemotherapy because of their apoptotic properties.⁵⁰⁻⁶⁵
5. Fluoroquinolones may harm the Central Nervous System,¹⁸⁻²⁸ the Peripheral Nervous System¹⁰⁻¹⁷ as well as many other endocrine and non-endocrine organs.⁸³⁻⁹⁷
6. Fluoroquinolones appear to be able to either induce or worsen an existing autoimmune diseases as well as give rise to an immune-allergic mediated reaction.⁶⁶⁻⁷⁵

Patients may present with a wide array of symptoms: *Joints: pain, swelling, redness, fluid. Cartilage damage. Meniscus tears. Tendons: Pain, tears, rupture, swelling. Ligament damage. Muscles: pain, weakness and wasting, involuntary muscle contraction, twitching or jerks. Weight loss, nausea, diarrhea, hair loss, visual abnormalities, severe fatigue, exertion inability, headache, feelings of head pressure, dizziness, tremors, insomnia or sleep disturbance, hallucinations, convulsions, anxiety, psychosis. neuropathy pain, tingling, prickling, burning, "shocks," buzzing, squeezing, or "pressure" in the arms, legs, body, or head, paresthesia, blood pressure changes, autonomic neuropathy and sensory disturbance, inability to sweat, excessive sweating, loss of bladder control, orthostatic hypotension, tinnitus, dizziness, lightheadedness, fainting. Hypersensitivity to pain or to light touch. Insomnia. Disturbance of glucose regulation, signs of hypo or hyperglycemia. Elevated liver enzymes, liver failure, kidney damage or failure. Heart: irregular heart beat with palpitations, QT prolongation, torsade de point. Vision disturbance like floaters. Difficulty walking, difficulty talking, difficulty swallowing, difficulty thinking.*^{76,108}

Acknowledgment of these often complex AEs is important for the patient. If AEs to FQs are not viewed as inter-related, it is easy to miss the diagnosis of FTS. Patients are then diagnosed as having fibromyalgia, somatoform or other psychiatric illness because doctors who are unaware of the potential severity and duration of some fluoroquinolone AEs. Of course It is also important to exclude other pathology that was either provoked by or already existing but only become apparent after the use of fluoroquinolone antibiotics.

It is my hope that many patients will benefit as medical professionals become more aware of the information in this letter. Thank you for your time and consideration.

Respectfully yours,

Miriam J. de Jonge M.D.
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Postscript and Accountability. To write this letter I have done a PUB Med and Google scholar search for fluoroquinolones and the several adverse events. I tried to refer to human research only as much as possible, although animal studies may provide valuable data. I also tried to use recent publications except when I thought older ones to be of importance.

Being harmed myself by the adverse events to these antibiotics, I wanted to find out for myself what could be the explanation for my ongoing symptoms. I also wanted to update the last "Dear Doctor" letter that was written in 2006 by

yet another physician who was harmed after the use of Fluoroquinolones Antibiotics.¹⁰⁷

As you might know medical literature post marketing has a tendency to emphasize a more favorable outcome than is the reality ^{105,106} Lately two citizens petitions for two more black box warnings were submitted to the FDA by professor Charles Bennet from SONAR : one for psychiatric EAs. ⁸² And one for Mitochondrial damage. ⁸¹

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